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Original Research Article

Smoking and the Probability of Developing Parkinson's Disease

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Abstract

Objective: To look at the relationship between current cigarette use and the risk of Parkinson disease (PD).

Methods: In the Research, which included 30,000 male doctors, we evaluated the chances of PD death with smoking habits among survivors who had been periodically polled for five decades. For 65 years, cause-specific mortality was tracked, and 283 fatalities from PD were among them. Utilizing CoX models for smoking habits (smoking status, amount smoked, and years since stopping) at baseline or revised behaviors at resurvey, the respective risks (RRs) of PD (and 95% confidence intervals [CIs]) were calculated.

Results: Between 1972 and 2022, there was a progressive decrease in the prevalence of current smoking, from 67% to 8%. At baseline, the crude rates of PD death were lower among current smokers (30 vs. 46/100,000 persons-years) than in nonsmokers. After age at risk was considered, the risk of Parkinson's disease (PD) was 30% lower in current smokers at baseline (RR 0.71; 95% CI 0.60-0.84) and 40% lower in continuous smokers at the follow-up survey (RR 0.60; 95% CI 0.46-0.77) as contrasted with never smokers. Negative correlations were found between cigarette use and PD risks. By raising the amount of time after quitting smoking, the protective effect of current smoking versus never smoking for PD was diminished.

Conclusions: In contrast to previous suggestions, the present report demonstrates a causally protective effect of current smoking on the risk of PD, which may provide insights into the etiology of PD.

Keywords: Parkinson disease, Tobacco smoking, Cox models

INTRODUCTION

Consumption of tobacco contributed to around 100 million fatalities in the 21st century and is expected to contribute to 1 billion deaths in the 21st century in high-, middle-, and low-income nations [1-6]. Ongoing cigarette smoking resulted in more deaths from vascular, respiratory, and other neoplastic disorders than from lung cancer solely in the 50-year follow-up of male Indian doctors [6-11]. Nearly all non-communicable diseases (ischemic heart disease, cerebrovascular disease, diabetes, chronic lung disease, pneumonia, cirrhosis of the liver, and cancers of the mouth, esophagus, lung, and pancreas) have been shown to have higher risks for current smokers than for non-smokers, with the exception of Parkinson disease (PD), which is said to have an inverse relationship with smoking (PD), according to studies) [11,12].

Parkinson's disease (PD) is a progressive neurological condition characterized by bradykinesia, resting tremor, and rigidity of the muscles. The start of nonmotor indicators of PD, such as old-factory dysfunction, constipation, disturbed sleep, and dis-ordered mood, may occur up to ten years before the onset of motor symptoms [13-15]. The cause of Parkinson's disease (PD) is unknown, although the pathology includes Lewy body buildup and dopaminergic neuron loss in the substantia nigra region of the basal ganglia [13,14]. Globally, PD is second in terms of prevalent neurodegenerative illness and the most prevalent motion disorder, affecting approximately 6.1 million people in 2015 and expected to reach 9 million by 2030 [16,17]. Modifiable risk variables for Parkinson's disease are not well understood, however prior research has found positive connections between the disease and head trauma, pesticide exposure, and dairy product intake, as well as negative associations with caffeine, serum urate, physical activity, ibuprofen, and tobacco use [18].

Current smoking was linked to a 60% decreased risk of Parkinson's disease, according to a meta-analysis of observational studies (relative risk [RR] 0.42; 95% confidence interval [CI] 0.38-0.47) [12]. Regarding the causal significance of this inverse connection, there is, however, a great deal of ambiguity.

A recently published broad case-control research in Denmark, which included 1,808 PD instances and 1,876 controls, indicated that the lower incidence of PD in current smokers was an artefact of inverse causality bias. The research proposed that early nonmotor signs of PD

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may include a decreased reaction to nicotine stimulation, prompting current smokers to quit smoking before the diagnosis of PD can be made.[19] Retrospective case-control research designs, in which data on smoking behaviors was gathered after the beginning of disease, were utilized in the majority of earlier studies examining the relationship between smoking and the risk of Parkinson's disease (PD). These investigations are particularly vulnerable to the effects of reverse causality bias.

