Supplementary material – Fassora et al.

Intensity-dependent effects of exercise therapy on walking performance and aerobic fitness in symptomatic patients with lower extremity peripheral artery disease: a systematic review and meta-analysis

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Suppl 1. Search strategy

1.1 Vocabulary

Concepts	Peripheral Artery Disease (PAD)	Exercise	Walking performance
Free terms Syntaxe Embase	1	Exercise Rehabilitation (Physical NEAR/3 (activit* OR therap*)) Training Walking OR cycling OR swimming Plantar flexion exertion "heart rate" OR "oxygen consumption" OR "VO2 max" OR "VO2 peak" OR "VO2max" OR "VO2peak" OR "borg" OR "workload" OR "work rate" OR "oxygen uptake"	U
Emtree	disease*) 'peripheral vascular disease'/de OR 'arterial insufficiency'/de OR 'arteriosclerosis'/de OR 'atherosclerosis'/exp OR 'peripheral occlusive artery disease'/de OR 'artery occlusion'/de OR 'claudication'/exp	<pre>'exercise'/exp OR 'kinesiotherapy'/exp OR 'rehabilitation'/de OR 'rehabilitation'/de OR 'training'/de OR 'endurance'/de OR 'walking'/de OR 'cycling'/de OR 'swimming'/de 'exercise test'/exp 'heart rate'/de OR 'oxygen consumption'/de OR 'maximal oxygen uptake'/de OR 'maximal oxygen uptake'/de</pre>	'treadmill exercise'/exp OR 'walk test'/exp 'walking distance'/exp OR 'walking parameters'/de 'walking'/de
MeSH	"Peripheral Vascular Diseases"[Mesh:NoExp] OR "Peripheral Arterial Disease"[Mesh] OR	oxygen consumption'/de ("Exercise"[Mesh]) OR "Exercise Therapy"[Mesh] OR "Exercise Movement Techniques"[Mesh:NoExp] OR	Exercise Tolerance"[Mes h:NoExp]

Arterial Occlusive	"Exercise Test"[Mesh]	"Exercise
Diseases"[Mesh:NoExp]		Test"[Mesh]
OR	Exercise	
"Arteriosclerosis"[Mesh:No	Tolerance"[Mesh:NoExp]	"Walking"[Mes
Exp] OR "Arteriosclerosis		h:NoExp]
Obliterans"[Mesh]	"Rehabilitation"[Mesh:NoExp]	
"Intermittent		
Claudication"[Mesh]	"Physical Exertion"[Mesh]	
	"Physical Endurance"[Mesh]	
"Atherosclerosis"[Mesh]		
	"Heart Rate"[Mesh:NoExp]	
	"Oxygen	
	Consumption"[Mesh:NoExp]	

1.2. Bibliographic database search – strategies

Embase.com

1756 references on 2020.06.17

('peripheral vascular disease'/de OR 'arterial insufficiency'/de OR 'arteriosclerosis'/de OR 'atherosclerosis'/exp OR 'peripheral occlusive artery disease'/de OR 'artery occlusion'/de OR 'claudication'/exp OR ((Peripheral NEAR/3 (vascular OR arter*) NEAR/3 disease*) OR (peripheral NEAR/3 angiopath*) OR Arterial-Occlusive-Disease* OR Arterial-Obstructive-Disease* OR arterial-occlusion* OR arterial-stenos* OR Artery-narrowing OR artery-obstruction OR arteryobstructive-disease* OR artery-stenos* OR arterial-insufficiency OR arteriosclerosis OR atherosclerosis OR claudication OR ("Lower extremity" NEAR/3 arter* NEAR/3 disease*)):ab,ti,kw) AND ('exercise'/exp OR 'kinesiotherapy'/exp OR 'rehabilitation'/de OR 'training'/de OR 'physical activity'/de OR 'endurance'/de OR 'walking'/de OR 'cycling'/de OR 'swimming'/de OR 'heart rate'/de OR 'oxygen consumption'/de OR 'maximal oxygen uptake'/de OR 'maximal oxygen consumption'/de OR (Exercise* OR Rehabilitation OR exertion OR (Physical NEAR/3 (activit* OR therap*)) OR training OR walking OR cycling OR swimming OR "heart rate" OR "oxygen consumption" OR "VO2 max" OR "VO2 peak" OR "VO2max" OR "VO2peak" OR "borg" OR "workload" OR "work rate" OR "oxygen uptake"):ab,ti,kw) AND ('treadmill exercise'/exp OR 'walk test'/exp OR 'walking distance'/exp OR 'walking parameters'/de OR 'walking'/de OR (treadmill* OR walk*):ab,ti,kw) AND (((random* OR factorial* OR crossover* OR cross NEXT/1 over* OR placebo* OR doubl* NEXT/1 blind* OR singl* NEXT/1 blind* OR assign* OR allocat* OR volunteer*):de,ab,ti OR 'crossover procedure'/exp OR 'double blind procedure'/exp OR 'randomized controlled trial'/exp OR 'single blind procedure'/exp) NOT ([animals]/lim NOT [humans]/lim))

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MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to June 16, 2020

