

QUESTION

Should offering echocardiograms vs. no echocardiograms be used for untested adult siblings of people with Friedreich ataxia?

POPULATION:	untested adult siblings of people with Friedreich ataxia
INTERVENTION:	offering echocardiograms
COMPARISON:	no echocardiograms
MAIN OUTCOMES:	Cardiomyopathy diagnosed; Anxiety;

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <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 	<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"> <input type="radio"/> Trivial <input type="radio"/> Small <input checked="" type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know 	<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>If a sibling of a person with FRDA does not wish to have genetic testing to identify if they have the condition then they can be offered echocardiography to see if they have evidence of cardiac involvement from FRDA. Since cardiac involvement is the main cause of mortality in FRDA and can be treated to reduce the chance of cardiac morbidity/mortality, offering echocardiography is middle ground that enables a person to</p>

		avoid possible definitive diagnosis of FRDA but maintains safety. Normal echocardiography may result in reduced anxiety for the individual.
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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Large ○ Moderate ○ Small ○ Trivial ○ Varies ○ Don't know 	<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>Identification of cardiac abnormality by echocardiography may be a surrogate for a genetic diagnosis of FRDA and this may result in significant psychological morbidity for the individual.</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"> ○ Very low ○ Low ○ Moderate ○ High ● No included studies 	<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"> ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability 	<table border="1" style="width: 100%; text-align: center;"> <tr> <td style="width: 33%;">Outcomes</td> <td style="width: 15%;">Importance</td> <td style="width: 52%;">Certainty of the evidence (GRADE)</td> </tr> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	
Outcomes	Importance	Certainty of the evidence (GRADE)			

	<table border="1"> <tr> <td>Cardiomyopathy diagnosed - not measured</td> <td>CRITICAL^a</td> <td>-</td> </tr> <tr> <td>Anxiety - not measured</td> <td>IMPORTANT^b</td> <td>-</td> </tr> </table> <p>a. identified as critical by expert authors on this topic b. Identified as important by expert authors on this topic</p>	Cardiomyopathy diagnosed - not measured	CRITICAL ^a	-	Anxiety - not measured	IMPORTANT ^b	-	
Cardiomyopathy diagnosed - not measured	CRITICAL ^a	-						
Anxiety - not measured	IMPORTANT ^b	-						

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"> <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 	<p>No published evidence.</p>	<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 Echocardiograms as a management strategy for untested adult siblings.</p> <p>Reflecting on the impact of Echocardiograms on Cardiomyopathy diagnosed and treated, 75% (3/4) clinical experts reported a benefit (large, moderate or small), and 0% (0/4) reported observing a harm (large, moderate or small). 1 clinician could not provide any information on this outcome.</p> <p>Reflecting on the impact on Anxiety, 75% (3/4) clinical experts reported a benefit, 0% (0/4) reported no effect. 1 expert clinician could not provide any information on this outcome.</p> <p>If a sibling of a person with FRDA does not wish to have genetic testing to identify if they have the condition then they can be offered echocardiography to see if they have evidence of cardiac involvement from FRDA. Since cardiac involvement is the main cause of mortality in FRDA and can be treated to reduce the chance of cardiac morbidity/mortality, offering echocardiography is middle ground that enables a person to avoid possible definitive diagnosis of FRDA but maintains safety. Normal echocardiography may result in reduced anxiety for the individual.</p>

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.	

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	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	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	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 suggest that adult siblings of a person with Friedreich ataxia, who do not wish to have genetic testing to confirm whether or not they have Friedreich ataxia, be offered echocardiography to see if they have any cardiac signs that may require treatment.

Justification

Cardiac involvement is the main cause of mortality in FRDA (Tsou et al, 2011) and can be treated to reduce the chance of cardiac morbidity and mortality. Offering echocardiography can enable a person who does not wish to have genetic testing to avoid possible definitive diagnosis of FRDA, while at the same time maintaining safety. Identification of cardiac abnormality by echocardiography may lead to treatment that can reduce morbidity and mortality. Normal echocardiography may result in reduced anxiety for the individual.

Subgroup considerations

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

Research priorities

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