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Prevalence of Restless Legs Syndrome in North American and Western European Populations: A Systematic Review

Kim E Innes, MSPH, PhD^{1,2,*}, Terry Kit Selfe, DC, PhD^{1,2}, and Parul Agarwal, MS¹

¹Department of Community Medicine, West Virginia University School of Medicine, PO Box 9190, Morgantown, WV 26506-9190

²Center for the Study of Complementary and Alternative Therapies, University of Virginia Health System, PO Box 800782, McLeod Hall, Charlottesville, Virginia 22908-0782

Abstract

Background—Restless legs syndrome (RLS) is a potentially debilitating sleep disorder that affects a significant percentage of North American and European adults. Although standardized RLS diagnostic criteria are now established and widely accepted, reported prevalence estimates have varied widely. In this paper, we review the literature regarding RLS prevalence in North American and Western European adult populations, examine potential sources of variation, briefly discuss the impact of RLS, and offer recommendations for future research.

Methods—To identify qualifying studies, we searched 6 scientific databases and scanned bibliographies of relevant review papers and all identified articles. Studies including fewer than 300 participants that did not use any of the 4 standard diagnostic criteria were published prior to 1995, or targeted clinical populations were excluded.

Results—Thirty-four papers detailing results of large, population-based studies in 16 North American and Western European countries met our inclusion criteria, including 5 multi-country studies (N=69,992 participants) and 29 single country studies (N=163,188 participants); all but one were cross-sectional. Reported general prevalence rates ranged from 4 to 29% of adults, averaging $14.5 \pm 8.0\%$ across studies. Reported prevalence averaged higher in primary care populations than in populations derived from random sampling or geographically defined cohorts ($19.5 \pm 7.9\%$ vs. $12.3 \pm 7.2\%$). Diagnostic and severity criteria differed considerably among studies, as did inclusion criteria, with corresponding variation in prevalence estimates. Prevalence averaged higher in women and older adults; more limited data suggest race/ethnicity, parity, health status, and other factors may also contribute to the observed variation in prevalence. RLS has profound, negative effects on health, well-being, and quality of life, yet detection rates remain low.

* K Innes, corresponding author: Dept of Community Medicine, WVU School of Medicine, PO Box, 9190, Morgantown, WV 26506; Tel: 304-293-5206; Fax: 304-293-2700, kinnes@hsc.wvu.edu.
TK Selfe. Tel: 304-293-2082 Fax: 304-293-2700; tselfe@hsc.wvu.edu
P Agarwal. Tel: 304-293-2968; Fax: 304-293-2700; pagarwal@hsc.wvu.edu

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Conclusions—Collectively, these studies indicate that RLS is a common disorder of major clinical and public health significance in the Western industrialized world, affecting between 4 and 29% of adults. The wide variation in reported prevalence likely reflects differences in demographic factors, health status, and other population characteristics; study population source and sampling frame; and inconsistencies in RLS diagnostic criteria and procedures. In addition, prospective studies and corresponding incidence data on RLS are lacking, hindering the evaluation of both causal factors and sequelae.

Keywords

Restless legs syndrome; RLS; prevalence; epidemiology; diagnostic criteria; quality of life; gender; sleep disorders; sensorimotor disorders; pain

INTRODUCTION

Restless legs syndrome (RLS) is a potentially debilitating sleep and sensorimotor disorder that affects a significant percentage of North American and Western European adults.¹⁻⁴ RLS is characterized by a distressing, irresistible urge to move the legs which is usually accompanied by uncomfortable sensations in the lower extremities, that begins or worsens during periods of inactivity, is worse during the evening and nighttime hours, and is partially or totally relieved by movement.^{1, 3, 5} Recognition of RLS as an important clinical condition is growing, in part aided by standardized minimal clinical criteria developed by international expert consensus in 1995⁶ and revised in 2003¹(Table 1). While there remains some debate regarding the specificity of these criteria, the diagnostic guidelines developed by the International Restless Legs Syndrome Study Group (IRLSSG)¹ are now widely accepted.^{2, 4} The establishment of standardized diagnostic criteria, coupled with the increasing appreciation of RLS as a disorder of significant clinical and economic impact have, in turn, led to a growing number of population-based studies regarding RLS prevalence and epidemiology in both North American and Western European populations. However, despite apparent broad disparities in reported estimates and corresponding uncertainty regarding the public health significance of RLS, prevalence data from these studies have not, to our knowledge, been comprehensively reviewed. In this paper, we present a systematic review of the published literature regarding RLS prevalence in the general Western European and North American populations, discuss potential sources of variation, outline the implications regarding the clinical and public health impact of RLS, and offer recommendations for future research.

METHODS

Included in this review are original population-based studies published 1995-2010 in the peer-reviewed scientific literature that provided data on prevalence of RLS in North American and/or Western European populations. We excluded studies that targeted clinical populations, were based only on chart or medical record review, were not available in English, did not target North American or Western European populations, included fewer than 300 participants, did not specifically target RLS, did not specify diagnostic criteria for RLS, or did not incorporate any of the 4 diagnostic criteria for RLS outlined by the IRLSSG.

Studies published only in dissertation or abstract form or that did not report quantitative outcome data were also excluded.

To identify potentially eligible studies, we searched 6 scientific databases from 1995 through July, 2010, including MEDLINE, CINAHL, Academic Search Complete, PsycINFO, PsycARTICLES, and Health Source: Nursing/Academic Edition. Search terms included (restless leg* OR RLS) AND (prevalence OR epidemiology). Titles and abstracts of the citations were scanned to identify potential articles for the review. In addition, we manually searched our own files, the citation sections of all identified articles, and the reference sections of recent (2000-2010) review articles concerning restless legs syndrome. Potentially eligible papers were retrieved in hard copy form for more detailed review.

Data extraction for each eligible paper was performed by at least two of the three authors according to predefined criteria, and recorded on standardized forms. Discrepancies or disagreements during the data extraction and evaluation process were resolved by discussion and consensus by at least two reviewers (KEI and PA/TKS).

RESULTS AND DISCUSSION

Of over 1300 potentially relevant abstracts and citation indices scanned, 55 possibly eligible papers were identified for detailed review; of these, 21 were excluded for the following reasons: one targeted clinical populations only, 6 did not present original data or reported data included in another paper, 2 were not available in English, 3 were available only in abstract or report form, 4 did not specifically target RLS, 3 used a definition of RLS that did not include any of the four IRLSSG standard criteria, and in 2, estimates were based solely on medical records with no specified diagnostic criteria.

Tables 2 and 3 summarize findings from the remaining 34 eligible population-based North American and Western European studies. To date, large population-based studies yielding data on RLS prevalence have been conducted in at least 16 North American and Western European countries, including the United States,⁷⁻¹⁸ Canada,¹⁹ United Kingdom,^{8, 10, 20-22} Ireland,^{20, 23-24} France,^{8, 10, 25-26} Germany,^{8, 10, 20, 22, 27-30} the Netherlands,²⁰ Denmark,^{20, 31} Norway,³¹ Sweden,³²⁻³⁶ Switzerland,³⁷ Finland,³⁸ Italy,^{8, 22, 39} Spain,^{8, 10, 20, 22} Portugal,²² and Greece.⁴⁰ (Table 2) All were published within the last decade, with almost 75% published in 2005 or later. Collectively, these studies represent a combined total of 233,180 participants and include 5 multi-country studies (N=69,992 total participants)^{8, 10, 20, 22, 31} and 29 single country studies (N=163,188 total participants) (Table 2). Study populations ranged in size from 346²³ to 88,673⁹; in all but seven investigations^{13, 19, 23, 25, 30, 38-39} RLS prevalence estimates were based on data from at least 1000 adults. Studies in US populations account for over one-third of all investigations to date and almost half of all participants (N=12 studies, 115,056 total participants combined).

