QUESTION

Should lower limb strengthening vs. no treatment be used for non-ambulant people with Friedreich ataxia?	
POPULATION:	non-ambulant people with Friedreich ataxia
INTERVENTION:	lower 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; Lower 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 54 individuals with FRDA, weakness of the lower limbs was absent or minimal in ambulatory patients, whereas it rapidly became prominent 1 year after loss of ambulation (Pandolfo, 2020). There is evidence suggesting changes to skeletal muscles in individuals with FRDA. This includes studies demonstrating deficits in energy production, delayed muscle oxygenation after exercise (Lynch et al, 2002), homogeneously increased muscle density and reduced muscle force (Sival et al, 2011), increased muscle specific fatigue (Bossie et al, 2017), and a reduction of 70% of strength at the time of wheelchair use (Beauchamp et al, 1995). A further decline in lower limb strength to 56% of normal occurred approximately 2 years after initial wheelchair use (Beauchamp et al, 1995).	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).

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 **lower limb strengthening as a management strategy for non-ambulant individuals.** Reflecting on the impact of lower 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, 100% (2/2) clinical experts reported a benefit. 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, 50% (1/2) clinical experts reported a benefit, 50% (1/2) reported no effect. Reflecting on the impact on Lower 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.	No undesirable effects have been observed in clinical practice.

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		

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[a]	-
Capacity to stand - not measured	IMPORTANT[c]	-
Sitting balance - not measured	IMPORTANT[c]	-
Quality of life - not measured	CRITICAL[d]	-
Lower limb strength - not measured	IMPORTANT[e]	-

a. Identified as critical (4/6), 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 (3/6), important (3/6) by people with FA and important by expert authors on this topic
d. Identified as critical (3/6), important (3/6) by people with FA and critical by expert authors on this topic
e. Identified as critical (2/6) and important (4/6) 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.	Although there is no published evidence examining the effects of lower limb strengthening on individuals who are non-ambulant; in clinical practice there appears to be a beneficial effect.

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 lower 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
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			**No included studies**

	JUDGEMENT						
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 conditionally recommend lower limb strengthening over no lower limb strengthening for individuals with Friedreich ataxia who are no longer ambulant.

Justification

Although there is no published evidence examining the effects of lower limb strengthening on individuals who are non-ambulant, in clinical practice there appears to be a beneficial effect.

Subgroup considerations

This recommendation is for non-ambulant individuals with Friedreich ataxia. There might be a greater benefit when a person first commences use of a wheelchair; however, this is unclear.

Research priorities

Future research should examine the effectiveness of strengthening for non-ambulant individuals, alongside other exercise or rehabilitation approaches. Therapy should aim for the most efficient and effective exercise intervention to maintain and increase function while minimising the time burden for individuals with FRDA. Exploring the best dosage, intensity and timing of implementing a strengthening program is critical to ensure accurate prescription of exercises.

References

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