

	participants (studies) Follow-up	the evidence (GRADE)	effect (95% CI)	Risk with no activity programme (exercise such as aerobic exercise, strengthening exercise, yoga, tai chi, dancing)	Risk difference with physical activity programme (exercise such as aerobic exercise, strengthening exercise, yoga, tai chi, dancing)
Reported fatigue assessed with: BORG	1 (1 observational study) ¹	⊕○○○ Very low ^a	-	A 17 year old male with Friedreich ataxia underwent a physiotherapy programme, 3 sessions per week for 6 weeks. Fatigue during resting decreased from 4 to 3 and fatigue during movement decreased from 5 to 4 on the Borg Scale. (Kaplan et al 2015).	
Reported fatigue assessed with: Rhoten Fatigue Scale	61 (1 RCT) ²	⊕○○○ Very low ^{b,c,d}	-	61 people with multiple sclerosis were randomly assigned to 3 groups of yoga (n=20), aerobics (n=20) or control (n=21). The exercise programmes were performed as 3 sessions per week for 12 weeks. Paired t-test determined a significant decrease in fatigue severity in the yoga ($p<0.05$) and exercise ($p<0.05$) groups but not in the control group. (Hasanpour Dehkordi 2016).	
Reported fatigue assessed with: Modified Fatigue Impact Scale	140 (2 RCTs) ^{3,4}	⊕⊕○○ Moderate ^b	-	120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. All dimensions of fatigue were significantly improved in the exercise group in comparison with usual care at 3 months ($p<0.0001$), with the change in total fatigue scores being positively correlated with baseline levels. The improvements in fatigue were not maintained at 9 months. (Carter et al 2014). 20 people with multiple sclerosis were randomised to 2 groups A or B in a 16 week crossover study: participants either received 20 sessions of upper limb	

				<p>aerobic training and task oriented exercises and then an 8 week rest period or vice versa. Group A received sessions first. There was a statistically significant treatment effect in the MFIS ($p=0.05$) without any carryover effect. MFIS was lower after treatment compared to the waiting list. The combined differences for Groups A and B between WL-T periods for MFIS was [median and interquartile range (Q1-Q3)] 5.2 (10.7) points. Fatigue was present in our sample with a median MFIS baseline score of 32 out of 84 points. At the end of the treatment, there was a median reduction of 5 points, in 70% in the treatment period and 30% in the waiting list period showing reduced fatigue after rehabilitation. In addition, 66% in the treatment period and 10% in the waiting list period showed a 10-point reduction in MFIS, which is the cut-off score that defines a clinically relevant improvement. (Gervasoni et al 2019).</p>
Reported fatigue assessed with: Fatigue Intensity Test	59 (1 RCT) ⁵	⊕○○○ Very low ^{b,c,e,f}	-	<p>59 people with multiple sclerosis were randomised to an intervention (n=39) or control (n=20) group. The intervention group received 10 weeks of combination therapy. Assessments were conducted 1 week before the intervention, 1 week after the 10 weeks of intervention and 1 year after the intervention. The intervention group reported a significant decrease in the scores in the second ($p = 0.02$) and third timepoints ($p = 0.04$) compared to the baseline. There were no significant changes in fatigue scores in the control group. The degree of change in the second timepoint compared to the first timepoint was significant in the intervention group when compared with the control ($p = 0.02$). (Sangelaji et al 2014)</p>
Reported fatigue assessed with:	38 (1 RCT) ⁶	⊕○○○ Very low ^{b,f,g,h}	-	<p>38 people with multiple sclerosis were randomly allocated to 3 groups: mat nilates, reformer nilates and control. The</p>

Fatigue Severity Scale				<p>pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. There was a significant decrease in the FSS score in both mat ($p=0.034$) and reformer ($p=0.008$) Pilates groups. There was no significant change in the control group. (Bulguroglu et al 2017)</p>
Reported fatigue assessed with: Motor Fatigability Index	20 (1 RCT) ⁴	 Very low ^{b,g,i}	-	<p>20 people with multiple sclerosis were randomised to 2 groups A or B in a 16 week crossover study: participants either received 20 sessions of aerobic training and task oriented exercises and then an 8 week rest period or vice versa. Group A received sessions first. The MFI showed a statistically significant treatment effect ($p = 0.05$) with no carryover effect ($p = 0.23$). The between-period differences (waiting list-treatment) for the MFI was -0.007 (<0.001) Hz/s meaning a reduction in motor fatigue index after treatment ($p=0.05$). (Gervasoni et al 2019).</p>
Reported fatigue assessed with: Fatigue Scale of Motor and Cognitive Functions	32 (1 observational study) ⁷	 Very low ^{b,g,i,k}	-	<p>32 people with multiple sclerosis were allocated to a Tai Chi group (2x weekly sessions of 90mins for 6 months), or treatment as usual TAU group. Assessments were conducted prior to and following the 6-month interval. For Fatigue, a significant Time by Group interaction [$F(1,25) = 7.83, p = 0.01, \text{partial } \eta^2 = 0.24$] and a significant main effect of Group emerged [$F(1,25) = 5.91, p < 0.05, \text{partial } \eta^2 = 0.19$]. Post-hoc comparisons indicated a significant increase in fatigue scores in the TAU group from pre to post assessments. Scores in the Tai Chi group remained relatively stable. At pre-treatment assessments the groups did not differ</p>

