QUESTION

Should high intensity (defined at 3+ days per week) exercise vs. less intense (defined as <3 days per week) exercise be used for ambulant people with Friedreich ataxia?	
POPULATION:	ambulant people with Friedreich ataxia
INTERVENTION:	high intensity (defined at 3+ days per week) exercise
COMPARISON:	less intense (defined as <3 days per week) exercise
MAIN OUTCOMES:	Independence of ambulation; Independence of ambulation; Independence of ambulation; Independence of ambulation; Independence of ambulation; Balance; Balance; Walking capacity; Quality of life;

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Gait instability is the most frequently reported initial symptom in individuals with FRDA, occurring as the first symptom in 76 - 88% of individuals (Reetz et al, 2015). Mobility typically declines, with loss of mobility for individuals with onset <15 years of age typically 11.5 years after first symptom onset; 18.3 years for individuals with onset 15-24 years of age and 23.5 years for individuals with onset >24 years (Rumney et al, 2020).	The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of the topic. 1/7 indicated the consequences of the disturbance of strength, balance, mobility and reduction of falls were probably serious, 5/7 indicated serious, 1/7 indicated didn't know if serious. 1/7 indicated the consequences of the disturbance of strength, balance, mobility and reduction of falls were probably not urgent, 1/7 indicated probably urgent, 5/7 indicated urgent. 1/7 indicated the consequences of the disturbance of strength, balance, mobility and reduction of falls were probably a priority, 6/7 indicated priority. (Aug 2020). 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).

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know		There are no studies that have compared three days or greater frequency of exercise versus less than 3 days per week. However, a systematic review found the average frequency of rehabilitation interventions for individuals with hereditary cerebellar ataxia was 4.4 days per week (Milne et al, 2017) and three studies have found greater frequency of training was associated with better outcomes (Milne et al, 2018; Ilg et al, 2009; Ilg et al, 2010; Ilg et al, 2012).

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with less intense (defined as <3 days per week) exercise	Risk difference with high intensity (defined at 3+ days per week) exercise
Independence of ambulation assessed with: Functional Independence Measure	0 (2 RCTs)[1,2]	⨁⨁◯◯ LOW[a,b]	-	19 participants with Friedreich ataxia were randomised to a six-week outpatient rehabilitation programme immediately (intervention group) or after a six-week delayed-start (control group). The rehabilitation was followed by a six-week home exercise programme. Rehabilitation effectiveness was analysed using independent sample t-tests to compare change from baseline and six-week visit between groups. No significant difference was found in the FIM, between the groups from baseline to six-week visit. There was no significant between-group difference in the FIM motor domain, however there was a significant within-group increased for the intervention group. (Milne et al 2018). A case study of a 17 year old male with Friedreich ataxia underwent a physiotherapy treatment programme involving stretching and strengthening exercises, special scoliosis exercises, PNF techniques, kinesiobant exercises and coordination exercises were implemented. Three sessions of physiotherapy program per week was carried out for 6 weeks. FIM score improved from 100 to 105. (Kaplan et al 2015).	
Independence of ambulation	0	⨁⨁◯◯	-	19 participants with Friedreich ataxia were randomised to a six-week	

assessed with: Friedreich Ataxia Rating Scale	(1 RCT)[1]	LOW[c,d]		outpatient rehabilitation programme immediately (intervention group) or after a six-week delayed-start (control group). The rehabilitation was followed by a six-week home exercise programme. Paired t-tests were used to determine change in baseline and immediately post-rehab, and baseline and immedidately after post-home exercise programme (HEP). Significant improvements between baseline (mean 97.3, SD 22.2) and post-HEP (mean 94.0, SD 23.2) were found in the FARS (p=0.017). (Milne et al 2018).
Independence of ambulation assessed with: Functional Ambulation Category	0 (1 observational study)[3]	⊕◯◯◯ VERY LOW[e,f,g,h]	-	37 people with Friedriech ataxia who received inpatient rehabilitation between Jan 2000 and Dec 2012 were included in this retrospective study. Mean rehabilitation duration was 4.7 weeks (SD 1.4 weeks). At the end of the rehabilitation program, a statistically significant difference was found in the FAC pre- and post- treatment (p=0.016).
Independence of ambulation assessed with: Hoffer Ambulation Scale	0 (1 observational study)[3]	⊕◯◯◯ VERY LOW[e,f,g,h]	-	37 people with Friedriech ataxia who received inpatient rehabilitation between Jan 2000 and Dec 2012 were included in this retrospective study. Mean rehabilitation duration was 4.7 weeks (SD 1.4 weeks). At the end of the rehabilitation program, a statistically significant difference was found in the Hoffer Ambulation scale pre- and post-treatment (p<0.05).
Independence of ambulation assessed with: Barthel Index	0 (1 observational study)[3]	⊕◯◯◯ VERY LOW[e,f,g,h]	-	37 people with Friedriech ataxia who received inpatient rehabilitation between Jan 2000 and Dec 2012 were included in this retrospective study. Mean rehabilitation duration was 4.7 weeks (SD 1.4 weeks). At the end of the rehabilitation program, a statistically significant difference was found in the Barthel Index pre- (mean 46.8, SD 8.8) and post- (mean 54.2, SD 10.3) treatment (p<0.001).

