**Personal Perceptions of Exercise and Restless Legs Syndrome:**

**Results from a nation-wide, mixed-methods survey**

**Authors:** Cederberg, K.L.J.,1\* Sikes, E.M.2, Camillo Ricciardiello Mejia, G.1,3 and Mignot, E.1

1 Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Palo Alto, CA USA

2 Department of Occupational Therapy, Shenandoah University, Winchester, VA, USA

3 Epidemiology and Population Health, Stanford University, Palo Alto, CA USA

\* Corresponding Author: Katie L.J. Cederberg; kcederb@stanford.edu; 3165 Porter Drive, Palo Alto, CA 94304

**Funding Information:** This work was supported, in part, by the National Heart, lung, and Blood institute [T32HL110952]. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The funding sources had no involvement in (a) the study design; (b) data collection, analysis or interpretation; (c) in writing of the report; or in the decision to submit the article for publication.

**Acknowledgments**: We would like to thank the Restless Legs Syndrome Foundation, the Northern California Restless Legs Syndrome Support Group, and study participants for their contribution to this manuscript.

**Conflict of Interest Statements:** Drs. Katie Cederberg and E. Morghen Sikes declare no conflict of interest. Dr. Emmanuel Mignot occasionally consults and has received contracts from Jazz Pharmaceuticals, Orexia/Centessa, Tekeda, Dreem, and ActiGraph; has received grant/clinical trial funding from Haromony, Tekeda, Apple, Humani, Sunovion, Indorsia, Eisai; is and has been a Principal Investigator on clinical trials using sodium oxybate and Solriamfetol, Jazz Pharmaceutical products, for the treatment of Type 1 Narcolepsy; all outside the scope of this work.

**Abstract**

**Background:** Restless legs syndrome (RLS) is a prevalent, sensorimotor sleep disorder that is temporarily relieved by movement. There is evidence of inter-individual variation in the response to exercise, whereby some people experience the health benefits associated with exercise (i.e., responders), but some do not experience the physiological changes associated with exercise (i.e., non-responders). The present study examined inter-individual factors that may account for differences in the perceived response to exercise as a mode of treatment for RLS symptoms.

**Methods:** Participants (N=528) completed a mixed-methods, nationwide survey including items assessing RLS diagnosis, RLS severity, current physical activity levels, personal experiences with exercise and RLS (both positive and negative), and demographic and clinical characteristics. Participants were classified as perceived positive responders (i.e., exercise improves symptoms), perceived negative responders (i.e., exercise exacerbates symptoms), and perceived non-responders (i.e., exercise does not impact symptoms).

**Results:**

**Conclusions:** The present study presents unique factors that might account for individual differences in the response to exercise. Such individual differences and specific attributes should be considered in exercise-based management to further optimize personalized treatment plans to prevent and manage symptoms in people with RLS.

**Keywords:** restless legs syndrome, exercise, personal perceptions, survey, treatment

**Introduction**

Restless legs syndrome (RLS) is a sensorimotor sleep disorder that affects roughly 10% of people.1 It significantly disrupts sleep2 and increases the risk of cardiovascular disease, hypertension, stroke,3,4 depression and anxiety,5 and causes overall poorer health1,6 and decreased quality of life.7,8 Despite the identification of genetic variants associated with RLS,9,10 the pathophysiology of RLS is not well understood, hindering the development of targeted disease modifying therapies. As two key diagnostic features of RLS include the worsening of symptoms at rest and relief by movement,11 there is increasing interest in utilizing physical activity and exercise to manage symptoms.

Previous research highlights exercise as one of the most promising non-pharmacological approaches for managing symptoms of RLS.12-20 Despite the current evidence for the benefit of exercise in RLS symptoms, there are anecdotal reports of certain parameters of exercise (e.g., high-intensity) exacerbating symptom of RLS, suggesting that the differential response to exercise may involve inter-personal or exercise parameter-specific variability (i.e., response heterogeneity). Understanding the aspects of exercise (e.g., intensity, timing) that can benefit and/or exacerbate symptoms in different individuals may improve our approach in managing symptoms. Further, the development of exercise studies, programs, and prescription recommendations for managing RLS should consider the needs of people with RLS. Indeed, including the target population in the development of an exercise program is an imperative step in clinical and translational research that increases the success of subsequent implementation research efforts.21