				significantly in fatigue. In contrast, fatigue differed following the six-months interval. (Burschka et al 2014)
Improved quality of life assessed with: SF-36	61 (1 RCT) ²	⊕○○○ Very low ^{b,c,d}	-	61 people with multiple sclerosis were randomly assigned to 3 groups of yoga (n=20), aerobics (n=20) or control (n=21). The exercise programmes were performed as 3 sessions per week for 12 weeks. ANOVA was used to compare the dimensions of the SF-36 scale in each group. After the 12 weeks, components of the SF-36 improved significantly in the yoga group. (Hasanpour Dehkordi 2016).
Improved quality of life assessed with: MSQoL-54	179 (2 RCTs) ^{3,5}	⊕⊕⊕○ Moderate ^b	-	<p>120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. Positive changes in many quality of life domains in favour of the exercise group were also observed at 3 months, with improvements in emotional wellbeing ($p = 0.01$), social function ($p = 0.004$) and overall quality of life ($p = 0.001$) being maintained for 9 months. (Carter et al 2014)</p> <p>59 people with multiple sclerosis were randomised to an intervention (n=39) or control (n=20) group. The intervention group received 10 weeks of combination therapy. Assessments were conducted 1 week before the intervention, 1 week after the 10 weeks of intervention and 1 year after the intervention. For mental QOL, the intervention group reported significant changes at the second time point compared to the first or third timepoints. There was significant change in the intervention group between the first and second timepoints compared to the control group ($p = 0.001$) as well as between for the third and first timepoint ($p=0.02$). For physical QOL, the intervention group also reported</p>

				significant changes at the second time point compared to the first timepoint ($p=0.001$). After 9 months however, values returned to baseline. Comparison of changes between the two groups also indicated that the values of second time point compared to the first and the third timepoint compared to the first had significant changes ($p < 0.05$). (Sangelaji et al 2014)
Improved quality of life assessed with: Questionnaire of Life Satisfaction	32 (1 observational study) ⁷	⊕○○○ Very low ^{b,d,i,k}	-	32 people with multiple sclerosis were allocated to a Tai Chi group (2x weekly sessions of 90mins for 6 months), or treatment as usual TAU group. Assessments were conducted prior to and following the 6-month interval. In case of life satisfaction, a significant Time by Group interaction [$F(1,24) = 8.64, p < 0.01, \text{partial } \eta^2 = 0.27$] and a significant main effect Group emerged [$F(1,24) = 8.64, p < 0.01, \text{partial } \eta^2 = 0.19$]. Post-hoc comparisons indicated a significant rise in the life-satisfaction score in the Tai Chi group relative to the TAU group. At pretreatment assessments the groups did not differ significantly in life satisfaction. In contrast, life satisfaction differed following the six-months interval. (Burschka et al 2014)
Improved quality of life assessed with: Turkish version of the MSQOL-54	38 (1 RCT) ⁵	⊕○○○ Very low ^{b,f,g,h}	-	38 people with multiple sclerosis were randomly allocated to 3 groups: mat pilates, reformer pilates and control. The pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. In the MSQOL, there were statistically significant improvements in the Mat (mental $p=0.006$, physical $p=0.005$), Reformer (mental $p=0.002$, physical

				$p=0.002$) Pilates and control groups (physical $p=0.023$). (Bulguroglu et al 2017)
Improved energy levels assessed with: SF-36	61 (1 RCT) ²	⊕○○○ Very low ^{b,c,d}	-	61 people with multiple sclerosis were randomly assigned to 3 groups of yoga (n=20), aerobics (n=20) or control (n=21). The exercise programmes were performed as 3 sessions per week for 12 weeks. ANOVA was used to compare the dimensions of the SF-36 scale in each group. After the 12 weeks, the component measuring energy improved significantly in the yoga group. (Hasanpour Dehkordi 2016).
Improved physical capacity assessed with: SF-36	61 (1 RCT) ²	⊕○○○ Very low ^{b,c,d}	-	61 people with multiple sclerosis were randomly assigned to 3 groups of yoga (n=20), aerobics (n=20) or control (n=21). The exercise programmes were performed as 3 sessions per week for 12 weeks. ANOVA was used to compare the dimensions of the SF-36 scale in each group. After the 12 weeks, the component measuring physical performance and limited activity following physical problems improved significantly in the yoga group. (Hasanpour Dehkordi 2016).
Improved physical capacity assessed with: Godin Leisure Time Exercise Questionnaire	120 (1 RCT) ³	⊕⊕⊕○ Moderate ^b	-	120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. An increase in GLTEQ was observed in the exercise group versus usual care at 3 months ($p = 0.01$). The improvement in GLTEQ was accompanied by increases in daily step counts at 3 months ($p = 0.009$) in the exercise group versus usual care, but at 9 months daily step counts were similar to baseline levels. (Carter et al 2014)

Improved physical capacity assessed with: Multiple Sclerosis Functional Composite	120 (1 RCT) ³	⊕⊕⊕○ Moderate ^b	-	120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. The exercise intervention had no effect on the MSFC. (Carter et al 2014)
Improved physical capacity assessed with: Six minute walk test	179 (2 RCTs) ^{3,5}	⊕⊕⊕○ Moderate ^b	-	<p>120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. The exercise intervention had no effect on the 6MWT. (Carter et al 2014)</p> <p>59 people with multiple sclerosis were randomised to an intervention (n=39) or control (n=20) group. The intervention group received 10 weeks of combination therapy. Assessments were conducted 1 week before the intervention, 1 week after the 10 weeks of intervention and 1 year after the intervention. There were significant differences in the 6MWT in the first and second timepoints and in the second and third timepoints in the intervention group ($p < 0.0001$). The changes were also statistically significant in control group in the first and third timepoints and in the second and third timepoints ($p < 0.0001$). The comparison of changes in the two groups indicated that changes were significant when comparing the first with the second timepoints ($p < 0.0001$) and the first and the third timepoints ($p = 0.001$). (Sangelaji et al 2014)</p>
Improved physical capacity assessed with: Berg balance test	59 (1 RCT) ⁵	⊕○○○ Very low ^{b,c,e,f}	-	59 people with multiple sclerosis were randomised to an intervention (n=39) or control (n=20) group. The intervention group received 10 weeks of combination therapy. Assessments were conducted 1 week before the intervention, 1 week after the 10 weeks of intervention and 1

