QUESTION

Should orthotic devices (i.e. braces, ankle-foot-orthotics) vs. no orthotic support be used for ambulant people with Friedreich ataxia?	
POPULATION:	ambulant people with Friedreich ataxia
INTERVENTION:	orthotic devices (i.e. braces, ankle-foot-orthotics)
COMPARISON:	no orthotic support
MAIN OUTCOMES:	Independence of ambulation; Balance; Falls; 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 (Rummey et al, 2020). There are significant gait pattern changes in people with FRDA, including increased double stance time, decreased swing phase as a percentage of the gait cycle, decreased speed of walking, greater step width, reduced step length (Croarkin et al, 2009; Serrao et al, 2012; Vasco et al, 2016; Stephenson et al, 2015) and increased variability (Serrao et al, 2012; Gouelle et al, 2013). In two separate studies, changes to kinematic parameters around the ankle suggest altered antagonist and agonist activity of the calf and anterior shin muscles during ambulation (Serrao et al, 2012; Vasco et al, 2016). These changes may be due to ankle spasticity, peripheral neuropathy, ataxia, and/or postural instability resulting in altered distal limb activity during gait.	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		There is currently no evidence examining the effect of orthotic

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

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with no orthotic support	Risk difference with orthotic devices (i.e. braces, ankle-foot-orthotics)
Independence of ambulation - not measured	-	-	-	-	-
Balance - not measured	-	-	-	-	-
Falls - not measured	-	-	-	-	-
Walking capacity assessed with: Walking speed	0 (4 observational studies)[1,2,3,4]	⨁◯◯◯ VERY LOW[a,b]	-	8 patients with Charcot-Marie-Tooth were fitted with custom AFOs. After at least 10 weeks, measurements of plantar- and dorsiflexor strength were obtained. Participants then walked unbraced and braced on an intrumentied walkway while being tracked with a 12-camera motion capture system. All participants had quicker walking speed (89.4±13.3 vs 115.6±18.0 cm/s) in the braced condition. There was a strong inverse relationship between braced change in walking velocity and dorsiflexor (r = 0.708) and plantarflexor (r = 0.823) strength. (Dufek et al 2014) 7 patients with Charcot-Marie-Tooth were asked to walk on a circut at self-selected speeds in two walking conditions: with shoes only or with an anterior elastic ankle-foot orthosis. Each condition lasted 5 mins and 5 mins was given for recovery between each condition. Comparisons between the 2 conditions at the self-selected speeds were completed by ANOVA for repeated measures followed by t-tests	

devices for ambulant individuals with FRDA. Studies examining orthotic devices for CMT show beneficial changes in gait; however, the neuropathology in FRDA is significantly different to that in CMT and therefore results may not be directly transferable.

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 orthotic devices (i.e. Braces, ankle-foot-orthotics) as a management strategy for ambulant individuals.

Reflecting on the impact of orthotic devices (i.e. Braces, ankle-foot-orthotics) on Independence of ambulation, 61.54% (16/26) 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). 10 clinicians could not provide any information on this outcome.

Reflecting on the impact on Balance, 50% (13/26) clinical experts reported a benefit, 11.54% (3/26) reported no effect and, 0% (0/26) reported observing a harm. 10 expert clinicians could not provide any information on this outcome.

Reflecting on the impact on Falls, 56% (14/25) clinical experts reported a benefit, 4% (1/25) reported no effect and, 0% (0/25) reported observing a harm. 10 expert clinicians could not provide any information on this outcome.

Reflecting on the impact on Walking capacity, 61.54% (16/26) clinical experts reported a benefit, 0% (0/26) reported no effect and, 0% (0/26) reported observing a harm. 10 expert clinicians could not provide any information on this outcome.