To that end, the present study utilized a mixed-methods, nationwide survey of adults with RLS to (1) describe personal experiences regarding exercise parameters that are perceived to benefit and/or exacerbate RLS symptoms; (2) identify inter-personal and clinical factors that may account for individual differences in the perceived response to exercise as a mode of treatment for RLS symptoms (i.e., response heterogeneity); and (3) inquire about specific questions people with RLS have about exercise that can inform the development of future exercise-based research studies and programs. We expected most participants to report that exercise reduces symptoms of RLS and fewer to report that exercise only worsens symptoms. We further expected certain non-modifiable factors (e.g., age, sex, RLS duration and severity, and secondary conditions) and modifiable factors (e.g., physical activity and sedentary levels) to be significant determinants of the perceived response to exercise.22 Lastly, we anticipated participants to ask questions about exercise parameters that would maximize the benefit of exercise (e.g., the optimal exercise intensity and what time of day is best for minimizing symptoms and avoiding exacerbations).

**Materials & Methods**

*Participants and Procedure*

The present study was a secondary analysis of a previously published description of perceptions of exercise in people with RLS1 and the procedure was approved by Stanford’s Institutional Review Board. The Restless Legs Syndrome Foundation (RLSF) distributed the survey to 3,644 registered members with RLS via an email notification (i.e., “eblast”) in October 2021. Persons interested in participating were instructed to proceed to the internet-based survey by clicking on the survey link provided in the eblast advertisement. An RLSF member who completed the survey also shared the survey link to the “RLS SUCKS! Restless Legs Syndrome – Willis-Ekbom Support Group” Facebook group, which includes approximately 1,804 members. Upon entry into the survey, all participants were provided with a detailed description of the survey and all participants provided electronic informed consent followed by the anonymous completion of the questionnaire. All questionnaires were checked for completeness; however, the survey was conducted completely anonymously. Therefore, in the event of missing data, a survey was considered incomplete and excluded from formal analyses. The survey was closed to participants in June 2022, at which time 1,935 (53%) of the 3,644 emails sent by the RLSF were opened with 727 (38%) recorded unique clicks to proceed to the survey. We were unable to track the number of individuals in the Facebook group who completed the survey. In total, there were 587 survey responses with a total of 528 people (90%) who completed all relevant outcomes for the present study.

*Mixed-Methods Survey*

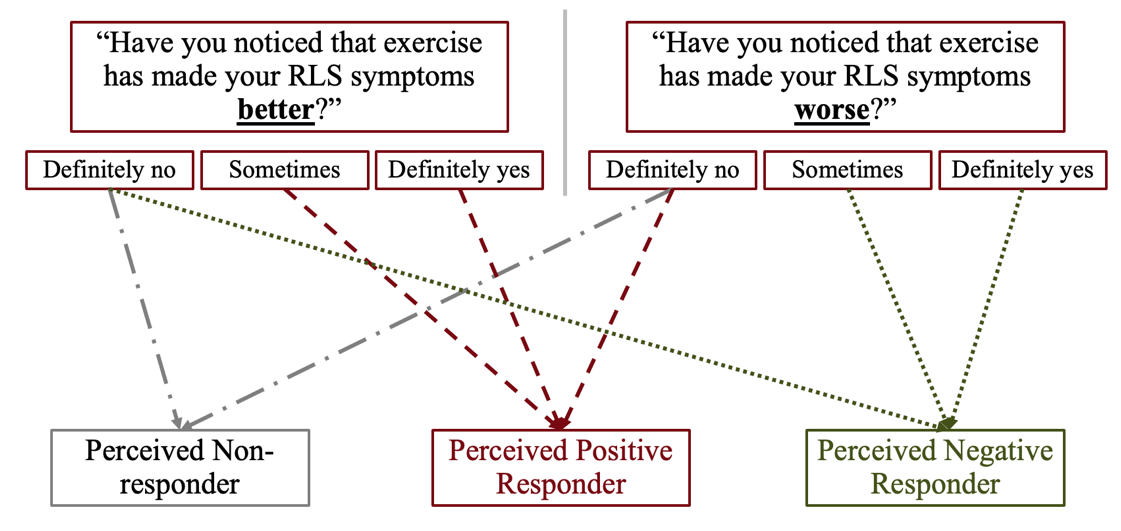
The survey was designed in collaboration with the Northern California Restless Legs Syndrome Support Group. The first author (KLJC) presented the proposed survey items to 20 members of the group in June 2021, whereby members engaged in an active discussion and provided feedback and suggestions regarding survey items thought to be important to address for people with RLS. The final, distributed version of the mixed-methods survey included items assessing RLS diagnosis, RLS severity, current physical activity levels, personal experiences with exercise and RLS (both positive and negative), and demographic and clinical characteristics.