Balance assessed with: Berg Balance Scale	0 (1 RCT)[1]	⊕⊕⊕◯ MODERATE[c]	-	19 participants with Friedreich ataxia were randomised to a six-week outpatient rehabilitation programme immediately (intervention group) or after a six-week delayed-start (control group). The rehabilitation was followed by a six-week home exercise programme. Paired t-tests were used to determine change in baseline and immediately post-rehab, and baseline and immedidately after post-home exercise programme (HEP). Significant improvements between baseline and post-rehab were found in the Berg Balance Scale (*p*=0.039). as well as between baseline and post-HEP (*p*=0.026) for non-ambulant participants. (Milne et al 2018).	
Balance assessed with: Scale for the Assessment and Rating of Ataxia	0 (1 observational study)[4]	⊕◯◯◯ VERY LOW[g,i,j,k,l]	-	11 people with autosomal dominant spinocerebellar ataxia (n=6) or Friedriech ataxia (n=5) wore a wearable proprioceptive stabilizer for 5 days/week, 180 min/day for 3 weeks. The Friedman analysis of variance by ranks was used to identify treatment effects across timepoints and the Wilcoxon-signed rank test was used to identify post hoc comparisons in the case of statistically significance. Statistically signficant improvement in the SARA between baseline (mean 10.7, SD 3.1) and 3 weeks of device use (mean 9.6, SD 3.1, *p*=0.027) was identified. (Leonardi et al 2016)	
Walking capacity assessed with: 6 min walking test	0 (1 observational study)[4]	⊕◯◯◯ VERY LOW[g,i,j,k,l]	-	11 people with autosomal dominant spinocerebellar ataxia (n=6) or Friedriech ataxia (n=5) wore a wearable proprioceptive stabilizer for 5 days/week, 180 min/day for 3 weeks. The Friedman analysis of variance by ranks was used to identify treatment effects across timepoints and the Wilcoxon-signed rank test was used to identify post hoc comparisons in the case of statistically significance. Statistically signficant improvement in	

				the 6MWT between baseline (mean 322.1 metres, SD 182.9) and 3 weeks of device use (mean 380.1 metres, SD 120.7, *p*=0.049) was identified. (Leonardi et al 2016)
Quality of life assessed with: Friedreich Ataxia Impact Scale	19 (1 RCT)[1]	⨁⨁⨁◯ MODERATE[c]	-	19 participants with Friedreich ataxia were randomised to a six-week outpatient rehabilitation programme immediately (intervention group) or after a six-week delayed-start (control group). The rehabilitation was followed by a six-week home exercise programme. Rehabilitation effectiveness was analysed using independent sample t-tests to compare change from baseline and six-week visit between groups. There was a significant between-group difference in the FAIS body movement scale (*p*=0.003). Paired t-tests were used to determine change in baseline and immediately post-rehab, and baseline and immedidately after post-home exercise programme (HEP). Significant improvements between baseline (mean 35.2 SD 21.9) and post-rehab (mean 27.7, SD 19.7) were found in the FAIS body movement scale (*p*=0.009) and in the FAIS lower limb (mean 65.2, SD 28.5 to mean 48.5, SD 31.5, *p*=0.033) and upper limb subscales (mean 29.3, SD 23.7 to mean 25.2, SD 20.4, *p*=0.044). (Milne et al 2018).

