

QUESTION

Should systemic pharmacotherapy (non-licenced: cannabis, other) vs. no intervention be used for people with spasticity and spasms/cramps with Friedreich ataxia?

POPULATION:	people with spasticity and spasms/cramps with Friedreich ataxia
INTERVENTION:	systemic pharmacotherapy (non-licenced: cannabis, other)
COMPARISON:	no intervention
MAIN OUTCOMES:	Mobility related to spasticity ; Frequency and severity of spasms; Frequency and severity of spasms; Pain; Pain; Frequency and severity of cramps; Severity of spasticity; Severity of spasticity; Upper limb function;

ASSESSMENT

Problem

Is the problem a priority?



JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> No <input type="radio"/> Probably no <input type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>Data from the FA Clinical Outcome Measures (FA-COMS) registry found in individuals still ambulating, 68.2% (230/337) adults and 55.9% (157/281) children reported leg spasms (Lynch, 2017). The prevalence of spasms was higher for individuals not ambulating, with 80.0% (340/425) of adults and 57.1% (44/77) of children reporting leg spasms. In adults still ambulating, 55.1% (207/376) had pes cavus, while 61.4% (183/298) of children had pes cavus. In individuals no longer ambulating, 67.6% (288/426) of adults and 73.3% (55/75) of children had pes cavus.</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of the topic.</p> <p>1/7 indicated spasticity and spasms were probably not serious, 2/7 indicated probably serious, 4/7 indicated serious.</p> <p>3/7 indicated spasticity and spasms were probably not urgent, 2/7 indicated probably urgent, 2/7 indicated urgent.</p> <p>1/7 indicated spasticity and spasms were not a priority, 2/7 indicated probably not a priority, 1/7 indicated probably a priority, 3/7 indicated priority. (Aug 2020).</p>



Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS										
<ul style="list-style-type: none"> <input type="radio"/> Trivial <input type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input checked="" type="radio"/> Don't know 	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 15%;">Outcomes</th> <th style="width: 15%;">No of</th> <th style="width: 15%;">Certainty of</th> <th style="width: 15%;">Relative</th> <th style="width: 40%;">Anticipated absolute effects* (95% CI)</th> </tr> </thead> <tbody> <tr> <td> </td> <td> </td> <td> </td> <td> </td> <td> </td> </tr> </tbody> </table>	Outcomes	No of	Certainty of	Relative	Anticipated absolute effects* (95% CI)						<p>Clinical experts report efficacy in individuals who have been resistant to other treatments. Reduction in anxiety and improvement in sleep.</p>
Outcomes	No of	Certainty of	Relative	Anticipated absolute effects* (95% CI)								

	participants (studies) Follow-up	the evidence (GRADE)	effect (95% CI)	Risk with no intervention	Risk difference with systemic pharmacotherapy (non-licensed: cannabis, other)
Mobility related to spasticity assessed with: timed 10-metre walk	241 (1 RCT) ¹	⊕⊕○○ Low ^{a,b,c}	-	241 people with multiple sclerosis were part of a post hoc analysis of a clinical trial of THC:CBD oromucosal spray vs placebo to treat spasticity. Group 1 included patients with >=1 failed therapy attempt with baclofen or tizanidine (n=162). Group 2 included patients with >=2 failed therapy attempts with both baclofen and tizanidine (n=57). There were no differences in the timed 10-metre walk time between THC:CBD spray vs placebo for any of the groups. (Haupts et al 2016).	
Frequency and severity of spasms assessed with: Numeric Rating Scale	241 (1 RCT) ¹	⊕⊕○○ Low ^{a,b,c}	-	241 people (intention to treat analysis) with multiple sclerosis were part of a post hoc analysis of a clinical trial of THC:CBD oromucosal spray vs placebo to treat spasticity. Group 1 included patients with >=1 failed therapy attempt with baclofen or tizanidine (n=162). Group 2 included patients with >=2 failed therapy attempts with both baclofen and tizanidine (n=57). In all groups, response on the NRS for spasticity was significantly greater with patients receiving the THC:CBD spray vs placebo (minimal clinically important difference (MCID) ≥18% improvement vs baseline, and clinically important difference (CID) ≥30% improvement vs baseline). (Haupts et al 2016). A 54-year old man with multiple sclerosis and severe lower limb spasticity was started on treatment with nabiximols (a cannabinoid compound consisting of THC and CBD in a 1:1 ratio). Before the procedure, he reported a spasticity NRS score of 8/10. After 1 month of therapy, he reported a spasticity NRS score of 6/10. (Gajofatto 2016).	
Frequency and severity of	433 (1 observational)	⊕○○○ Very low ^{a,d}	-	433 participants with multiple sclerosis prescribed add on THC:CBD oromucosal spray were followed for 3 months. After 1	