Prevalence of RLS

The research design and population characteristics, sample size, RLS diagnostic criteria, and prevalence rates for each study, stratified by country, are given in Table 3. Reported general prevalence rates from recent community-based studies in the United States,⁷⁻¹⁸ Canada,¹⁹

and Western Europe^{8, 10, 20-40} have ranged from approximately 4^{12, 40} to 29%¹¹ of adults in the general population. For example, estimates from large population-based US studies (N > 1000) defining RLS using the IRLSSG diagnostic criteria^{8, 10, 14} have ranged from 7.6% in a random sample of US adults aged 18 and older⁸ to 24% of predominantly white patients in an Idaho primary care clinic¹⁴(Table 3); using these same diagnostic criteria, prevalence of RLS with symptoms at least once/week has varied from approximately 5%¹⁸ to 15.7%¹⁴ of the overall population. Estimates based on less stringent RLS diagnostic criteria were somewhat higher: 15.9%¹⁷ to 29.3%¹¹ for symptoms of any frequency, and 10.6%¹⁷ to 28.2%⁷ with symptoms at least weekly.

Similarly, prevalence rates from recent population-based studies in Western Europe and based on the four IRLSSG diagnostic criteria (N=18 studies)^{8, 10, 20, 24-32, 34-36, 38-40} have ranged from 3.9% in random samples of Greek adults (N=3303) aged 20 or older⁴⁰ to 26% in a Finnish population of 995 residents 57 years of age.³⁸ Among those studies using these same criteria and reporting information on symptom frequency (10 studies^{8, 10, 20, 24-26, 28, 32, 38, 40}), reported prevalence of RLS in adults experiencing symptoms at least once/week varied from 2.7% in a large random sample of German adults⁸ to 25.8% in a smaller study of healthy French seniors with no previous diagnosis of sleep disorder (N=667)²⁵; estimates of RLS with symptoms occurring at least twice per week and associated with at least moderate distress ranged from 1.3% of German adults aged 18 or older⁸ to 7.6% of primary care patients in Western Europe²⁰ (Table 3).

Of the 30 studies with data on general population prevalence (excluding those which presented only gender-specific information),^{9, 21, 35-36} 70% reported general RLS prevalence rates of at least 10%, 40% reported prevalence rates of at least 15%, and 30% reported prevalence rates of at least 20% (Table 3), with a combined average reported prevalence rate of 14.5±8.0%. Excluding studies that targeted older adults^{21, 25, 30, 38-39} reduced the overall mean prevalence slightly (X=13.9±7.9%), as did considering reported data for each country within multi-country studies as distinct studies (X=12.1±7.65%). Inclusion of studies that reported only gender-specific data also decreased the overall prevalence estimates slightly (X=14.2±8.0%). Restricting studies to those using the four IRLSSG diagnostic criteria to define RLS either with^{9, 12, 15-16, 18, 20, 25, 38} or without a minimum symptom frequency requirement^{8, 10, 14, 19, 24, 26-32, 34-36, 39-40} also reduced average prevalence estimates (X=12.3±7.1%), with 60% of these studies reporting prevalence rates of at least 10%, and 32% of studies indicating prevalence rates of at least 15%. In contrast, prevalence rates reported in studies employing less restrictive criteria (N=9 studies)^{7, 11, 13, 17, 21-23, 33, 37} averaged considerably higher (19.6±8.2%).

Prevalence: Potential Sources of Variation

The broad variation in prevalence reported in these recent population-based studies may reflect several factors, including discrepancies in the RLS diagnostic and severity criteria used, as well as population characteristics and sampling frame. Unfortunately from the standpoint of comparison across studies, definitions of RLS differed considerably among the 34 studies despite the establishment of specific diagnostic criteria by the IRLSSG. Eight studies used the four minimal/essential IRLSSG criteria to define RLS^{14, 24, 26, 31, 34-36, 40},

17 defined RLS as meeting the four diagnostic criteria in addition to experiencing RLS symptoms at a specified minimal frequency or severity^{9, 12, 15-16, 18, 20, 25, 38} and/or reporting general^{8-10, 15-16, 19, 25, 27-30, 32, 38-39} or specific¹² unpleasant leg sensations; in two of these studies, additional estimates were based on both IRLSSG screening criteria and confirmation by a trained physician.^{20, 24} Six studies used questionnaires that included some, but not all standard criteria,^{7, 11, 17, 22-23, 33} with 5 also requiring a minimal symptom frequency^{7, 17, 23} and/or unpleasant leg sensations,^{17, 22-23, 33} and three studies used relatively nonspecific diagnostic criteria that could pertain to periodic limb movement disorder as well.^{13, 21, 37} Even among those using the four IRLSSG diagnostic criteria, several used different wording and/or questionnaires, with, e.g., one study using a 7-item questionnaire with specifically described leg sensations,¹² two using a single complex survey question,^{16, 38} and seven using an interview by a neurologist or other health professional to address the 4 criteria or confirm diagnosis.^{20, 24, 27, 29-30, 39-40} Some of these discrepancies may stem from apparent inconsistencies in the 2003 paper outlining the IRLSSG criteria, in which the suggested diagnostic questions for epidemiologic studies diverge somewhat from the 4 stated criteria (which mention but do not require unpleasant leg sensations).¹ In addition, the diagnostic questionnaires used differed with respect to the specific time interval addressed, potentially contributing further to variation in prevalence estimates⁴¹; while most studies included in this review used questionnaires apparently designed to measure current RLS symptoms, some employed instruments assessing lifetime prevalence^{38, 40} or prevalence over the past 12 months^{15, 18, 26}; in other studies, no time interval was specified for the screening questionnaire.^{8, 10, 12, 14, 24, 31-32, 35-36} However, most of these studies provided data on recent symptom frequency and/or severity.^{8, 10, 12, 14-15, 18, 24, 26, 31-32, 34, 38, 40}

Clearly, there is a need to establish concise, unambiguous questions that adequately capture the established criteria, address a specific, standardized time interval, yet are easy to understand and are culturally appropriate. Confirmation of diagnosis by an expert clinician and/or using a more detailed diagnostic questionnaire may also help increase accuracy of prevalence estimates. For example, in two of the studies reviewed, subjects screening positive for moderate to severe RLS were examined by a physician with expertise in RLS; RLS was confirmed in only a subset of these participants, raising the possibility that the use of a simple screening questionnaire alone might contribute to an overestimation of the RLS prevalence.^{20, 24} Likewise, improving assessor understanding of RLS criteria and/or more detailed questioning of participants may aid both in identifying true RLS cases and in differentiating RLS from conditions such as positional discomfort or ischemia, simple leg cramps, neuropathy, akathisia, and other “mimics” that share some (although not all) of the core features of RLS.⁴¹⁻⁴³ For example, validation studies of a structured telephone diagnostic interview⁴³ and a more comprehensive self-administered diagnostic questionnaire⁴⁴ have demonstrated relatively high sensitivity, specificity, and positive predictive value relative to the simple screening questionnaire.

In addition, the wide range in reported RLS prevalence, even within the same geographic region, may reflect differences in population age, gender, and race/ethnicity distribution, cultural factors, genetic predisposition, and other population characteristics. Less than 40% of the 34 studies reported age and/or gender-adjusted risk estimates,^{9, 12, 16, 26, 39} and/or

used stratified sampling methods.^{8, 15, 22-23, 26-28, 30, 39-40} In addition, although 71% of studies either used random sampling or targeted an entire population within a specific geographic area, age and/or gender distributions of respondents were often skewed (Table 3). Most, although not all^{7, 12, 31, 39} studies have shown RLS prevalence to increase strongly with age, with rates generally plateauing in the 6th or 7th decade of life (Table 3). For example, in those studies reporting age-specific data (N=17), reported prevalence among young adults ranged from 1.2%⁴⁰ to 16.1%¹⁴ ($X=7.6\pm4.8\%$); in contrast, reported prevalence among adults in their 6th to 7th decade ranged from approximately 5.0%⁴⁰ to 32.4%¹⁴ ($X=17.8\pm7.2\%$).