*RLS Diagnosis.* The Cambridge-Hopkins Restless Legs Syndrome Short Form Diagnostic Questionnaire (RLS-SFDQ13) 23 was used to assess a positive screen for RLS. A positive screen for RLS requires that participants present with the following criteria: (1) the desire to move the legs in association with uncomfortable sensations; (2) the need to move the legs in response to these sensations; (3) the worsening of sensations at rest; (4) the partial or complete relief of the urge with movement; and (5) the sensations occurring most frequently during the evening or early part of the night. All participants either had a positive screen for RLS or a previous diagnosis of RLS from a medical professional.

*RLS Severity.* The Self-Administered version of the International Restless Legs Syndrome Study Group Scale (sIRLS) is a validated 10-question survey that provides a global score regarding the severity and frequency of symptoms over the previous week.24 Overall symptom severity scores range between 0 and 40 and are determined by summing item scores, with higher scores indicating a greater severity of symptoms. Severity scores can further be categorized as no symptoms (0), and mild (scores 1-10), moderate (scores 10-20), severe (scores 20-30), and very severe (scores 30-40) symptoms.

*Perceived Responsiveness to Exercise.* Questions related to participant’s personal experiences with exercise were preceded by the following instructions: “The following questions ask about your own, personal experience with exercise and how exercise has affected your symptoms of RLS. Please consider your overall experience with exercise on average (not just the best or worst).” Perceived responsiveness to exercise groups (Figure 1) were defined by responses to “Have you noticed that exercise has made your RLS symptoms better?” (i.e., exercise benefits RLS symptoms) and “Have you noticed that exercise has made your RLS symptoms worse?” (i.e., exercise worsens RLS symptoms). Perceived positive responders included participants that responded “Definitely yes” or “sometimes” to exercise benefits RLS symptoms and “Definitely no” to exercise worsens RLS symptoms. Perceived negative responders included participants that responded “Definitely no” to exercise benefits RLS symptoms and “Definitely yes” or “sometimes” to exercise worsens RLS symptoms. Non-responders included participants that responded “Definitely no” to exercise benefits and “Definitely no" to exercise worsens RLS symptoms.

**Figure 1: Allocation of participants into perceived responsiveness groups.**



*Physical Activity and Sedentary Levels.* The abbreviated International Physical Activity Questionnaire (IPAQ) was designed for population surveillance of physical activity among adults and contains 6 items that measure the frequency and duration of vigorous-intensity activities, moderate-intensity activities, and walking during a seven-day period. The duration component was not included in this study based on previous research that identified problems with accurate recall of physical activity duration in persons with another neurological disorder (e.g., multiple sclerosis).2 The respective frequency values for vigorous, moderate, and walking activities were multiplied by 8, 4, and 3.3 metabolic equivalents, respectively, and then summed to form a continuous measure of physical activity that ranged between 0 and 107 METs/week. The IPAQ further includes an item for estimating daily sitting time in hours and minutes, including time spent sitting at a desk, visiting friends, reading, or sitting/lying down to watch television.

*Demographic and Clinical Characteristics.* Participants completed items for assessing age, sex, race, height, and weight. Several questions were included to examine RLS-specific clinical characteristics, including previous diagnosis of RLS, age at diagnosis, bilateral or unilateral symptomology, duration of RLS symptoms, and time of symptom onset on a typical day/night (e.g., 2 AM). Female participants were also asked if symptoms began during pregnancy and stopped after pregnancy. Participants were further asked questions regarding current RLS-specific treatments, including the responsiveness of symptoms to the treatment as well as treatment type, dosage, timing and regularity of administration. We further examined the presence of conditions highly associated with RLS including periodic limb movements (PLMs) and conditions considered to mimic RLS or be related to secondary forms of RLS (e.g., iron deficiency anemia, renal disease, diabetes, radiculopathy, peripheral edema, and peripheral neuropathy).

*Statistical Analyses*

*Quantitative Analyses.* All quantitative analyses were conducted using Python 3.7.4 in Jupyter Notebook (version 6.0.1) using the statsmodels package (version 0.10.1).25 Descriptive statistics are reported as mean and standard deviation (SD) for continuous variables and number and percentage for dichotomous variables. We examined frequency distributions and conducted Shapiro-Wilks analysis for establishing normality of the variables, whereby a *p*-value of >0.05 was indicative of a normal distribution.

