

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

Mattia Fassora¹, Luca Calanca², Cecile Jaques³, Lucia Mazzolai², Bengt Kayser¹ ([0000-0002-9776-7501](https://orcid.org/0000-0002-9776-7501)), **Stefano Lanzi^{2*} (0000-0003-1089-6309)**

¹ Institute of Sport Sciences of the University of Lausanne, Switzerland

² Division of Angiology, Heart and Vessel Department, Lausanne University Hospital, Switzerland

³ Medical Library, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland.

***Corresponding author**

Stefano Lanzi, PhD

Division of Angiology, Heart and Vessel Department, Lausanne University Hospital

Ch. de Mont-Paisible 18 - 1011 Lausanne, Switzerland

Tél. +41 079 556 49 11

stefano.lanzi@chuv.ch

<https://orcid.org/0000-0003-1089-6309>

@ste_lanzi

Suppl 1. Search strategy

1.1 Vocabulary

Concepts	Peripheral Artery Disease (PAD)	Exercise	Walking performance
Free terms Syntaxe Embase	(Peripheral NEAR/3 (vascular OR arter*) NEAR/3 disease*) 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* arterial-insufficiency OR arteriosclerosis OR atherosclerosis (peripheral NEAR/3 angiopath*) claudication ("Lower extremity" NEAR/3 arter* NEAR/3 disease*)	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"	walk* treadmill
Emtree	'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	'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 'exercise test'/exp 'heart rate'/de OR 'oxygen consumption'/de OR 'maximal oxygen uptake'/de OR 'maximal oxygen consumption'/de	'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	("Exercise"[Mesh]) OR "Exercise Therapy"[Mesh] OR "Exercise Movement Techniques"[Mesh:NoExp] OR	Exercise Tolerance"[Mesh:NoExp]

Arterial Occlusive Diseases"[Mesh:NoExp] OR "Arteriosclerosis"[Mesh:NoExp] OR "Arteriosclerosis Obliterans"[Mesh] "Intermittent Claudication"[Mesh] "Atherosclerosis"[Mesh]	"Exercise Test"[Mesh] Exercise Tolerance"[Mesh:NoExp] "Rehabilitation"[Mesh:NoExp] "Physical Exertion"[Mesh] "Physical Endurance"[Mesh] "Heart Rate"[Mesh:NoExp] "Oxygen Consumption"[Mesh:NoExp]	"Exercise Test"[Mesh] "Walking"[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 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'/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))

Medline Ovid SP

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 "VO2max" 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

