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Parkinson's disease research in a prospective cohort in China

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ABSTRACT

Introduction: China has the largest population of Parkinson's disease (PD) patients; however few etiological studies of PD have been conducted in China.
Methods: The Shanghai Women's Health Study recruited 74,941 women in urban Shanghai, aged 40 to 70, from 1996 to 2000. Self-reported PD cases were invited for a neurological examination and diagnoses were made by a movement disorder specialist.
Results: This cohort had very few smokers (2.7%), alcohol drinkers (2.3%), and post-menopausal hormone users (4.3%); however, tea drinking (29.9%) and exposure to tobacco smoke from husbands (61.8%) were common. A total of 301 participants reported PD diagnosis during the follow-up. The diagnosis was confirmed in 76 (57%) of the 133 clinically examined patients. An additional 19 (53%) PD cases were identified out of 36 participants who self-confirmed the diagnosis and provided a history on PD symptoms and treatments. As expected, increasing age was strongly associated with PD risk. Further, PD risk appears to be inversely associated with exposures to second-hand tobacco smoke from husbands and tea drinking, and positively with education, although none of these reached statistical significance. The age-adjusted odds ratio (OR) was 0.7 (95% confidence interval: 0.4–1.1) for participants whose husbands were current smokers at baseline and 0.8 (0.5–1.3) for ever tea-drinkers. Compared with primary education or lower, the age-adjusted OR was 1.3 (0.7–2.4) for middle school and 1.6 (1.0–2.7) for high school or above.
Conclusion: PD research in this unique cohort is feasible and, with extended follow-up, will allow for prospective PD etiological research in China.

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Parkinson's disease (PD) is the second most prevalent neurodegenerative disease and affects more than 1% of the elderly population. The causes for late-onset sporadic PD are largely unknown, and likely involve both genetic and environmental factors and interactions among these factors [1]. To date, most PD etiological studies have been conducted in the United States and western European countries. Research efforts in China have been limited, despite the fact that China has the largest elderly population and is believed to have the largest PD population worldwide [2,3]. PD epidemiological research in China will have important public health and economic impacts. Further, such research may potentially lead to the identification of environmental or genetic risk factors that are less common in western countries [4,5] and may facilitate cross-cultural comparison of study results from different regions of the world [4,6]. We therefore conducted PD research in a well-established large community-based prospective cohort in China: the Shanghai Women's Health Study (SWHS).

1. Methods

The SWHS cohort was a joint effort by Vanderbilt University, the Shanghai Cancer Institute, and the US National Cancer Institute to investigate diet and lifestyle risk factors for cancers among Chinese

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women [7]. Details of this cohort were published previously [7]. From 1996 to 2000, the SWHS recruited 74,941 Chinese women, ages 40 to 70, from seven communities in the Changning district of Shanghai with an overall consent rate of 92%. At baseline, in-person interviews collected information on demographics, dietary habits, lifestyle, reproductive and medical histories, and residential and employment histories from each women, as well as lifestyle and medical history for her husband. All interviews were tape-recorded and randomly checked by quality control staff to monitor the quality of the interview. In addition, 87.7% of the study participants donated urine and 75.8% donated blood, and among those who did not donate blood, 49.3% provided buccal cells for genetic research [7].

The comprehensive baseline survey included questions that are potentially useful for PD research. Participants were queried about their smoking and tea drinking habit as well as the smoking habit of their husbands. Ever smoking was defined as at least one cigarette per day continuously for six months or longer, and tea drinking was defined as continuous drinking of at least three times a week for six months or longer. Education level was ascertained with the following categorical choices: no formal education, elementary, junior high, high, professional high education, college or above, unknown. In addition, these women also provided information on their reproductive characteristics, including oral contraceptive use and use of post-menopausal hormones. After the baseline survey, this cohort has been followed by in-person interviews every 2–3 years to update exposures and to ascertain the occurrence of cancer and selected chronic diseases with response rates consistently over 92%. Participants were first asked in the third follow-up survey in 2004–2007 whether they had ever been told by a physician that they had PD, and those who answered yes or probably yes further reported the year and month of diagnosis. Similar questions were included in the fourth follow-up survey (2008–2011) to ascertain PD diagnosis since last follow-up. These two follow-up surveys identified a total of 301 self-reported PD diagnoses: 220 from the third follow-up survey and 81 additional from the fourth follow-up.

