



## Original Article

## Prevalence of restless legs syndrome in Parkinson's disease: a systematic review and meta-analysis of observational studies



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## ABSTRACT

**Objective:** Restless legs syndrome (RLS) and Parkinson's disease (PD) are common neurological disorders that respond to dopaminergic therapy. RLS prevalence among people with PD varies widely (0–38%) in the literature, complicating efforts to understand whether the two diseases might be associated.

**Method:** The databases Web of Science, PubMed, Embase, Chinese National Knowledge Infrastructure, Wanfang, and SinoMed were searched for observational and case-control studies of RLS prevalence in PD. Eligible studies were meta-analyzed using Stata 12.0.

**Results:** Pooled RLS prevalence in PD among various patient populations was 14%, and prevalence in Asia (12%) was slightly lower than outside Asia (16%). Prevalence was higher among patients who had previously received PD treatment (15%) than among drug-naïve patients (11%). Prevalence of RLS was higher in female PD patients (13%) than in male patients (11%). RLS prevalence was much higher among PD patients than among healthy controls (OR 2.86, 95% CI 2.10–3.90;  $p < 0.001$ ).

**Conclusion:** This meta-analysis may provide the first reliable pooled estimate of RLS prevalence in PD, and strong evidence that RLS risk is higher among PD patients than among healthy individuals.

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## 1. Introduction

Restless legs syndrome (RLS), also referred to as Willis-Ekbom disease, is a chronic neurological disorder that may require life-long treatment. People with RLS experience an urge to move their legs, as well as other unpleasant sensations; these symptoms often occur at rest, especially in the evening, and they decrease during motor activity. RLS has been associated with various diseases,

including renal failure, hypertension, headache and Parkinson's disease (PD) [1].

Parkinson's disease is the second most common neurodegenerative disease, and its clinical characteristics include tremor, rigidity, bradykinesia and postural instability. Several studies have shown higher RLS prevalence in PD patients than in controls [2–6]. Another study showed that the risk of PD was more than two-fold higher in the presence of RLS [7]. Both PD and RLS respond to dopaminergic treatment, implicating the dopaminergic pathway in both diseases [8]. Yet, brain pathology differs between the two diseases: the pathological hallmark of PD is synuclein aggregation and degeneration of dopaminergic neurons in the substantia nigra pars compacta region; while RLS has been associated with a decrease in iron levels in the brain [9], and PD has been associated with iron accumulation in the brain. These observations suggest that while the two diseases may share elements in common, they also show significant differences in pathophysiology.

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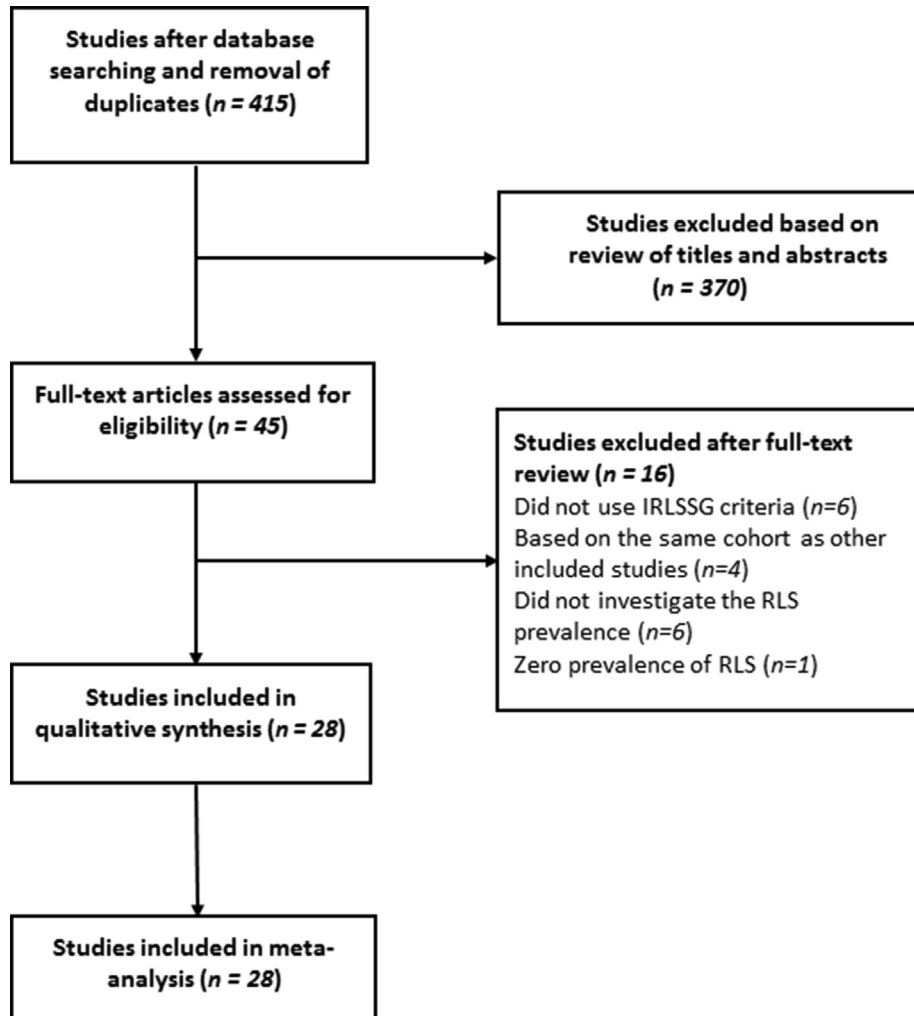


Fig. 1. Flow diagram of study selection and meta-analysis. IRLSSG, diagnostic criteria of the International Restless Legs Syndrome Study Group; RLS, restless legs syndrome.

RLS prevalence among people with PD has been reported to be 0–38.3% based on the criteria of the International RLS Study Group (IRLSSG) [2–6,10–32]. This wide variation, coupled with the fact that only some of those previous studies included parallel case and control cohorts, suggests the need for comprehensive meta-analysis in order to determine a more reliable estimate of RLS prevalence in PD populations. This estimate may then provide a better basis for formulating clinical intervention strategies.

Therefore, the current study meta-analyzed the available literature to: (1) evaluate overall RLS prevalence in PD populations; (2) compare RLS prevalence between drug-naïve PD patients and patients who have received any PD treatment; and (3) compare RLS prevalence between PD patients and the general population.

## 2. Methods

This meta-analysis was performed according to the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. This statement was designed to improve the quality of reporting of observational studies, and it involves checking study content against a 22-item list [33].

### 2.1. Search strategy

The following six databases were systematically searched for eligible studies published up to May 2017: PubMed, Web of Science, Embase, Chinese National Knowledge Infrastructure, Wanfang, and SinoMed. The search terms were “restless legs syndrome” and “Parkinson’s disease”. Searching was restricted to studies in humans, without language or date restrictions.

### 2.2. Study selection criteria

To be included in the meta-analysis, studies had to: be observational studies with a cross-sectional, case-control or cohort design analyzing RLS in PD patients at least 18 years old; diagnose PD based on UK PD Society Brain Bank criteria; diagnose RLS according to IRLSSG criteria based on questionnaires or clinical interviews [34]; and report point prevalence of RLS or sufficient data to calculate it. If more than one study evaluated the same population, only the study with the most complete data was included.

Studies were excluded if they: were discussions, editorials, reviews, case reports, letters, commentaries or critiques; did not report sufficient data and efforts to contact the authors were

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