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. Kaplan T., Maden C.,Yakut H.,Pelin Z.,Bayramlar K.. Conference Abstract: Evaluation of a Patient with Friedreich's Ataxia in Aspect of Physiotherapy Applications: Case Report. . Fiz. Rehab.; 2015.
3. Dogan-Aslan M., Buyukvural-Sen S.,Nakipoglu-Yuzer G.F.,Ozgirgin N.. Demographic and clinical features and rehabilitation outcomes of patients with Friedreich ataxia: A retrospective study. . Turkish Journal of Physical Medicine and Rehabilitation. ; 2018.
4. Leonardi L., Aceto M.G.,Marcotulli C.,et al. A wearable proprioceptive stabilizer for rehabilitation of limb and gait ataxia in hereditary cerebellar ataxias: a pilot open-labeled study. . Neurol. Sci.; 2017.

a. Small sample size (n=20) from all studies.
b. One study case study design.
c. Small sample size (n=19).
d. Outcome measure not specific to independence of ambulation.
e. Diagnosis of FRDA based on Harding's criteria not genetic results.
f. Small sample size (n=37).
g. Confidence intervals not reported.
h. No control group.
i. Only 5 participants had a diagnosis of FRDA (from total participant numbers of n=11).
j. One non-randomised study only, with small sample size and no control group.
k. Small sample size (n=11).
l. No intention to treat analysis (two participants not included in the analysis).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT

○ Large
○ Moderate
● Small
○ Trivial
○ Varies
○ Don't know

RESEARCH EVIDENCE

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with less intense (defined as <3 days per week) exercise	Risk difference with high intensity (defined at 3+ days per week) exercise
Independence of ambulation assessed with: Functional Independence Measure	0 (2 RCTs)[1,2]	⨁⨁◯◯ LOW[a,b]	-	19 participants with Friedreich ataxia were randomised to a six-week outpatient rehabilitation programme immediately (intervention group) or after a six-week delayed-start (control group). The rehabilitation was followed by a six-week home exercise programme. Rehabilitation effectiveness was analysed using independent sample t-tests to compare change from baseline and six-week visit between groups. No significant difference was found in the FIM, between the groups from baseline to six-week visit. There was no significant	

ADDITIONAL CONSIDERATIONS

There appear to be no undesirable effects from exercising greater than 3 days per week. Monitoring of fatigue and impact on daily function is important to ensure exercise and rehabilitation programs are prescribed appropriately for ambulant individuals with FRDA.

				between-group difference in the FIM motor domain, however there was a significant within-group increased for the intervention group. (Milne et al 2018). A case study of a 17 year old male with Friedreich ataxia underwent a physiotherapy treatment programme involving stretching and strengthening exercises, special scoliosis exercises, PNF techniques, kinesiobant exercises and coordination exercises were implemented. Three sessions of physiotherapy program per week was carried out for 6 weeks. FIM score improved from 100 to 105. (Kaplan et al 2015).
Independence of ambulation assessed with: Friedreich Ataxia Rating Scale	0 (1 RCT)[1]	⊕⊕◯◯ LOW[c,d]	-	19 participants with Friedreich ataxia were randomised to a six-week outpatient rehabilitation programme immediately (intervention group) or after a six-week delayed-start (control group). The rehabilitation was followed by a six-week home exercise programme. Paired t-tests were used to determine change in baseline and immediately post-rehab, and baseline and immedidately after post-home exercise programme (HEP). Significant improvements between baseline (mean 97.3, SD 22.2) and post-HEP (mean 94.0, SD 23.2) were found in the FARS (*p*=0.017). (Milne et al 2018).
Independence of ambulation assessed with: Functional Ambulation Category	0 (1 observational study)[3]	⊕◯◯◯ VERY LOW[e,f,g,h]	-	37 people with Friedriech ataxia who received inpatient rehabilitation between Jan 2000 and Dec 2012 were included in this retrospective study. Mean rehabilitation duration was 4.7 weeks (SD 1.4 weeks). At the end of the rehabilitation program, a statistically significant difference was found in the FAC pre- and post- treatment (*p*=0.016).
Independence of ambulation	0 (1	⊕◯◯◯	-	37 people with Friedriech ataxia who received inpatient rehabilitation

