QUESTION

Should upper limb strengthening vs. no treatment be used for non-ambulant people with Friedreich ataxia?	
POPULATION:	non-ambulant people with Friedreich ataxia
INTERVENTION:	upper limb strengthening
COMPARISON:	no treatment
MAIN OUTCOMES:	Independence in transfers; Pain; Independence in activities of daily living; Capacity to stand; Sitting balance; Quality of life; Upper limb strength;

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	In a study of 19 individuals with FRDA, 84% (16/19) had intrinsic hand muscle weakness as assessed by manual muscle strength testing (MMST) (Corben et al, 2019). A second study assessed forearm muscle dysfunction in 16 individuals with FRDA. Results demonstrated decreased muscle endurance and reduced feelings of physical energy (Bossie et al, 2017). Two further studies also found upper limb weakness in individuals with FRDA, but lower limb weakness was more severe and was present earlier in the disease (Beauchamp et al, 1995; Sival et al, 2011).	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 non-ambulant mobility was not serious, 2/7 indicated probably serious, 4/7 indicated serious. 3/7 indicated non-ambulant mobility was probably not urgent, 4/7 indicated urgent. 2/7 indicated non-ambulant mobility was probably not a priority, 1/7 indicated probably a priority, 4/7 indicated priority. (Aug 2020). In clinical practice, shoulder injuries (such as rotator cuff tears) appear with greater frequency. This is likely due to the increased demands on the upper limbs to enable independence in transferring and other mobility activities.

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	A search of four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 24 September 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.	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 **upper limb strengthening as a management strategy for non-ambulant**

		individuals. Reflecting on the impact of **upper limb strengthening** on Independence in transfers, 100% (2/2) clinical experts reported a benefit (large, moderate or small), 0% (0/2) reported no effect and, 0% (0/2) reported observing a harm (large, moderate or small). Reflecting on the impact on Pain, 100% (2/2) clinical experts reported a benefit. Reflecting on the impact on Independence in activities of daily living, 100% (2/2) clinical experts reported a benefit. Reflecting on the impact on Capacity to stand, 50% (1/2) clinical experts reported a benefit, 50% (1/2) reported no effect. Reflecting on the impact on Sitting balance, 50% (1/2) clinical experts reported a benefit, 50% (1/2) reported no effect. Reflecting on the impact on Quality of life, 100% (2/2) clinical experts reported a benefit. Reflecting on the impact on Upper limb strength, 100% (2/2) clinical experts reported a benefit.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	A search of four databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 24 September 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.	In clinical practice, no undesirable effects from upper limb strengthening have been seen. However, caution should be taken not to 'over-exercise' the upper limbs due to their increased involvement in mobility and potential for fatigue.

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	No published evidence.	

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	See table below	Although pain was considered of low importance by individuals with FRDA, pain is not typically the main indication for prescribing an upper limb strengthening program.

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]	-
Capacity to stand - not measured	IMPORTANT[d]	-
Sitting balance - not measured	IMPORTANT[d]	-
Quality of life - not measured	CRITICAL[e]	-
Upper limb strength - not measured	IMPORTANT[f]	-

a. Identified as critical (4/6) and important (2/6) by people with FA and critical by expert authors on this topic
b. Identified as critical (2/6), important (2/6) and low importance (2/6) by people with FA and important by expert authors on this topic
c. Identified as critical (4/6) and important (2/6) by people with FA and critical by expert authors on this topic
d. Identified as critical (3/6) and important (3/6) by people with FA and important by expert authors on this topic
e. Identified as critical (3/6) and important (3/6) by people with FA and

	critical by expert authors on this topic f. Identified as important (6/6) by people with FA and important 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	No published evidence.	Choosing the right exercises to maintain muscle balance (i.e. posterior and anterior muscles) should take into account how the upper limbs are being used during everyday function. Strengthening can prevent or reduce the risk of shoulder or wrist injuries.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	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). 5/5 indicated that upper limb strengthening 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

	JUDGEMENT						
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

We recommend upper limb strengthening versus no upper limb strengthening in individuals with Friedreich ataxia who are no longer ambulant. Caution should be taken to not 'over-exercise', especially when there is reliance on the upper limbs to transfer or mobilise.

Justification

There is no published evidence for upper limb strengthening; however, benefits from upper limb strengthening are seen in clinical practice. Prescription of upper limb exercises should aim to maintain muscle balance, considering how the upper limbs are being used during everyday function. Strengthening can prevent or reduce the risk of shoulder or wrist injuries.

Subgroup considerations

This recommendation is for non-ambulant individuals with Friedreich ataxia.

Research priorities

Future studies should examine the best approach to upper limb strengthening to target maximising function (mobility and independence during activities of daily living) and minimising risk of injury for non-ambulant individuals with FRDA.

References

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Corben LA, Yiu EM, Tai G, Milne SC, Lynch B, Delatycki MB. Probing the multifactorial source of hand dysfunction in Friedreich ataxia. J Clin Neurosci. 2019;64:71-6.

Sival DA, Pouwels ME, Van Brederode A, Maurits NM, Verschuuren-Bemelmans CC, Brunt ER, et al. In children with Friedreich ataxia, muscle and ataxia parameters are associated. Dev Med Child Neurol. 2011;53(6):529-34.