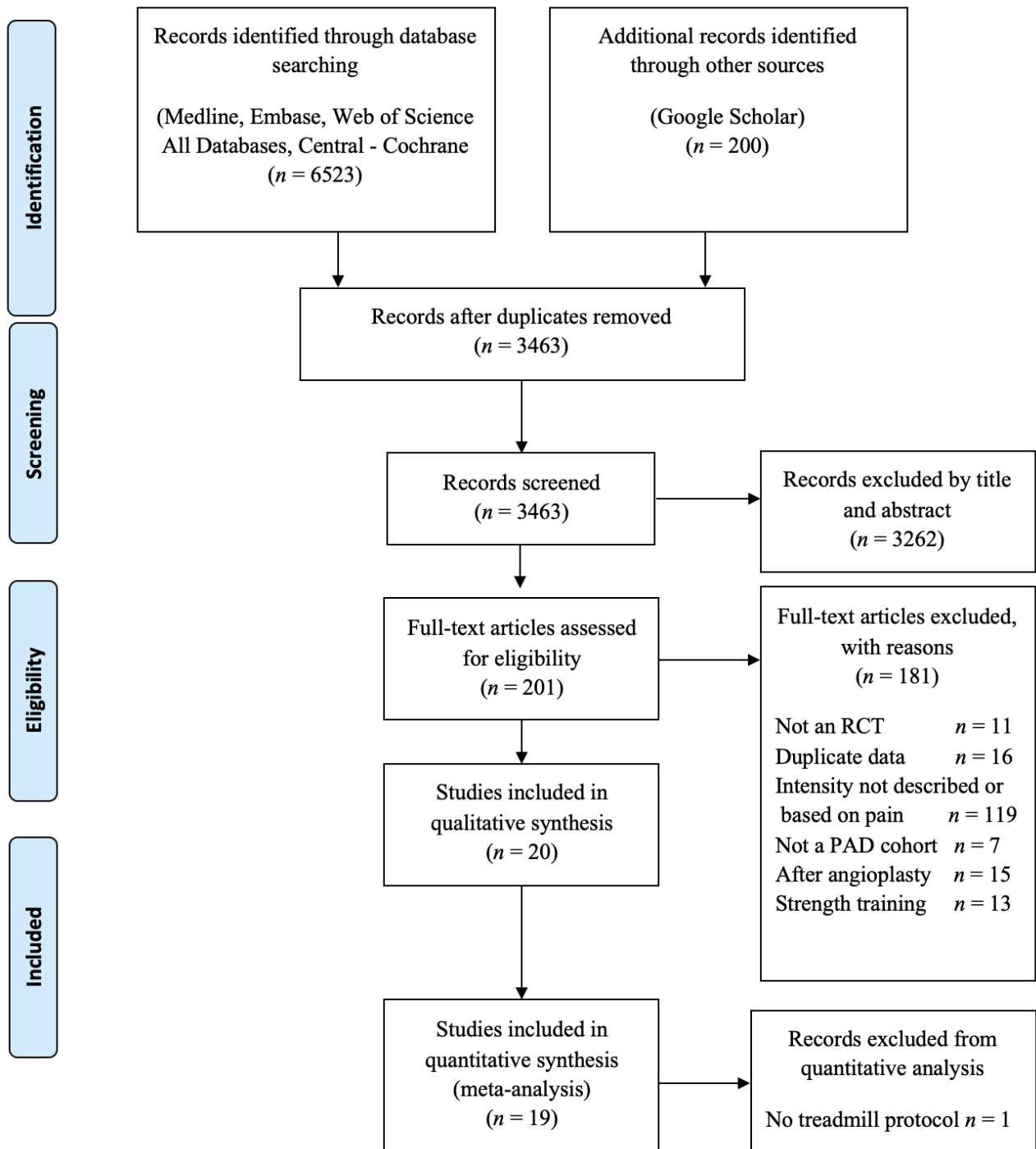
1271 references on 2020.06.17

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.



Suppl 3. Included studies and intervention characteristics.

Author, year	Control group	Intervention group	Mean exercise intensity*	Claudication pain severity	Supervision	Program length (weeks)	Frequency (per week)	Mean duration (min)
Vigorous exercise intensity								
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
Sanderson et al. 2006 ⁵⁰	Usual care	Treadmill walking	90% V'O _{2peak}	Mild pain	Yes	6	3	40 with rest periods
		Cycling	90% V'O _{2peak}	Mild pain	Yes	6	3	40 with rest periods
Treat-Jacobson et al. 2009 ⁵²	Walking advice	Treadmill walking	RPE 14	Severe pain	Yes	12	3	70 with rest periods
		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
Walker et al. 2000 ⁵³	Walking advice	Arm-ergometer	77.5% HR _{max}	No pain	Yes	6	2	40 with rest periods
		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
Zwierska et al. 2005 ⁵⁵	Walking advice	Arm-ergometer	87.5% V'O _{2peak} RPE 14.5	No pain	Yes	24	2	40 with rest periods
		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.