1822 references on 2020.06.17

("Peripheral Vascular Diseases"/ OR exp "Peripheral Arterial Disease"/ OR "Arterial Occlusive Diseases"/ OR exp "Arteriosclerosis Obliterans"/ OR "Arteriosclerosis"/ OR exp "Intermittent Claudication"/ OR exp "Atherosclerosis"/ OR ((Peripheral ADJ3 (vascular OR arter*) ADJ3 disease*) OR (peripheral ADJ3 angiopath*) OR Arterial-Occlusive-Disease* OR Arterial-Obstructive-Disease* OR arterial-occlusion* OR arterial-stenos* OR Artery-narrowing OR artery-

obstruction OR artery-obstructive-disease* OR artery-stenos* OR arterial-insufficiency OR arteriosclerosis OR atherosclerosis OR claudication OR ("Lower extremity" ADJ3 arter* ADJ3 disease*)).ab,ti,kf.) AND (Exp Exercise/ OR exp Exercise Therapy/ OR Exercise Movement Techniques/ OR exp Exercise Test/ OR Exercise Tolerance/ OR exp Physical Endurance/ OR Rehabilitation/ OR exp Physical Exertion/ OR Heart Rate/ OR Oxygen Consumption/ OR (Exercise* OR Rehabilitation OR exertion OR (Physical ADJ3 (activit* OR therap*)) OR training OR walking OR cycling OR swimming OR "heart rate" OR "oxygen consumption" OR "VO2 max" OR "VO2 peak" OR "VO2max" OR "VO2peak" OR "borg" OR "workload" OR "work rate" OR "oxygen uptake").ab,ti,kf.) AND (Exercise Tolerance/ OR exp Exercise Test/ OR Walking/ OR (treadmill* OR walk*).ab,ti,kf.) AND ((randomized controlled trial.pt. OR controlled clinical trial.pt. OR randomized.ab,ti,kf. OR placebo.ab,ti,kf. OR randomly.ab,ti,kf. OR trial.ab,ti,kf. OR groups.ab,ti,kf.) NOT (exp animals/ not humans.sh.))

Cochrane Central Register of Controlled Trials Wiley

Issue 6 of 12, June 2020

1674 references on 2020.06.17

(((Peripheral NEAR/3 (vascular OR arter*) NEAR/3 disease*) OR (peripheral NEAR/3 angiopath*) OR Arterial-Occlusive-Disease* OR Arterial-Obstructive-Disease* OR arterial-occlusion* OR arterial-stenos* OR Artery-narrowing OR artery-obstruction OR artery-obstructive-disease* OR artery-stenos* OR arterial-insufficiency OR arteriosclerosis OR atherosclerosis OR claudication OR ("Lower extremity" NEAR/3 arter* NEAR/3 disease*)):ab,ti,kw) AND ((Exercise* OR Rehabilitation OR exertion OR (Physical NEAR/3 (activit* OR therap*)) OR training OR walking OR cycling OR swimming OR "heart rate" OR "oxygen consumption" OR "VO2 max" OR "VO2 peak" OR "VO2peak" OR "borg" OR "workload" OR "work rate" OR "oxygen uptake"):ab,ti,kw) AND ((treadmill* OR walk*):ab,ti,kw)

Web of Science – ALL Databases

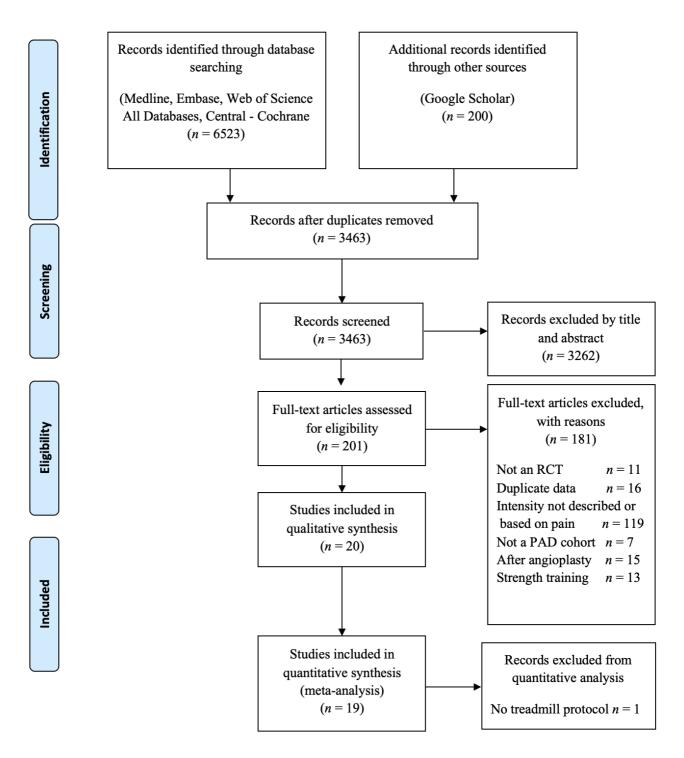
1271 references on 2020.06.17

TS=(((Peripheral NEAR/3 (vascular OR arter*) NEAR/3 disease*) OR (peripheral NEAR/3 angiopath*) OR Arterial-Occlusive-Disease* OR Arterial-Obstructive-Disease* OR arterial-occlusion* OR arterial-stenos* OR Artery-narrowing OR artery-obstruction OR artery-obstructive-disease* OR artery-stenos* OR arterial-insufficiency OR arteriosclerosis OR atherosclerosis OR claudication OR ("Lower extremity" NEAR/3 arter* NEAR/3 disease*)) AND ((Exercise* OR "Rehabilitation" OR "exertion" OR (Physical NEAR/3 (activit* OR therap*))) OR "training" OR "walking" OR "cycling" OR "swimming" OR "heart rate" OR "oxygen consumption" OR "VO2 max" OR "VO2 peak" OR "VO2max" OR "VO2peak" OR "borg" OR "workload" OR "work rate" OR "oxygen uptake")) AND ((treadmill* OR walk*))) AND TS=(randomized OR randomly OR randomised)

Google Scholar

"peripheral artery disease"|"lower extremity artery disease"|claudication "exercise intensity"|"heart rate"|"oxygen consumption"|"VO2max"|"VO2peak"|"borg"|"workload"|"work rate"|"rate of perceived exertion"|"oxygen uptake" walking randomized|randomly

Suppl 2. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow chart for study identification. PAD, peripheral artery disease; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; RCT, randomized controlled trial.