As many variables were not normally distributed, we adopted nonparametric analyses for examining factors that may be driving perceived response heterogeneity to exercise. We examined the difference among the three response groups (i.e., perceived positive responders, perceived negative responders, and non-responders) using Chi-squared tests for dichotomous variables and the Kruskal-Wallis H-test for continuous variables. For factors significantly different among groups, we utilized Dunn’s test for post-hoc analysis with Bonferroni correction using the scikit-posthocs package (version 0.7.0) in Python. We examined demographic factors (i.e., age, sex, race, body mass index [BMI]), clinical factors (i.e., duration of RLS, severity of RLS, bilateral vs. unilateral symptoms, if RLS was pregnancy-related, presence of secondary conditions [e.g., iron deficiency anemia, diabetes, PLMs]), medication factors (i.e., medication use, responsiveness to medication, medication frequency), and exercise-specific factors (i.e., physical activity levels, sedentary time) as potential factors that could influence perceived responsiveness to exercise.22 We then conducted a logistic regression with response group as the dependent variable and factors significantly different among groups (identified with Kruskal-Wallis tests) as independent variables to examine significant determinants of the perceived response to exercise.

**Results**

*Participant Characteristics*

The summary of demographic and clinical characteristics for the final sample of participants completing the survey (N=528) is presented in Table 2. The sample had a mean age of 68.1±10.0 years and were primarily White (97%) females (65%) with an average BMI of 26.5±6.0 kg/m2. Regarding RLS characteristics, participants reported experiencing RLS symptoms for an average of 30.0±18.2 years with an average RLS severity of 20.0±8.2 (i.e., moderate RLS) and a median RLS peak onset time of 19:00 (i.e., 7:00 PM). Most participants reported symptoms bilaterally (95%) and symptoms were mostly unrelated to pregnancy (90%). Most participants (91%) were taking medications on a regular basis (95%) to manage their symptoms with 98% reporting that medications either partially or completely relieve symptoms. Only 27% of participants reported a concomitant, secondary condition (e.g., anemia, peripheral neuropathy) and most participants (63%) reported the presence of PLMs in addition to having RLS. Regarding physical activity and sedentary behavior, participants reported an average of 48.6±26.1 METS/day of physical activity and 6.2±3.4 hours/day of sitting time.

|  |  |  |
| --- | --- | --- |
| Table 2: Summary of demographic and clinical characteristics in the final sample (N=528). | | |
|  | Mean (SD) | Range | |
| Age (years) | 68.1 (10.0) | 18-89 | |
| Sex (n (%) Female) | 341 (65%) |  | |
| Race (n (%) White) | 512 (97%) |  | |
| BMI | 26.5 (6.0) | 16.1-53.2 | |
| RLS Duration | 30.0 (18.2) | 1.0-81.0 | |
| RLS Severity | 20.0 (8.2) | 0.0-39.0 | |
| No Symptoms (IRLS 0) | 13 (2%) |  | |
| Mild (IRLS 1-10) | 56 (11%) |  | |
| Moderate (IRLS 11-20) | 198 (38%) |  | |
| Severe (IRLS 21-30) | 213 (40%) |  | |
| Very Severe (IRLS >30) | 48 (9%) |  | |
| RLS Onset Time (median [IQR]) | 19:00 [15:00-21:00] | 1:00-24:00 | |
| Bilateral vs. Unilateral (n (%) bilateral) | 504 (95%) |  | |
| Pregnancy Related (n (%) yes) | 34 (10%) |  | |
| RLS Medication Use (n (%) yes) | 479 (91%) |  | |
| Responsiveness to RLS Medications (n (%) non-responsive) | 8 (2%) |  | |
| Medication Frequency (n (%) regularly) | 454 (95%) |  | |
| Secondary Conditions (n (%) yes) | 141 (27%) |  | |
| Presence of PLMs | 332 (63%) |  | |
| Physical Activity Level (METs) | 48.6 (26.1) | 0.0-107.1 | |
| Sedentary time (hours/day) | 6.2 (3.4) | 0.5-21.0 | |
| *Notes:* Data are presented as mean (standard deviation) unless otherwise specified. *SD* standard deviation; *BMI* body mass index; *RLS* restless legs syndrome; *IRLS* International Restless Legs Syndrome Study Group Scale; *IQR* interquartile range; *PLMs* periodic limb movements; *METs* metabolic equivalents. | | |