RLS is also more common in women, as illustrated in Table 3. Of the 23 studies with gender-specific data on both sexes (including Gao et al⁹), overall female to male ratio in RLS prevalence averaged 1.61 ± 0.35 ; all but 5 studies^{11, 17, 29, 33, 38} reported at least 35% greater prevalence of RLS in women relative to men, with two US^{12, 18} and four European studies^{22, 30, 39-40} reporting rates in women at least double those in men. In certain subgroups, including individuals with frequent or severe symptoms,^{8, 12} or without sleep apnea,²⁵ excess prevalence among women can be even greater, with reported rates up to 2 1/2 times those of men (Table 3).^{8, 12, 25}

Whether RLS prevalence varies significantly by race/ethnicity remains unclear. For example, while reported prevalence rates in East Asia have been consistently lower than those observed in Western populations,⁴⁵⁻⁴⁹ it is unknown if rates are correspondingly lower in Asian populations residing in North America and Western Europe. To our knowledge, only three studies to date have specifically examined potential variation by race/ethnicity. In a recent US study of two large health professional cohorts, reported prevalence of RLS was higher in white than in non-white participants of both sexes.⁹ In contrast, an investigation of 1028 Baltimore adults did not find significant differences between white and African American participants in RLS prevalence after adjustment for age, gender, and comorbidities;¹² Likewise, in their study of 1934 primary care patients in North Carolina, Alattar and colleagues found no differences between white and black adults, but reported significantly lower RLS prevalence in Latino adults,⁷ although this finding may have been in part due to the apparent younger age distribution of Latino participants.

Because cultural and linguistic factors can affect the reporting of both somatic and psychological symptoms,⁵⁰⁻⁵³ and RLS assessment is based on self-report, cultural differences both within and across geographic regions may also contribute to the heterogeneity of findings. In addition, differences in the distribution of predisposing genetic factors might also contribute to the variability across studies. Familial aggregation of RLS is well-established, with up to 60% or more of those with idiopathic RLS reporting a positive family history.^{4, 54-55} Recent genome-wide association studies have discovered several genetic variants associated with increased RLS risk in populations of European ancestry,^{4, 54-55} including 5 genes and 10 different risk alleles.⁵⁶ However, no causal genes or functional relationships with RLS have yet been identified.^{4, 54-55}

Differences in reported RLS prevalence may also reflect variation in the health status of the study population. Prevalence of RLS can be significantly elevated in association with

specific clinical conditions, with reported rates up to 40% or higher in those diagnosed with certain chronic disorders, including type 2 diabetes,^{29, 57} cardiovascular disease,³³ chronic kidney disease,³ pulmonary hypertension,⁵⁸ fibromyalgia,⁵⁹ depression,³³ and attention deficit/hyperactivity disorder.⁶⁰⁻⁶¹ Increased risk for RLS has also been linked to obesity,^{7, 9, 21, 29, 33, 62} osteoarthritis,³⁶ hypertension,^{7, 15, 22, 29, 33, 35} and respiratory disease,⁶³⁻⁶⁴ as well as to low iron stores and folate deficiency.^{4, 54, 56, 65} In addition, the use of certain medications, including anti-histamines, many anti-emetics, and possibly certain anti-depressants may trigger or exacerbate RLS symptoms.⁶⁶⁻⁶⁷ RLS incidence is significantly elevated during pregnancy,³ and recent research suggests that pregnancy itself may increase risk for the subsequent development of RLS^{27, 68} and may account in part for the observed gender difference in RLS prevalence, at least in those with a family history of RLS.⁶⁹ As illustrated in Table 3, eligibility criteria differed widely among studies, ranging from none other than restriction to adults in a given age range to exclusion of pregnant women,^{9, 20, 24} and/or those with a history of specific conditions linked to RLS, including diabetes,^{9, 25} arthritis,⁹ diagnosis of sleep disorder or heart failure, or history of MI, pacemaker, stroke, or neurological disorder.²⁵

Finally, variation in observed RLS prevalence may be due in part to differences in population source and sampling frame. For example, reported prevalence of RLS in studies of primary care populations (N=9 studies) averaged considerably higher than that reported in studies using random sampling of registries or geographically defined populations (N=25) ($19.5 \pm 7.9\%$ vs. $12.3 \pm 7.2\%$, respectively); restricting this comparison to studies that employed the IRLSSG standard criteria reduced but did not eliminate the disparity in average RLS prevalence ($15.4 \pm 7.8\%$ vs. $11.9 \pm 6.8\%$, respectively). Reasons for this discrepancy are unclear, but may reflect differences in age and gender distribution as well as in health status. For example, adults attending primary care clinics might be more likely to have health conditions associated with RLS, or to have RLS symptoms for which they are seeking medical attention; while comparative studies specific to RLS are lacking, patients attending primary care clinics have been reported to have higher rates of insomnia and poorer health functioning than the general population.⁷⁰⁻⁷¹

Impact of RLS on health, functioning and quality of life

RLS can profoundly affect health, well-being, and quality of life.⁷²⁻⁷⁵ A number of population-based studies have documented significant reductions in health-related quality of life in those with RLS relative to the general population, including increased pain and impairment in physical and social functioning, mental health, general health, and vitality.^{8, 20, 27, 72-73, 76-77} Typified by symptom exacerbation in the evening and nighttime hours, RLS has been repeatedly associated with significant impairment in sleep quality and duration,^{74-75, 78} especially in those suffering more severe symptoms.⁷⁶ Likewise, mood disturbance, including depression and anxiety, is common in those affected by RLS,^{66, 74} and both can result from and contribute to sleep deficits.⁷⁹ Numerous studies have demonstrated strong, bidirectional relationships between mood disturbance and sleep impairment.⁷⁹ Sleep disturbance can interfere with daily role functioning^{72, 75} and is itself associated with increased risk for a host of adverse mental and physical health outcomes, including depression, fatigue, hypertension, impaired glucose tolerance and insulin

resistance, obesity, proinflammatory changes, and cardiovascular disease morbidity and mortality.⁸⁰⁻⁸⁴ Similarly, mood disturbance has been linked to significantly increased risk for stroke, diabetes, cardiovascular disease, metabolic syndrome, and other chronic conditions.^{83, 85-89} Findings from several recent investigations indicate that the adverse impact of RLS on quality of life is comparable to^{8, 72, 74-75} or worse than^{72, 74, 90} that in other serious chronic conditions,⁷³ including diabetes,^{8, 72, 74-75, 90} depression,^{8, 75, 90} hypertension,⁷² angina,⁷² myocardial infarction within the last year,⁷² congestive heart failure,⁷² osteoarthritis,^{72, 90} Parkinson's Disease,⁷² and stroke.⁷²

However, despite the relatively high prevalence of RLS, and the documented adverse effects of RLS on health, functioning, and well-being,⁷³ RLS remains underdiagnosed and undertreated in most populations.^{8, 10, 19-20, 29, 78, 91-92} For example, in a recent international study of RLS, only 6.2% of those suffering frequent, moderate to severe RLS symptoms (N=416) had received a correct diagnosis, although over 80% of these patients had consulted physicians concerning their condition.⁸ Likewise, in two recent large scale European studies of primary care patients, only 9^{10, 20} to 20%²⁹ of those with RLS had been diagnosed correctly. Detection rates in vulnerable populations are likely to still be lower. For example, in a Canadian study of RLS in 3 indigenous North American populations, only 3.9% with symptoms had received a diagnosis of RLS.¹⁹ Findings from medical record studies are also suggestive; for example, in a UK study of 1,561,692 primary care patients (1994-1999), RLS was diagnosed in only 0.25% of the population.⁹² This figure represents approximately 2-3% of the general RLS prevalence estimates from two recent large, UK population-based studies,^{8, 22} and only 5.4% of reported prevalence of physician-confirmed, clinically significant RLS in a recent, smaller investigation of primary care patients in the UK,²⁰ again highlighting overall poor RLS detection rates in medical settings.