Author, year	Control group	Intervention group	Mean exercise intensity*	Claudication pain severity	Supervision	Program length (weeks)	Frequency (per week)	Mean duration (min)
Vigorous exercise intens	ity							
Bronas et al. 2011 ⁴³	Usual care	Arm-ergometer	RPE 14	No pain	Yes	12	3	60 with rest periods
Collins et al. 2005 ⁴⁵	Usual care	Pole striding	77% V'O _{2peak} 85% HR _{max}	Maximal pain	Yes	24	3	30-60 w/o rest periods
Cucato et al. 2013 ⁶²	Stretching	Treadmill walking	80% V'O _{2peak} 82% HR _{max}	Mild pain	NR	12	2	60 with rest periods
Park et al. 2019 ⁴⁸	Usual care	Aquatic walking	66% HRR	NR	Yes	12	4	60 with rest periods
Sandercock et al. 2007 ⁴⁹	Walking advice	Treadmill walking	72.5% V'O _{2peak}	NR	Yes/No	12	2 supervised 1 unsupervised	30 w/o rest periods
G 1 000 <i>c</i> 50	TT 1	Treadmill walking	90% V'O _{2peak}	Mild pain	Yes	6	3	40 with rest periods
Sanderson et al. 2006 ⁵⁰	Usual care	Cycling	90% V'O _{2peak}	Mild pain	Yes	6	3	40 with rest periods
		Treadmill walking	RPE 14	Severe pain	Yes	12	3	70 with rest periods
Treat-Jacobson et al. 2009^{52}	Walking advice	Arm-ergometer	RPE 14	No pain	Yes	12	3	70 with rest periods
		Combined	RPE 14	Severe pain	Yes	12	3	70 with rest periods
NL 11 1 - 200053		Arm-ergometer	77.5% HR _{max}	No pain	Yes	6	2	40 with rest periods
Walker et al. 2000 ⁵³	Walking advice	Leg-ergometer	77.5% HR _{max}	NR	Yes	6	2	40 with rest periods
Wang et al. 2008 ⁶⁵	Walking advice	Plantar flexion	80% W _{peak}	NR	Yes	8	3	40 with rest periods
Wood et al. 2006 ⁵⁴	Usual care	Treadmill walking	90% V'O _{2peak}	Pain (but not specify)	Yes	6	3	40 with rest periods
7 1 1 000755		Arm-ergometer	87.5% V'O _{2peak} RPE 14.5	No pain	Yes	24	2	40 with rest periods
Zwierska et al. 2005 ⁵⁵	Walking advice	Leg-ergometer	87.5% V'O _{2peak} RPE 14.5	NR	Yes	24	2	40 with rest periods

*According to American College of Sports Medicine (Garber et al. ³²) or Hansen et al. ⁴⁰ HR_{max}, maximal heart rate; HRR, heart rate reserve; NR, not reportable; RPE, rate of perceived exertion; V'O_{2peak}, peak oxygen consumption; w/o, without. W_{peak}, peak workload.

Suppl 3. Continued

Light-to-moderate exerci	ise intensity							
Brenner et al. 2019 ⁶¹	Usual care	Walking	≤40% HRR RPE 12	Mild pain	No	12	5	33.7 w/o rest periods
Chehuen et al. 2017 ⁴¹	Stretching	Treadmill walking	61% HR _{max}	Mild pain	Yes	12	2	60 with rest periods
Collins et al. 2003 ⁴⁴	Usual care (placebo)	Pole striding	75% HR	Mild-moderate Pain	Yes	24	3	45-60 w/o rest periods
Gardner et al. 2011 ⁶³	Walking advice	Treadmill walking	$40\% W_{\text{peak}}$	Maximal pain	Yes	12	3	15-40 w/o rest periods
Gardner et al. 2012 ⁴⁶	Walking advice	Treadmill walking	65% W _{peak}	Severe pain	Yes	24	3	15-40 w/o rest periods
Nicolaï et al. 201047	Walking advice	Walking	55% V'O _{2peak} RPE 13	Mild-moderate Pain	Yes	12	2 or 3	20-40 w/o rest periods
Neurshania et al. 201064	Walling advise	Treadmill walking at moderate pain	70% HR	Moderate pain	Yes	12	2 or 3	60 with rest periods
Novakovic et al. 2019 ⁶⁴	Walking advice	Treadmill walking at pain-free	70% HR	No pain	Yes	12	2 or 3	60 with rest periods
Sandercock et al. 2007 ⁴⁹	Walking advice	Walking (home- based)	RPE 13	NR	No	12	3	30 w/o rest periods
Tew et al. 2009 ⁵¹	Usual care	Arm-ergometer	65% W _{peak} RPE 13	No pain	Yes	12	2	40 with rest periods

*According to American College of Sports Medicine (Garber et al. ³²) or Hansen et al. ⁴⁰ HR_{max}, maximal heart rate; HRR, heart rate reserve; NR, not reportable; RPE, rate of perceived exertion; V'O_{2peak}, peak oxygen consumption; w/o, without. W_{peak}, peak workload.

Suppl 4. Maximal walking distance (m) following vigorous and light-to-moderate exercise intensity (post and change score) CI: confidence interval; IV: inverse variance; SD: standard deviation of change.