Numerous upcoming investigations Inverse relationships between smoking and Parkinson's disease (PD) have also been observed in studies [11,12,20,22]. However, few of these researches included enough PD cases or had long enough follow-up periods to rule out the influence of reverse causality bias. The current report's objectives were to evaluate the risks of PD linked with tobacco smoking behaviors, the quantity of tobacco smoked, and effects of time since stopping smoking among ex-smokers. It involved assessments of the 65-year follow-up of 30,000 male doctors.

METHODS

Standard protocol approvals, registrations, and patient consents

In 1972, Study was conceived upon and the initial questionnaires were distributed, there were no pertinent research ethics committees. The researchers explained the consequences and the methodology of the investigation to doctors who opted to respond to the first questionnaire. At any point throughout the follow-up, participants might decide to stop, and all information was kept private.

Population

A postal survey was issued to every doctor who was a member of the Indian Medical Association and who resided in the Uttar Pradesh in 1972. Two-thirds of the 59,600 doctors who were notified responded, and 34,439 (58.8%) of the male doctors gave complete information about their smoking habits. Six times between 1978 and 1998, survivors were resurveyed on changes in their smoking behaviors. The monitoring of cause-specific mortality continued until November 30, 2016.

Smoking habits

Seven self-completed postal questionnaires were used to gather data on each participant's smoking behaviors. Six to eleven doctors identified themselves as current smokers, former smokers, or never smokers. Those who currently smoke was also asked how old they were when they first started, how much they smoked per day, and whether they smoked cigarettes or pipes. The same questions on when they last smoked and their reasons for giving up were also posed to EX-smokers. Doctors who had never smoked were those who had never smoked even one cigarette a day, or the equivalent in pipe or cigar tobacco, for at least a year. Resurvey questions asked respondents if their habits had changed after showing them their responses from the initial survey. Individuals who already declined to answer questions, those who requested not to be approached again, or those who had been removed from the medical register were not provided questionnaires. Response rates to the 6 resurveys after reminders ranged from 94% to 98%. For every evaluation, tobacco smokers included those who smoked cigarettes, pipes, and cigars. On the basis of missing data, there were no exclusions imposed. The most current survey that was accessible was used to determine the smoking behaviors of non-responders to the resurvey.

Smoking history (current, ex-, and never smoker), typical daily cigarette consumption, or the equivalent in pipe or cigar tobacco (hereafter referred to as "cigarette equivalents/day"), and time since last smoking as determined prospectively from recruitment (smoking-free years prior to 1951 were not counted) were all considered tobacco use behaviors **(Table 1)**.

Follow-up and PD

Between November 1, 1972, and October 31, 2016, data on vital statistics and the reason of death for persons who passed away were gathered from national records and augmented by individual inquiries. Patients were defined as medical professionals with an International Classification of Diseases, Seventh Revision (ICD-7) code 350, ICD-9 code 332.0, or ICD-10 code G20 (hence referred to as "PD") on their death certificates. The evaluations comprised doctors who left the research early or were lost to follow-up until withdrawal or attrition, at which point they were censored. About 99% of those who participated had comprehensive follow-up on mortality accessible to them.

Strategies to minimize reverse causality bias

The effect of reverse causality bias in observational studies participants with prior sickness at enrolment; and excluding a pertinent window of early follow-up to reduce the effect of illness cases that were undiagnosed at enrollment on the findings. In order to reduce the impacts of reverse causality bias, the first 10 years of follow-up were omitted from all analysis [23-26].

Statistical Methods

To study the links between cigarette, use and the risk of Parkinson's disease, two statistical models were used. First, a CoX proportional hazards model (hence referred to as the "baseline model") evaluated the impact of smoking behaviors at baseline in 1951. Second, a CoX proportional hazards model that was routinely updated following each resurvey questionnaire (referred to as the "updated model") evaluated the impact of smoking habits. To be sure that changes in habits weren't brought on by inherent sickness, the model only updated smoking patterns over a decade after they had been documented.

Table 1. Characteristics of study participants at baseline and at resurveys.