spasms assessed with: Spasm counts per day	study) ²			month, only responders (FAS group, n=349) ($\geq 20\%$ improvement in spasticity) continued treatment. 281 patients continued treatment after 3 months (CAS group). Data was collected at V0 (baseline), V1 (end of trial period, 1 month after enrolment, V3 (study completion, 3 months after enrolment). Spasms count per day in the CAS group decreased from mean of 7 (SD 10.6) at baseline to 4.9 (SD 7.2) after 3 months' treatment ($p < 0.001$). (Vermesch et al 2018)
Pain assessed with: Numerical Rating Scale	434 (2 observational studies) ^{2,3}	 Very low ^{a,d,e}	-	433 participants with multiple sclerosis prescribed add on THC:CBD oromucosal spray were followed for 3 months. After 1 month, only responders (FAS group, n=349) ($\geq 20\%$ improvement in spasticity) continued treatment. 281 patients continued treatment after 3 months (CAS group). Data was collected at V0 (baseline), V1 (end of trial period, 1 month after enrolment, V3 (study completion, 3 months after enrolment). Mean pain NRS score in CAS group decreased from mean of 5.0 (SD 3.3) at baseline to 3.8 (SD 2.8) after 3 months' treatment ($p < 0.001$). (Vermesch et al 2018) A 54-year old man with multiple sclerosis and severe lowe limb spasticity was started on treatment with nabiximols (a cannabinoid compound consisting of THC and CBD in a 1:1 ratio). Before the procedure, he reported a pain NRS score of 4/10. After 1 month of therapy, he reported a pain NRS score of 0/10. (Gajofatto 2016).
Pain assessed with: SF-36	241 (1 RCT) ¹	 Low ^{a,b,c}	-	241 people with multiple sclerosis were part of a post hoc analysis of a clinical trial of THC:CBD oromucosal spray vs placebo to treat spasticity. Group 1 included patients with ≥ 1 failed therapy attempt with baclofen or tizanidine (n=162). Group 2 included patients with ≥ 2 failed therapy attempts with both baclofen and tizanidine (n=57). There was a significantly greater mean difference in favour of the THC:CBD group for the SF-36 domain of bodily pain ($p = 0.035$) in Group 1. (Haupts et al 2016).