	Expe	rimental		C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Vigorous intensity (Change score)									
Bronas 2011 (arm-ergometer) 43	181.1	127	10	46.3	92.5	8	5.0%	134.80 [33.29, 236.31]	
Cucato 2013 62	316	141	13	-57	174.78	12	4.1%	373.00 [247.88, 498.12]	
Sanderson 2006 (cycling) 50	36	94.8	15	-7.5	103.91	7	5.4%	43.50 [-47.20, 134.20]	
Sanderson 2006 (walking) 50	180	150	13	-7.5	103.91	7	4.6%	187.50 [75.37, 299.63]	
Freat-Jacobson 2009 (arm-ergometer) 52	182.1	126.7	10	45.3	92.7	3	3.9%	136.80 [5.76, 267.84]	
Freat-Jacobson 2009 (combination) 52	217.2	72.7	12	45.3	92.7	3	4.5%	171.90 [59.23, 284.57]	
Freat-Jacobson 2009 (treadmill) 52	294.7		11	45.3	92.7	3	3.6%	249.40 [106.78, 392.02]	
Wood 2006 54	218.25		7		387.63	6		165.00 [-194.78, 524.78]	
Zwierska 2005 (arm-ergometer) 55	94.72	71.26			46.99	17	7.8%	107.53 [74.78, 140.28]	-
Zwierska 2005 (leg-ergometer) 55	113.89	91.8		-12.81		17	7.6%	126.70 [89.63, 163.77]	
Subtotal (95% CI)	115.69	91.0	162	-12.01	40.99	83		153.25 [108.40, 198.11]	
Heterogeneity: $Tau^2 = 2512.34$; $Chi^2 = 24.0$	a d f = 0	B - 0.00		620/		05	47.570	199129 [100.10, 190.11]	•
Test for overall effect: $Z = 6.70 (P < 0.0000)$		P = 0.00	(4); I [_] =	03%					
1.1.2 Vigorous intensity (Post score)									
Collins 2005 45	829.5	255	25	520.8	211.8	24	3.9%	308.70 [177.66, 439.74]	
Sandercock 2007 (supervised) 49	649.1	338	13	380.9	380.9	15	1.5%	268.20 [1.90, 534.50]	
Walker 2000 (arm-ergometer) 53	391.67	85.19		273.33		8	5.7%	118.34 [35.54, 201.14]	
Walker 2000 (leg-ergometer) 53	318.67	48.15		273.33		8	6.0%	45.34 [-32.54, 123.22]	
Nang 2008 65	1.099.56		14	920		11	1.9%	179.56 [-46.24, 405.36]	
Subtotal (95% CI)	1,035.50	207.11	100	520	555.1	66	19.0%	162.70 [58.79, 266.62]	-
Heterogeneity: $Tau^2 = 8528.78$; $Chi^2 = 12.9$ Fest for overall effect: Z = 3.07 (P = 0.002)	93, df = 4 (P = 0.01); $I^2 = 6$	59%					
1.1.3 Light-to-moderate (Change score)									
Gardner 2011 (supervised) 63	192.2	185.07	33	-8.88	157.4	30	5.7%	201.08 [116.47, 285.69]	
Nicolaï 2010 47	437.33	487.41	169	136.67	222.22	83	5.5%	300.66 [212.99, 388.33]	
Few 2009 51	165	194.62	27	26	181.87	24	4.9%	139.00 [35.64, 242.36]	
Subtotal (95% CI)			229			137	16.1%	216.37 [126.33, 306.41]	
Heterogeneity: Tau ² = 4141.38; Chi ² = 5.80 Fest for overall effect: Z = 4.71 (P < 0.0000		= 0.05);	$1^2 = 66$	5%					
1.1.4 Light-to-moderate (Post score)									
Brenner 2019 61	488.5	209.5	18	278.1		15	3.9%	210.40 [78.63, 342.17]	
Chehuen 2017 41	941	334	22	678	275	20	2.6%	263.00 [78.60, 447.40]	
Collins 2003 44	862.3	306.9	11	535.1	207.5	10	2.0%	327.20 [104.87, 549.53]	
Gardner 2012 46	666.98	265.54	106	398.76	275.37	36	4.9%	268.22 [165.04, 371.40]	
Novakovic 2019 (moderate) 64	235.33	195.56	10	147.33	108.15	4	3.1%	88.00 [-73.01, 249.01]	
Novakovic 2019 (pain-free) 64	359.33			147.33		4	1.1%	212.00 [-97.79, 521.79]	
Subtotal (95% CI)	000.00		178			89		228.93 [165.70, 292.16]	•
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4.47$, df Test for overall effect: $Z = 7.10$ (P < 0.0000).48); I ² =	= 0%						-
Fotal (95% CI)			669			375	100.0%	177.94 [142.29, 213.60]	•
Heterogeneity: $Tau^2 = 3981.04$; $Chi^2 = 65.0$	06. df = 23	(P < 0.0	0001)	$l^2 = 65\%$					
			0001),	00/0					-500 -250 0 250 50
Test for overall effect: $Z = 9.78 (P < 0.0000)$									

Suppl 5. Pain-free walking distance (m) following vigorous and light-to-moderate exercise intensity (post and change score) CI: confidence interval; IV: inverse variance; SD: standard deviation of change.

