**Appendix E. Table 7. Evidence Table for the nonpharmacologic studies**

| **Study Characteristics****and Design** | **Inclusion/Exclusion criteria** | **Participant Characteristics** | **Intervention (daily dose) /Comparator (daily dose)** | **Study Quality and Applicability** |
| --- | --- | --- | --- | --- |
| **Study ID**Mitchell, 2011**Near-infrared light****Geographical Location**: US**Funding source**: Academic**Study Design**:Prospective, randomized, single-blind, sham-controlled trial**Duration:** 4 weeks | **Inclusion criteria:*** Met the 4 minimal criteria established by the IRLS for the diagnosis of RLS
* IRLS score 11-20 points
* good skin integrity and no obvious signs of impaired circulation

**Exclusion criteria:*** decreased sensation
 | **N**=34**Age (mean yr)**: 55**Gender (Male %):** 41**Race/Ethnicity (%):** NR**Comorbidities:** NR**Baseline Severity:** IRLSS 24.1**Previous RLS medication history:**  50% (n=17) were also taking RLS medication (dopamine agonist 82% (n=14), gabapentin 12% (n=2), hydrocodone 6% (n=1))**Iron Status:** 18 patientshad low ferritin levels. Means were 19.2 μg/L (range 3.4 to 42.6) for near-infrared group (n=9) and 20.12 μg/L (range 5.8 to 38.7) for sham group (n=9) | **Intervention:** monochromatic near- infrared light (n=17). Anodyne® Therapy System 480 which delivers pulsed light at 290 Hz with a wavelength of 890 nm. Active unit provides 62.4 Joules/cm2 of energy density. 12 30-minute treatments over 4 weeks.**Comparator:** Sham therapy (n=17)**A.** **Change in Disease Status and Impact**IRLS Scale Score**B. Quality of life**None**Subjective Sleep Quality**None**Definition of clinically significant Improvement:** none provided | **Assessment of Internal Validity**Sequence generation: Allocation concealment: unclearBlinding: patientsIncomplete outcome data: noSelective outcome reporting: no**Applicability**Some patients may have had secondary RLS as over one half of the subjects (53%, n=18) had low ferritin levels (see iron status).  |
| **Study ID**Cuellar, 200932**Botanical preparation****Geographical Location**: US**Funding source**: NR**Study Design**:parallel design**Duration**: 8 weeks | **Inclusion criteria**: * Met diagnostic criteria based on the IRLS criteria including akathisia brought on by rest, relieved with moving or walking, and worsening at night or in the evening
* at least 21 years old; not satisfied with current treatment outcomes
* willing to use valerian as treatment with possibility of being in control group; have symptoms of RLS 3 nights a week or more; commitment to treatment fidelity.

**Exclusion criteria:** * Positive toxicology report, liver function profile abnormal, and 3 *yes* answers on CAGE 2
* participation in a clinical study with an investigation drug within 3 months
* current use of vitamins or minerals beyond the recommended RDA requirements
* current use of any herbs or natural products; current use of benzodiazepines or barbiturates
* sleep disorder other than RLS
* use of valerian within 120 days of baseline visit
* history of liver disease including cirrhosis, alcoholism, and hepatitis
* pregnant, nursing, or intending to become pregnant in 3 months.
 | **N**=48**Age (mean yr)**: 49.5**Gender (Male %)**: 25**Race/Ethnicity (%)**: white 68**Comorbidities**: NR**Baseline Severity**: IRLSS 23.5**Previous RLS medication history**: yes**Iron Status**: NR | **Intervention:** Valerian 800 mg (n=24)**Comparator:** Placebo (identical in taste, color, etc.) (n=24)**A.** **Change in Disease Status and Impact**IRLS Scale Score**B. Quality of life**None**Subjective Sleep Quality**Pittsburgh Sleep Quality Index (PSQI)Epworth Sleepiness Scale (ESS)**Definition of clinically significant Improvement:** none provided**Adverse Effects Reported:** Yes | **Assessment of Internal Validity**Sequence generation: adequateAllocation concealment: adequate, pharmacy controlledBlinding: patients, personnel, data enterer, outcome assessmentIncomplete outcome data: yes, needed to take at least one dose of study medicationSelective outcome reporting: No**Applicability**Yes |
| **Study ID**Lettieri, 200933**Compression device****Geographical Location**: US**Funding source**: NR**Study Design**:Prospective, randomized, double-blind, sham-controlled trial**Duration**: 28 days | **Inclusion criteria**: * Subjects >17 years of age with a reliable diagnosis of RLS in accordance with the *International Classification of* *Sleep Disorders, Revised Diagnostic and Coding Manual* of the American Academy of Sleep Medicine