Frequency and severity of cramps - not measured	-	-	-	-	-
Severity of spasticity assessed with: Modified Ashworth Scale	674 (2 RCTs) ^{1,2}	 Low ^{a,f}	-	<p>241 people with multiple sclerosis were part of a post hoc analysis of a clinical trial of THC:CBD oromucosal spray vs placebo to treat spasticity. Group 1 included patients with >=1 failed therapy attempt with baclofen or tizanidine (n=162). Group 2 included patients with >=2 failed therapy attempts with both baclofen and tizanidine (n=57). There were no differences in MAS score in any of the groups. (Haupts et al 2016). 433 participants with multiple sclerosis prescribed add on THC:CBD oromucosal spray were followed from 3 months. After 1 month only responders (FAS group, n=349) (≥20% improvement in spasticity) continued treatment. 281 patients continued treatment after 3 months (CAS group). Data was collected at V0 (baseline), V1 (end of trial period, 1 month after enrolment), V3 (study completion, 3 months after enrolment). At V1, the mean MAS score in all groups had decreased to 2.3, 2.2, and 2.4 compared to V0 (p<0.0001). At V3, mean MAS for FAS total patients and initial responders had also improved to 2.3 compared to baseline (p < 0.0001). (Vermesch et al 2018)</p>	
Severity of spasticity assessed with: Numeric Rating Scale	840 (3 observational studies) ^{1,2,4}	 Very low ^{a,g,h}	-	<p>241 people with multiple sclerosis were part of a post hoc analysis of a clinical trial of THC:CBD oromucosal spray vs placebo to treat spasticity. Group 1 included patients with >=1 failed therapy attempt with baclofen or tizanidine (n=162). Group 2 included patients with >=2 failed therapy attempts with both baclofen and tizanidine (n=57). There were significant differences in spasticity NRS score in the ITT group (p<0.001) and Group 1 (p=0.002). (Haupts et al 2016). 433 participants with multiple sclerosis prescribed add on THC:CBD</p>	

				<p>oromucosal spray were followed from 3 months. After 1 month only responders (FAS group, n=349) ($\geq 20\%$ improvement in spasticity) continued treatment. 281 patients continued treatment after 3 months (CAS group). Data was collected at V0 (baseline), V1 (end of trial period, 1 month after enrolment), V3 (study completion, 3 months after enrolment). There were significant difference in mean spasticity NRS score in the FAS (from mean 6.9 (SD 1.9) to mean 5.4 (SD 1.8), $p < 0.001$) and CAS groups (mean 6.9 (SD 1.9) to 5.32 (SD 1.8), $p < 0.0001$). (Vermesch et al 2018)</p> <p>166 patients with multiple sclerosis were treated with THC:CBD spray over a 15-month timeframe. 120 patients continued on therapy. The mean spasticity NRS score in responders was 7.0 (range 4-10) before treatment and 3.0 (range 0-6) within the first 10 days of treatment. (Koehler et al 2014).</p>	
Upper limb function - not measured	-	-	-	-	-
<ol style="list-style-type: none"> 1. Haupts M, Vila C, Jonas A, Witte K, Alvarez-Ossorio L. Influence of Previous Failed Antispasticity Therapy on the Efficacy and Tolerability of THC:CBD Oromucosal Spray for Multiple Sclerosis Spasticity. <i>European Neurology</i>; 2016. 2. Vermersch P, Trojano M.. Tetrahydrocannabinol:Cannabidiol Oromucosal Spray for Multiple Sclerosis-Related Resistant Spasticity in Daily Practice.. <i>European Neurology</i>; 2016. 3. A, Gajofatto. Refractory trigeminal neuralgia responsive to nabiximols in a patient with multiple sclerosis. <i>Multiple Sclerosis and Related Disorders</i>; 2016. 4. Koehler J., Feneberg W., Meier M., Pollmann W. Clinical experience with THC:CBD oromucosal spray in patients with multiple sclerosis-related spasticity. <i>International Journal of Neuroscience</i>; 2014. <ol style="list-style-type: none"> a. All participants with multiple sclerosis (none with FRDA). b. Allocation concealment not reported. c. Significant differences in disability at baseline between control and intervention group. d. Confidence intervals not reported. e. One study case study (n=1). f. One observational study, for the RCT allocation concealment not reported 					



and significant differences in disability at baseline between the control and intervention group.



g. Confidence intervals not reported in two studies.

h. Two observational studies, for the RCT (n=241) allocation concealment not reported and significant differences in disability at baseline between the control and intervention group. Eligibility criteria not selective and short follow up period in one observational study (n=166).