assessed with: Hoffer Ambulation Scale	observational study)[3]	VERY LOW[e,f,g,h]		between Jan 2000 and Dec 2012 were included in this retrospective study. Mean rehabilitation duration was 4.7 weeks (SD 1.4 weeks). At the end of the rehabilitation program, a statistically significant difference was found in the Hoffer Ambulation scale pre- and post-treatment (p<0.05).
Independence of ambulation assessed with: Barthel Index	0 (1 observational study)[3]	⨁◯◯◯ VERY LOW[e,f,g,h]	-	37 people with Friedriech ataxia who received inpatient rehabilitation between Jan 2000 and Dec 2012 were included in this retrospective study. Mean rehabilitation duration was 4.7 weeks (SD 1.4 weeks). At the end of the rehabilitation program, a statistically significant difference was found in the Barthel Index pre- (mean 46.8, SD 8.8) and post- (mean 54.2, SD 10.3) treatment (p<0.001).
Balance assessed with: Berg Balance Scale	0 (1 RCT)[1]	⨁⨁⨁◯ MODERATE[c]	-	19 participants with Friedreich ataxia were randomised to a six-week outpatient rehabilitation programme immediately (intervention group) or after a six-week delayed-start (control group). The rehabilitation was followed by a six-week home exercise programme. Paired t-tests were used to determine change in baseline and immediately post-rehab, and baseline and immedidately after post-home exercise programme (HEP). Significant improvements between baseline and post-rehab were found in the Berg Balance Scale (p=0.039). as well as between baseline and post-HEP (p=0.026) for non-ambulant participants. (Milne et al 2018).
Balance assessed with: Scale for the Assessment and Rating of Ataxia	0 (1 observational study)[4]	⨁◯◯◯ VERY LOW[g,i,j,k,l]	-	11 people with autosomal dominant spinocerebellar ataxia (n=6) or Friedriech ataxia (n=5) wore a wearable proprioceptive stabilizer for 5 days/week, 180 min/day for 3 weeks. The Friedman analysis of variance by ranks was used to identify treatment

				effects across timepoints and the Wilcoxon-signed rank test was used to identify post hoc comparisons in the case of statistically significance. Statistically signficant improvement in the SARA between baseline (mean 10.7, SD 3.1) and 3 weeks of device use (mean 9.6, SD 3.1, *p*=0.027) was identified. (Leonardi et al 2016)
Walking capacity assessed with: 6 min walking test	0 (1 observational study)[4]	⨁◯◯◯ VERY LOW[g,i,j,k,l]	-	11 people with autosomal dominant spinocerebellar ataxia (n=6) or Friedriech ataxia (n=5) wore a wearable proprioceptive stabilizer for 5 days/week, 180 min/day for 3 weeks. The Friedman analysis of variance by ranks was used to identify treatment effects across timepoints and the Wilcoxon-signed rank test was used to identify post hoc comparisons in the case of statistically significance. Statistically signficant improvement in the 6MWT between baseline (mean 322.1 metres, SD 182.9) and 3 weeks of device use (mean 380.1 metres, SD 120.7, *p*=0.049) was identified. (Leonardi et al 2016)
Quality of life assessed with: Friedreich Ataxia Impact Scale	19 (1 RCT)[1]	⨁⨁⨁◯ MODERATE[c]	-	19 participants with Friedreich ataxia were randomised to a six-week outpatient rehabilitation programme immediately (intervention group) or after a six-week delayed-start (control group). The rehabilitation was followed by a six-week home exercise programme. Rehabilitation effectiveness was analysed using independent sample t-tests to compare change from baseline and six-week visit between groups. There was a significant between-group difference in the FAIS body movement scale (*p*=0.003). Paired t-tests were used to determine change in baseline and immediately post-rehab, and baseline and immedidately after post-home exercise programme (HEP). Significant improvements between baseline (mean

				35.2 SD 21.9) and post-rehab (mean 27.7, SD 19.7) were found in the FAIS body movement scale (p=0.009) and in the FAIS lower limb (mean 65.2, SD 28.5 to mean 48.5, SD 31.5, p=0.033) and upper limb subscales (mean 29.3, SD 23.7 to mean 25.2, SD 20.4, p=0.044). (Milne et al 2018).

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4. Leonardi L., Aceto M.G.,Marcotulli C.,et al. A wearable proprioceptive stabilizer for rehabilitation of limb and gait ataxia in hereditary cerebellar ataxias: a pilot open-labeled study. . Neurol. Sci.; 2017.

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d. Outcome measure not specific to independence of ambulation.
e. Diagnosis of FRDA based on Harding's criteria not genetic results.
f. Small sample size (n=37).
g. Confidence intervals not reported.
h. No control group.
i. Only 5 participants had a diagnosis of FRDA (from total participant numbers of n=11).
j. One non-randomised study only, with small sample size and no control group.
k. Small sample size (n=11).
l. No intention to treat analysis (two participants not included in the analysis).