	Exp	erimenta	l.	c	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.1.1 Vigorous intensity (Change score)								
Bronas 2011 (arm–ergometer) 43	89.6	74	10	7.3	43.8	8	8.0%	82.30 [27.30, 137.30]	
Sanderson 2006 (cycling) 50	-6	138.06	15	41.25	203.51	7	1.6%	-47.25 [-213.41, 118.91]	
Treat-Jacobson 2009 (arm-ergometer) 52	89.6	74	10	4	45.4	3	6.3%	85.60 [16.73, 154.47]	
Treat-Jacobson 2009 (combination) 52	61.94	109.94	12	4	45.4	3	5.1%	57.94 [-22.74, 138.62]	
Treat-Jacobson 2009 (treadmill) 52	91.6	148.4	11	4	45.4	3	3.7%	87.60 [-14.04, 189.24]	
Zwierska 2005 (arm-ergometer) 55	44.41	68.53	34	-20	95.17	17	8.6%	64.41 [13.64, 115.18]	
Zwierska 2005 (leg–ergometer) ^{ss} Subtotal (95% CI)	52.37	69.41	37 129	-20	95.17	17 58	8.7% 42.0%	72.37 [21.90, 122.84] 71.07 [46.14, 96.00]	•
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.55$, Test for overall effect: Z = 5.59 (P < 0.00		= 0.86); l ²	^e = 0%						
2.1.2 Vigorous intensity (Post score)									
Cucato 2013 62	413	201	13	253	118	12	2.5%	160.00 [31.95, 288.05]	
Sanderson 2006 (walking) 50		276.75		334.5	331.5	7		120.75 [-167.24, 408.74]	· · · · · · · · · · · · · · · · · · ·
Walker 2000 (arm-ergometer) 53		120.74		148.33	71.11	8	6.3%	118.34 [49.34, 187.34]	
Walker 2000 (leg-ergometer) 53	250.33	89.63		148.33	71.11	8	7.2%	102.00 [41.06, 162.94]	
Wood 2006 54	456	301.5		296.25	156	6	0.7%	159.75 [-96.11, 415.61]	
Subtotal (95% CI)			81			41	17.3%	116.23 [74.26, 158.20]	•
Heterogeneity: Tau ² = 0.00; Chi ² = 0.77, Test for overall effect: Z = 5.43 (P < 0.00		= 0.94); l ²	^e = 0%						
2.1.3 Light-to-moderate (Change score	2)								
Chehuen 2017 41	94	120.04	22	-31	92.92	20	6.8%	125.00 [60.39, 189.61]	
Gardner 2011 (supervised) 63	147.52	154.67	33	-14.3	111.76	30	6.6%	161.82 [95.61, 228.03]	
Novakovic 2019 (moderate) ⁶⁴ Subtotal (95% CI)	78.67	67.91	12 67	7.33	45.26	6 56	8.3% 21.6%	71.34 [18.54, 124.14] 116.32 [62.88, 169.76]	
Heterogeneity: Tau ² = 1261.50; Chi ² = 4		(P = 0.10)	$(); I^2 =$	57%					
Test for overall effect: $Z = 4.27 (P < 0.00)$	01)								
2.1.4 Light-to-moderate (Post score)									
Gardner 2012 ⁴⁶		207.43	106		142.16	36	7.2%	172.56 [111.60, 233.52]	
Nicolaï 2010 47		331.11			229.63	83	6.1%	197.66 [127.43, 267.89]	
Novakovic 2019 (pain-free) 64		244.44	12	97		6	1.9%	125.00 [-25.00, 275.00]	
Tew 2009 51	225	167	27	192	195	24	3.8%	33.00 [-67.27, 133.27]	
Subtotal (95% CI)			314			149	19.0%	141.40 [71.87, 210.93]	-
Heterogeneity: Tau ² = 2890.78; Chi ² = 7 Test for overall effect: Z = 3.99 (P < 0.00		(P = 0.00	5); I ² =	60%					
Total (95% CI)			591			304	100.0%	103.13 [80.78, 125.48]	▲
Heterogeneity: Tau ² = 837.94; Chi ² = 28		8 (P = 0.0)	05); I ² =	= 37%					-200 -100 0 100 200
Test for overall effect: $Z = 9.04$ (P < 0.00 Test for subgroup differences: $Chi^2 = 6.7$		P = 0.08)	$1^{2} = 5$	5.4%					Favors [control] Favors [experimental]

Suppl 6. Maximal walking distance (m) following high-intensity interval training (HIIT), moderate-intensity interval training (MIIT), and moderate-intensity training (MIT). CI: confidence interval; IV: inverse variance; SD: standard deviation of change.

	Expe	rimental	ľ.	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
I.3.1 HIIT									
Cucato 2013 62	316	141	13	-57	174.78	12	4.2%	373.00 [247.88, 498.12]	
anderson 2006 (cycling) ^{so}	36	94.8	15	-7.5	103.91	7	5.5%	43.50 [-47.20, 134.20]	
anderson 2006 (walking) ⁵⁰	180	150	13	-7.5	103.91	7	4.6%	187.50 [75.37, 299.63]	
Vood 2006 54	218.25	246.12	7	53.25	387.63	6	0.9%	165.00 [-194.78, 524.78]	
wierska 2005 (arm-ergometer) 55	94.72	71.26	34	-12.81	46.99	17	7.9%	107.53 [74.78, 140.28]	
wierska 2005 (leg-ergometer) ⁵⁵ ubtotal (95% CI)	113.89	91.8	37 119	-12.81	46.99	17 66	7.7% 30.8%	126.70 [89.63, 163.77] 148.85 [87.91, 209.79]	
leterogeneity: $Tau^2 = 3375.33$; $Chi^2 = 20$.	51, df = 5 (P = 0.00	(1); $I^2 =$	76%					
est for overall effect: $Z = 4.79 (P < 0.000)$	01)								
.3.2 MIIT									
ronas 2011 (arm-ergometer) 43	181.1	127	10	46.3	92.5	8	5.0%	134.80 [33.29, 236.31]	
hehuen 2017 41	941	334	22	678	275	20	2.6%	263.00 [78.60, 447.40]	
ollins 2003 44	862.3	306.9	11	535.1	207.5	10	2.0%	327.20 [104.87, 549.53]	
collins 2005 45	829.5	255	25	520.8	211.8	24	4.0%	308.70 [177.66, 439.74]	
ew 2009 51	165	194.62	27	26	181.87	24	5.0%	139.00 [35.64, 242.36]	
reat-Jacobson 2009 (arm-ergometer) 52	182.1	126.7	10	45.3	92.7	3	4.0%	136.80 [5.76, 267.84]	
reat-Jacobson 2009 (combination) 52	217.2	72.7	12	45.3	92.7	3	4.6%	171.90 [59.23, 284.57]	
/alker 2000 (arm-ergometer) 53	391.67	85.19	24	273.33	108.89	8	5.8%	118.34 [35.54, 201.14]	
/alker 2000 (leg-ergometer) 53	318.67	48.15	24	273.33	108.89	8	6.0%	45.34 [-32.54, 123.22]	
Vang 2008 65	1,099.56	207.11	14	920	335.1	11	2.0%	179.56 [-46.24, 405.36]	
ubtotal (95% CI)			179			119	41.0%	158.74 [105.64, 211.84]	•
leterogeneity: Tau ² = 3224.18; Chi ² = 17.	17, df = 9(P = 0.05	5); $ ^2 = 4$	18%					1 Arc.
est for overall effect: $Z = 5.86 (P < 0.000)$	01)								
1.3.3 MIT (Claudication)									
renner 2019 61	488.5	209.5	18	278.1	176.7	15	4.0%	210.40 [78.63, 342.17]	
ardner 2011 (supervised) 63	192.2	185.07	33	-8.88	157.4	30	5.7%	201.08 [116.47, 285.69]	
ardner 2012 46	666.98	265.54	106	398.76	275.37	36	5.0%	268.22 [165.04, 371.40]	
icolaï 2010 47	437.33	487.41	169	136.67	222.22	83	5.6%	300.66 [212.99, 388.33]	
ovakovic 2019 (moderate) 64	235.33	195.56	10	147.33	108.15	4	3.1%	88.00 [-73.01, 249.01]	
lovakovic 2019 (pain-free) 64	359.33	492.59	11	147.33	108.15	4	1.2%	212.00 [-97.79, 521.79]	
reat-Jacobson 2009 (treadmill) ⁵² Iubtotal (95% CI)	294.7	163.5	11 358	45.3	92.7	3 175	3.6% 28.2%	249.40 [106.78, 392.02] 234.50 [187.77, 281.23]	•
leterogeneity: Tau ² = 352.29; Chi ² = 6.57 Fest for overall effect: Z = 9.84 (P < 0.000		= 0.36);	l ² = 9%						
Total (95% CI)			656			360	100.0%	176.67 [140.63, 212.70]	•
leterogeneity: Tau ² = 4022.50; Chi ² = 64.	25, df = 22	(P < 0.0)0001);	$I^2 = 66\%$					-500 -250 0 250 5
est for overall effect: $Z = 9.61 (P < 0.000)$	01)								-500 -250 0 250 5 Favors [control] Favors [experimental]
			$^{2} = 69.$						