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE					ADDITIONAL CONSIDERATIONS	
<ul style="list-style-type: none"> ○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know 	Outcomes	No of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	Clinical experience has identified patients reporting deteriorating function and mobility with self-prescribed administration.	
Risk with no intervention	Risk difference with systemic pharmacotherapy (non-licenced: cannabis, other)						
Mobility related to spasticity assessed with: timed 10-metre walk	241 (1 RCT) ¹	 Low ^{a,b,c}	-	241 people with multiple sclerosis were part of a post hoc analysis of a clinical trial of THC:CBD oromucosal spray vs placebo to treat spasticity. Group 1 included patients with >=1 failed therapy attempt with baclofen or tizanidine (n=162). Group 2 included patients with >=2 failed therapy attempts with both baclofen and tizanidine (n=57). There were no differences in the timed 10-metre walk time between THC:CBD spray vs placebo for any of the groups. (Haupts et al 2016).			
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Upper limb function - not	-	-	-	-

	<table border="1" data-bbox="520 110 1417 180"> <tr> <td data-bbox="520 110 638 180">measured</td> <td data-bbox="638 110 779 180"></td> <td data-bbox="779 110 919 180"></td> <td data-bbox="919 110 1060 180"></td> <td data-bbox="1060 110 1201 180"></td> <td data-bbox="1201 110 1417 180"></td> </tr> </table> <ol style="list-style-type: none"> 1. Haupts M, Vila C, Jonas A, Witte K, Alvarez-Ossorio L. Influence of Previous Failed Antispasticity Therapy on the Efficacy and Tolerability of THC:CBD Oromucosal Spray for Multiple Sclerosis Spasticity. <i>European Neurology</i>; 2016. 2. Vermersch P, Trojano M.. Tetrahydrocannabinol:Cannabidiol Oromucosal Spray for Multiple Sclerosis-Related Resistant Spasticity in Daily Practice.. <i>European Neurology</i>; 2016. 3. A, Gajofatto. Refractory trigeminal neuralgia responsive to nabiximols in a patient with multiple sclerosis. <i>Multiple Sclerosis and Related Disorders</i>; 2016. 4. Koehler J., Feneberg W., Meier M., Pollmann W. Clinical experience with THC:CBD oromucosal spray in patients with multiple sclerosis-related spasticity. <i>International Journal of Neuroscience</i>; 2014. <ol style="list-style-type: none"> a. All participants with multiple sclerosis (none with FRDA). b. Allocation concealment not reported. c. Significant differences in disability at baseline between control and intervention group. d. Confidence intervals not reported. e. One study case study (n=1). f. One observational study, for the RCT allocation concealment not reported and significant differences in disability at baseline between the control and intervention group. g. Confidence intervals not reported in two studies. h. Two observational studies, for the RCT (n=241) allocation concealment not reported and significant differences in disability at baseline between the control and intervention group. Eligibility criteria not selective and short follow up period in one observational study (n=166). 	measured						
measured								