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Very low ○ Low ● Moderate ○ High ○ No included studies	Moderate to very low certainty of evidence as per the evidence profile table.	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability		

Outcomes	Importance	Certainty of the evidence (GRADE)
Independence of ambulation assessed with: Functional Independence Measure	IMPORTANT[a]	⨁⨁◯◯ LOW[b,c]
Independence of ambulation assessed with: Friedreich Ataxia Rating Scale	IMPORTANT[a]	⨁⨁◯◯ LOW[d,e]
Independence of ambulation assessed with: Functional Ambulation Category	IMPORTANT[a]	⨁◯◯◯ VERY LOW[f,g,h,i]
Independence of ambulation assessed with: Hoffer Ambulation Scale	IMPORTANT[a]	⨁◯◯◯ VERY LOW[f,g,h,i]
Independence of ambulation assessed with: Barthel Index	IMPORTANT[a]	⨁◯◯◯ VERY LOW[f,g,h,i]
Balance assessed with: Berg Balance Scale	IMPORTANT	⨁⨁⨁◯ MODERATE[d]
Balance assessed with: Scale for the Assessment and Rating of	IMPORTANT[j]	⨁◯◯◯

Ataxia		VERY LOW[h,k,l,m,n]
Walking capacity assessed with: 6 min walking test	IMPORTANT[o]	⊕◯◯◯ VERY LOW[h,k,l,m,n]
Quality of life assessed with: Friedreich Ataxia Impact Scale	CRITICAL[p]	⊕⊕⊕◯ MODERATE[d]

a. Identified as critical (1/6), important (3/6), low (2/6) importance by people with FA and critical by expert authors on this topic
b. Small sample size (n=20) from all studies.
c. One study case study design.
d. Small sample size (n=19).
e. Outcome measure not specific to independence of ambulation.
f. Diagnosis of FRDA based on Harding's criteria not genetic results.
g. Small sample size (n=37).
h. Confidence intervals not reported.
i. No control group.
j. Identified as important (3/5), critical (2/5) by people with FA and important by expert authors on this topic
k. Only 5 participants had a diagnosis of FRDA (from total participant numbers of n=11).
l. One non-randomised study only, with small sample size and no control group.
m. Small sample size (n=11).
n. No intention to treat analysis (two participants not included in the analysis).
o. Identified as critical (2/6), important (3/6), low (1/6) importance by people with FA and important by expert authors on this topic
p. Identified as critical (3/6), important (3/6) 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

○ 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		A survey designed to systematically collect expert-based opinions from clinicians involved in the development of these guidelines 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 High intensity (defined as 3+ days per week) exercise as a management strategy for ambulant individuals. Reflecting on the impact of High intensity (defined as 3+ days per week) exercise on Independence of ambulation, 69.24% (18/26) clinical experts reported a benefit (large, moderate or small), 0% (0/26) reported no effect and, 0% (0/26) reported observing a harm (large, moderate or small). 8 clinicians could not provide any information on this outcome. Reflecting on the impact on Balance, 65.39% (17/26) clinical experts reported a benefit, 3.85% (1/26) reported no effect and, 0% (0/26) reported observing a harm. 8 expert clinicians could not provide any information on this outcome. Reflecting on the impact on Falls, 69.23% (18/26) clinical experts reported a benefit, 0% (0/26) reported no effect and, 0% (0/26) reported observing a harm. 8 expert clinicians could not provide any information on this outcome. Reflecting on the impact on Walking capacity, 69.23% (18/26) clinical experts reported a benefit, 0% (0/26) reported no effect and, 0% (0/26) reported observing a harm. 8 expert clinicians could not provide any information on this outcome. Reflecting on the impact on Quality of life, 68% (17/25) clinical experts reported a benefit, 0% (0/25) reported no effect and, 0% (0/25) reported observing a harm. 8 expert clinicians could not provide any information on this outcome. Reflecting on the impact on Lower limb strength, 69.23% (18/26) clinical experts reported a benefit, 0% (0/26) reported no effect and, 0% (0/26) reported observing a harm. 8 expert clinicians could not provide any information on this outcome.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies	No published evidence.	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).

○ Don't know		4/4 indicated high intensity exercise for people who are walking was reasonable. (Aug 2020).

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	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	**Strong recommendation for the intervention**
○	○	○	○	●

CONCLUSIONS

Recommendation

For individuals with Friedreich ataxia who are ambulant, we recommend completing rehabilitation or exercises 3 days per week or more frequently over completing these exercises less than 3 days per week.

Justification

Although there are no studies that have compared three days or greater frequency of exercise versus less than 3 days per week, a systematic review found the average frequency of rehabilitation interventions for individuals with hereditary cerebellar ataxia was 4.4 days per week (Milne et al, 2017) and three studies have found greater frequency of independent training was associated with better outcomes (Milne et al, 2018; Ilg et al, 2009; Ilg et al, 2010; Ilg et al, 2012). This is supported by observations in clinical practice.

Subgroup considerations

This recommendation is for individuals with Friedreich ataxia who are ambulant.

Research priorities

An evaluation of the optimal intensity and dosage of exercise or rehabilitation is required. This will offer more certainty to clinicians and individuals with FRDA when considering the best approach to take in regard to physical activity and training.

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