LIMITATIONS

As described above, studies included in this review were heterogeneous in many respects; thus, summary estimates of prevalence must be interpreted with caution. An additional limitation includes restriction to papers published in the English language, potentially introducing bias and narrowing the scope of the review. However, only two (German language) publications were excluded on these grounds;⁹³⁻⁹⁴ these papers reported prevalence estimates consistent with those of other studies in our review, and their inclusion would not substantively alter either the specific or overall findings of this paper.

CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE RESEARCH

Collectively, these studies suggest that RLS is a condition of major public health significance in the Western industrialized world, affecting between approximately 4 and 29% of adults and exacting substantial costs in terms of health, functioning, and quality of life. Estimates of prevalence in recent large population-based studies have varied considerably, likely reflecting differences in RLS diagnostic and severity criteria, population characteristics, and study population source. While standard criteria for RLS have been established, standardized diagnostic questions and wording that incorporate these 4 criteria and have been validated in multiple languages are still needed. Investigators continue to

employ modifications of the standard criteria, either omitting specific criteria and/or rendering the criteria more restrictive, and, in some cases, using alternative criteria. Wording varies from study to study, as does the rating of severity and the definition of clinically significant RLS, rendering interpretation and comparison across studies still more demanding.

The establishment and consistent use not only of standardized criteria for RLS diagnosis and determination of clinical significance but also of standardized questionnaires would facilitate interpretation of prevalence estimates and comparison of prevalence across studies, aid in evaluating detection and treatment rates, and help inform the investigation of potential causal factors underlying the etiology and progression of this common and potentially debilitating disorder. While diagnosis of RLS remains challenging, clear understanding and careful application of the diagnostic criteria, recognition of conditions that share certain features of RLS, and the use of specific, validated diagnostic questionnaires designed both to adequately capture RLS symptoms and to exclude mimics may aid in improving estimates of RLS prevalence. Confirmation of diagnosis by an expert clinician in at least a subset of the study population could also be useful in assessing accuracy of RLS screening procedures. In addition, while the number of cross-sectional studies on RLS has grown rapidly in the past decade, published data on RLS incidence are lacking, and the need for prospective studies of RLS remains. Few studies have examined potential differences in RLS prevalence among ethnic or racial minorities in Western countries, and the relative contribution and causal association of various chronic, co-occurring conditions to RLS is still uncertain. Continued assessment of putative causal or precipitating factors, such as anemia, pregnancy, and use of certain medications, along with prospective evaluation of metabolic, psychosocial, and neuroendocrine profiles of common comorbidities, and of lifestyle, environmental, and other potential contributing factors will aid in determining the relative contribution of these variables to RLS prevalence, help enhance our still incomplete understanding regarding the etiology of RLS, and ultimately help inform the development of new therapies.

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Table 1
Commonly used diagnostic criteria for restless legs syndrome (RLS)

IRLSSG Minimal Criteria (1995) ⁶	
1	Desire to move the limbs usually associated with paresthesias/dysesthesias;
2	Motor restlessness;
3	Symptoms are worse or exclusively present at rest (i.e. lying, sitting) with at least partial and temporary relief by activity;
4	Symptoms are worse in evening/night.
IRLSSG Essential Criteria (2003) ¹	
1	An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs (Sometimes the urge to move is present without the uncomfortable sensations and sometimes the arms or other body parts are involved in addition to the legs);
2	The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting;
3	The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues;
4	The urge to move or unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night. (When symptoms are very severe, the worsening at night may not be noticeable but must have been previously present.)
ICSD-90 Criteria ^{* 95}	
Criterion A: A complaint of unpleasant sensations in the legs at night or difficulties in initiating sleep. Criterion B: Disagreeable sensations of 'creeping' inside the calves often associated with general aches and pains in the legs. Criterion C: The discomfort is relieved by movement of the limbs.	
ICSD-2 Diagnostic Criteria for Adults (2nd Edition, 2005) ^{** 96}	
A.	The patient reports an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs.
B.	The urge to move or the unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting.
C.	The urge to move or the unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.
D.	The urge to move or the unpleasant sensations are worse, or only occur, in the evening or night.
E.	The condition is not better explained by another current sleep disorder, medical or neurological disorder, mental disorder, medication use, or substance use disorder.

Abbreviations: ICSD=International Classification of Sleep Disorders; IRLSSG = International Restless Legs Syndrome Study Group

* Used in one multi-national study included in this review.²²

** Not used by any of the studies included in this review.

Table 2
Population-based studies (N>300 participants) reporting RLS prevalence estimates, by country

Country	Single Country Studies (N=29*)		Multi-Country Studies (N=5)		Total Studies	Total Participants (all studies)	% Total Studies	% Total Subjects
	N	Participants	N	Participants				
United States	10	105437	2	9619	12	115056	23.08%	49.34%
Canada	1	430			1	430	1.92%	0.18%
United Kingdom (Wales)	1	1871	4	10047	5	11918	9.62%	5.11%
Ireland	1	346	1	2628	2	2974	3.85%	1.28%
France	2	10930	2	6692	4	17622	7.69%	7.56%
Germany	4	22319	4	14127	8	36446	15.38%	15.63%
Italy	1	701	2	5738	3	6439	5.77%	2.76%
Spain			4	13760	4	13760	7.69%	5.90%
Portugal			1	1858	1	1858	1.92%	0.80%
Holland			1	2121	1	2121	1.92%	0.91%
Denmark			2	2402	2	2402	3.85%	1.03%
Norway			1	1000	1	1000	1.92%	0.43%
Finland	1	995			5	995	9.62%	0.43%
Sweden	5	11955			1	11955	1.92%	5.13%
Switzerland	1	4901			1	4901	1.92%	2.10%
Greece	1	3303			1	3303	1.92%	1.42%
Totals	28	163188	5	69992	52	233180	100.0%	100.0%

* One Irish study reported original data as both a single country and a multi-country study; The 2628 participants were only counted once in this table (included in the multi-country total).

Reported prevalence of restless legs syndrome in recent population-based studies of North American and Western European populations

Table 3

First Author, year (Location)	Study Population and Assessment Procedures	Sample size		RLS definition and determination	General (%)	RLS Prevalence By Age, Sex, and Frequency/ Severity
		Analyzed	Total			
Phillips, 2000 ¹⁶ (US)	Sample of Kentucky adults (18 y) using random digit dialing [1996 Kentucky Behavioral Risk Factor Surveillance survey]. Telephone interview (limited to only one RLS question)	1803	2146	IRLSSG criteria w/ unpleasant feelings in legs required, plus sleep interference; Sx 5x/mo; based on one question	19.4 (any freq); 9.4 (5x/mo); 10.0 (age-adj, 5x/mo)	By Age (5x/mo): 18-29: 3%; 30-79: 10%; 80-93: 19% By Freq: Never: 80.6%; 1x/mo: 2.4%; 2-4x/mo: 7.6%; 5-15x/mo: 3.5%; 16x/mo: 5.9%
Kushida, 2000 ¹¹ (US)	All patients (18 y) attending a rural Idaho private practice during 12-mo period (2/97-2/98). Questionnaires completed in clinic (n=962) or via mail (n=292). Mean age: 47.9±18.5 y; Mean BMI: 26.7±9.1; Female: 54.3%; White: 98.8%	1254	2087	Restless or crawling feeling in legs, before going to sleep, that may go away w/movement; based on one RLS dx (and one freq) question in sleep questionnaire	29.3	By Gender (F, M): 31.3%, 27.1% [R 1.15] By Age: Prevalence increased with age
Nichols, 2003 ¹⁴ (US)	All patients (18 y) attending a rural Idaho primary care practice during 12-mo period (12/99-12/00). Questionnaires completed in clinic (n=1905) or via mail (n=194). Mean age: 45.6±18.9 y (range: 18-93); Female: 51.7%; White: 98.0%	2099	2649	IRLSSG criteria: based on RLSQ	24.0	By Gender (F, M): 27.6%, 20.2% [R 1.37] By Age: 18-29: 16.1%; 30-39: 28.2%; 40-49: 25.8%; 50-59: 32.4%; 60-69: 27.4%; 70-79: 23.4%; 80-93: 14.8% By Freq: <1x/mo: 24.0%; 1-3x/mo: 20.6%; 1-3x/wk: 15.3%; <3x/wk: 6.6%; Severity mildly distressing sx when they occur: <1x/mo: 20.7%; 1-3x/mo: 18.2%; 1-3x/wk: 13.7%; <3x/wk: 6.0%
Mustafa, 2005 ¹³ (US)	Outpatients in 5 Northeast Ohio VA Medical Center clinics (4 primary care, 1 cardiology clinic) over a 2-month period at each site. Anonymous survey questionnaire; data collected 6/01-3/02. Mean age: 62.5 y (range: 19-85); Mean BMI: 29.3 (range: 15.1-57.5), BMI <30: 36.9%; Male: 95%; White: 67.2%, Black: 24.6%, Hispanic: 3.6%,	886	1496	Persistent report of both leg jerks during sleep and leg sensations and positive sleepiness score; based on Cleveland Sleep Habits Questionnaire	19	