**Exclusion criteria**: * Individuals <17 years old
* Mental/physical limitations that would preclude data collection on questionnaires
* medical conditions that would preclude the use of PCDs, such as known or suspected deep vein thrombosis, active skin infections, recent vein ligation or skin graft, or extreme deformity of the legs. We also excluded individuals if they had previously used PCDs for deep vein thrombosis prophylaxis, as this would have potentially unblinded subjects randomized to sham devices.
 | N=35Age (mean yr): 51.0Gender (Male %): 60Race/Ethnicity (%): NRComorbidities: NR**Criteria used to define RLS**see inclusion criteriaBaseline Severity: IRLS 19.8Previous RLS medication history: Subjects taking iron or prescription medications for RLS were offered enrollment only if they had been on a stable dose of medications for more than two months and reported persistent symptoms.Iron Status: Current iron therapy 17.1% | **Intervention:** Compression device (n=21)**Comparator:** Control (n=14)**A.** **Change in Disease Status and Impact**IRLS Scale Score**B. Quality of life**Yes**Subjective Sleep Quality**Yes**Definition of clinically significant Improvement:** No**Adverse Effects Reported:** Yes | **Assessment of Internal Validity**Sequence generation: adequateAllocation concealment: adequateBlinding: patients, physicians, investigatorsIncomplete outcome data: adequateSelective outcome reporting: no |
| **Study ID**Aukerman, 200634**Exercise****Geographical Location**: US**Funding source**: non-industry**Study Design**:parallel design**Duration**: 12 weeks | **Inclusion criteria**: * Meeting diagnostic criteria for RLS

**Exclusion criteria**: * Secondary causes of RLS
* orthopedic condition that limited ambulation on a treadmill or ability to perform prescribed resistance exercises
* recent coronary event in the preceding six months
* uncontrolled hypertension, renal dysfunction (serum creatinine >1.5 mg/dL) or anemia (hemoglobin <13 g/dL in males and <11 g/dL in females).
 | N=41, demographic data for 28 subjects who completed trial (9 exercise and 4 controls dropped out)Age (mean yr): 53.7Gender (Male %): 39Race/Ethnicity (%): white 96Comorbidities: NR**Criteria used to define RLS**Primary or secondary RLS: primaryBaseline Severity: NRPrevious RLS medication history: NRIron Status: NR | **Intervention:** Exercise (lower body resistance exercises performed 3 times/week for 12 weeks and treadmill walking for aerobic exercise) (n=11)**Comparator:** Control (n=17)Both groups were instructed in lifestyle interventions that are thought to improve RLS, including cigarette and alcohol cessation, avoidance of excessive caffeine, and proper sleep hygiene.**A.** **Change in Disease Status and Impact**IRLS Scale Score**B. Quality of life**None**Subjective Sleep Quality**No**Definition of clinically significant Improvement:** none provided**Adverse Effects Reported:** yes | **Assessment of Internal Validity**Sequence generation: adequateAllocation concealment: unclearBlinding: study personnel blinded to allocation called participants at 3 and 9 weeks to complete the questionnaire over the phoneIncomplete outcome data: yesSelective outcome reporting: no |

IRLS = International RLS Study Group Rating Scale; NR = not reported