

## QUESTION

Should offering a physical examination vs. no physical examination be used for for adult siblings of people with Friedreich ataxia?	
POPULATION:	for adult siblings of people with Friedreich ataxia
INTERVENTION:	offering a physical examination
COMPARISON:	no physical examination
MAIN OUTCOMES:	Anxiety;

## 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>Nil</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of genetic testing of adult siblings.</p> <p>1/7 indicated that the problem was serious, 1/7 indicated probably serious, 2/7 indicated probably not serious, 1/7 indicated they didn't know if serious, 2/7 indicated varied or sometimes serious.</p> <p>1/7 indicated that the problem was urgent, 1/7 indicated probably urgent, 3/7 indicated probably not urgent, 1/7 indicated they didn't know if urgent, 1/7 indicated varied or sometimes serious.</p> <p>2/7 indicated that the problem was a priority, 3/7 indicated probably not a priority, 1/7 indicated they didn't know if a priority, 1/7 indicated varied or sometimes 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 checked="" type="radio"/> Moderate</li> <li><input type="radio"/> Large</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>A search of four databases (CENTRAL, MEDLINE, EMBASE, PsycINFO) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 20 August 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	<p>Clinical experience indicates that a normal physical examination prior to genetic testing of a sibling of an individual with FRDA can reduce anxiety.</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 four databases (CENTRAL, MEDLINE, EMBASE, PsycINFO) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 20 August 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.</p>	<p>Conversely, identification of unrealised signs that could be due to FRDA will markedly increase anxiety.</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" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 33%;">Outcomes</th> <th style="width: 33%;">Importance</th> <th style="width: 33%;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Anxiety - not measured</td> <td>IMPORTANT<sup>a</sup></td> <td style="text-align: center;">-</td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	Anxiety - not measured	IMPORTANT <sup>a</sup>	-	
Outcomes	Importance	Certainty of the evidence (GRADE)						
Anxiety - not measured	IMPORTANT <sup>a</sup>	-						

	a. Identified as important by expert authors on this topic	
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## 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 checked="" type="radio"/> Probably favors the intervention</li> <li><input type="radio"/> Favors the intervention</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	No published evidence.	<p>A survey designed to systematically collect expert-based opinions from clinicians involved in developing the recommendations for this topic and providing clinical care for individuals with Friedreich ataxia, was conducted. Clinical experts from Australia, Europe, UK, South America, Canada and the USA were asked to consider the harms/benefits of <b>Physical Examination as a management strategy for adult siblings</b>.</p> <p>Reflecting on the impact of <b>Physical Examination</b> on <u>Anxiety</u>, 100% (4/4) clinical experts reported a benefit (large, moderate or small).</p> <p>Clinical experience indicates that siblings of people with FRDA who request genetic testing often value the outcome of a physical examination. The key here is that it should be offered as an option and not be made mandatory. In offering the option, the possibility of identifying signs of FRDA should be made known to the individual before the examination.</p>

## 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 type="radio"/> Probably yes</li> <li><input checked="" type="radio"/> Yes</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	No published evidence.	

## SUMMARY OF JUDGEMENTS

JUDGEMENT

	JUDGEMENT						
PROBLEM	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	<b>Moderate</b>	Large		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	Probably yes	<b>Yes</b>		Varies	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 suggest that adult siblings of people with Friedreich ataxia should be offered a physical examination. They should be made aware that this could identify signs of Friedreich ataxia. Absence of signs of Friedreich ataxia does not mean that they will not be found to have biallelic pathogenic variants in *FXN*. The older the individual with a normal examination, the less likely they are to have biallelic pathogenic variants in *FXN*.

### Justification

Although there is no published evidence, clinical experience indicates that siblings of people with FRDA who request genetic testing often value the outcome of a physical examination. The key here is that it should be offered as an option and not be made mandatory. In offering the option, the possibility of identifying signs of FRDA should be made known to the individual before the examination.

## Subgroup considerations

This recommendation is for adult siblings of individuals with Friedreich ataxia.

## Research priorities

A study of siblings about this topic would be of interest.