				<p>year after the intervention. In the intervention group, the Berg increased from 49.02 to 51.7 from the first and second timepoint. The score decreased to 48.63 at the third timepoint. The significance of changes between the two groups was also statistically tested. There was a significant change in the second timepoint compared to the first in the intervention group when compared to control ($p < 0.0001$). Changes in the third timepoint were also significantly different from the first ($p = 0.03$). (Sangelaji et al 2014)</p>
Improved physical capacity assessed with: Single leg stance	38 (1 RCT) ⁵	⊕○○○ Very low ^{b,f,g,h}	-	<p>38 people with multiple sclerosis were randomly allocated to 3 groups: mat pilates, reformer pilates and control. The pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. There was improvement in the single leg stance before and after intervention in both pilates groups ($p < 0.05$). There was no significant change in the control group. (Bulguroglu et al 2017).</p>
Improved physical capacity assessed with: Timed Up and Go Test	38 (1 RCT) ⁵	⊕○○○ Very low ^{b,f,g,h}	-	<p>38 people with multiple sclerosis were randomly allocated to 3 groups: mat pilates, reformer pilates and control. The pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. There was improvement in the TUG before and</p>

				after intervention in mat ($p=0.006$) and reformer pilates groups ($p=0.011$). There was no significant change in the control group. (Bulguroglu et al 2017).
Improved physical capacity assessed with: Core stability	38 (1 RCT) ⁶	⊕○○○ Very low ^{b,f,g,h}	-	38 people with multiple sclerosis were randomly allocated to 3 groups: mat pilates, reformer pilates and control. The pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. There was improvement in core stability before and after intervention in both pilates groups. There was no significant change in the control group. (Bulguroglu et al 2017)
Improved physical capacity assessed with: Nine hole peg test	20 (1 RCT) ⁴	⊕○○○ Very low ^{b,g,i}	-	20 people with multiple sclerosis were randomised to 2 groups A or B in a 16 week crossover study: participants either received 20 sessions of aerobic training and task oriented exercises and then an 8 week rest period or vice versa. Group A received sessions first. NHPT of the affected hand showed no statistically significant treatment effect ($P = 0.63$) with no carryover effect ($P = 0.67$) and a mean (SD) between-period (waiting list – treatment) NHPT difference of 3.6 (25.0) s. (Gervasoni et al 2019)
Improved physical capacity assessed with: Action Research Arm Test	20 (1 RCT) ⁴	⊕○○○ Very low ^{b,g,i}	-	20 people with multiple sclerosis were randomised to 2 groups A or B in a 16 week crossover study: participants either received 20 sessions of aerobic training and task oriented exercises and then an 8 week rest period or vice versa. Group A received sessions first. No statistically significant between-group differences were found in the ARAT. (Gervasoni et al

				2019)	
Improved physical capacity assessed with: Balance test	32 (1 observational study) ⁷	⊕○○○ Very low ^{b,g,k}	-	32 people with multiple sclerosis were allocated to a Tai Chi group (2x weekly sessions of 90mins for 6 months), or treatment as usual TAU group. Assessments were conducted prior to and following the 6-month interval. In case of balance performance, a significant Time by Group interaction emerged [F (1,30) = 5.70, p < 0.05, partial η ² = 0.16]. Post-hoc comparisons revealed that performance in the Tai Chi group improved, while it remained relatively stable in the TAU group. (Burschka et al 2014)	
Improved physical capacity assessed with: Coordination test	32 (1 observational study) ⁷	⊕○○○ Very low ^{b,g,k}	-	32 people with multiple sclerosis were allocated to a Tai Chi group (2x weekly sessions of 90mins for 6 months), or treatment as usual TAU group. Assessments were conducted prior to and following the 6-month interval. For coordination, there was a significant main effect of Time [F (1,30) = 4.89, p < 0.05, partial η ² = 0.14] and a significant Time by Group interaction [F (1,30) = 6.57, p < 0.05, partial η ² = 0.18]. Post-hoc comparisons indicated that the increase in coordination performance scores was significant in the Tai Chi group whereas scores remained relatively stable in the TAU group. (Burschka et al 2014)	
Improved capacity to participate in daily tasks assessed with: Functional Independence Measure	1 (1 observational study) ¹	⊕○○○ Very low ^a	-	A 17 year old male with Friedreich ataxia underwent a physiotherapy programme, 3 sessions per week for 6 weeks. FIM score improved from 100 to 105. (Kaplan et al 2015).	
Reduced falls - not measured	-	-	-	-	-

	<ol style="list-style-type: none"> 1. Kaplan T., Maden C. Yakut H. Pelin Z. Bayramlar K. Evaluation of a Patient with Friedreich's Ataxia in Aspect of Physiotherapy Applications: Case Report. Fiz. Rehab; 2015. 2. A, Hasanpour,Dehkordi. Influence of yoga and aerobics exercise on fatigue, pain and psychosocial status in patients with multiple sclerosis: a randomized trial. Journal of sports medicine and physical fitness; 2016. 3. Carter A., Daley A. Humphreys L. et al. Pragmatic intervention for increasing self-directed exercise behaviour and improving important health outcomes in people with multiple sclerosis: A randomised controlled trial. Multiple Sclerosis Journal; 2014. 4. Gervasoni E, Cattaneo D Bertoni R et al. Effect of arm cycling and task-oriented exercises on fatigue and upper limb performance in multiple sclerosis: a randomized crossover study. International Journal of Rehabilitation Research; 2019. 5. Sangelaji B., Nabavi S.M. Estebarsari F. et al. Effect of combination exercise therapy on walking distance, postural balance, fatigue and quality of life in multiple sclerosis patients: A clinical trial study. Iranian Red Crescent Medical Journal; 2014. 6. Bulguroglu I, Guclu-Gunduz A Yazici G et al. The effects of Mat Pilates and Reformer Pilates in patients with Multiple Sclerosis: A randomized controlled study. NeuroRehabilitation; 2017. 7. Burschka J.M., Keune P.M. Oy U.H.-V. Oschmann P. Kuhn P. Mindfulness-based interventions in multiple sclerosis: Beneficial effects of Tai Chi on balance, coordination, fatigue and depression. BMC Neurol.; 2014. <ol style="list-style-type: none"> a. Single case study only. b. All participants had a diagnosis of multiple sclerosis (none with FRDA). c. Estimated sample size not achieved in the one study published. Confidence intervals not published. d. 20 participants were excluded from the study after allocation. No blinded-assessments conducted. e. Enrolment process and randomization not clearly described. f. No accounting for dropouts. g. Low absolute numbers of participants h. No between group analyses to compare control and intervention (pilates groups) i. Crossover study design. j. Confidence intervals not reported. k. 6 dropouts in intervention group, non-randomised design. 	
--	---	--

