



Effective Health Care

Effectiveness of Treatments for Restless Leg Syndrome Nomination Summary Document

Results of Topic Selection Process & Next Steps

- *Effectiveness of Treatments for Restless Leg Syndrome* was found to be addressed by a 2012 AHRQ report entitled, *Treatment for Restless Legs Syndrome*. Given that the existing report covers this nomination, no further activity will be undertaken on this topic.
 - Wilt TJ, MacDonald R, Ouellette J, Tacklind J, Khawaja I, Rutks I, Butler M, Fink HA. *Treatment for Restless Legs Syndrome*. Comparative Effectiveness Review No. 86. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 290-2007-10064-I.) AHRQ Publication No. 12(13)-EHC147-EF. Rockville, MD: Agency for Healthcare Research and Quality. November 2012. http://effectivehealthcare.ahrq.gov/ehc/products/334/1327/CER86_RestlessLegsSyndrome_FinalReport_20121119.pdf

Topic Description

Nominator(s): Individual

Nomination Summary: The nomination was submitted by a patient with restless leg syndrome (RLS). The nominator is interested in the effectiveness of low-dose methadone for relieving symptoms of RLS, particularly in patients with severe, refractory RLS.

Staff-Generated PICO

Population(s): Individuals diagnosed with RLS

Intervention(s): Pharmacologic and non-pharmacologic therapies for treating RLS

Comparator(s): Available treatments including non-pharmacologic, pharmacologic and alternative treatments

Outcome(s): Improvement in symptoms of RLS; improved social and occupational functioning; improved health-related quality of life

Key Questions from Nominator: What is the comparative effectiveness of treatments for restless legs syndrome (RLS)?

Considerations

- The topic meets EHC Program appropriateness and importance criteria. (For more information, see <http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/>.)

- Restless legs syndrome (RLS) is a neurological disorder characterized by unpleasant sensations in the legs and an uncontrollable urge to move them. Symptoms occur primarily at night when a person is relaxing or at rest or can increase in severity during the night. As much as 10% of the US population may have RLS. Most people with RLS have difficulty falling asleep and staying asleep. Left untreated, the condition causes exhaustion and daytime fatigue. Many people with RLS report that their job, personal relations and activities of daily living are strongly affected as a result of their sleep deprivation. They are often unable to concentrate, have impaired memory or fail to accomplish daily tasks.
- RLS can be treated using dopaminergic agents (e.g. ropinirole, pramipexole, and rotigotine) that are FDA approved to treat moderate to severe RLS. It is also often treated off-label with benzodiazepines (e.g. clonazepam, diazepam), opioids (e.g. codeine, propoxyphene, oxycodone or methadone) and anticonvulsant calcium channel (alpha-2-delta) ligands (e.g. gabapentin).
- The nominator was specifically interested in the use of methadone for the treatment of RLS. Although methadone has been prescribed for the treatment of RLS, methadone and other opioids are not currently approved by the Food and Drug Administration for treating RLS.
- The topic was found to be addressed by a 2012 AHRQ report entitled, *Treatment for Restless Legs Syndrome*. Key questions from this report include:

Key Question 1. What is the comparative effectiveness of treatments for restless legs syndrome (RLS)?

- a. What are the benefits from RLS treatments when compared with placebo or no treatment?
- b. What are the benefits from RLS treatments when compared with other active treatments?
- c. What is the durability and sustainability of treatment benefits?

Key Question 2. What are the harms from RLS treatments?

- a. What are the harms from RLS treatments when compared with placebo or no treatment?
- b. What are the harms from RLS treatments when compared with other active treatments?
- c. What are the long-term harms from treatment?

Key Question 3. What is the effect of patient characteristics (age, sex, race, comorbidities, disease severity, etiology, iron status, pregnancy, end-stage renal disease) on the benefits and harms of treatments for RLS?

- The AHRQ report does address off-label opioid treatment for RLS, noting that it found no eligible studies evaluating these agents. The report states that for individuals unable to initiate or tolerate dopaminergic agents, or for whom these drugs have failed, potential pharmacologic treatments include off-label opioids (morphine, oxycodone, and methadone), sedative hypnotics, and tramadol.
- Since the AHRQ report, there are a number of recently published trials. . However, these studies do not examine novel treatments for RLS and the new trials are not likely to change the existing treatment recommendations.