Suppl 7. Pain-free walking distance (m) following high-intensity interval training (HIIT), moderate-intensity interval training (MIIT), and moderate-intensity training (MIT). CI: confidence interval; IV: inverse variance; SD: standard deviation of change.

	Exp	erimenta	I .	c	Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.5.1 HIIT									
Cucato 2013 62	413	201	13	253	118	12	2.5%	160.00 [31.95, 288.05]	
Sanderson 2006 (cycling) 50	-6	138.06	15	41.25	203.51	7	1.6%	-47.25 [-213.41, 118.91]	
Sanderson 2006 (walking) 50	455.25	276.75	13	334.5	331.5	7	0.6%	120.75 [-167.24, 408.74]	
Wood 2006 54	456	301.5	7	296.25	156	6	0.7%	159.75 [-96.11, 415.61]	
Zwierska 2005 (arm-ergometer) 55	44.41	68.53	34	-20	95.17	17	8.6%	64.41 [13.64, 115.18]	
Zwierska 2005 (leg–ergometer) ^{ss} Subtotal (95% CI)	52.37	69.41	37 119	-20	95.17	17 66	8.7% 22.8%	72.37 [21.90, 122.84] 72.20 [38.96, 105.43]	•
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4.44$, o	f = 5 (P =	= 0.49); l ²	= 0%						
Test for overall effect: $Z = 4.26$ (P < 0.000	1)								
2.5.2 MIIT									
Bronas 2011 (arm-ergometer) 43	89.6	74	10	7.3	43.8	8	8.0%	82.30 [27.30, 137.30]	
Chehuen 2017 ⁴¹		120.04	22	-31		20	6.8%	125.00 [60.39, 189.61]	
Tew 2009 51	225	167	27	192	195	24	3.8%	33.00 [-67.27, 133.27]	
Treat–Jacobson 2009 (arm–ergometer) 52	89.6	74	10	4	45.4	3	6.3%	85.60 [16.73, 154.47]	
Treat-Jacobson 2009 (combination) 52	61.94	109.94	12	4	45.4	3	5.1%	57.94 [-22.74, 138.62]	
Walker 2000 (arm-ergometer) 53	266.67	120.74	24	148.33	71.11	8	6.3%	118.34 [49.34, 187.34]	
Walker 2000 (leg-ergometer) 53	250.33	89.63		148.33	71.11	8	7.2%	102.00 [41.06, 162.94]	
Subtotal (95% CI)			129			74	43.4%	92.31 [66.61, 118.02]	•
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.83$, c Test for overall effect: $Z = 7.04$ (P < 0.000		= 0.70); l²	= 0%						
2.5.3 MIT (claudication)									
Gardner 2011 (supervised) 63	147.52	154.67	33	-14.3	111.76	30	6.6%	161.82 [95.61, 228.03]	
Gardner 2012 46	367.46	207.43	106	194.9	142.16	36	7.2%	172.56 [111.60, 233.52]	
Nicolaï 2010 47	334.33	331.11	169	136.67	229.63	83	6.1%	197.66 [127.43, 267.89]	
Novakovic 2019 (moderate) 64	78.67	67.91	12	7.33	45.26	6	8.3%	71.34 [18.54, 124.14]	
Novakovic 2019 (pain-free) 64	222	244.44	12	97	72.59	6	1.9%	125.00 [-25.00, 275.00]	
Treat-Jacobson 2009 (treadmill) 52	91.6	148.4	11	4	45.4	3	3.7%	87.60 [-14.04, 189.24]	+
Subtotal (95% CI)			343			164	33.8%	138.35 [91.73, 184.96]	•
Heterogeneity: $Tau^2 = 1812.05$; $Chi^2 = 11$ Test for overall effect: $Z = 5.82$ (P < 0.000		5 (P = 0.0))4); I ² =	= 57%					
Total (95% CI)			591			304	100.0%	103.13 [80.78, 125.48]	•
Heterogeneity: $Tau^2 = 837.94$; $Chi^2 = 28.7$	$^{\prime}8 df = 1$	8(P = 0.0)		= 37%					
Test for overall effect: $Z = 9.04$ (P < 0.000		0.0		5170					-200 -100 Ó 100 200
Test for subgroup differences: $Chi^2 = 5.14$									Favors [control] Favors [experimental]

Suppl 8. Cardiorespiratory fitness (V'O_{2peak}, mLO₂·kg⁻¹·min⁻¹) following high-intensity interval training (HIIT), moderate-intensity interval training (MIIT), and moderate-intensity training (MIT). CI: confidence interval; IV: inverse variance; SD: standard deviation of change.