Reflecting on the impact on Quality of life, 57.7% (15/26) clinical experts reported a benefit, 3.85% (1/26) reported no effect and, 0% (0/26) reported observing a harm. 10 expert clinicians could not provide any information on this outcome.

				for repeated measures. Speed of walking at the three self-selected speeds did not differ between shoes only and anterior elastic anklefoot orthoses. (Menotti et al 2014) 15 patients with Charcot-Marie-Tooth were analysed barefoot and with prescribed AFOs using a standardised motion analysis protocol. Walking velocity improved from 95±26 to 108±21 cm/sec demonstrating the functional benefits of AFOs. (Ounpuu et al 2017) 37 patients with neuromuscular disorders were provided with dorsal leaf spring ankle foot orthosis (DLS-AFO) of which stiffness could be varied (flexible K1-stiff K5). Walking speed was higher compared to shoes-only for all AFO stiffness configurations (shoes only: 0.87 ± 0.21 m/s, smallest improvement K5: + 0.17 ± 0.17 m/s (+19.5%), largest improvement K2: + 0.21 ± 0.17 m/s (+24.1%)), with significant differences found between AFO stiffness (p = 0.013). Post-hoc analysis revealed that walking speed was significantly higher in K2 compared to K5 (+ 0.04 m/s (+ 3.7%)). (Waterval et al 2019)	
Quality of life - not measured	-	-	-	-	-

1. Dufek J.S., Neumann E.S.,Hawkins M.C.,O'Toole B.. Functional and dynamic response characteristics of a custom composite ankle foot orthosis for Charcot-Marie-Tooth patients. . Gait Posture. ; 2014.
2. Menotti F., Laudani L.,Damiani A.,Mignogna T.,Macaluso A.. An anterior ankle-foot orthosis improves walking economy in Charcot-Marie-Tooth type 1A patients. . Prosthet. Orthot. Int.; 2014.
3. Ounpuu S., Pogemiller K.,Pierz K.,Acsadi G.. Do orthoses improve gait in children and adolescents with Charcot-Marie-Tooth?. . J. Peripher. Nerv. Syst.; 2017.
4. Waterval N.F.J., Nollet F.,Harlaar J.,Brehm M.-A.. Modifying ankle foot orthosis stiffness in patients with calf muscle weakness: Gait responses on group and individual level. . J. NeuroEng. Rehabil.; 2019.

a. No participants with a diagnosis of FRDA.

b. Small sample size.

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 no orthotic support	Risk difference with orthotic devices (i.e. braces, ankle-foot-orthotics)
Independence of ambulation - not measured	-	-	-	-	-
Balance - not measured	-	-	-	-	-
Falls - not measured	-	-	-	-	-
Walking capacity assessed with: Walking speed	0 (4 observational studies)[1,2,3,4]	⨁◯◯◯ VERY LOW[a,b]	-	8 patients with Charcot-Marie-Tooth were fitted with custom AFOs. After at least 10 weeks, measurements of plantar- and dorsiflexor strength were obtained. Participants then walked unbraced and braced on an intrumentied walkway while being tracked with a 12-camera motion capture system. All participants had quicker walking speed (89.4±13.3 vs 115.6±18.0 cm/s) in the braced condition. There was a strong inverse relationship between braced change in	

ADDITIONAL CONSIDERATIONS

Not infrequent complications associated with orthotics include pressure ulcers, pain, altered gait dynamics and unnecessary restriction to ankle range of movement. These complications are most likely to occur when orthotics are incorrectly fitted or wrongly prescribed.

					walking velocity and dorsiflexor (r = 0.708) and plantarflexor (r = 0.823) strength. (Dufek et al 2014) 7 patients with Charcot-Marie-Tooth were asked to walk on a circut at self-selected speeds in two walking conditions: with shoes only or with an anterior elastic ankle-foot orthosis. Each condition lasted 5 mins and 5 mins was given for recovery between each condition. Comparisons between the 2 conditions at the self-selected speeds were completed by ANOVA for repeated measures followed by t-tests for repeated measures. Speed of walking at the three self-selected speeds did not differ between shoes only and anterior elastic anklefoot orthoses. (Menotti et al 2014) 15 patients with Charcot-Marie-Tooth were analysed barefoot and with prescribed AFOs using a standardised motion analysis protocol. Walking velocity improved from 95±26 to 108±21 cm/sec demonstrating the functional benefits of AFOs. (Ounpuu et al 2017) 37 patients with neuromuscular disorders were provided with dorsal leaf spring ankle foot orthosis (DLS-AFO) of which stiffness could be varied (flexible K1-stiff K5). Walking speed was higher compared to shoes-only for all AFO stiffness configurations (shoes only: 0.87 ± 0.21 m/s, smallest improvement K5: + 0.17 ± 0.17 m/s (+19.5%), largest improvement K2: + 0.21 ± 0.17 m/s (+24.1%)), with significant differences found between AFO stiffness (p = 0.013). Post-hoc analysis revealed that walking speed was significantly higher in K2 compared to K5 (+ 0.04 m/s (+ 3.7%)). (Waterval et al 2019)	
Quality of life - not measured	-	-	-	-	-	