*Factors Influencing Perceived Response Heterogeneity to Exercise.*

The summary of factors that could influence perceived response heterogeneity among groups is presented in Table 3. Most participants (n=172, 54%) were classified as perceived positive responders (i.e., responded as exercise sometimes or definitely makes symptoms better and exercise definitely does not make symptoms worse), followed by perceived non-responders (n=76, 24%; responded as exercise definitely does not make symptoms better or worse), and perceived negative responders (n=72; 23%; responded as exercise definitely does not make symptoms better and exercise sometimes or definitely makes symptoms worse). There were significant differences among groups for BMI (H=7.059; *p*=0.029), RLS severity (H=6.837; *p*=0.033), and presence of PLMs (*p*=0.034), whereby posthoc analyses indicated that the perceived negative responders had significantly higher BMI, higher RLS severity, and a higher proportion of individuals with PLMs compared with the perceived positive responders. There were no other statistically significant differences among groups.

Logistic regression analysis (F=6.192; R2=0.061) of the significant factors identified in univariate analyses indicated that BMI (β= –0.0168; *p*=0.038) and the presence of PLMs (β= –0.2819; *p*=0.009) were independently associated with response category, whereby perceived negative responders had higher BMI and a higher probability of also having PLMs and positive responders had a lower probability of having PLMs as a secondary condition.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Table 3: Summary of differences in demographic and clinical characteristics among perceived response to exercise groups. | | | | |
|  | Perceived Positive Responders (n=172) | Perceived Non-Responders  (n= 76) | Perceived Negative Responders  (n= 72) | *p* | |
| Age (years) | 69.0 (10.4) | 68.9 (8.6) | 67.8 (10.2) | 0.727# | |
| Sex (n (%) Female) | 104 (60%) | 41 (54%) | 47 (65%) | 0.366+ | |
| Race (n (%) White) | 169 (98%) | 75 (99%) | 70 (97%) | 0.298+ | |
| BMI | 26.4 (5.6) | 26.4 (6.1) | 28.7 (6.6) | **0.034#\*** | |
| RLS Duration | 30.0 (19.4) | 29.6 (15.5) | 32.3 (18.1) | 0.600# | |
| RLS Severity | 19.6 (8.3) | 20.8 (8.6) | 22.7 (8.1) | **0.033#\*** | |
| RLS Onset Time (median [IQR]) | 19:00  [15:00-21:00] | 20:00  [16:00-21:00] | 19:00  [16:00-21:00] |  | |
| Bilateral vs. Unilateral (n (%) bilateral) | 163 (95%) | 72 (95%) | 70 (97%) | 0.534+ | |
| Pregnancy Related (n (%) yes) | 8 (8%) | 3 (7%) | 6 (13%) | 0.141+ | |
| RLS Medication Use (n (%) yes) | 150 (87%) | 73 (96%) | 63 (88%) | 0.096+ | |
| Responsiveness to RLS Medications (n (%) non-responsive) | 4 (2%) | 1 (1%) | 0 (0%) | 0.084+ | |
| Medication Frequency (n (%) regularly) | 142 (95%) | 69 (95%) | 61 (67%) | 0.773+ | |
| Secondary Conditions (n (%) yes) | 53 (31%) | 14 (18%) | 17 (24%) | 0.136+ | |
| Presence of PLMs | 104 (60%) | 54 (71%) | 54 (75%) | **0.034+\*** | |
| Physical Activity Level (METs) | 50.4 (26.8) | 44.2 (27.1) | 43.3 (24.4) | 0.093# | |
| Sedentary time (hours/day) | 9.5 (18.0) | 6.3 (4.9) | 8.7 (10.4) | 0.182# | |
| *Notes:* Data are presented as mean (standard deviation) unless otherwise specified. # Kruskal-Wallis H-test; + Chi-squared test; \* significant difference between perceived negative responders and perceived positive responders identified by Dunn’s post-hoc tests. *BMI* body mass index; *RLS* restless legs syndrome; *IQR* interquartile range; *PLMs* periodic limb movements; *METs* metabolic equivalents. | | | | |