	Expe	rimen	tal	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.3.1 HIIT									
Sanderson 2006 (cycling) 50	1.4	2.93	15	-0.2	3.1	7	4.6%	1.60 [-1.13, 4.33]	
Sanderson 2006 (walking) 50	0.6	2.73	13	-0.2	3.1	7	4.6%	0.80 [-1.93, 3.53]	
Wood 2006 54	1.4	2.69	7	0.4	3.99	6	2.8%	1.00 [-2.76, 4.76]	
Zwierska 2005 (arm-ergometer) 55	16.21	2.29	34	12.77	1.07	17	11.7%	3.44 [2.52, 4.36]	
Zwierska 2005 (leg-ergometer) 55	2.49	1.28		-0.63	0.81	17	13.4%	3.12 [2.56, 3.68]	
Subtotal (95% CI)			106			54	37.1%	2.91 [2.19, 3.63]	•
Heterogeneity: Tau ² = 0.18; Chi ² =	5.57, df	= 4 (P	= 0.23); $I^2 = 2$	8%				
Test for overall effect: $Z = 7.93$ (P <	0.0000	1)							
3.3.2 MIIT									
Bronas 2011 (arm–ergometer) 43	1.47	1.9	10	-0.38	2	8	7.4%	1.85 [0.03, 3.67]	
Chehuen 2017 41	0.1	2.53	22	-0.3	2.89	19	8.0%	0.40 [-1.28, 2.08]	
Collins 2005 45	19.5	4.6	25	15.6	3.5	24	5.8%	3.90 [1.62, 6.18]	
Tew 2009 51	1	2.04	27	-0.6	3.17	24	8.9%	1.60 [0.12, 3.08]	
Wang 2008 65	25.8	3.8	14	22.3	5	11	3.1%	3.50 [-0.06, 7.06]	
Subtotal (95% CI)			98			86	33.2%	1.92 [0.76, 3.09]	-
Heterogeneity: $Tau^2 = 0.72$; $Chi^2 =$	6.88, df	= 4 (P	= 0.14); $I^2 = 4$	2%				
Test for overall effect: $Z = 3.23$ (P =	= 0.001)								
3.3.3 MIT									
Gardner 2011 (supervised) 63	0.3	1.9	33	-0.9	1.9	30	11.6%	1.20 [0.26, 2.14]	
Gardner 2012 46	15.4	3.6	106	14.5	3.8	36	9.2%	0.90 [-0.52, 2.32]	
Tew 2009 51	1	2.04	27	-0.6	3.17	24	8.9%	1.60 [0.12, 3.08]	
Subtotal (95% CI)			166			90	29.7%	1.22 [0.52, 1.91]	•
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 =$	0.45, df	= 2 (P	= 0.80); $I^2 = 0$	%				
Test for overall effect: Z = 3.44 (P =	= 0.0006))							
Total (95% CI)			370			230	100.0%	1.97 [1.26, 2.67]	•
Heterogeneity: Tau ² = 0.88; Chi ² =	33.93, d	f = 12	(P = 0.	0007);	$^{2} = 65$	5%			
Test for overall effect: $Z = 5.47$ (P <									-'4 -'2 Ó Ż Á
Test for subgroup differences: Chi ²			P(P = 0)	004)	$^{2} = 82$	0%			Favors [control] Favors [experimental]

Suppl 9. Pain-free walking distance (m) following vigorous and light-to-moderate exercise intensity in different training modalities (walking vs. others). CI: confidence interval; IV: inverse variance; SD: standard deviation of change.

	Exp	erimental			ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.6.1 Walking (Vigorous)									
Treat-Jacobson 2009 (treadmill) 52	91.6	148.4	11	4	45.4	3	5.2%	87.60 [-14.04, 189.24]	
Wood 2006 54	456	301.5		296.25	156	6	1.1%	159.75 [-96.11, 415.61]	
Subtotal (95% CI)			18			9	6.3%	97.43 [2.98, 191.89]	
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.26$, c Test for overall effect: $Z = 2.02$ (P = 0.04)	if = 1 (P =	= 0.61); I ²	= 0%						
2.6.2 Cycling and others (Vigorous)									
Bronas 2011 (arm-ergometer) 43	89.6	74	10	7.3	43.8	8	9.8%	82.30 [27.30, 137.30]	
Sanderson 2006 (cycling) 50	-6	138.06	15	41.25	203.51	7	2.5%	-47.25 [-213.41, 118.91]	
Treat-Jacobson 2009 (arm-ergometer) 52	89.6	74	10	4	45.4	3	8.1%	85.60 [16.73, 154.47]	
Zwierska 2005 (arm-ergometer) 55	44.41	68.53	34	-20	95.17	17	10.4%	64.41 [13.64, 115.18]	
Zwierska 2005 (leg-ergometer) 55	52.37	69.41	37	-20	95.17	17	10.4%	72.37 [21.90, 122.84]	
Subtotal (95% CI)			106			52	41.2%	71.38 [44.24, 98.51]	•
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.35$, d	if = 4 (P =	= 0.67); I ²	= 0%						
Test for overall effect: $Z = 5.16$ (P < 0.000	001)								
2.6.3 Walking (Light-to-moderate)									
Chehuen 2017 41	94	120.04	22	-31	92.92	20	8.6%	125.00 [60.39, 189.61]	
Gardner 2011 (supervised) 63	147.52	154.67	33	-14.3	111.76	30	8.4%	161.82 [95.61, 228.03]	
Gardner 2012 46	367.46	207.43	106	194.9	142.16	36	9.1%	172.56 [111.60, 233.52]	
Nicolaï 2010 47	334.33	331.11	169	136.67	229.63	83	8.0%	197.66 [127.43, 267.89]	
Novakovic 2019 (moderate) 64	78.67	67.91	12	7.33	45.26	6	10.1%	71.34 [18.54, 124.14]	
Novakovic 2019 (pain-free) 64	222	244.44	12	97	72.59	6	2.9%		
Subtotal (95% CI)			354			181	47.1%	141.56 [99.75, 183.37]	•
Heterogeneity: Tau ² = 1401.21; Chi ² = 10 Test for overall effect: Z = 6.64 (P < 0.000		5 (P = 0.0	6); I ² =	= 54%					
2.6.4 Cycling and others (Light-to-mode	erate)								
Tew 2009 51	225	167	27	192	195	24	5.3%	33.00 [-67.27, 133.27]	
Subtotal (95% CI)			27			24	5.3%	33.00 [-67.27, 133.27]	
Heterogeneity: Not applicable									
Test for overall effect: $Z = 0.65$ (P = 0.52)									
Total (95% CI)			505			266	100.0%	102.94 [74.54, 131.34]	•
Heterogeneity: $Tau^2 = 1349.02$; $Chi^2 = 26$.	61 df -	13 (P - 0		- 51%		-00	20010/0		
Test for overall effect: $Z = 7.10$ (P < 0.000		15(r = 0.	UI), I	- 31/0					-200 -100 Ó 100 200
Test for subgroup differences: $Chi^2 = 8.92$		2 - 0.02)	$1^2 - 6$	6 1%					Favors [control] Favors [experimental]
rescrot subgroup unterences. cfll = 6.92	, ui – 5 (i	- 0.05),	0	0.4/0					

