

QUESTION

Should sitting and standing balance exercises vs. no treatment be used for non-ambulatory people with Friedreich ataxia?

POPULATION:	non-ambulatory people with Friedreich ataxia
INTERVENTION:	sitting and standing balance exercises
COMPARISON:	no treatment
MAIN OUTCOMES:	Independence in transfers; Pain; Independence in activities of daily living; Capacity to stand; Sitting balance; Quality of life;

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>No published evidence directly evaluating the impact of loss of balance in non-ambulant people with FRDA. However, it is assumed that truncal ataxia results in progressively difficult sitting with eventual need for a back and/or side supports to prevent falls. In a recent paper analysing sitting balance decline, as reflected by Item 1 of the Friedreich Ataxia Rating Scale E sub score, in a cohort of 301 individuals with FRDA sitting posture remains with none to minimal disability for many years and only a few individuals completely lose the ability to sit completely (Rummey et al, 2020).</p> <p>In a separate study evaluating neurological disease progression in 54 individuals with FRDA, once individuals were non-ambulant, sitting balance continued to decline, as reflected by changes seen in the SARA sitting item (Pandolfo, 2020).</p> <p>Although not examined specifically in individuals with FRDA, a 2015 systematic review found that loss of balance and activities requiring dynamic stability (such as reaching and transfers) were associated with an increased risk of falls in non-ambulant adults (Rice et al, 2015).</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.</p> <p>1/7 indicated non-ambulant mobility was not serious, 2/7 indicated probably serious, 4/7 indicated serious.</p> <p>3/7 indicated non-ambulant mobility was probably not urgent, 4/7 indicated urgent.</p> <p>2/7 indicated non-ambulant mobility was probably not a priority, 1/7 indicated probably a priority, 4/7 indicated priority. (Aug 2020).</p> <p>In a public forum entitled "Voice of the patient", held on 2 June 2017 in the USA to inform the United States Food and Drug Administration approximately 400 attendees (in-person and online) were asked to choose top three symptoms that would be most meaningful to treat. 55% of people chose improving balance or improved walking as two of their top symptoms (weblink: http://curefa.org/pdf/news/FA-Voice-of-the-Patient.pdf).</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 	<table border="1"> <thead> <tr> <th>Outcomes</th> <th>No of</th> <th>Certainty of</th> <th>Relative</th> <th>Anticipated absolute effects* (95% CI)</th> </tr> </thead> <tbody> <tr> <td> </td> <td> </td> <td> </td> <td> </td> <td> </td> </tr> </tbody> </table>	Outcomes	No of	Certainty of	Relative	Anticipated absolute effects* (95% CI)						
Outcomes	No of	Certainty of	Relative	Anticipated absolute effects* (95% CI)								

- o Large
- o Varies
- o Don't know

	participants (studies) Follow up	the evidence (GRADE)	effect (95% CI)	Risk with no treatment	Risk difference with sitting and standing balance exercises
Independence in transfers - not measured	-1	-	-	-	-
Pain - not measured	-	-	-	-	-
Independence in activities of daily living - not measured	-1	-	-	-	-
Capacity to stand assessed with: Scale for the Assessment and Rating of Ataxia	0 (1 observational study) ²	⊕○○○ VERY LOW ^{a,b}	-	10 young people with advanced degenerative spinocerebellar ataxia underwent 12 weeks of home based training with body-controlled video games, in 2 6-week phases. Non-parametric Friedman tests were used to determine within group differences between assessments (E1: 2 wks before training, E2: immediately before training, E3: after phase 1, E4: after phase 2). SARA scores remained unchanged at E1 and E2 however decreased by average 2.5 points between E2 and E3 ($p<0.002$) and E2 and E4 ($p<0.006$).	
Sitting balance assessed with: Scale for the Assessment and Rating of Ataxia	0 (1 observational study) ²	⊕○○○ VERY LOW ^{a,b}	-	10 young people with advanced degenerative spinocerebellar ataxia underwent 12 weeks of home based training with body-controlled video games, in 2 6-week phases. Non-parametric Friedman tests were used to determine within group differences between assessments (E1: 2 wks before training, E2: immediately before training, E3: after phase 1, E4: after phase 2). SARA scores remained unchanged at E1 and E2 however decreased by average 2.5 points between E2 and E3 ($p<0.002$) and E2	

					and E4 ($p < 0.006$).
Quality of life - not measured	-.1	-	-	-	-
<ol style="list-style-type: none"> 1. Milne S.C., Corben L.A., Roberts M., et al. Can rehabilitation improve the health and well-being in Friedreich's ataxia: a randomized controlled trial?. Clin Rehabil. ; 2018. 2. Schatton C., Synofzik M., Fleszar Z., Giese M.A., Schols L., Ilg W.. Individualized exergame training improves postural control in advanced degenerative spinocerebellar ataxia: A rater-blinded, intra-individually controlled trial. .parkreldis.2017.03.016. Parkinsonism Relat. Disord.; 2017. <ol style="list-style-type: none"> a. 50% (5/10) of participants had a diagnosis of FRDA, other diagnoses included ataxia with oculomotor ataxia type 1, ataxia teleangiectasia and autosomal-recessive ataxia (not FRDA). b. Small sample size/confidence intervals not reported. 					