Undesirable Effects
How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
------------------	--------------------------	----------------------------------

- 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)	
				Risk with no activity programme (exercise such as aerobic exercise, strengthening exercise, yoga, tai chi, dancing)	Risk difference with physical activity programme (exercise such as aerobic exercise, strengthening exercise, yoga, tai chi, dancing)
Reported fatigue assessed with: BORG	1 (1 observational study) ¹	⊕○○○ Very low ^a	-	A 17 year old male with Friedreich ataxia underwent a physiotherapy programme, 3 sessions per week for 6 weeks. Fatigue during resting decreased from 4 to 3 and fatigue during movement decreased from 5 to 4 on the Borg Scale. (Kaplan et al 2015).	
Reported fatigue assessed with: Rhoten Fatigue Scale	61 (1 RCT) ²	⊕○○○ Very low ^{b,c,d}	-	61 people with multiple sclerosis were randomly assigned to 3 groups of yoga (n=20), aerobics (n=20) or control (n=21). The exercise programmes were performed as 3 sessions per week for 12 weeks. Paired t-test determined a significant decrease in fatigue severity in the yoga ($p<0.05$) and exercise ($p<0.05$) groups but not in the control group. (Hasanpour Dehkordi 2016).	
Reported fatigue assessed with: Modified Fatigue Impact Scale	140 (2 RCTs) ^{3,4}	⊕⊕⊕○ Moderate ^b	-	120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. All dimensions of fatigue were significantly improved in the exercise group in comparison with usual care at 3 months ($p<0.0001$) with the change in total	

The level of drop-out in some studies may indicate some undesirable effects of exercise programs, although a survey of expert clinicians suggest harms from exercise programs are trivial at most.

				<p>fatigue scores being positively correlated with baseline levels. The improvements in fatigue were not maintained at 9 months. (Carter et al 2014).</p> <p>20 people with multiple sclerosis were randomised to 2 groups A or B in a 16 week crossover study: participants either received 20 sessions of upper limb aerobic training and task oriented exercises and then an 8 week rest period or vice versa. Group A received sessions first. There was a statistically significant treatment effect in the MFIS ($p=0.05$) without any carryover effect. MFIS was lower after treatment compared to the waiting list. The combined differences for Groups A and B between WL-T periods for MFIS was [median and interquartile range (Q1-Q3)] 5.2 (10.7) points. Fatigue was present in our sample with a median MFIS baseline score of 32 out of 84 points. At the end of the treatment, there was a median reduction of 5 points, in 70% in the treatment period and 30% in the waiting list period showing reduced fatigue after rehabilitation. In addition, 66% in the treatment period and 10% in the waiting list period showed a 10-point reduction in MFIS, which is the cut-off score that defines a clinically relevant improvement. (Gervasoni et al 2019).</p>	
Reported fatigue assessed with: Fatigue Intensity Test	59 (1 RCT) ⁵	⊕○○○ Very low ^{b,c,e,f}	-	<p>59 people with multiple sclerosis were randomised to an intervention (n=39) or control (n=20) group. The intervention group received 10 weeks of combination therapy. Assessments were conducted 1 week before the intervention, 1 week after the 10 weeks of intervention and 1 year after the intervention. The intervention group reported a significant decrease in the scores in the second ($p = 0.02$) and third timepoints ($p = 0.04$) compared to the baseline. There were no significant changes in fatigue scores in the control group. The degree of change in the second timepoint compared to the</p>	

				first timepoint was significant in the intervention group when compared with the control ($p = 0.02$). (Sangelaji et al 2014)
Reported fatigue assessed with: Fatigue Severity Scale	38 (1 RCT) ⁶	⊕○○○ Very low ^{b,f,g,h}	-	38 people with multiple sclerosis were randomly allocated to 3 groups: mat pilates, reformer pilates and control. The pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. There was a significant decrease in the FSS score in both mat ($p=0.034$) and reformer ($p=0.008$) Pilates groups. There was no significant change in the control group. (Bulguroglu et al 2017)
Reported fatigue assessed with: Motor Fatigability Index	20 (1 RCT) ⁴	⊕○○○ Very low ^{b,g,i}	-	20 people with multiple sclerosis were randomised to 2 groups A or B in a 16 week crossover study: participants either received 20 sessions of aerobic training and task oriented exercises and then an 8 week rest period or vice versa. Group A received sessions first. The MFI showed a statistically significant treatment effect ($p = 0.05$) with no carryover effect ($p = 0.23$). The between-period differences (waiting list-treatment) for the MFI was -0.007 (<0.001) Hz/s meaning a reduction in motor fatigue index after treatment ($p=0.05$). (Gervasoni et al 2019).
Reported fatigue assessed with: Fatigue Scale of Motor and Cognitive Functions	32 (1 observational study) ⁷	⊕○○○ Very low ^{b,g,i,k}	-	32 people with multiple sclerosis were allocated to a Tai Chi group (2x weekly sessions of 90mins for 6 months), or treatment as usual TAU group. Assessments were conducted prior to and following the 6-month interval. For Fatigue, a significant Time by Group interaction [$F(1, 25) = 7.82, p = 0.01$]

