

## QUESTION

### Should anti-anxiety medication vs. none be used for anxiety patients with Friedreich ataxia?

POPULATION:	anxiety patients with Friedreich ataxia
INTERVENTION:	anti-anxiety medication
COMPARISON:	none
MAIN OUTCOMES:	Less anxiety; Side effect frequency; QOL;

## 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>In cohort of 650 individuals with FA 20/560 (3.1%) reported anxiety. Within the subset of those in the typical age of onset group (n=540), 3.3% reported anxiety (Reetz et al, 2018). Notably, 60% of individuals with anxiety had co-morbidities related to visual disturbance.</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of anxiety.</p> <p>4/6 indicated that the problem was serious, 2/6 indicated probably serious.</p> <p>4/6 indicated that the problem was urgent, 1/6 indicated probably urgent, 1/6 indicated probably not urgent.</p> <p>4/6 indicated that the problem was a priority, 2/6 indicated probably 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 checked="" type="radio"/> Large</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>A search of five databases (CENTRAL, MEDLINE, EMBASE, CINAHL, PsycINFO) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 29 July 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	<p>If treatment is efficacious then desirable effect on individuals who are anxious would be large. Clinical experience is there is no difference in response to medication for individuals with FRDA, when they accept the use of medication, compared to those without FRDA. It is important to make sure individuals with FRDA are screened and clinicians are alert to the possibility of anxiety.</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 five databases (CENTRAL, MEDLINE, EMBASE, CINAHL, PsycINFO) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 29 July 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	<p>Side effects of antianxiety medication may be undesirable such as dizziness, reduced balance and mobility</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>No published evidence.</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"> <thead> <tr> <th>Outcomes</th> <th>Importance</th> <th>Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Less anxiety - not measured</td> <td>CRITICAL<sup>a</sup></td> <td>-</td> </tr> <tr> <td>Side effect frequency - not measured</td> <td>IMPORTANT<sup>b</sup></td> <td>-</td> </tr> <tr> <td>QOL - not measured</td> <td>CRITICAL<sup>a</sup></td> <td>-</td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	Less anxiety - not measured	CRITICAL <sup>a</sup>	-	Side effect frequency - not measured	IMPORTANT <sup>b</sup>	-	QOL - not measured	CRITICAL <sup>a</sup>	-	
Outcomes	Importance	Certainty of the evidence (GRADE)												
Less anxiety - not measured	CRITICAL <sup>a</sup>	-												
Side effect frequency - not measured	IMPORTANT <sup>b</sup>	-												
QOL - not measured	CRITICAL <sup>a</sup>	-												



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

## TYPE OF RECOMMENDATION

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

### Recommendation

We conditionally recommend the use of anti-anxiety medication in individuals with Friedreich ataxia who present with symptoms of anxiety.

### Justification

Cohort studies indicate the presence of anxiety symptoms in individuals with FRDA. Whilst there is no published evidence in FRDA. If treatment is efficacious then the desirable effect on individuals who are anxious would be large. Clinical experience of the authors indicates there is no difference in response to medication in individuals with FRDA, when they accept the use of medication, compared to those without FRDA. It is important to make sure individuals with FRDA are screened and clinicians are alert to the possibility of anxiety.

## Subgroup considerations

This recommendation is for individuals with Friedreich ataxia and symptoms of anxiety and should be implemented according to an assessment of the severity of anxiety. Balance of side-effects versus efficacy needs to be taken into account when considering treatment options.

## Research priorities

Further research to confirm the prevalence of anxiety and determine the efficacy of treatment options for anxiety symptoms is required.

### Reference

Reetz K, Dogan I, Hohenfeld C, Didszun C, Giunti P, Mariotti C, et al. Nonataxia symptoms in Friedreich Ataxia: Report from the Registry of the European Friedreich's Ataxia Consortium for Translational Studies (EFACTS). *Neurology*. 2018;91(10):e917-e30.