For the current study, a field coordinator from the Shanghai Cancer Institute visited the home of self-reported PD patients and invited them to a clinical examination at the Hua-Shan hospital of Fudan University, one of the leading hospitals in China on neurology clinical care and research. During the clinical examination, a neurologist took medical and neurological history, conducted a video-taped structured examination for PD diagnosis, and collected blood and urine samples. The patient was then examined by a senior movement disorder specialist, and based on all information collected, the movement disorder specialist made the PD diagnosis according to established diagnostic criteria [8,9]. For self-reported cases that refused clinical examination, a neurologist from the Hua-Shan hospital visited each participant's home and completed a screening questionnaire that collected information on PD diagnostic history, including where the diagnosis was made, primary clinical symptoms, and responsiveness to dopaminergic therapy. These data were subsequently reviewed by the senior movement disorder specialist who made a determination regarding PD diagnosis.

The current analysis was limited to women who participated in the third or the fourth follow-up surveys (n = 71,600). We first described the basic population characteristics of cohort participants and self-reported cases. Means and standard deviations were presented for continuous variables and proportions for categorical variables. We also examined age (in 5 year groups), education (primary school or under, middle school, high school or above), smoking status (never, ever), husband's smoking status (never, ever/current), tea drinking (never, ever), and oral contraceptive use (never, ever) in relation to PD risk. Odds ratios (OR) and 95% confidence intervals (CI) were derived from unconditional logistic regression models, adjusting for age as a continuous variable when appropriate. Self-reported PD patients whose diagnoses were not confirmed were excluded from these analyses. Statistical analysis was performed by using the Statistical Analysis Systems (SAS) release 9.3 (SAS Institute, Cary, NC, USA) with two-tailed α of 0.05.

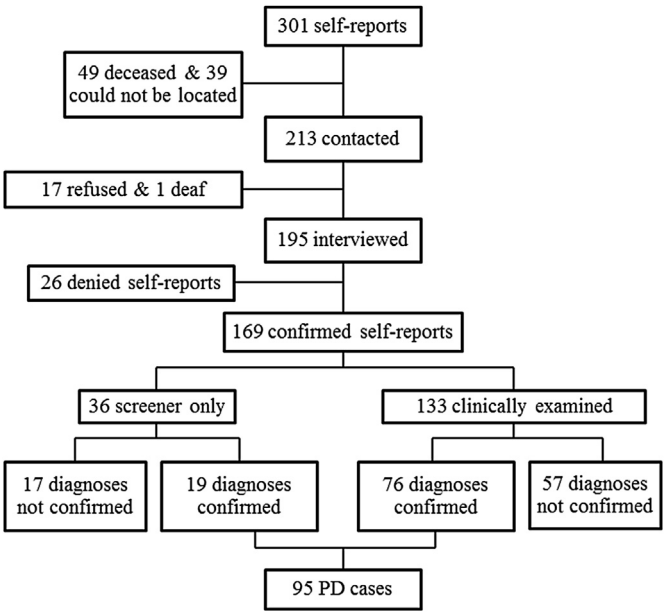

Fig. 1. Flowchart of PD confirmation.

All SWHS participants provided written consent at the baseline survey; participants who underwent the clinical examination further provided written consent for the clinical examination. The study protocol was approved by the Institutional Review Boards of the US National Institute of Environmental Health Sciences, the Shanghai Hua-Shan hospital, Vanderbilt University, and the Shanghai Cancer Institute.

2. Results

Fig. 1 shows the disease confirmation process. Of the 301 women who self-reported PD, 49 had died, 39 could not be located, 17 refused participation, and 1 was deaf and unable to communicate. Of the remaining 195 self-reported patients, 26 denied ever having a diagnosis of PD, 36 refused an examination but completed the screening interview and 133 were clinically examined. PD was confirmed in 76 of those clinically examined. For those whose PD diagnosis was not confirmed at the clinical examination, 34 had essential tremor, 8 secondary parkinsonisms (4 vascular, 2 drug-induced, 1 neurotoxicant induced, 1 other), 4 progressive supranuclear palsy, 4 enhanced physiological tremor, 2 dementia, 2 dystonia, 1 ischemic stroke, 1 spinocerebellar ataxia and 1 had no neurological disease. Of the 36 potential cases who only provided medical history data, 19 were considered to have PD after review by the movement disorder specialist. Therefore a total of 95 PD patients were confirmed and the prevalence (/100,000) was 71.8 for ages <55 years, 124.8 for ages 55–64 years, 256.3 for ages 65–74 years, and 106.7 for ages 75–84 years.

Table 1 presents population characteristics of all cohort participants and self-reported cases with various PD confirmation results. The average age of cohort participants was 52.0 years at study baseline, and few were ever smokers or alcohol drinkers, or had ever used postmenopausal hormones. However, about 30% of these

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