				partial $\eta^2 = 0.24$] and a significant main effect of Group emerged [$F(1,25) = 5.91$, $p < 0.05$, partial $\eta^2 = 0.19$]. Post-hoc comparisons indicated a significant increase in fatigue scores in the TAU group from pre to post assessments. Scores in the Tai Chi group remained relatively stable. At pre-treatment assessments, the groups did not differ significantly in fatigue. In contrast, fatigue differed following the six-months interval. (Burschka et al 2014)
Improved quality of life assessed with: SF-36	61 (1 RCT) ²	⊕○○○ Very low ^{b,c,d}	-	61 people with multiple sclerosis were randomly assigned to 3 groups of yoga (n=20), aerobics (n=20) or control (n=21). The exercise programmes were performed as 3 sessions per week for 12 weeks. ANOVA was used to compare the dimensions of the SF-36 scale in each group. After the 12 weeks, components of the SF-36 improved significantly in the yoga group. (Hasanpour Dehkordi 2016).
Improved quality of life assessed with: MSQoL-54	179 (2 RCTs) ^{3,5}	⊕⊕⊕○ Moderate ^b	-	120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. Positive changes in many quality of life domains in favour of the exercise group were also observed at 3 months, with improvements in emotional wellbeing ($p = 0.01$), social function ($p = 0.004$) and overall quality of life ($p = 0.001$) being maintained for 9 months. (Carter et al 2014) 59 people with multiple sclerosis were randomised to an intervention (n=39) or control (n=20) group. The intervention group received 10 weeks of combination therapy. Assessments were conducted 1 week before the intervention, 1 week after the 10 weeks of intervention and 1 year after the intervention. For mental QoL the intervention group reported

				<p>significant changes at the second time point compared to the first or third timepoints. There was significant change in the intervention group between the first and second timepoints compared to the control group ($p = 0.001$) as well as between for the third and first timepoint ($p=0.02$). For physical QOL, the intervention group also reported significant changes at the second time point compared to the first timepoint ($p=0.001$). After 9 months however, values returned to baseline. Comparison of changes between the two groups also indicated that the values of second time point compared to the first and the third timepoint compared to the first had significant changes ($p < 0.05$). (Sangelaji et al 2014)</p>
Improved quality of life assessed with: Questionnaire of Life Satisfaction	32 (1 observational study) ⁷	⊕○○○ Very low ^{b,g,i,k}	-	<p>32 people with multiple sclerosis were allocated to a Tai Chi group (2x weekly sessions of 90mins for 6 months), or treatment as usual TAU group. Assessments were conducted prior to and following the 6-month interval. In case of life satisfaction, a significant Time by Group interaction [$F(1,24) = 8.64, p < 0.01, \text{partial } \eta^2 = 0.27$] and a significant main effect Group emerged [$F(1,24) = 8.64, p < 0.01, \text{partial } \eta^2 = 0.19$]. Post-hoc comparisons indicated a significant rise in the life-satisfaction score in the Tai Chi group relative to the TAU group. At pretreatment assessments the groups did not differ significantly in life satisfaction. In contrast, life satisfaction differed following the six-months interval. (Burschka et al 2014)</p>
Improved quality of life assessed with: Turkish version of the MSQOL-54	38 (1 RCT) ⁵	⊕○○○ Very low ^{b,f,g,h}	-	<p>38 people with multiple sclerosis were randomly allocated to 3 groups: mat pilates, reformer pilates and control. The pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of</p>

				<p>the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. In the MSQOL, there were statistically significant improvements in the Mat (mental $p=0.006$, physical $p=0.005$), Reformer (mental $p=0.002$, physical $p=0.002$) Pilates and control groups (physical $p=0.023$). (Bulguroglu et al 2017)</p>
Improved energy levels assessed with: SF-36	61 (1 RCT) ²	⊕○○○ Very low ^{b,c,d}	-	<p>61 people with multiple sclerosis were randomly assigned to 3 groups of yoga (n=20), aerobics (n=20) or control (n=21). The exercise programmes were performed as 3 sessions per week for 12 weeks. ANOVA was used to compare the dimensions of the SF-36 scale in each group. After the 12 weeks, the component measuring energy improved significantly in the yoga group. (Hasanpour Dehkordi 2016).</p>
Improved physical capacity assessed with: SF-36	61 (1 RCT) ²	⊕○○○ Very low ^{b,c,d}	-	<p>61 people with multiple sclerosis were randomly assigned to 3 groups of yoga (n=20), aerobics (n=20) or control (n=21). The exercise programmes were performed as 3 sessions per week for 12 weeks. ANOVA was used to compare the dimensions of the SF-36 scale in each group. After the 12 weeks, the component measuring physical performance and limited activity following physical problems improved significantly in the yoga group. (Hasanpour Dehkordi 2016).</p>
Improved physical capacity assessed with: Godin Leisure Time Exercise Questionnaire	120 (1 RCT) ³	⊕⊕⊕○ Moderate ^b	-	<p>120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. An increase in GLTEQ was observed in the exercise group versus usual care at 3</p>

				months ($p = 0.01$). The improvement in GLTEQ was accompanied by increases in daily step counts at 3 months ($p = 0.009$) in the exercise group versus usual care, but at 9 months daily step counts were similar to baseline levels. (Carter et al 2014)
Improved physical capacity assessed with: Multiple Sclerosis Functional Composite	120 (1 RCT) ³	⊕⊕⊕○ Moderate ^b	-	120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. The exercise intervention had no effect on the MSFC. (Carter et al 2014)

	<p>Improved physical capacity assessed with: Six minute walk test</p>	<p>179 (2 RCTs)^{3,5}</p>	<p>⊕⊕⊕○ Moderate^b</p>	<p>-</p>	<p>120 people with multiple sclerosis were randomised equally to either usual care or a 3-month exercise intervention plus usual care. Outcomes were assessed at baseline, at 3 months (post intervention) and 9 months after randomisation. The exercise intervention had no effect on the 6MWT. (Carter et al 2014)</p> <p>59 people with multiple sclerosis were randomised to an intervention (n=39) or control (n=20) group. The intervention group received 10 weeks of combination therapy. Assessments were conducted 1 week before the intervention, 1 week after the 10 weeks of intervention and 1 year after the intervention. There were significant differences in the 6MWT in the first and second timepoints and in the second and third timepoints in the intervention group ($p < 0.0001$). The changes were also statistically significant in control group in the first and third timepoints and in the second and third timepoints ($p < 0.0001$). The comparison of changes in the two groups indicated that changes were significant when comparing the first with the second timepoints ($p < 0.0001$) and the first and the third timepoints ($p = 0.001$). (Sangelaji et al 2014)</p>	
	<p>Improved physical capacity assessed with: Berg balance test</p>	<p>59 (1 RCT)⁵</p>	<p>⊕○○○ Very low^{b,c,e,f}</p>	<p>-</p>	<p>59 people with multiple sclerosis were randomised to an intervention (n=39) or control (n=20) group. The intervention group received 10 weeks of combination therapy. Assessments were conducted 1 week before the intervention, 1 week after the 10 weeks of intervention and 1 year after the intervention. In the intervention group, the Berg increased from 49.02 to 51.7 from the first and second timepoint. The score decreased to 48.63 at the third timepoint. The significance of changes between the two groups was also statistically tested. There was a significant change in the second timepoint compared to the first in the intervention group when</p>	

				<p>compared to control ($p < 0.0001$). Changes in the third timepoint were also significantly different from the first ($p = 0.03$). (Sangelaji et al 2014)</p>
Improved physical capacity assessed with: Single leg stance	38 (1 RCT) ⁶	⊕○○○ Very low ^{b,f,g,h}	-	<p>38 people with multiple sclerosis were randomly allocated to 3 groups: mat pilates, reformer pilates and control. The pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. There was improvement in the single leg stance before and after intervention in both pilates groups ($p < 0.05$). There was no significant change in the control group. (Bulguroglu et al 2017).</p>
Improved physical capacity assessed with: Timed Up and Go Test	38 (1 RCT) ⁶	⊕○○○ Very low ^{b,f,g,h}	-	<p>38 people with multiple sclerosis were randomly allocated to 3 groups: mat pilates, reformer pilates and control. The pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. There was improvement in the TUG before and after intervention in mat ($p = 0.006$) and reformer pilates groups ($p = 0.011$). There was no significant change in the control group. (Bulguroglu et al 2017).</p>
Improved physical capacity assessed with:	38 (1 RCT) ⁶	⊕○○○ Very low ^{b,f,g,h}	-	<p>38 people with multiple sclerosis were randomly allocated to 3 groups: mat pilates, reformer pilates and control. The pilates groups completed mat or reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. There was improvement in the TUG before and after intervention in mat ($p = 0.006$) and reformer pilates groups ($p = 0.011$). There was no significant change in the control group. (Bulguroglu et al 2017).</p>

Core stability				reformer pilates for 8 weeks, 2 days/week. The control groups completed breathing and relaxation exercises at home. The measurements of the groups prior to and after treatment were compared with the Wilcoxon Test. The gain obtained in the Mat Pilates and Reformer Pilates groups was compared with the Mann Whitney U Test. There was improvement in core stability before and after intervention in both pilates groups. There was no significant change in the control group. (Bulguroglu et al 2017)
Improved physical capacity assessed with: Nine hole peg test	20 (1 RCT) ⁴	⊕○○○ Very low ^{b,g,i}	-	20 people with multiple sclerosis were randomised to 2 groups A or B in a 16 week crossover study: participants either received 20 sessions of aerobic training and task oriented exercises and then an 8 week rest period or vice versa. Group A received sessions first. NHPT of the affected hand showed no statistically significant treatment effect ($P = 0.63$) with no carryover effect ($P = 0.67$) and a mean (SD) between-period (waiting list – treatment) NHPT difference of 3.6 (25.0) s. (Gervasoni et al 2019)
Improved physical capacity assessed with: Action Research Arm Test	20 (1 RCT) ⁴	⊕○○○ Very low ^{b,g,i}	-	20 people with multiple sclerosis were randomised to 2 groups A or B in a 16 week crossover study: participants either received 20 sessions of aerobic training and task oriented exercises and then an 8 week rest period or vice versa. Group A received sessions first. No statistically significant between-group differences were found in the ARAT. (Gervasoni et al 2019)
Improved physical capacity assessed with: Balance test	32 (1 observational study) ⁷	⊕○○○ Very low ^{b,g,k}	-	32 people with multiple sclerosis were allocated to a Tai Chi group (2x weekly sessions of 90mins for 6 months), or treatment as usual TAU group. Assessments were conducted prior to and following the 6-month interval. In case of balance performance a

				significant Time by Group interaction emerged [F (1,30) = 5.70, p < 0.05, partial η^2 = 0.16]. Post-hoc comparisons revealed that performance in the Tai Chi group improved, while it remained relatively stable in the TAU group. (Burschka et al 2014)
Improved physical capacity assessed with: Coordination test	32 (1 observational study) ⁷	⊕○○○ Very low ^{b,g,k}	-	32 people with multiple sclerosis were allocated to a Tai Chi group (2x weekly sessions of 90mins for 6 months), or treatment as usual TAU group. Assessments were conducted prior to and following the 6-month interval. For coordination, there was a significant main effect of Time [F (1,30) = 4.89, p < 0.05, partial η^2 = 0.14] and a significant Time by Group interaction [F (1,30) = 6.57, p < 0.05, partial η^2 = 0.18]. Post-hoc comparisons indicated that the increase in coordination performance scores was significant in the Tai Chi group whereas scores remained relatively stable in the TAU group. (Burschka et al 2014)
Improved capacity to participate in daily tasks assessed with: Functional Independence Measure	1 (1 observational study) ¹	⊕○○○ Very low ^a	-	A 17 year old male with Friedreich ataxia underwent a physiotherapy programme, 3 sessions per week for 6 weeks. FIM score improved from 100 to 105. (Kaplan et al 2015).
Reduced falls - not measured	-	-	-	-

1. Kaplan T., Maden C. Yakut H. Pelin Z. Bayramlar K. Evaluation of a Patient with Friedreich's Ataxia in Aspect of Physiotherapy Applications: Case Report. Fiz. Rehab; 2015.
2. A, Hasanpour,Dehkordi. Influence of yoga and aerobics exercise on fatigue, pain and psychosocial status in patients with multiple sclerosis: a randomized trial. Journal of sports medicine and physical fitness; 2016.
3. Carter A., Daley A. Humphreys L. et al. Pragmatic intervention for increasing self-directed exercise behaviour and improving important health outcomes in people with multiple sclerosis: A randomised controlled trial.