	Year of survey					
	1972	**1982**	**1992**	**2002**	**2012**	**2022**
No. of participants[a]-n (%)	29,737 (100)	29,737 (100)	27,617 (100)	24,800 (100)	18,515 (100)	12,146 (100)
Age, y-mean (SD)	41.9 (12.6)	48.9 (12.6)	55.6 (11.6)	59.1 (10.4)	64.6 (9.1)	73.3 (7.1)
Smoking status-n (%)						
Never smoker	5,319 (17.9)	5,114 (17.2)	4,799 (17.4)	4,465 (18.0)	3,319 (17.9)	2,501 (20.6)
Ex-smoker	4,446 (14.9)	8,027 (27.0)	9,994 (36.2)	10,307 (41.6)	10,545 (57.0)	7,688 (63.3)
Current smoker	19,972 (67.2)	16,595 (55.8)	12,824 (46.4)	10,028 (40.4)	4,651 (25.1)	1,957 (16.1)
Daily amount smoked[b]-n (%)						
0 cigarettes/d (never smoker)	5,319 (17.9)	5,114 (17.2)	4,799 (17.4)	4,465 (18.0)	3,319 (17.9)	2,501 (20.6)
<15 cigarettes/d	8,205 (27.6)	7,469 (25.1)	6,363 (23.0)	5,658 (22.8)	2,715 (14.7)	1,235 (10.2)
15+ cigarettes/d	11,767 (39.6)	9,127 (30.7)	6,462 (23.4)	4,370 (17.6)	1,936 (10.5)	722 (5.9)
Time since last smoked[c]-n (%)						
Quit, 10+ y ago	0 (0)	0 (0)	3,356 (12.2)	7,703 (31.1)	5,596 (30.2)	6,059 (49.9)
Quit, >0–9 y ago	4,446 (14.9)	8,027 (27.0)	6,638 (24.0)	2,604 (10.5)	4,949 (26.8)	1,629 (13.4)
Current smoker, 0 y	19,972 (67.2)	16,595 (55.8)	12,824 (46.4)	10,028 (40.4)	4,651 (25.1)	1,957 (16.1)

All percent values represent the fraction of surviving participants in the relevant survey.

[a] *All analyses exclude the first 10 years of follow-up and participants who died during these 10 years.*

[b] *Cigarettes per day or equivalent in pipe and cigar tobacco: 1 cigar = 5 cigarettes, 1 small cigar = 3 cigarettes, 1 very small cigar = 1 cigarette, and 1 oz oftobacco per week = 4 cigarettes per day.*

[c] *Time since last smoked assessed prospectively during follow-up. Analyses assume that ex-smokers at baseline have just quit.*

RESULTS

Baseline characteristics of the study population

After subtracting the 4,67 (1.4%), 17, (0.05%), and 2,459 (7.1%), participants who were known to be alive but no longer residing in the country in 1971 were no longer being followed up on, there were 29,737 (86.3%) male doctors who could be included in the current analyses (table). These individuals were male doctors who had been recruited in 1972. The prevalence of current smoking decreased from 67% in 1951 to 8% in 1998 among doctors aged 65 to 69. The proportion of smokers who were cigarette smokers also declined from 63% in 1972 to 33% in 2022.

Smoking status and the risk of PD

Subjects were tracked for an average of 35 years (range: 11-65 years) between 1972 and 2016. In 743,920 person-years, 25,379 fatalities were documented, excluding the first 10 years of follow-up. Amongst them, PD was recognized as the underlying cause of death in 283 cases (1.1%). After categorizing smoking patterns at baseline, current smokers had a lower crude mortality rate from PD than nonsmokers (30 vs. 46 per 100,000 person-years; an uncorrected RR decrease of 34.7%). The average length of time spent following doctors who passed away from PD was 42 years, while the average length of time spent following doctors who passed away from reasons other than PD was 35 years, with a mean age of death of 77 years.

Smoking frequency and the risk of Parkinson's disease the investigation of current smokers' smoking patterns revealed an inverse dose-response association between daily tobacco consumption and the risk of Parkinson's disease (PD). In both the baseline ($p = 0.0006$) and revised ($p = 0.002$) models, the link between daily amount of smoking and PD risk was statistically significant after adjusting for age at risk **(Figure 1)**.