	1. Dufek J.S., Neumann E.S.,Hawkins M.C.,O'Toole B.. Functional and dynamic response characteristics of a custom composite ankle foot orthosis for Charcot-Marie-Tooth patients. . Gait Posture. ; 2014. 2. Menotti F., Laudani L.,Damiani A.,Mignogna T.,Macaluso A.. An anterior ankle-foot orthosis improves walking economy in Charcot-Marie-Tooth type 1A patients. . Prosthet. Orthot. Int.; 2014. 3. Ounpuu S., Pogemiller K.,Pierz K.,Acsadi G.. Do orthoses improve gait in children and adolescents with Charcot-Marie-Tooth?. . J. Peripher. Nerv. Syst.; 2017. 4. Waterval N.F.J., Nollet F.,Harlaar J.,Brehm M.-A.. Modifying ankle foot orthosis stiffness in patients with calf muscle weakness: Gait responses on group and individual level. . J. NeuroEng. Rehabil.; 2019. a. No participants with a diagnosis of FRDA. b. Small sample size.	

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	There is low certainty of the evidence of effects 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 - not measured	IMPORTANT[a]	-
Balance - not measured	IMPORTANT[b]	-
Falls - not measured	CRITICAL[c]	-
Walking capacity assessed with: Walking speed	IMPORTANT[d]	⨁◯◯◯ VERY LOW[e,f]
Quality of life - not measured	CRITICAL[g]	-

a. Identified as critical (1/6), important (3/6) and low importance (2/6) by people with FA and critical by expert authors on this topic
b. Identified as critical (2/5) and important (3/5) by people with FA and important by expert authors on this topic.
c. Identified as critical (3/5) and important (2/5) by people with FA and important by expert authors on this topic.
d. Identified as critical (2/6), important (3/6) and low importance (1/6) by people with FA and important by expert authors on this topic.
e. No participants with a diagnosis of FRDA.
f. Small sample size.
g. Identified as critical (3/6) and 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		In clinical practice, the following strategies are more likely to avoid complications and provide greater benefit: - trialling different orthotics (including different orthotic materials) - customised fitting - prescription, design and fabrication by experienced clinicians, including both orthotist and physiotherapist to review fit and impact on mobility.

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). 3/4 indicated orthotic devices for people who are walking are reasonable, 1/4 indicated they varied or were sometimes reasonable. (Aug 2020). Cost of customised orthotics can be prohibitive in some circumstances.

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	Does not favor either	**Probably favors the**	Favors the intervention	Varies	Don't know

	JUDGEMENT						
		comparison	the intervention or the comparison	**intervention**			
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

In individuals with Friedreich ataxia who are ambulant, we suggest customised orthotics (including lateral ankle support braces, ankle-foot-orthotics) over no orthotic devices when ankle joint kinematics are altered during gait and this has a significant impact on the independence, safety and ease of walking. It is important that orthotics are customised and fitted professionally to avoid complications, such as pressure ulcers and incorrectly altered ankle range of motion.

Justification

Although there is no published evidence examining the effect of orthotics on gait and independence of ambulation, expert-based clinical observations indicate benefits for individuals with FRDA.

Subgroup considerations

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

Research priorities

Future research should examine the effectiveness of orthotic prescription on ambulant individuals with FRDA. Further exploration of the perspectives and experiences of individuals with FRDA would support clinicians in the decision-making around orthotic prescription.

References

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