First Author, year (Location)	Study Population and Assessment Procedures	Sample size		RLS definition and determination	General (%)	RLS Prevalence By Age, Sex, and Frequency/ Severity
		Analyzed	Total			
	Other: 4.6%					
Winkelman, 2006 ¹⁷ (US)	Random sample of adults (30-60 y) drawn in 1992 (n=6569) from employee payroll records of 4 Wisconsin state agencies [Wisconsin Sleep Cohort]; data from third survey (2002). Mailed questionnaire. Mean age: 53±8 y (range: 40-75 y)	2821	4210	RLS Sx: urge to move legs, when sitting or lying down, relieved by movement, w/ uncomfortable feelings in the legs and sleep disruption required; Sx 1x/wk; based on multi-level questions	15.9 (1x/mo); 10.6 (1x/wk)	<i>By Freq & Gender (F, M):</i> 1x/mo: 15.9% (17.5%, 14.1%) [R 1.24]; 1x/wk: 10.6% (11.2%, 9.9%) [R 1.13]; 1x/day: (5.4%, 4.2%) <i>By Freq, Age & Gender (F, M):</i> 1x/mo: 40-50: 16.1%, 11.2%; 50-60: 15.5%, 14.7%; 60-70: 25.2%, 14.9%; 1x/wk: 40-50: 10.6%, 8.5%; 50-60: 9.1%, 9.7%; 60-70: 17.4%, 12.2%
Lee, 2006 ¹² (US)	Wave 4 of the Baltimore ECA follow-up study, original sample (n=3481) in 1981 selected by probability sampling methods from 3 catchment areas in East Baltimore. Interviewed ~75% of surviving participants in 2004. Mean age 58.11±12.13 y; Caucasian: 61.8%, African-American: 35.0%, Other: 3.2%	1028	1071	IRLSSG criteria w/ creepy/crawly feelings and concurrent sx required; Sx 2x/wk deemed clinically significant; based on 7-item RLS questionnaire	4.1	<i>By Gender (F,M):</i> OR 2.64 <i>By Race: African-American:</i> 4.7%; <i>Caucasian:</i> 3.8% (NS) <i>By Freq (2x/wk):</i> 1.8% <i>By Age:</i> Not associated with age
Phillips, 2006 ¹⁵ (US)	Random sample of community-dwelling adults (18 y) living w/in continental US, stratified by region and age. Telephone interview from Sept 20 to Nov 7, 2004 [2005 NSF Sleep in America poll]. Mean age 49 y; Female: 51%; White: 84%	1506	22504 contacted [23% response]	IRLSSG criteria w/ unpleasant feelings in legs required; Sx at least a few times/wk and worse at night; based on two questions	9.7	<i>By Freq & Gender (F, M):</i> At least a few nights/wk: 9.7 (11%, 8%) [R 1.375]; Every or almost every night: 6%, 5%
Alattar, 2007 ⁷ (US)	All patients (18 y) with appt at 1 of 5 primary care sites in North Carolina over a 1-mo period [NC-FP-RN Study]. Questionnaire or interview. Mean age: 50.1±18.1 y; mean BMI 29.3±7.1; Female: 67.7%; White: 58.1%, African-American: 30.0%, Latino: 9.2%	1934 [of 1935, 1 m.d.]	2963	Unpleasant, tingling, creeping, or restless feelings in legs at night while trying to sleep; Sx 1x/wk; based on one screening question	28.2	<i>By age: <65:</i> 28.2%; 65: 28.9% (NS) <i>By Ethnicity (Latino:white):</i> OR=0.46
Winkelman, 2008 ¹⁸ (US)	Community-based population drawn from ongoing longitudinal studies (ARIC, CHS, FHS, NY cohorts, SHS, and Tucson cohorts),	3433 [of 4586, 1153 m.d.]	6441	IRLSSG criteria; Sx occur at least 5-15 days/mo, w/ at least moderate distress;	5.2	<i>By Gender (F, M)</i> 5x/mo & moderate distress: 6.8%, 3.3% [R 2.06]

First Author, year (Location)	Study Population and Assessment Procedures	Sample size		RLS definition and determination	General (%)	RLS Prevalence By Age, Sex, and Frequency/ Severity
		Analyzed	Total			
	examined 2000–2003 [SHHS-2]. Interview questionnaire. Mean age: 67.9±10.2 y (range: 44–98); Mean BMI: 29.1±5.4; Female: 54.6%			based on SHHS-2 Health Interview Questionnaire		<i>By Freq:</i> 5–15x/mo: 1.5%; 16–23x/mo: 1.5%; 24x/mo: 2.2% <i>By Severity:</i> Moderate: 2.9%; Severe (“a lot” or “extremely” bothersome): 2.3%
Gao, 2009 ⁹ (US)	NHS II cohort (women 25–42 yoa in 1989) & HPFS cohort (men 40–75 yoa in 1986); data collected from follow up questionnaires in 2002 [HPFS] and 2005 [NHS II]; excluded from analysis those with diabetes, arthritis, and pregnancy. Mean age: NHS: 50.4±5 y & HPFS: 68.9±9 y	88673 [of 111721 completed] Women: 65554 Men: 23119	135073	IRLSSG criteria w/ unpleasant leg sensations required; Sx 5x/mo; based on 3 RLS dx questions	Female: 6.4; Male: 4.1	<i>By Freq & Gender (F, M):</i> 5x/mo: 6.4%, 4.1% [R 1.56]; 15x/mo: 2.7%, 1.7% <i>By Age:</i> Prevalence increased with age <i>By Race & Gender (F, M):</i> White: 6.6%, 4.2%; Non-white: 3.8%, 2.4%
Hening, 2004 ¹⁰ (US, France, Germany, Spain, UK)	Patients of 182 primary care physicians who visited clinic during a 2-wk enrollment period. Screening questionnaires distributed on site (those screening positive for RLS given additional, more detailed questionnaires) [REST Primary Care Study]. Mean age: 51.4±17.6 y	23052 US: 3655; France: 4808; Germany: 6723; Spain: 5752; UK: 2114	Not given	IRLSSG dx criteria w/ uncomfortable feelings in legs required; based on 4 dx screening questions; Sx 1x/wk given Patient Follow up Questionnaire and Physician Questionnaire	Any Freq: Total: 11.1; US: 13.3; France: 7.4; Germany: 11.4; Spain: 5.5; UK: 14.2	<i>By Country & Freq (Any freq, 1x/wk, 2x/wk with at least moderate impact on QOL):</i> France: 7.4%, 5.0%, 2.1%; Germany: 11.4%, 7.9%, 3.7%; Spain: 5.5%, 3.6%, 1.9%; UK: 14.2%, 11.3%, 5.6%; US: 13.3%, 11.3%, 5.8%; All: 11.1%, 9.6%, 3.4%
Allen, 2005 ⁸ (US, France, Germany, Italy, Spain, UK)	Nationally representative, random sample of adults (18 y) from 6 countries (sample stratified by age, sex, working/social status and region). Interviewed via telephone (US) or in person (Europe); those screening positive for RLS administered more detailed questions [REST General Population Study]. (Age: 20–29 y slightly over-represented; 80 y under-represented)	15 391 US: 5964; France: 1884; Germany: 1929; Italy: 1768; Spain: 1896; UK: 1950	16 202 US: 6014; France: 2010; Germany: 2040; Italy: 2036; Spain: 2020; UK: 2082	IRLSSG dx criteria w/ uncomfortable feelings in legs required; based on 4 dx screening questions; Severity based on postscreening questions	Any Freq: Total: 7.2; US: 7.6; France: 10.8; Germany: 4.1; Italy: 6.7; Spain: 4.9; UK: 8.6	<i>By Country & Freq (Any freq, 1x/wk, 2x/wk with at least moderate distress):</i> France: 10.8%, 6.6%, 5.5%, 4.2%; Germany: 4.1%, 2.7%, 2.0%, 1.3%; Italy: 6.7%, 4.2%, 3.1%, 2.4%; Spain: 4.9%, 3.5%, 3.1%, 2.0%; UK: 8.6%, 5.6%, 4.9%, 2.3%; US: 7.6%, 5.8%, 4.8%, 3.1%; All: 7.2%, 5.0%, 4.1%, 2.7% <i>By Freq & Gender (F, M):</i> Any freq: 9.0%,