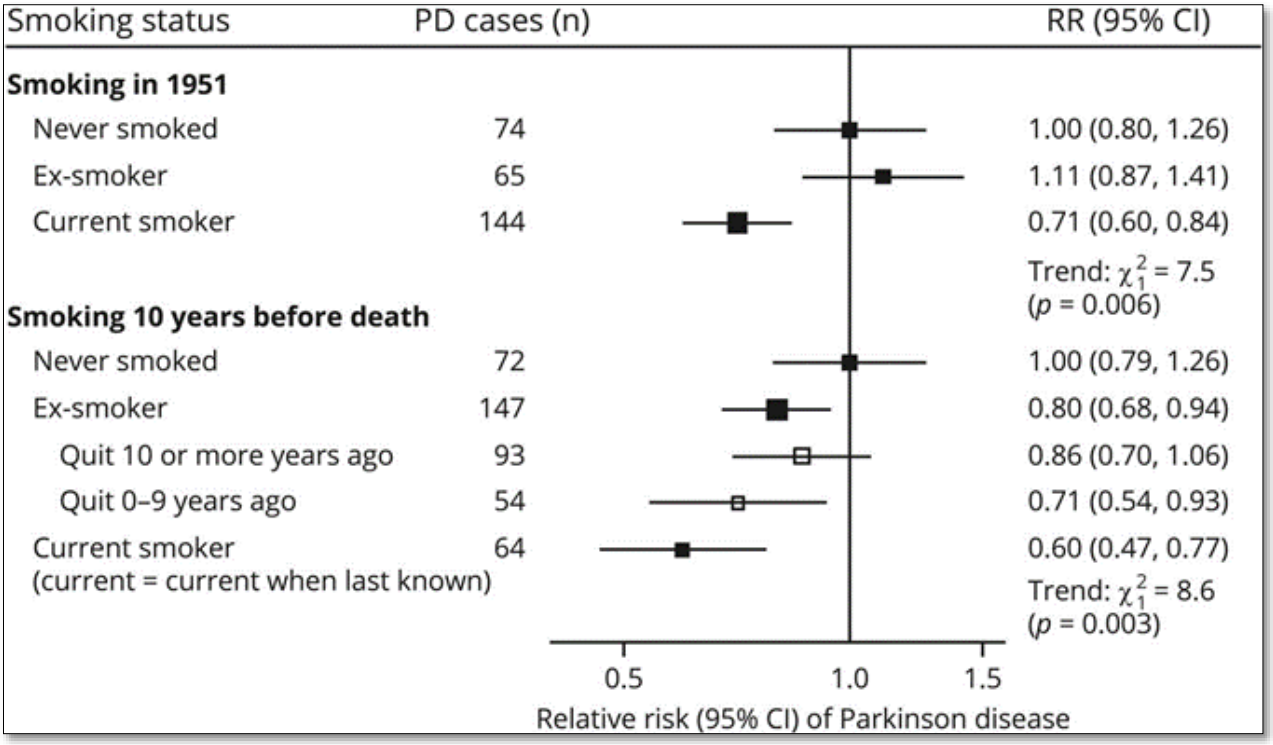

Figure 1. Relative risk of PD by smoking status (never, ex-, and current smoker) at baseline survey in 1972 and at resurveysand by years since quitting smoking.

Duration since quitting smoking and the risk of PD

In the modified model, the risks of PD were calculated for former smokers compared to those who had never smoked, and by how long it had been since they had last smoked (10 or more years ago vs. 0-9 years ago). Duration since quitting was connected to PD risk even after age at risk was considered **(Figure 1).** People who stopped smoking 10 or more years ago had a 14% reduced risk of Parkinson's disease compared to never smokers (RR 0.86; 95% CI 0.70-1.06), while people who stopped within the past nine years had a 29% lower risk (RR 0.71; CI 0.54-0.93).

The smoking status at resurveys was updated at each resurvey, with a 10-year time lag to minimize reverse causality bias. CI, group-specific confidence intervals. n, number of deaths from PD. Tests for trend of PD risk across categories of never, ex-, and current smoker. PD = Parkinson disease.