**Discussion**

The present study identified inter-individual factors that may influence perceived responsiveness to exercise. Our results demonstrated that higher BMI and the presence of PLMs were independently associated with perceived response categories, whereby perceived negative responders (i.e., those who perceived exercise only worsens symptoms) had higher BMI and a higher probability of also having PLMs than positive responders (i.e., those who perceived exercise only improves symptoms). These two factors have been previously associated with higher RLS severity (REFs), suggesting that those with higher RLS severity may be more prone to exacerbations with exercise. This is consistent with our inferential results indicating a significant difference between groups, whereby negative responders had higher RLS severity than positive responders. These specific factors might account for individual differences in the response to exercise as a mode of treatment and should be considered in exercise-based management to optimize personalized treatment plans for patients with RLS. For example, health professionals should inquire about present RLS severity, previous experiences with exercise, and take into account BMI and the presence of PLMs when prescribing specific exercise parameters (e.g., initial exercise intensity).

*Limitations*

The present study has important limitations that should be considered when interpreting our results. The cross-sectional design of this study precludes any inferences on causality in the effect of exercise on symptoms of RLS. Although we recruited from an RLS-specific organization and we utilized the validated RLS-SFDQ1323 in assessing the presence of RLS, we did include an official physician diagnosis of RLS. As all data were self-report in nature, our results are subject to recall bias. The use of open-ended questions for participants to share their experiences rather than a formal qualitative approach precludes the ability for discussion to elaborate on specific responses. Further, this method may have led to more contradictory responses than another method (e.g., some participants reported that exercise worsens RLS, but only described exercise as improving symptoms). The survey was conducted through Qualtrics using the “Anonymize responses” mode, whereby we did not record respondents’ IP address, location data, or contact information; therefore, we were unable to contact participants for missing data or unclear responses. Lastly, our cohort was primarily White, limiting the generalizability to people of different racial and ethnic backgrounds who are likely to experience RLS differently (REFs).

**Conclusions**

**References**

1. Ohayon MM, O'Hara R, Vitiello MV. Epidemiology of restless legs syndrome: a synthesis of the literature. Sleep Med Rev.2012; 16 (4): 283-295. doi:DOI: 10.1016/j.smrv.2011.05.002

2. Budhiraja P, Budhiraja R, Goodwin JL, et al. Incidence of restless legs syndrome and its correlates. J Clin Sleep Med.2012; 8 (2): 119-124. doi:10.5664/jcsm.1756

3. Gottlieb DJ, Somers VK, Punjabi NM, Winkelman JW. Restless legs syndrome and cardiovascular disease: a research roadmap. Sleep Med.2017; 31: 10-17. doi:10.1016/j.sleep.2016.08.008

4. Janes F, Lorenzut S, Bevilacqua F, et al. Cerebrovascular Risk in Restless Legs Syndrome: Intima-Media Thickness and Cerebral Vasomotor Reactivity: A Case-Control Study. Nat Sci Sleep.2021; 13: 967-975. doi:10.2147/nss.S302749

5. Becker PM, Sharon D. Mood disorders in restless legs syndrome (Willis-Ekbom disease). J Clin Psychiatry.2014; 75 (7): e679-694. doi:10.4088/JCP.13r08692

6. Allen RP, Bharmal M, Calloway M. Prevalence and disease burden of primary restless legs syndrome: results of a general population survey in the United States. Mov Disord.2011; 26 (1): 114-120. doi:10.1002/mds.23430

7. Allen RP, Walters AS, Montplaisir J, et al. Restless legs syndrome prevalence and impact: REST general population study. Arch Intern Med.2005; 165 (11): 1286-1292. doi:10.1001/archinte.165.11.1286

8. Dodel R, Happe S, Peglau I, et al. Health economic burden of patients with restless legs syndrome in a German ambulatory setting. Pharmacoeconomics.2010; 28 (5): 381-393. doi:10.2165/11531030-000000000-00000

9. Schormair B, Zhao C, Bell S, et al. Identification of novel risk loci for restless legs syndrome in genome-wide association studies in individuals of European ancestry: a meta-analysis. Lancet Neurol.2017; 16 (11): 898-907. doi:10.1016/s1474-4422(17)30327-7

10. Didriksen M, Nawaz MS, Dowsett J, et al. Large genome-wide association study identifies three novel risk variants for restless legs syndrome. Commun Biol.2020; 3 (1): 703. doi:10.1038/s42003-020-01430-1

11. Allen RP, Picchietti DL, Garcia-Borreguero D, et al. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria--history, rationale, description, and significance. Sleep Med.2014; 15 (8): 860-873. doi:10.1016/j.sleep.2014.03.025

12. Aukerman MM, Aukerman D, Bayard M, Tudiver F, Thorp L, Bailey B. Exercise and restless legs syndrome: a randomized controlled trial. J Am Board Fam Med.2006; 19 (5): 487-493. doi:10.3122/jabfm.19.5.487

13. Esteves A, de Mello M, Benedito-Silva A, Tufik S. Impact of aerobic physical exercise on Restless Legs Syndrome. Sleep Sci.2011; 4 (2): 45-48.