	<p>Multiple Sclerosis Journal; 2014.</p> <ol style="list-style-type: none"> 4. Gervasoni E, Cattaneo D Bertoni R et al. Effect of arm cycling and task-oriented exercises on fatigue and upper limb performance in multiple sclerosis: a randomized crossover study. International Journal of Rehabilitation Research; 2019. 5. Sangelaji B., Nabavi S.M. Estebarsari F. et al. Effect of combination exercise therapy on walking distance, postural balance, fatigue and quality of life in multiple sclerosis patients: A clinical trial study. Iranian Red Crescent Medical Journal; 2014. 6. Bulguroglu I, Guclu-Gunduz A Yazici G et al. The effects of Mat Pilates and Reformer Pilates in patients with Multiple Sclerosis: A randomized controlled study. NeuroRehabilitation; 2017. 7. Burschka J.M., Keune P.M. Oy U.H.-V. Oschmann P. Kuhn P. Mindfulness-based interventions in multiple sclerosis: Beneficial effects of Tai Chi on balance, coordination, fatigue and depression. BMC Neurol.; 2014. <ol style="list-style-type: none"> a. Single case study only. b. All participants had a diagnosis of multiple sclerosis (none with FRDA). c. Estimated sample size not achieved in the one study published. Confidence intervals not published. d. 20 participants were excluded from the study after allocation. No blinded-assessments conducted. e. Enrolment process and randomization not clearly described. f. No accounting for dropouts. g. Low absolute numbers of participants h. No between group analyses to compare control and intervention (pilates groups) i. Crossover study design. j. Confidence intervals not reported. k. 6 dropouts in intervention group, non-randomised design. 	
--	---	--

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Very low ○ Low ● Moderate ○ High ○ No included studies 	<p>Moderate to very low certainty of the evidence of effects as per the evidence profile table.</p>	

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" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%;">Outcomes</th> <th style="width: 20%;">Importance</th> <th style="width: 30%;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Reported fatigue assessed with: BORG</td> <td>IMPORTANT^a</td> <td>⊕○○○ VERY LOW^b</td> </tr> <tr> <td>Reported fatigue assessed with: Rhoten Fatigue Scale</td> <td>IMPORTANT^a</td> <td>⊕○○○ VERY LOW^{c,d,e}</td> </tr> <tr> <td>Reported fatigue assessed with: Modified Fatigue Impact Scale</td> <td>IMPORTANT^a</td> <td>⊕⊕⊕○ MODERATE^c</td> </tr> <tr> <td>Reported fatigue assessed with: Fatigue Intensity Test</td> <td>IMPORTANT^a</td> <td>⊕○○○ VERY LOW^{c,d,f,g}</td> </tr> <tr> <td>Reported fatigue assessed with: Fatigue Severity Scale</td> <td>IMPORTANT^a</td> <td>⊕○○○ VERY LOW^{c,g,h,i}</td> </tr> <tr> <td>Reported fatigue assessed with: Motor Fatigability Index</td> <td>IMPORTANT^a</td> <td>⊕○○○ VERY LOW^{c,h,j}</td> </tr> <tr> <td>Reported fatigue assessed with: Fatigue Scale of Motor and Cognitive Functions</td> <td>IMPORTANT^a</td> <td>⊕○○○ VERY LOW^{c,h,k,l}</td> </tr> <tr> <td>Improved quality of life assessed with: SF-36</td> <td>IMPORTANT^m</td> <td>⊕○○○ VERY LOW^{c,d,e}</td> </tr> <tr> <td>Improved quality of life assessed with: MSQoL-54</td> <td>IMPORTANT^m</td> <td>⊕⊕⊕○ MODERATE^c</td> </tr> <tr> <td>Improved quality of life assessed with: Questionnaire of Life Satisfaction</td> <td>IMPORTANT^m</td> <td>⊕○○○</td> </tr> </tbody> </table>			Outcomes	Importance	Certainty of the evidence (GRADE)	Reported fatigue assessed with: BORG	IMPORTANT ^a	⊕○○○ VERY LOW ^b	Reported fatigue assessed with: Rhoten Fatigue Scale	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,d,e}	Reported fatigue assessed with: Modified Fatigue Impact Scale	IMPORTANT ^a	⊕⊕⊕○ MODERATE ^c	Reported fatigue assessed with: Fatigue Intensity Test	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,d,f,g}	Reported fatigue assessed with: Fatigue Severity Scale	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,g,h,i}	Reported fatigue assessed with: Motor Fatigability Index	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,h,j}	Reported fatigue assessed with: Fatigue Scale of Motor and Cognitive Functions	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,h,k,l}	Improved quality of life assessed with: SF-36	IMPORTANT ^m	⊕○○○ VERY LOW ^{c,d,e}	Improved quality of life assessed with: MSQoL-54	IMPORTANT ^m	⊕⊕⊕○ MODERATE ^c	Improved quality of life assessed with: Questionnaire of Life Satisfaction	IMPORTANT ^m	⊕○○○	
Outcomes	Importance	Certainty of the evidence (GRADE)																																			
Reported fatigue assessed with: BORG	IMPORTANT ^a	⊕○○○ VERY LOW ^b																																			
Reported fatigue assessed with: Rhoten Fatigue Scale	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,d,e}																																			
Reported fatigue assessed with: Modified Fatigue Impact Scale	IMPORTANT ^a	⊕⊕⊕○ MODERATE ^c																																			
Reported fatigue assessed with: Fatigue Intensity Test	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,d,f,g}																																			
Reported fatigue assessed with: Fatigue Severity Scale	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,g,h,i}																																			
Reported fatigue assessed with: Motor Fatigability Index	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,h,j}																																			
Reported fatigue assessed with: Fatigue Scale of Motor and Cognitive Functions	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,h,k,l}																																			
Improved quality of life assessed with: SF-36	IMPORTANT ^m	⊕○○○ VERY LOW ^{c,d,e}																																			
Improved quality of life assessed with: MSQoL-54	IMPORTANT ^m	⊕⊕⊕○ MODERATE ^c																																			
Improved quality of life assessed with: Questionnaire of Life Satisfaction	IMPORTANT ^m	⊕○○○																																			