First Author, year (Location)	Study Population and Assessment Procedures	Sample size		RLS definition and determination	General (%)	RLS Prevalence By Age, Sex, and Frequency/ Severity
		Analyzed	Total			
						5.4% [R 1.67]; 1x/wk: 6.2%, 2.8% [R 2.21]; 2x/wk with moderate distress: 3.7%, 1.7% [R 2.18] Age (70-79): Highest Prevalence
Obayon, 2002 ²² (UK, Germany, Italy, Portugal, Spain)	Random sample of non-institutionalized residents from 5 (15 y, except Portugal (18 y)); sample stratified by geographic distribution, age, and gender. Telephone interview, 1994-99. Age: 15-100 y; Female: 51.3%	18980 UK: 4972; Germany: 4115; Italy: 3970; Portugal: 1858; Spain: 4065	23620 UK: 6249; Germany: 6047; Italy: 4442; Portugal: 2234; Spain: 4648	ICSD-90 Criteria ["shivering or creeping" feeling in calves required]	Total: 5.5	By Gender (F, M): 7.1 %, 3.6% [R 1.97] By Age: 15-19: 2.7%; 20-29: 3.7%; 30-39: 3.5%; 40-49: 4.7%; 50-59: 7.2%; 60-69: 8.3%; 70-79: 8.7%; 80: 8.2%
Allen, 2010 ²⁰ (Denmark, Germany, Ireland, Netherlands, Spain, UK)	10,564 adults (18 y) visiting 1 of 62 primary care practices over a 1-wk period. 804 screened positive for clinically significant RLS (A) & referred to physician; 630 completed interview with physician; Patients attending pre-natal clinics excluded	10564 Denmark: 1397; Germany: 1360; Ireland: 2628; Netherlands: 2121; Spain: 2047; UK: 1011	Not given	A. IRLSSG criteria; based on 4 RLS dx screening questions; B. Physician confirmed: based on structured diagnostic interview; Sx 2x/wk and at least moderately distressing	A. Self-report Total: 7.6; B. MD Dx Total: 4.4; Denmark: 3.5; Germany: 2.4; Ireland: 4.6; Netherlands: 6.0; Spain: 4.6; UK: 4.6	General (clinically significant sx 2x/wk and at least moderately distressing): A) Self-report: 7.6%; B) Physician confirmed: 4.4% By Country (Physician Diagnosed): Denmark: 3.5%; Germany: 2.4%; Ireland: 4.6%; Netherlands: 6.0%; Spain: 4.6%; UK: 4.6% [adjusted for missing interviews]
Bjorvatn, 2005 ³¹ (Denmark, Norway)	Nationwide research survey of adults (18 y) in Denmark and Norway, random sample drawn from each country's phone number register, household member randomly selected using next-birthday technique. Telephone interview. Mean age: 46.6±17.8 y (range: 18-99); Female: 51%	2005 Norway: 1000; Denmark: 1005	4279 Norway: 2141; Denmark: 2138	IRLSSG criteria; Severity during past wk based on IRLS	Total: 11.5; Norway: 14.3; Denmark: 8.8	By Gender (F, M): 11.5% (13.4%, 9.4%) [R 1.43] By Age: 18-29: 6.3%; 30-44: 12.6%; 45-59: 14.2%; 60: 11.9% Severity (past 7 days): No sx: 0.8%; Mild: 5.2%; Moderate: 3.9%; Severe: 1.3%; Very Severe: 0.4% [Based on 193]

First Author, year (Location)	Study Population and Assessment Procedures	Sample size		RLS definition and determination	General (%)	RLS Prevalence By Age, Sex, and Frequency/ Severity
		Analyzed	Total			
Froese, 2008 ¹⁹ (British Columbia, Canada)	Community-based survey of 3 indigenous North American Indian groups living in northwestern BC. Phone & door-to-door survey from May to Sept 2006. Mean age: 43.2±14.3 y; Mean BMI: 31.0±9.2, BMI >30: 45%, BMI >40: 11% (n=393 for BMI); Female: 56%	430	1020	IRLSSG criteria w/ abnormal sensations required; based on 4 RLS dx questions	17.7	General: 17.7% [only 3.9% of whom reported a physician dx (0.007% of total population)]
Ulfberg, 2001 ³⁵ (Sweden)	Men 18-64 y randomly selected from register of all Dalarna County residents. Mailed questionnaire, 10% of nonrespondents contacted at random by telephone. Mean age: 47 y	2608 [of 2980, 372 m.d.]	3961 eligible [of 4000]	IRLSSG criteria; based on 4 RLS dx questions	5.8 (all male)	By Age (all male): 18-24: 1.2%; 25-34: 4.0%; 35-44: 6.2%; 45-54: 8.0%; 55-64: 10.5%
Ulfberg, 2007 ³⁴ (Sweden)	Nationwide survey of adults; random sample from register of phone numbers; household member randomly selected using next-birthday technique. Telephone interview. Age range: 18-90 y; Female: 51%	1000	2016	IRLSSG criteria; based on interview; Severity based on IRLS	5	By Gender (F, M): 5.7%, 3.5% [R 1.63] Severity [of those w/sx during the last week]: Mild: 0.5%; Moderate: 1.3%; Severe: 1.8%; Very Severe: 1.4%
Mallon, 2008 ³³ (Sweden)	Random sample of adults (30-65 y), using population registry of Dalarna & Gävleborg Counties (1983). RLS findings based on data collected via postal questionnaire in 1983. Mean age: 46±10 y; Female: 51%	3496 [of 3550, 54 m.d.]	5102	RLS proxy: At least sometimes 'bothered by creeping sensations in legs when trying to fall asleep' PLUS at least moderate daytime sleepiness (Uppsala Sleep Inventory)	25.3 (with or w/o daytime sleepiness); 10.3 (w/daytime sleepiness)	By Gender (F, M): With or w/o daytime sleepiness: 25.3% (28.1%, 22.5%) [R 1.25]; At least moderate problem w/ daytime sleepiness: 10.3% (10.6%, 10.0%)
Broman, 2008 ³² (Sweden)	Residents in Uppsala Municipality (20-59 y); select every 50th person from national registration records. Mailed questionnaire. 56% female (mean age: 38±11 y); 44% male (mean age: 39±12 y)	1335	1962	IRLSSG criteria w/ unpleasant leg sensations required; based on 4-question set (3 standardized dx & 1 freq) recommended by IRLSSG for epidemiology studies	18.8	By Freq & Gender (F, M): Any freq: 18.8 (21.6%, 15.2%) [R 1.42]; 2x/wk: 5.8% (6.3%, 5.3%) By Age & Freq (Any freq, 2x/wk): 20-39: 14.8%; 2.5%; 40-59: 23.5%, 9.8%
Wesstrom, 2008 ³⁶ (Sweden)	Random sample of women 18-64 y residing in Dalarna County and drawn from SPAR database. Mailed questionnaire. BMI>25: 43.1%	3516	5000	IRLSSG criteria; based on questionnaire	15.7 (all female)	By Age (all female): 25-34: 11.0%; 35-44: 11.7%; 45-54: 18.1%;