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 	<table border="1"> <thead> <tr> <th rowspan="2">Outcomes</th> <th rowspan="2">№ of participants (studies) Follow up</th> <th rowspan="2">Certainty of the evidence (GRADE)</th> <th rowspan="2">Relative effect (95% CI)</th> <th colspan="2">Anticipated absolute effects* (95% CI)</th> </tr> <tr> <th>Risk with no treatment</th> <th>Risk difference with sitting and standing balance exercises</th> </tr> </thead> <tbody> <tr> <td>Independence in transfers - not measured</td> <td>-.1</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> </tr> <tr> <td>Pain - not measured</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> </tr> <tr> <td>Independence</td> <td>-.1</td> <td>-</td> <td>-</td> <td>-</td> <td>-</td> </tr> </tbody> </table>	Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)		Risk with no treatment	Risk difference with sitting and standing balance exercises	Independence in transfers - not measured	-.1	-	-	-	-	Pain - not measured	-	-	-	-	-	Independence	-.1	-	-	-	-	<p>There is no specific evidence to suggest balance training in non-ambulant individuals results in undesirable effects. Similar to any rehabilitation/exercise therapeutic intervention, direct effects may be increased fatigue and increased risk of falls. In the Milne et al (2018) pilot study no participants in the intervention group reported any falls and one person reported fatigue.</p> <p>There is no evidence evaluating the effect of increased physical activity on falls or muscle or generalised fatigue</p> <p>In clinical practice, balance exercises are individualised and prescribed by a qualified physical therapist/physiotherapist to directly target the impairments of people with FRDA and therefore undesirable effects are minimised due to this approach.</p>
Outcomes	№ of participants (studies) Follow up					Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)																				
		Risk with no treatment	Risk difference with sitting and standing balance exercises																									
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Pain - not measured	-	-	-	-	-																							
Independence	-.1	-	-	-	-																							

in activities of daily living - not measured					
Capacity to stand assessed with: Scale for the Assessment and Rating of Ataxia	0 (1 observational study) ²	⊕○○○ VERY LOW ^{a,b}	-	10 young people with advanced degenerative spinocerebellar ataxia underwent 12 weeks of home based training with body-controlled video games, in 2 6-week phases. Non-parametric Friedman tests were used to determine within group differences between assessments (E1: 2 wks before training, E2: immediately before training, E3: after phase 1, E4: after phase 2). SARA scores remained unchanged at E1 and E2 however decreased by average 2.5 points between E2 and E3 ($p<0.002$) and E2 and E4 ($p<0.006$).	
Sitting balance assessed with: Scale for the Assessment and Rating of Ataxia	0 (1 observational study) ²	⊕○○○ VERY LOW ^{a,b}	-	10 young people with advanced degenerative spinocerebellar ataxia underwent 12 weeks of home based training with body-controlled video games, in 2 6-week phases. Non-parametric Friedman tests were used to determine within group differences between assessments (E1: 2 wks before training, E2: immediately before training, E3: after phase 1, E4: after phase 2). SARA scores remained unchanged at E1 and E2 however decreased by average 2.5 points between E2 and E3 ($p<0.002$) and E2 and E4 ($p<0.006$).	
Quality of life - not measured	-.1	-	-	-	-

1. Milne S.C., Corben L.A., Roberts M., et al. Can rehabilitation improve the health and well-being in Friedreich's ataxia: a randomized controlled trial?. Clin Rehabil. ; 2018.
2. Schatton C., Synofzik M., Fleszar Z., Giese M.A., Schols L., Ilg W.. Individualized exergame training improves postural control in advanced degenerative spinocerebellar ataxia: A rater-blinded, intra-individually controlled trial. .parkreldis.2017.03.016. Parkinsonism Relat. Disord.; 2017.

	<p>a. 50% (5/10) of participants had a diagnosis of FRDA, other diagnoses included ataxia with oculomotor ataxia type 1, ataxia teleangiectasia and autosomal-recessive ataxia (not FRDA).</p> <p>b. Small sample size/confidence intervals not reported.</p>	
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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>Very low certainty of evidence as per evidence profile table.</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%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%;">Outcomes</th> <th style="width: 20%;">Importance</th> <th style="width: 30%;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Independence in transfers - not measured</td> <td>CRITICAL^a</td> <td style="text-align: center;">-</td> </tr> <tr> <td>Pain - not measured</td> <td>IMPORTANT^b</td> <td style="text-align: center;">-</td> </tr> <tr> <td>Independence in activities of daily living - not measured</td> <td>CRITICAL^c</td> <td style="text-align: center;">-</td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	Independence in transfers - not measured	CRITICAL ^a	-	Pain - not measured	IMPORTANT ^b	-	Independence in activities of daily living - not measured	CRITICAL ^c	-	
Outcomes	Importance	Certainty of the evidence (GRADE)												
Independence in transfers - not measured	CRITICAL ^a	-												
Pain - not measured	IMPORTANT ^b	-												
Independence in activities of daily living - not measured	CRITICAL ^c	-												