DISCUSSION

Using a relatively long follow-up period, the research of 30,000 male British doctors showed an inverse relationship between current tobacco use and the risk of Parkinson's disease (PD). Current tobacco use was linked to a 40% reduced chance of PD utilizing baseline smoking habits and a 30% lower risk of PD using updated smoking habits from subsequent surveys, both as compared to never smoking. The amount of smoking and the risk of PD were inversely correlated, and the protective impact of smoking on the risk of PD diminished with longer periods of time since quitting. The extended follow-up period, repeated surveys of smoking behavior every decade for a period of five decades, and consistently high response rates to each survey are the research's main advantages. The present investigation also compared the effects of smoking on Parkinson's disease (PD) utilizing two statistical models that took into consideration age at risk for PD, causality in reverse, as well as shifts in smoking habits, all of which produced similar outcomes **(Figure 2)**.

The evaluations in this paper were based on only 283 PD patients, which was one of its limitations. Only male doctors were involved, and no information on caffeine consumption or other variables was gathered in the short survey questionnaires that had a high response rate. The results of this research, however, are in line with those of earlier Western population-centered cohorts which included both men and women and also made substantial multivariate adjustments.

The generalizability of these results could be confirmed by studies that control for reverse causality bias in non-Western populations while also adjusting for other significant PD risk factors [12,18]. Additionally, situations where PD was a contributing (secondary) cause of death were not considered. Although any bias from relying on fatal instances where PD was the underlying cause of death is likely to be minimal, the present report's results are consistent with those of earlier prospective studies that included incident nonfatal PD cases.

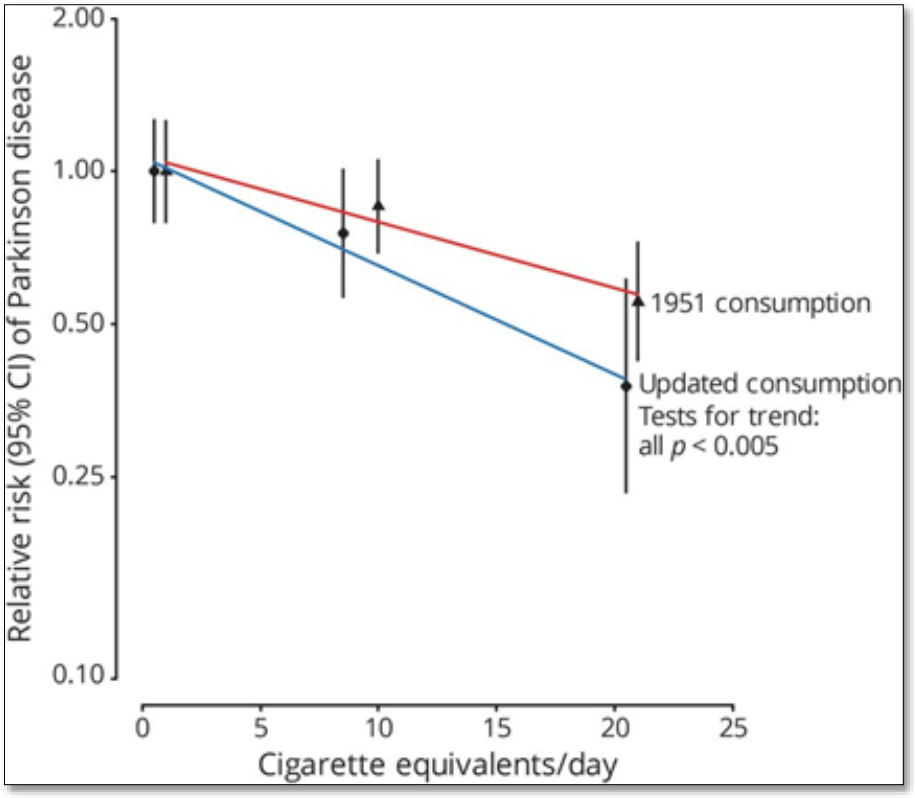

Figure 2. Association between daily amount of tobaccosmoked and the risk of PD.

Additionally, patients were classified using ICD codes for Parkinson's disease, which may not always distinguish between intrinsic PD and parkinsonism related to an unidentified cause or between various clinical subtypes of PD. On death certificates, PD is listed as the primary cause of death in some situations, however these cases are more likely to have more severe disease and definite PD diagnoses [29].

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