		VERY LOW ^{c,h,k,l}
Improved quality of life assessed with: Turkish version of the MSQOL-54	IMPORTANT ^m	⊕○○○ VERY LOW ^{c,g,h,j}
Improved energy levels assessed with: SF-36	IMPORTANT ⁿ	⊕○○○ VERY LOW ^{c,d,e}
Improved physical capacity assessed with: SF-36	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,d,e}
Improved physical capacity assessed with: Godin Leisure Time Exercise Questionnaire	IMPORTANT ^a	⊕⊕⊕○ MODERATE ^c
Improved physical capacity assessed with: Multiple Sclerosis Functional Composite	IMPORTANT ^a	⊕⊕⊕○ MODERATE ^c
Improved physical capacity assessed with: Six minute walk test	IMPORTANT ^a	⊕⊕⊕○ MODERATE ^c
Improved physical capacity assessed with: Berg balance test	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,d,f,g}
Improved physical capacity assessed with: Single leg stance	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,g,h,j}
Improved physical capacity assessed with: Timed Up and Go Test	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,g,h,j}
Improved physical capacity assessed with: Core stability	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,g,h,j}
Improved physical capacity assessed with: Nine hole peg test	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,h,j}
Improved physical capacity assessed with: Action Research Arm Test	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,h,j}

Improved physical capacity assessed with: Balance test	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,h,l}
Improved physical capacity assessed with: Coordination test	IMPORTANT ^a	⊕○○○ VERY LOW ^{c,h,l}
Improved capacity to participate in daily tasks assessed with: Functional Independence Measure	IMPORTANT ^a	⊕○○○ VERY LOW ^b
Reduced falls - not measured	CRITICAL ^o	-

- a. Identified as important (6/6) by people with FA and critical by expert authors on this topic.
- b. Single case study only.
- c. All participants had a diagnosis of multiple sclerosis (none with FRDA).
- d. Estimated sample size not achieved in the one study published. Confidence intervals not published.
- e. 20 participants were excluded from the study after allocation. No blinded-assessments conducted.
- f. Enrolment process and randomization not clearly described.
- g. No accounting for dropouts.
- h. Low absolute numbers of participants
- i. No between group analyses to compare control and intervention (pilates groups)
- j. Crossover study design.
- k. Confidence intervals not reported.
- l. 6 dropouts in intervention group, non-randomised design.
- m. Identified as critical (1/6) and important (5/6) by people with FA and important by expert authors on this topic.
- n. Identified as important (6/6) by people with FA and important by expert authors on this topic.
- o. 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

<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 Physical activity programme (exercise such as aerobic exercise, strengthening exercise, yoga, tai chi, dancing) as a management strategy for all individuals who report fatigue.</p> <p>Reflecting on the impact of Physical activity programme (exercise such on Reported fatigue, 58.33% (14/24) clinical experts reported a benefit (large, moderate or small), 4.17% (1/24) reported no effect and, 4.17% (1/24) reported observing a harm (large, moderate or small). 8 clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on quality of life, 66.67% (16/24) clinical experts reported a benefit, 0% (0/24) reported no effect and, 0% (0/24) reported observing a harm. 8 expert clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on energy levels, 62.5% (15/24) clinical experts reported a benefit, 4.17% (1/24) reported no effect and, 0% (0/24) reported observing a harm. 8 expert clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on physical capacity, 66.67% (16/24) clinical experts reported a benefit, 0% (0/24) reported no effect and, 0% (0/24) reported observing a harm. 8 expert clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on capacity to participate in daily tasks, 66.67% (16/24) clinical experts reported a benefit, 0% (0/24) reported no effect and, 0% (0/24) reported observing a harm. 8 expert clinicians could not provide any information on this outcome.</p> <p>Reflecting on the impact on Reduced falls, 45.83% (11/24) clinical experts reported a benefit, 16.67% (4/24) reported no effect and, 0% (0/24) reported observing a harm. 9 expert clinicians could not provide any information on this outcome.</p>
--	--	---

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ● Probably yes 	No published evidence.	The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were asked if a physical activity programme in people who report fatigue was acceptable

<ul style="list-style-type: none"> ○ Yes ○ Varies ○ Don't know 		<p>(weighing up the balance between benefits, harms and costs).</p> <p>3/4 indicated the intervention was probably acceptable, 1/4 indicated probably not acceptable (Aug 2020).</p>
---	--	--

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

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 suggest a physical activity program be used to manage fatigue in individuals with Friedreich ataxia.

Justification

Most of the evidence reviewed for this recommendation was based on studies in multiple sclerosis. These studies indicate a favorable effect of physical activity programs on fatigue. The majority of expert authors surveyed consider a physical activity program to be of benefit for managing fatigue in individuals with FRDA.

Subgroup considerations

This recommendation is for individuals with FRDA who have no medical contraindications to participating in a physical activity program. Those individuals with other medical comorbidities/contraindications for exercise should work with their healthcare team to carefully consider the risks and benefits of an exercise program before deciding to begin one.

Research priorities

An RCT on the benefits of a physical activity program on fatigue in individuals with FRDA is required.

Reference

da Silva CB, Chevis CF, D'Abreu A, Lopes-Cendes I, Franca MC, Jr. Fatigue is frequent and multifactorial in Friedreich's ataxia. *Parkinsonism Relat Disord*. 2013;19(8):766-7.