Suppl 10. Cardiorespiratory fitness (V'O_{2peak}, mLO₂·kg⁻¹·min⁻¹) following vigorous and light-tomoderate exercise intensity in different training modalities (walking vs. others). CI: confidence interval; IV: inverse variance; SD: standard deviation of change.

	Expe	rimen			ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
3.4.1 Walking (Vigorous)									
Park 2019 ⁴⁸	2.4	0.9	35	-1.4	3.1	37	10.1%	3.80 [2.76, 4.84]	
Sandercock 2007 (supervised) 49	13.7	4.2	13	14.3	5.1	8	2.4%	-0.60 [-4.81, 3.61]	
Sanderson 2006 (walking) 50	0.6	2.73	13	-0.2	3.1	7	4.5%	0.80 [-1.93, 3.53]	
Wood 2006 54	1.4	2.69	7	0.4	3.99	6	2.9%	1.00 [-2.76, 4.76]	
Subtotal (95% CI)			68			58	19.9%	1.73 [-0.55, 4.01]	
Heterogeneity: Tau ² = 3.31; Chi ² = 3	8.62, df	= 3 (P	= 0.03); $I^2 = 6$	5%				
Test for overall effect: Z = 1.49 (P =	0.14)								
3.4.2 Cycle and others (Vigorous)									
Bronas 2011 (arm–ergometer) 43	1.47	1.9	10	-0.38	2	8	7.1%	1.85 [0.03, 3.67]	
Collins 2005 45	19.5	4.6	25	15.6	3.5	24	5.6%	3.90 [1.62, 6.18]	
Sanderson 2006 (cycling) 50	1.4	2.93	15	-0.2	3.1	7	4.5%	1.60 [-1.13, 4.33]	
Wang 2008 65	25.8	3.8	14	22.3	5	11	3.1%	3.50 [-0.06, 7.06]	
Zwierska 2005 (arm-ergometer) 55	16.21	2.29	34	12.77	1.07	17	10.5%	3.44 [2.52, 4.36]	
Zwierska 2005 (leg-ergometer) 55	2.49	1.28	37	-0.63	0.81	17	11.8%	3.12 [2.56, 3.68]	
Subtotal (95% CI)			135			84	42.7%	3.11 [2.67, 3.56]	•
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 4$	4.01, df	= 5 (P	= 0.55); $I^2 = 0$	%				~~~~
Test for overall effect: Z = 13.68 (P	< 0.000	01)							
3.4.3 Walking (Light-to-moderate))								
Chehuen 2017 ⁴¹	0.1	2.53	22	-0.3	2.89	19	7.6%	0.40 [-1.28, 2.08]	
Gardner 2011 (supervised) 63	0.3	1.9	33	-0.9	1.9	30	10.5%	1.20 [0.26, 2.14]	
Gardner 2012 ⁴⁶	15.4	3.6	106	14.5	3.8	36	8.6%	0.90 [-0.52, 2.32]	
Sandercock 2007 (home-based) 49	13.7	4.1	15	14.3	5.1	8	2.5%		
Subtotal (95% CI)			176			93	29.1%	0.94 [0.24, 1.63]	◆
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1$		= 3 (P	= 0.74); $I^2 = 0$	%				
Test for overall effect: $Z = 2.62$ (P =	0.009)								
3.4.4 Cycle and others (Light-to-n	noderate	e)							
Tew 2009 51	1	2.04	27	-0.6	3.17	24	8.3%	1.60 [0.12, 3.08]	
Subtotal (95% CI)			27			24	8.3%	1.60 [0.12, 3.08]	
Heterogeneity: Not applicable									
Test for overall effect: $Z = 2.11$ (P =	0.03)								
Total (95% CI)			406				100.0%	2.05 [1.32, 2.77]	•
Heterogeneity: Tau ² = 1.08; Chi ² = 4	43.32, d	f = 14	(P < 0.	0001);	$ ^{2} = 68$	3%			
Test for overall effect: Z = 5.53 (P <	0.0000	1)							Favors [control] Favors [experimental]
Test for subgroup differences: Chi ²	20 12	df -	D /D / C	00001) 12 -	20 20/			ravors (control) ravors (experimental)