QUESTION

Should pharmacological agents (baclofen, botulinum toxin) to manage upper limb function vs. no pharmacological agents be used for individuals with spasticity or spasm with Friedreich ataxia?	
POPULATION:	individuals with spasticity or spasm with Friedreich ataxia
INTERVENTION:	pharmacological agents (baclofen, botulinum toxin) to manage upper limb function
COMPARISON:	no pharmacological agents
MAIN OUTCOMES:	Contracture, range of motion; Pain; Neurological function; Independence in daily activities;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know		The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of the topic. 8/8 indicated upper limb dysfunction was serious. 1/7 indicated upper limb dysfuction was not urgent; 1/7 indicated probably not urgent; 1/7 indicated probably urgent; 4/7 indicated urgent. 1/7 indicated upper limb dysfunction was probably not a priority, 3/7 indicated probably a priority, 3/7 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 4 databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 16 September 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.	

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 4 databases (CENTRAL, MEDLINE, EMBASE, CINAHL) identified no randomized, non-randomized controlled, cohort and case studies published from 2014 through to 16 September 2020. No further published evidence meeting the search criteria was identified in the Consensus Clinical Management Guidelines for Friedreich's ataxia, 2014.	Clinical experience (unpublished) demonstrated profound and devastating loss of function after botulinum toxin injections to long finger flexors in 2/2 patients treated.

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)
Contracture, range of motion - not measured	IMPORTANT[a]	-
Pain - not measured	CRITICAL[b]	-
Neurological function - not measured	IMPORTANT[c]	-
Independence in daily activities - not measured	IMPORTANT[d]	-

a. Identified as critical (2/6), important (3/6) and low importance (2/6) by people with FA and critical by expert authors on this topic.
b. Identified as critical (3/6), important (1/6) and low importance (2/6) by people with FA and critical by expert authors on this topic.
c. Identified as critical (1/6), important (4/6) and low importance (1/6) by people with FA and important 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.

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.	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 pharmalogicals (baclofen, botulinum toxin) to manage upperlimb function as a management strategy for individuals with upper limb spasticity or spasm. Reflecting on the impact of pharmalogicals (baclofen, botulinum toxin) to manage upperlimb function on Contracture, range of motion, 40.74% (11/27) clinical experts reported a benefit (large, moderate or small), 7.41% (2/27) reported no effect and, 0% (0/27) reported observing a harm (large, moderate or small). 14 clinicians could not provide any information on this outcome.

		Reflecting on the impact on Pain, 38.46% (10/26) clinical experts reported a benefit, 7.69% (2/26) reported no effect and, 0% (0/26) reported observing a harm. 14 expert clinicians could not provide any information on this outcome. Reflecting on the impact on Neurological function, 22.22% (6/27) clinical experts reported a benefit, 14.81% (4/27) reported no effect and, 11.11% (3/27) reported observing a harm. 14 expert clinicians could not provide any information on this outcome. Reflecting on the impact on independence during daily activities, 29.63% (8/27) clinical experts reported a benefit, 14.81% (4/27) reported no effect and, 3.7% (1/27) reported observing a harm. 14 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 ○ 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). 2/4 indicated that medications for people with arm and hand spasticity or spasm was reasonable; 1/4 indicated that it varies or was sometimes reasonable; 1/4 indicated that they didn't know if it 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

	JUDGEMENT						
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 against the use of pharmacological agents (baclofen and botulinum toxin) for specific management of upper limb function in individuals with Friedreich ataxia experiencing spasticity and spasm.

Justification

This recommendation was made in the absence of any evidence for the intervention (pharmacological therapy) and clinical experience of undesirable effects associated with the use of botulinum toxin for upper limb spasticity and spasm in individuals with FRDA. Anecdotally, baclofen can have multisystem effects which have potential to compromise postural control, alertness and swallowing safety. Non-pharmacological management strategies should be used for upper limb spasticity or spasm.

Subgroup considerations

This recommendation is for individuals with Friedreich ataxia with spasticity or spasm, for management of upper limb function.

Research priorities

Evaluation of the effects of non-pharmacological interventions on upper limb spasticity and spasm in individuals with FRDA.