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
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<ul style="list-style-type: none"> ● Very low ○ Low ○ Moderate ○ High ○ No included studies 	<p>Low to very low certainty of evidence as per the evidence profile table.</p>	
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Values
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS																								
<ul style="list-style-type: none"> ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ● No important uncertainty or variability 	<table border="1"> <thead> <tr> <th data-bbox="506 662 1016 743">Outcomes</th> <th data-bbox="1016 662 1167 743">Importance</th> <th data-bbox="1167 662 1430 743">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td data-bbox="506 743 1016 850"> <p>Mobility related to spasticity assessed with: timed 10-metre walk</p> </td> <td data-bbox="1016 743 1167 850"> <p>IMPORTANT^a</p> </td> <td data-bbox="1167 743 1430 850"> <p>⊕⊕○○ LOW^{b,c,d}</p> </td> </tr> <tr> <td data-bbox="506 850 1016 958"> <p>Frequency and severity of spasms assessed with: Numeric Rating Scale</p> </td> <td data-bbox="1016 850 1167 958"> <p>IMPORTANT^e</p> </td> <td data-bbox="1167 850 1430 958"> <p>⊕⊕○○ LOW^{b,c,d}</p> </td> </tr> <tr> <td data-bbox="506 958 1016 1065"> <p>Frequency and severity of spasms assessed with: Spasm counts per day</p> </td> <td data-bbox="1016 958 1167 1065"> <p>IMPORTANT^e</p> </td> <td data-bbox="1167 958 1430 1065"> <p>⊕○○○ VERY LOW^{b,f}</p> </td> </tr> <tr> <td data-bbox="506 1065 1016 1172"> <p>Pain assessed with: Numerical Rating Scale</p> </td> <td data-bbox="1016 1065 1167 1172"> <p>IMPORTANT^g</p> </td> <td data-bbox="1167 1065 1430 1172"> <p>⊕○○○ VERY LOW^{b,f,h}</p> </td> </tr> <tr> <td data-bbox="506 1172 1016 1279"> <p>Pain assessed with: SF-36</p> </td> <td data-bbox="1016 1172 1167 1279"> <p>IMPORTANT^g</p> </td> <td data-bbox="1167 1172 1430 1279"> <p>⊕⊕○○ LOW^{b,c,d}</p> </td> </tr> <tr> <td data-bbox="506 1279 1016 1349"> <p>Frequency and severity of cramps - not measured</p> </td> <td data-bbox="1016 1279 1167 1349"> <p>IMPORTANTⁱ</p> </td> <td data-bbox="1167 1279 1430 1349"> <p>-</p> </td> </tr> <tr> <td data-bbox="506 1349 1016 1456"> <p>Severity of spasticity assessed with: Modified Ashworth Scale</p> </td> <td data-bbox="1016 1349 1167 1456"> <p>CRITICAL^j</p> </td> <td data-bbox="1167 1349 1430 1456"> <p>⊕⊕○○ LOW^{b,k}</p> </td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	<p>Mobility related to spasticity assessed with: timed 10-metre walk</p>	<p>IMPORTANT^a</p>	<p>⊕⊕○○ LOW^{b,c,d}</p>	<p>Frequency and severity of spasms assessed with: Numeric Rating Scale</p>	<p>IMPORTANT^e</p>	<p>⊕⊕○○ LOW^{b,c,d}</p>	<p>Frequency and severity of spasms assessed with: Spasm counts per day</p>	<p>IMPORTANT^e</p>	<p>⊕○○○ VERY LOW^{b,f}</p>	<p>Pain assessed with: Numerical Rating Scale</p>	<p>IMPORTANT^g</p>	<p>⊕○○○ VERY LOW^{b,f,h}</p>	<p>Pain assessed with: SF-36</p>	<p>IMPORTANT^g</p>	<p>⊕⊕○○ LOW^{b,c,d}</p>	<p>Frequency and severity of cramps - not measured</p>	<p>IMPORTANTⁱ</p>	<p>-</p>	<p>Severity of spasticity assessed with: Modified Ashworth Scale</p>	<p>CRITICAL^j</p>	<p>⊕⊕○○ LOW^{b,k}</p>	
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Severity of spasticity assessed with: Numeric Rating Scale	CRITICAL ^l	⊕○○○ VERY LOW ^{b,l,m}
Upper limb function - not measured	CRITICAL ⁿ	-

- a. Identified as important (5/6) and low importance (1/6) by people with FA and critical by expert authors on this topic
- b. All participants with multiple sclerosis (none with FRDA).
- c. Allocation concealment not reported.
- d. Significant differences in disability at baseline between control and intervention group.
- e. Identified as critical (2/6), important (3/6) and low importance (1/6) by people with FA and critical by expert authors on this topic
- f. Confidence intervals not reported.
- g. Identified as critical (2/6), important (2/6) and low importance (2/6) by people with FA and critical by expert authors on this topic
- h. One study case study (n=1).
- i. Identified as critical (1/6) and important (5/6) by people with FA and critical by expert authors on this topic
- j. Identified as critical (3/6), important (2/6) and low importance (1/6) by people with FA and important by expert authors on this topic
- k. One observational study, for the RCT allocation concealment not reported and significant differences in disability at baseline between the control and intervention group.
- l. Confidence intervals not reported in two studies.
- m. Two observational studies, for the RCT (n=241) allocation concealment not reported and significant differences in disability at baseline between the control and intervention group. Eligibility criteria not selective and short follow up period in one observational study (n=166).
- n. 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