14. Giannaki CD, Hadjigeorgiou GM, Karatzaferi C, et al. A single-blind randomized controlled trial to evaluate the effect of 6 months of progressive aerobic exercise training in patients with uraemic restless legs syndrome. Nephrol Dial Transplant.2013; 28 (11): 2834-2840. doi:10.1093/ndt/gft288

15. Giannaki CD, Sakkas GK, Karatzaferi C, et al. Effect of exercise training and dopamine agonists in patients with uremic restless legs syndrome: a six-month randomized, partially double-blind, placebo-controlled comparative study. BMC Nephrology.2013; 14: 194. doi:10.1186/1471-2369-14-194

16. Mortazavi M, Vahdatpour B, Ghasempour A, et al. Aerobic exercise improves signs of restless leg syndrome in end stage renal disease patients suffering chronic hemodialysis. Scientific World J.2013: 628142. doi:10.1155/2013/628142

17. Sakkas GK, Hadjigeorgiou GM, Karatzaferi C, et al. Intradialytic aerobic exercise training ameliorates symptoms of restless legs syndrome and improves functional capacity in patients on hemodialysis: a pilot study. ASAIO.2008; 54 (2): 185-190. doi:10.1097/MAT.0b013e3181641b07

18. de Mello MT, Lauro FA, Silva AC, Tufik S. Incidence of periodic leg movements and of the restless legs syndrome during sleep following acute physical activity in spinal cord injury subjects. Spinal Cord.1996; 34 (5): 294-296. doi:DOI: 10.1038/sc.1996.53

19. Cederberg KL, Motl RW. Restless legs syndrome in multiple sclerosis: a call for better understanding and non-pharmacological management. Curr Trends Neurol.2016; 10: 65-73.

20. Giannaki CD, Sakkas GK, Karatzaferi C, et al. Combination of exercise training and dopamine agonists in patients with RLS on dialysis: A randomized, double-blind placebo-controlled study. ASAIO.2015; 61 (6): 738-741. doi:DOI: 10.1097/mat.0000000000000271

21. Goodman MS, Sanders Thompson VL. The science of stakeholder engagement in research: classification, implementation, and evaluation. Transl Behav Med.2017; 7 (3): 486-491. doi:10.1007/s13142-017-0495-z

22. Herold F, Törpel A, Hamacher D, et al. Causes and Consequences of Interindividual Response Variability: A Call to Apply a More Rigorous Research Design in Acute Exercise-Cognition Studies. Front Physiol.2021; 12: 682891. doi:10.3389/fphys.2021.682891

23. Allen RP, Burchell BJ, MacDonald B, Hening WA, Earley CJ. Validation of the self-completed Cambridge-Hopkins questionnaire (CH-RLSq) for ascertainment of restless legs syndrome (RLS) in a population survey. Sleep Med.2009; 10 (10): 1097-1100. doi:DOI: 10.1016/j.sleep.2008.10.007

24. Sharon D, Allen RP, Martinez-Martin P, et al. Validation of the self-administered version of the international Restless Legs Syndrome study group severity rating scale - The sIRLS. Sleep Med.2019; 54: 94-100. doi:10.1016/j.sleep.2018.10.014

25. Seabold S, Perktold J. Statsmodels: Econometric and statistical modeling with python. In: proceedings from the Proceedings of the 9th Python in Science Conference; 2010.

26. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res.2005; 15 (9): 1277-1288. doi:10.1177/1049732305276687

1. Cederberg KLJ, Sikes EM, Mignot E. Perceptions of exercise and restless legs syndrome: Results from a nationwide survey. *J Sleep Res*. 2023:e13980. doi: 10.1111/jsr.13980

2. Gosney JL, Scott JA, Snook EM, Motl RW. Physical activity and multiple sclerosis: validity of self-report and objective measures. *Fam Community Health*. 2007;30(2):144-50. doi: