

## QUESTION

Should antiplatelets/anticoagulation vs. no anticoagulation be used for patients with permanent or paroxysmal atrial fibrillation with Friedreich ataxia?

POPULATION:	patients with permanent or paroxysmal atrial fibrillation with Friedreich ataxia
INTERVENTION:	antiplatelets/anticoagulation
COMPARISON:	no anticoagulation
MAIN OUTCOMES:	Morbidity - reducing the chance of having a stroke; Morbidity - reducing the chance of bleeding in the brain;
BACKGROUND:	
CONFLICT OF INTERESTS:	

## ASSESSMENT

### Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	<p>Atrial fibrillation is common in individuals with FRDA (Harding et al, 1983; Ribaï et al, 2007).</p> <p>Post mortem stroke data are required.</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of the topic. 6 out of 7 indicated the consequences of cardiac arrhythmias was serious; 1 out of 7 was probably serious. 6 out of 7 indicated cardiac arrhythmias was urgent; 1 out of 7 was probably urgent. 6 out of 7 indicated cardiac arrhythmias was a priority; 1 out of 7 was probably a priority. (July 2020)</p>

### Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input checked="" type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know	<p>A search of three databases (CENTRAL, MEDLINE, EMBASE) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 16 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>The increased risk of stroke and peripheral embolism in young people warrants consideration of anticoagulants to reduce the risk of stroke.</p>

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## 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 three databases (CENTRAL, MEDLINE, EMBASE) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 16 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>Although no evidence, there are known risks.</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>		

Outcomes	Importance	Certainty of the evidence (GRADE)
Morbidity - reducing the chance of having a stroke - not measured	CRITICAL <sup>a</sup>	-
Morbidity - reducing the chance of bleeding in the brain - not measured	CRITICAL <sup>b</sup>	-

a. Identified as critical (5/6) and low importance (1/6) by people with FA and critical by expert authors on this topic.

b. Identified as critical (3/6), as important (2/6) and low importance (1/6) by people with FA and critical by expert authors on this topic.

## Balance of effects

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

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input checked="" type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know	No published evidence.	Expert consensus favours anticoagulation over antiplatelet therapy

## Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know	No published evidence.	The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were asked if the intervention was reasonable (weighing up the balance between benefits, harms and costs). 2 out of 3 individuals indicated management with antiplatelets/anticoagulation was reasonable; 1 indicated it was sometimes reasonable due to falling and potential for bleeding.

## SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	<b>Yes</b>		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	<b>Large</b>		Varies	Don't know
UNDESIRABLE EFFECTS	<b>Large</b>	Moderate	Small	Trivial		Varies	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	<b>Probably yes</b>	Yes		Varies	Don't know

## TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input type="radio"/>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input checked="" type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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## CONCLUSIONS

### Recommendation

We conditionally recommend anticoagulation over no anticoagulation in individuals with Friedreich ataxia with permanent, persistent or paroxysmal atrial fibrillation.

## Justification

There is no evidence to suggest treatment should be different for individuals with FRDA versus individuals without FRDA, where anticoagulation therapy would be appropriate for individuals with permanent, persistent or paroxysmal atrial fibrillation unless there is a contraindication. Shared decision-making should consider younger age of this cohort in the context of increased risk of falls, stroke, females with concomitant heavy menstrual bleeding and desire to maintain autonomy in decisions related to health.

## Subgroup considerations

The recommendation is for individuals with Friedreich ataxia with permanent, persistent or paroxysmal atrial fibrillation. Stroke happens across the age spectrum in FRDA. The recommendation does need to encourage clinicians to think across all ages; however, be mindful of specific groups as specified in the justification above.

## Research priorities

Reporting incidence/pattern of peripheral embolism, stroke.

### References

Harding AE, Hewer RL. The heart disease of Friedreich's ataxia: a clinical and electrocardiographic study of 115 patients, with an analysis of serial electrocardiographic changes in 30 cases. *Q J Med.* 1983;52(208):489-502.

Ribaï P, Pousset F, Tanguy M, Rivaud-Pechoux S, Le Ber I, Gasparini F, et al. Neurological, cardiological, and oculomotor progression in 104 patients with Friedreich ataxia during long-term follow-up. *Arch Neurol.* 2007;64:558-64.