	<p>Capacity to stand assessed with: Scale for the Assessment and Rating of Ataxia</p>	<p>IMPORTANT^d</p>	<p>⊕○○○ VERY LOW^{e,f}</p>	
	<p>Sitting balance assessed with: Scale for the Assessment and Rating of Ataxia</p>	<p>IMPORTANT^d</p>	<p>⊕○○○ VERY LOW^{e,f}</p>	
	<p>Quality of life - not measured</p>	<p>CRITICAL^g</p>	<p>-</p>	
	<p>a. Identified as important (2/6), critical (4/6) by people with FA and critical by expert authors in this topic</p> <p>b. Identified as low importance (2/6), important (2/6), critical (2/6) by people with FA and important by expert authors in this topic</p> <p>c. Identified as important (2/6), critical (4/6) by people with FA and critical by expert authors in this topic</p> <p>d. Identified as important (3/6), critical (3/6) by people with FA and important by expert authors in this topic</p> <p>e. 50% (5/10) of participants had a diagnosis of FRDA, other diagnoses included ataxia with oculomotor ataxia type 1, ataxia teleangiectasia and autosomal-recessive ataxia (not FRDA).</p> <p>f. Small sample size/confidence intervals not reported.</p> <p>g. Identified as important (3/6), critical (3/6) by people with FA and critical 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"> <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>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 sitting and standing balance exercises as a management strategy for non-ambulant individuals.</p> <p>Reflecting on the impact of sitting and standing balance exercises on <u>Independence in transfers</u>, 50% (1/2) clinical experts reported a benefit (large, moderate or small), 50% (1/2) reported no effect and, 0% (0/2) reported observing a harm (large, moderate or small).</p>

		<p>Reflecting on the impact on <u>Pain</u>, 0% (0/2) clinical experts reported a benefit, 100% (2/2) reported no effect.</p> <p>Reflecting on the impact on <u>Independence in activities of daily living</u>, 50% (1/2) clinical experts reported a benefit, 50% (1/2) reported no effect.</p> <p>Reflecting on the impact on <u>Capacity to stand</u>, 50% (1/2) clinical experts reported a benefit, 50% (1/2) reported no effect.</p> <p>Reflecting on the impact on <u>Sitting balance</u>, 50% (1/2) clinical experts reported a benefit, 50% (1/2) reported no effect.</p> <p>Reflecting on the impact on <u>Quality of life</u>, 50% (1/2) clinical experts reported a benefit, 50% (1/2) reported no effect.</p>
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Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <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 	No published evidence.	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were asked if the intervention was acceptable (weighing up the balance between benefits, harms and costs).</p> <p>5/5 indicated sitting and standing balance exercises were reasonable. (Aug 2020).</p>

SUMMARY OF JUDGEMENTS

PROBLEM	JUDGEMENT						
	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

	JUDGEMENT						
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

For individuals with Friedreich ataxia who are no longer ambulant, we conditionally recommend standing and sitting balance exercises over no balance exercises. Balance exercises should be individually tailored to address each person's specific impairments and functional goals and minimise risk of falls or fatigue.

Justification

A number of small studies indicate balance training can improve ataxia and assist in achieving functional goals (Bunn et al, 2015; Keller & Bastian, 2014; Milne et al, 2018). Clinical experience supports these findings.

Subgroup considerations

This recommendation is for non-ambulant individuals with Friedreich ataxia. Although there are no specific subgroup considerations, individualised balance exercises should be targeted at the appropriate level of mobility and sitting and standing balance control.

Research priorities

There is a sparsity of literature examining the effectiveness of rehabilitation interventions in individuals who are non-ambulant with neurological conditions. Further studies are required to evaluate the effectiveness of balance exercises on functional capacity, independence and quality of life in individuals with ataxia.

References

Bunn LM, Marsden JF, Giunti P, Day BL. Training balance with opto-kinetic stimuli in the home: a randomized controlled feasibility study in people with pure cerebellar disease. *Clin Rehabil.* 2015;29(2):143-53.

Keller JL, Bastian AJ. A home balance exercise program improves walking in people with cerebellar ataxia. *Neurorehabil Neural Repair.* 2014;28(8):770-8.

Milne SC, Corben LA, Roberts M, Murphy A, Tai G, Georgiou-Karistianis N, et al. Can rehabilitation improve the health and well-being in Friedreich's ataxia: a randomized controlled trial? *Clin Rehabil.* 2018;32(5):630-43.

Pandolfo M. Neurologic outcomes in Friedreich ataxia: Study of a single-site cohort. *Neurol Genet.* 2020;6(3):e415.

Rice LA, Ousley C, Sosnoff JJ. A systematic review of risk factors associated with accidental falls, outcome measures and interventions to manage fall risk in non-ambulatory adults. *Disabil Rehabil.* 2015;37(19):1697-705.

Rummey C, Farmer JM, Lynch DR. Predictors of loss of ambulation in Friedreich's ataxia. *EClinicalMedicine.* 2020;18:100213.