<ul style="list-style-type: none"> ○ 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 		<p>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 Systemic pharmacotherapy (non-licensed: Cannabis, other) as a management strategy for People with spasticity and spasms/cramps.</p> <p>Reflecting on the impact of Systemic pharmacotherapy (non-licensed: Cannabis, other) on Mobility related to spasticity, 26.92% (7/26) clinical experts reported a benefit (large, moderate or small), 0% (0/26) reported no effect and, 3.85% (1/26) reported observing a harm (large, moderate or small). 18 clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on Frequency & severity of spasms, 26.92% (7/26) clinical experts reported a benefit, 3.85% (1/26) reported no effect and, 3.85% (1/26) reported observing a harm. 17 expert clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on Pain, 34.61% (9/26) clinical experts reported a benefit, 0% (0/26) reported no effect and, 0% (0/26) reported observing a harm. 17 expert clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on Frequency & severity of cramps, 26.92% (7/26) clinical experts reported a benefit, 3.85% (1/26) reported no effect and, 3.85% (1/26) reported observing a harm. 17 expert clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on Severity of spasticity, 26.93% (7/26) clinical experts reported a benefit, 0% (0/26) reported no effect and, 3.85% (1/26) reported observing a harm. 18 expert clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on UL function, 7.69% (2/26) clinical experts reported a benefit, 19.23% (5/26) reported no effect and, 3.85% (1/26) reported observing a harm. 18 expert clinicians could not provide any information on this outcome.</p>
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Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ● Probably no ○ Probably yes 	<p>Data from all individuals with FRDA (with and without spasm/cramps) in the FA Clinical Outcome Measures (FA-COMS) registry found 3.3% (28/847) adults and 0.2% (1/454) children had used tetrahydrocannabinol/cannabis/marijuana. Magnesium supplements were used by 11.7% (99/847)</p>	<p>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</p>

<ul style="list-style-type: none"> <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>adults and 2.6% (12/454) children. The data did not discern the primary reason for prescription. https://clinicaltrials.gov/ct2/show/NCT03090789</p>	<p>and costs). 2/4 indicated systemic non-licensed oral medications were not reasonable, 1/4 indicated probably reasonable, 1/4 indicated reasonable. (Aug 2020).</p>
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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

<p>Strong recommendation against the intervention</p> <p><input type="radio"/></p>	<p>Conditional recommendation against the intervention</p> <p><input type="radio"/></p>	<p>Conditional recommendation for either the intervention or the comparison</p> <p><input checked="" type="radio"/></p>	<p>Conditional recommendation for the intervention</p> <p><input type="radio"/></p>	<p>Strong recommendation for the intervention</p> <p><input type="radio"/></p>
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CONCLUSIONS

Recommendation

We cannot recommend either the use or non-use of systemic pharmacotherapy (non-licensed: cannabis, other) to manage spasticity and spasms/cramps in people with Friedreich ataxia.

Justification

There is no published evidence related to the use or non-use of non-licensed systemic pharmacotherapy for individuals with FRDA. The clinical experience of the authors indicated patients reported deteriorating function and mobility with self-prescribed administration. Conversely, anecdotal information relayed to the expert authors report efficacy in individuals who have been resistant to other treatments, with associated reduction in anxiety and improvement in sleep.

Subgroup considerations

Although there is no conclusive evidence, clinical experience suggests this intervention may be more beneficial for individuals with treatment-resistant troubling spasticity and spasm.

Research priorities

There is a requirement to undertake future research evaluating the effect of non-licensed systemic pharmacotherapy on spasticity in individuals with FRDA.