First Author, year (Location)	Study Population and Assessment Procedures	Sample size		RLS definition and determination	General (%)	RLS Prevalence By Age, Sex, and Frequency/ Severity
		Analyzed	Total			
Rohdach, 2000 ³⁰ (Germany)	Adults (65 y on 10/01/97) and living in Augsburg or one of two suburbs, who participated in 2nd WHO MONICA survey. Face-to-face interviews (10/97-4/98) by 2 RLS-trained physicians [MEMO Study]. Mean age: 72.7 (65-83 y); SBP: 147±17.5; DBP: 82.6±9.7; BMI: 27.8±3.8; Male: 52.7%	369 [of 385, 16 m.d.]	635	IRLSSG criteria w/ unpleasant sensations or pain in legs required; based on 3 standardized RLS dx questions in interview by MID	9.8	<i>By Gender (F, M):</i> 13.9%, 6.1% [R 2.28] <i>By Age & Gender (F, M):</i> 65-69: 12.8% (13.2%, 12.2%); 70-74: 9.9% (15.2%, 4.6%); 75: 7.4% (13.0%, 3.7%) (NS)
Berger, 2004 ²⁷ (Germany)	Adults (20-79 y) of German nationality, drawn from population registers using 2-stage cluster sampling [Study of Health in Pomerania (NE Germany)]. Face-to-face interview and physical examination 10/01/97-10/31/2000	4107 [of 4310, 203 m.d. on RLS]	6267 eligible [of 7008]	IRLSSG criteria w/ sensory discomfort or pain in legs required; based on 3 standardized RLS dx questions in interview by health care professional	10.6	<i>By Gender (F, M):</i> 13.4%, 7.6% [R 1.76] <i>By Age & Gender (F, M):</i> 20-29: 4.9%, 3%; 30-39: 13.2%; 40-49: 13.2%; 50-59: 19.4%; 60-69: 13.2%; then decline
Happe, 2008 ²⁸ (Germany)	Age- and gender- stratified random sample of adults 25-75 y living in Dortmund, drawn from city register [Dortmund Health Study]. In-person interview and standardized examination (n=1312) or questionnaire w/o RLS questions (n=979). Interviewees: Female: 52.9%; Migrants: 16.0%	1312 interviews (for RLS) [the 979 questionnaires had no RLS info]	3425 eligible [of 3820]	IRLSSG criteria w/ sensory discomfort or pain in legs required OR previous dx by physician; based on 3 standardized RLS dx questions in interview	8.8	<i>By Gender (F, M):</i> 10.2%, 7.1% [R 1.44] <i>By Age & Gender (F, M):</i> 25-44: 8.6%, 3.9%; 45-75: 11.1%, 8.5%; 76+: 1.3%; <i>By Freq:</i> 1x/mo: 1.3%; 1-3x/mo: 2.3%; 1-2x/wk: 2.2%; 3-6x/wk: 1.6%; Daily: 1.4% <i>By Race/Ethnicity:</i> German descendants: 9.2%; Migrants: 6.7%
Moller, 2010 ²⁹ (Germany)	Patients (>18 y) visiting 1 of 312 primary care practices in Germany. Pt questionnaire completed in waiting room (10/8/2007). Physician assessed 4 RLS dx criteria in pts with unpleasant sensations in legs. Mean age: 54.5±17.3 y; Female: 57.9%	16531 [of 16543, 12 m.d.]	Not given	IRLSSG criteria w/ unpleasant leg sensations required; based on physician dx using RLSSQ; Severity measured with CGI-S	10.6	<i>By Gender (F, M):</i> 11.9%, 9.0% [R 1.32] <i>By Severity:</i> Moderately ill or worse: 5.7%
Hogl, 2005 ³⁹ (Italy)	Age- and sex-stratified random sample of 1000 adults (40-79 y in 1990) in northern Italy (n=936) [Bruneck study]; data for this study from follow-up clinical exams conducted over 8-wk period in 2000. Age 50-89 y; White: 100%	701	768 eligible	IRLSSG criteria w/ unpleasant sensations required; based on 4 RLS dx questions in interview w/ neurologist experienced in sleep med; Severity based	10.6; 11.0 (age/sex-adj)	<i>By Gender (F, M):</i> 10.6% (14.2%, 6.6%) [R 2.15]; (Age and sex-adjusted: 11.0% (14.3%, 7.0%) [R 2.04]) <i>By Age and Gender (F, M):</i> 50-59: 13.9%,

First Author, year (Location)	Study Population and Assessment Procedures	Sample size		RLS definition and determination	General (%)	RLS Prevalence By Age, Sex, and Frequency/ Severity
		Analyzed	Total			
				on IRLS		7.8%; 60-69 : 16.3%, 6.6%; 70-79 : 12.6%, 6.4%; 80-89 : 13.5%, 2.9% By Severity : Mild : 3.6%; Moderate : 4.7%; Severe : 2.3%
Tison, 2005 ²⁶ (France)	Nationwide random sample of adults 18 y in metropolitan France, stratified by age, sex, socioprofessional group, and employment status for women [INSTANT Study]. Face to face interviews Feb to June 2003 (133 pts w/RLS and specific comorbidities did not provide more detailed RLS info). Mean age: 48.2±17.3 y (range: 18-92); Female: 53.6%	10263 [of 870 w/RLS, 737 asked addtl RLS questions, 6 m.d.]	Not given	IRLSSG criteria [w/in previous 12 mo]; based on 4 of 5 dx questions. Severity based on IRLS [over the last 7 days]	8.5	By Gender (F, M) : 10.8%, 5.8% [R 1.86]; (Age and sex-adjusted: Same) By Age : Increased with age until 64 y, then decreased By Freq : At least 1x/year : 0.9%, Monthly : 3.1%, Weekly : 2.5%, Daily : 1.9% By Severity [past 7 days] : Mild : 3.7%, Moderate : 3.0%, Severe : 1.4%, Very Severe : 0.4% [Freq/Severity based on subset (n=731) who provided detailed RLS data]
Celle, 2009 ²⁵ (France)	Population-based cohort of healthy elderly (65±1 y) living in Saint- Etienne in 2001 [PROOF Study, n=1011]; at 7-yr follow-up, ancillary study [Synapse, n=851] conducted; excluded those with hx of MI, heart failure, stroke, pacemaker, DM 1, neurological disorder, or sleep disorder. Clinical assessment of these Ss via questionnaire and interview. Mean age: 68.6±0.8 y; BMI: 25.4±3.7; Female: 59%	667 completed RLS eval [318 w/o SDB]	851 accepted polygraphic recording	IRLSSG criteria w/ unpleasant leg sensations required; Sx >1x/wk for last 6 mos; based on 5 standardized questions; Severity based on IRLS	25.8; 24.2 (in those w/o SDB)	By Gender (F, M) (n=667): 25.8%, (29.9%, 21.0%) [R 1.42]; (n=318 w/o SDB: 24.2% (29.7%, 12.1%) [R 2.45]) By Severity : Mild : 30%; Moderate : 36.6%; Severe : 23.4%; Very severe : 0.0% [This was for subset of those w/o SDB (n=318)]
O'Keefe, 2003 ²³ (Ireland)	An age-sex stratified random sample of adults (18 y) drawn from register of a single general practice in Galway. Mailed questionnaires	346	455 eligible [of 500]	"Do you have unpleasant feelings in your legs for example creepy-crawling or tingling feelings when you lie down at night that make you feel restless and keep you from getting a good night's sleep?"; Sx > 5 nights/mo; based on	13.6 (based on respondents only); 10.3 (non- respondents assumed not to have RLS)	By Gender (F, M) : 13.6% (15.0%, 10.6%) [based on 328 responses]; (n=455 w/ non- respondents assumed not to have RLS); 10.3% (12.4%, 6.5%) [R 1.91]) By Age & Gender (F, M) : 18-29 : 6.9%; 10.0%; 30-39 : 7.7%, 0.0%; 40-49 : 12.5%,

