

## QUESTION

Should complementary/alternative treatments vs. none or medication or lifestyle or physiotherapy be used for patients with RLS symptoms with Friedreich ataxia?

POPULATION:	patients with RLS symptoms with Friedreich ataxia
INTERVENTION:	complementary/alternative treatments
COMPARISON:	none or medication or lifestyle or physiotherapy
MAIN OUTCOMES:	Impact on sleep quality/ arousal; Impact on sleep quantity/ sleep benefit; Impact on behaviour, cognition, mood; Degree of pain vs discomfort;

## ASSESSMENT

### Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> No</li> <li><input type="radio"/> Probably no</li> <li><input checked="" type="radio"/> Probably yes</li> <li><input type="radio"/> Yes</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>Data from the FA Clinical Outcome Measures (FA-COMS) registry (Lynch, 2017) found:</p> <p>44.8% (312/696) of adults and 34.9% (110/315) of children reported restless legs; 75.0% (522/696) of adults and 55.6% (175/315) of children reported leg spasms. By comparison, restless legs affect between 4% and 14% of the general population (Ohayon et al, 2012).</p> <p>For individuals who reported sleep disturbance:</p> <p>Restless legs were present in 46.3% (229/495) of adults and 32.9% (53/161) of children, and leg cramps in 58.6% (290/495) adults and 44.7% (72/161) of children (Lynch, 2017).</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of restless legs.</p> <p>2/7 indicated that the problem was serious, 4/7 indicated probably serious, 1/7 indicated probably not serious.</p> <p>2/7 indicated that the problem was urgent, 4/7 indicated probably urgent, 1/7 indicated probably not urgent.</p> <p>3/7 indicated that the problem was a priority, 3/7 indicated probably a priority, 1/7 indicated probably not a priority. (Aug 2020)</p>

### Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Trivial</li> <li><input type="radio"/> Small</li> <li><input type="radio"/> Moderate</li> <li><input type="radio"/> Large</li> <li><input type="radio"/> Varies</li> <li><input checked="" type="radio"/> Don't know</li> </ul>	<p>A search of four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 30 October. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	

## Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>○ Large</li> <li>○ Moderate</li> <li>○ Small</li> <li>○ Trivial</li> <li>○ Varies</li> <li>● Don't know</li> </ul>	<p>A search of four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 30 October. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	

## Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li>● Very low</li> <li>○ Low</li> <li>○ Moderate</li> <li>○ High</li> <li>○ No included studies</li> </ul>	<p>A 2016 review of alternative treatments for restless legs syndrome (not specific to any condition and not including any studies specifically related to FRDA) showed some evidence of effect for physical activity and some promising effects of other complementary/alternative therapies to treat RLS, but not enough to make any recommendations (Bega et al, 2016).</p> <p><b>Reference</b></p> <p>Bega D, Malkani R. Alternative treatment of restless legs syndrome: an overview of the evidence for mind-body interventions, lifestyle interventions, and nutraceuticals. Sleep Med 2016;17:99-105.</p>	

## Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS						
<ul style="list-style-type: none"> <li>● Important uncertainty or variability</li> <li>○ Possibly important uncertainty or variability</li> <li>○ Probably no important uncertainty or variability</li> <li>○ No important uncertainty or variability</li> </ul>	<table border="1" style="width: 100%; text-align: center;"> <thead> <tr> <th style="width: 50%;">Outcomes</th> <th style="width: 15%;">Importance</th> <th style="width: 35%;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td style="height: 40px;"> </td> <td> </td> <td> </td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)				
Outcomes	Importance	Certainty of the evidence (GRADE)						

	Impact on sleep quality/ arousal - not measured	IMPORTANT <sup>a</sup>	-
	Impact on sleep quantity/ sleep benefit - not measured	IMPORTANT <sup>a</sup>	-
	Impact on behaviour, cognition, mood - not measured	IMPORTANT <sup>a</sup>	-
	Degree of pain vs discomfort - not measured	CRITICAL <sup>b</sup>	-
	<p>a. Identified as critical (1/6), important (4/6) and low importance (1/6) by people with FA and important by expert authors on this topic.</p> <p>b. Identified as critical (3/6), important (2/6) and low importance (1/6) by people with FA and important by expert authors on this topic.</p>		

## Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Favors the comparison</li> <li><input type="radio"/> Probably favors the comparison</li> <li><input type="radio"/> Does not favor either the intervention or the comparison</li> <li><input type="radio"/> Probably favors the intervention</li> <li><input type="radio"/> Favors the intervention</li> <li><input type="radio"/> Varies</li> <li><input checked="" type="radio"/> Don't know</li> </ul>		

## Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> No</li> <li><input type="radio"/> Probably no</li> <li><input checked="" type="radio"/> Probably yes</li> <li><input type="radio"/> Yes</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	No published evidence.	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were asked if complementary/ alternative treatments in people with restless legs syndrome was acceptable (weighing up the balance between benefits, harms and costs).</p> <p>1/3 indicated the intervention was acceptable, 2/3 indicated</p>

		probably acceptable. (Aug 2020).
--	--	----------------------------------

## SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	<b>Don't know</b>
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	<b>Don't know</b>
CERTAINTY OF EVIDENCE	<b>Very low</b>	Low	Moderate	High			No included studies
VALUES	<b>Important uncertainty or variability</b>	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	<b>Don't know</b>
ACCEPTABILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know

## TYPE OF RECOMMENDATION

Strong recommendation against the intervention ○	<b>Conditional recommendation against the intervention</b> ●	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○
---	---	---	--	---

## CONCLUSIONS

### Recommendation

We suggest alternative/complementary treatments should not be used over no treatment/medication/lifestyle/physiotherapy for RLS in Friedreich ataxia.

### Justification

Based on no published evidence on complementary/alternative treatments in FRDA, we suggest that regular physical activity, sleep hygiene, regular hours for going to bed, avoiding caffeine before bed and the use of electronic devices in bed may assist in managing RLS. A review of current medication is also suggested, which should focus in particular on selective serotonin reuptake inhibitors (SSRI), tricyclics and metoclopramide.

RLS is a significant problem affecting 44.8% of adults with FRDA. Complementary/alternative treatments may have undesirable side-effects for a person with FRDA. There is no RCT on the use of complementary/alternative treatments on RLS in FRDA. However, if there are no undesirable side-effects, some people with RLS may find alternative treatments as helpful as medication and without the known side-effects of medication.

It should be borne in mind when recommending any complementary/alternative treatments that they may be expensive and private insurers may not cover the cost for a person with FRDA.

## Subgroup considerations

This recommendation is for individuals with Friedreich ataxia with symptoms of RLS. Restless legs are more common in those who have sleep disturbances.

## Implementation considerations

Not relevant

## Research priorities

There is narrative review published in this area and there would be significant difficulties to be overcome to do an RCT of complementary/alternative treatments in those who have RLS.

### References

Lynch D. FA Clinical Outcome Measures (FA-COMS) Registry (unpublished data): clinicaltrials.gov; 2017 [Available from: <https://clinicaltrials.gov/ct2/show/NCT03090789>].

Ohayon MM, O'Hara R, Vitiello MV. Epidemiology of restless legs syndrome: a synthesis of the literature. *Sleep Med Rev.* 2012;16(4):283-95.