First Author, year (Location)	Study Population and Assessment Procedures	Sample size		RLS definition and determination	General (%)	RLS Prevalence By Age, Sex, and Frequency/ Severity
		Analyzed	Total			
				one question		5.3%; 50-59 : 18.2%, 12.5%; 60-69 : 30.8%, 0.0%; 70-79 : 16.0%, 26.1%; 80 : 12.5%, 21.4% [Based on 328 respondents, 18/346 did not specify age/sex so were not included] By Age & Gender (F, M): 18-29 : 6.3%, 6.3%; 30-39 : 6.5%, 0.0%; 40-49 : 11.4%, 2.9%; 50-59 : 18.2%, 9.1%; 60-69 : 24.2%, 0.0%; 70-79 : 12.5%, 17.1%; 80 : 6.7%/10.3%; Men <70 : 3.6%, Men 70 : 14.1% [Based on all eligible, non- respondents assumed not to have RLS]
O'Keefe, 2007 ²⁴ (Ireland)	Patients > 18 y attending 1 of 19 general practices across Ireland over a one week period; women attending ante-natal clinics excluded. Pts completed screening questionnaire, those positive for moderate to severe RLS at least 2x/wk interviewed by GP (60/195 decline); GPs provided with educational material and training session on RLS	2628	Not given	A. IRLSSG criteria; based on screening questions; B. Positive screeners w/ moderate to severely distressing Sx 2x/wk [MS-RLS] interviewed by GP; MS-RLS based on GP interview	23.5 (any freq); 7.4 (MS-RLS); 2.8 (Dr dx MS-RLS)	By Freq/Severity: Any freq, any severity: 23.5%; Any freq w/ moderate distress: 9.6%; 2x/wk, any severity: 13.3%; 2x/wk w/ moderate distress [MS- RLS]: 7.4%; Physician confirmed MS-RLS: 2.8% [Patients declining interviews (60 of 195 eligible) counted as not having RLS; see Allen, 2010 for adjusted prevalence]
Elwood, 2006 ²¹ (Wales (UK))	Representative population sample of older men in South Wales [Caerphilly cohort]. Questionnaire completed with help of partner at 2nd follow-up exam: 1986 men completed questionnaires, 112 who had prior stroke or MI excluded from RLS analyses. Age: 55-69 y; Mean BMI: 26.8±3.7; Male: 100%	1871	Not given	“Restless legs or bothersome twitches”; 1-2x/wk or more; based on Wisconsin Sleep questionnaire	23 (all male)	

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		Analyzed	Total			
Schwegler, 2006 ³⁷ (Switzerland)	Customers of 804 Swiss pharmacies (49% of all community pharmacies). Questionnaires completed in pharmacy 10/15 - 11/15/2003. 66.1% female (mean age: 52.4±18.1 y, mean BMI: 23.8±4.3); 33.9% male (mean age: 55.1±17.1 y, mean BMI: 25.7±3.9)	4901	Not given [4915 submitted]	RLS assessed using the 9 RLS/PLM items from the SDQ	22	<i>By Gender (F, M): above 90th percentile of reference: 25%, 16% [R 1.56]; above cutoff score of 21: 59.3%, 46.8%</i>
Hadjigeorgiou, 2007 ⁴⁰ (Greece)	Sex- and age-stratified random sample of all adults (20 y) residing in city of Larissa, drawn from 2000 National Census registration file. Door-to-door interviews conducted by MDs trained in RLS clinical dx; those screening positive given detailed neurological exam. Female: 50%	3303	3365 contacted [of 4200]	IRLSSG criteria: based on interview by MD; Severity based on IRLS	3.9	<i>By Gender (F, M): 5.2%, 2.3% [R 2.26] By Age & Gender (F, M): 20-29: 1.2% (1.4%, 1.0%); 30-39: 2.9% (3.8%, 1.9%); 40-49: 3.1% (4.0%, 2.2%); 50-59: 5.2% (6.7%, 3.3%); 60-69: 5.0% (7.8%, 2.0%); 70-79: 6.0% (8.5%, 3.2%); 79: 3.8% (4.3%, 3.0%); Total: 3.9% (5.2%, 2.3%) By Freq: <1x/mo: 0.9%; 1-4x/mo: 1.2%; 5-15x/mo: 1.0%; 16x/mo: 0.6% By Severity: Mild: 1.7%; Moderate: 1.3%; Severe: 0.8%; Very Severe: 0.1%</i>
Juuti, 2010 ³⁸ (Finland)	All aged 57 y residents (as of 12/31/01) of city of Oulu, drawn from National Population Registry of Finland. Mailed questionnaires, clinical interviews, exams, and labs. Female: 56%	995	1332 eligible	IRLSSG criteria w/ unpleasant feelings in legs required; Sx 1x/wk; based on one dx question	26 (1x/mo); 18 (1x/wk)	<i>By Freq & Gender (F, M): >1x/mo: 26% (28%, 23%) [R 1.22]; 1x/wk: 18% (20%, 15%) [R 1.33]; 3x/wk: 12% (13%, 10%); Every or almost every day: 7% (6%, 7%)</i>

Abbreviations: appt=appointment; ARIC=Atherosclerosis Risk in Communities; btwn=between; CGI-S=Clinical Global Impressions-Severity of Illness scale; CHS=Cardiovascular Health Study; dx=diagnosis; ECA=Epidemiologic Catchment Area; F=Female; FHS=Framingham Heart Study; Freq=frequency; GP=General Practitioner; HPFS=Health Professionals Follow-up study; hx=history; ICSD=International Classification of Sleep Disorders; IRLS=Intl rLS Study Group Rating Scale; IRLSSG=International Restless Legs Syndrome Study Group; M=Male; MD=Doctor of Medicine; m.d.=missing data; MEMO=The Memory and Morbidity in Augsburg Elderly Study; MI=Myocardial Infarction; MONICA=Monitoring trends and determinants in CVD Survey-Augsburg; MOS sleep=Medical Outcome Study Sleep scale; MS-RLS=Moderate to severe RLS; NC-FP-RN=North Carolina Family Practice Research Network; NHS II=Nurses Health Study II; NSF poll=National Sleep Foundation Poll; NY cohorts=New York Hypertension cohorts; PLM=Periodic Limb Movement; R=ratio; REST=RLS Epidemiology, Symptoms and Treatment; RLS=Restless Legs Syndrome; RLSQ=Restless Legs Syndrome Questionnaire; RLSAQ=Restless Legs Syndrome Screening Questionnaire; SDB=Sleep Disordered Breathing; SDQ=Stanford Sleep Disorders Questionnaire; SHHS=Sleep Heart Health Study; SHS=Strong Heart Study; SPAR=the official database covering the total population of Sweden; Ss=Subjects; Sx=Symptoms; Tucson cohorts=Tucson Epidemiologic Study of Airways Obstructive Diseases and the Health and Environment Study; w/o=without; y=years

Age: mean age $\pm$ SD

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