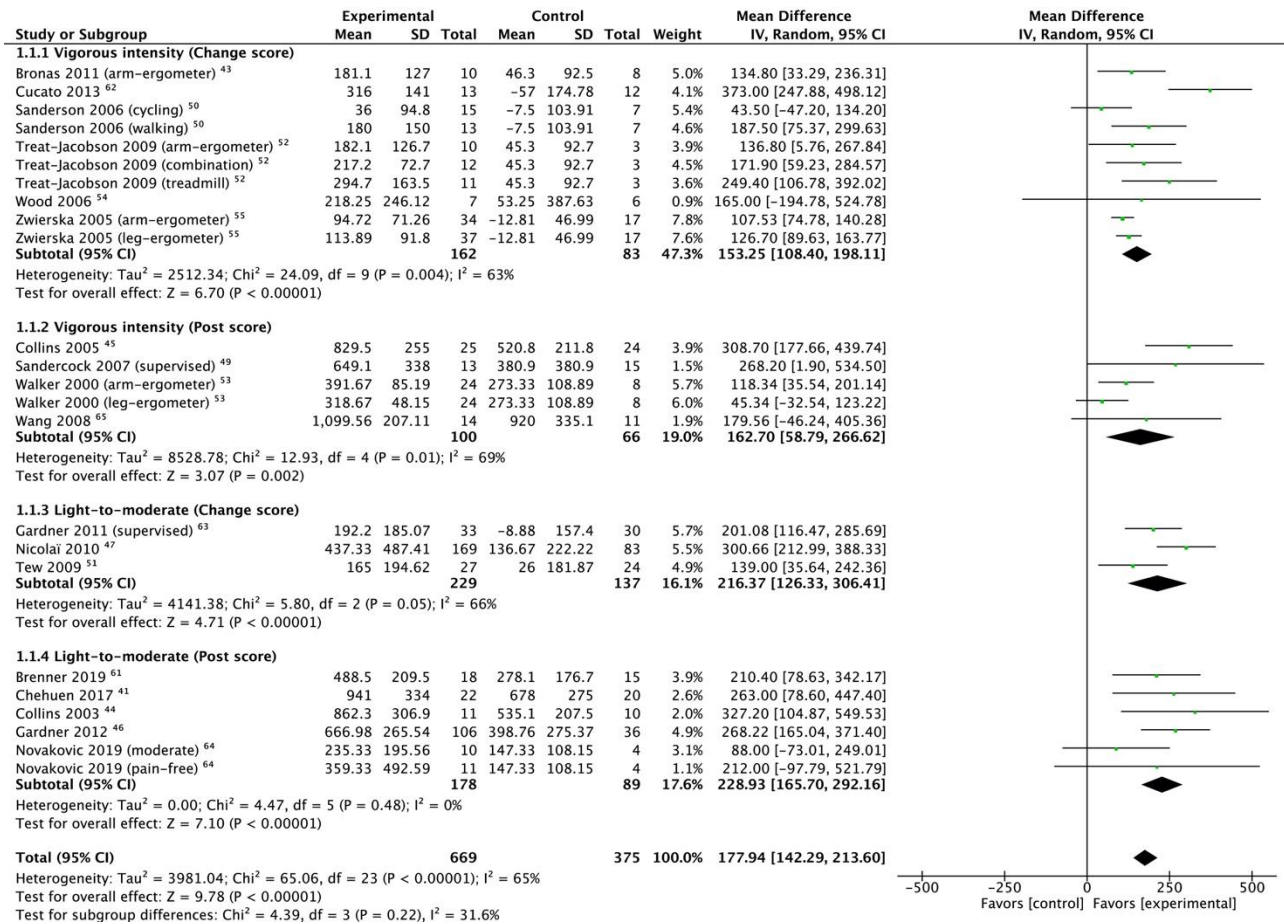
Suppl 3. Continued

Light-to-moderate exercise 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 _{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
Nicolai et al. 2010 ⁴⁷	Walking advice	Walking	55% V'O _{2peak} RPE 13	Mild-moderate Pain	Yes	12	2 or 3	20-40 w/o rest periods
Novakovic et al. 2019 ⁶⁴	Walking advice	Treadmill walking at moderate pain	70% HR	Moderate pain	Yes	12	2 or 3	60 with rest periods
		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

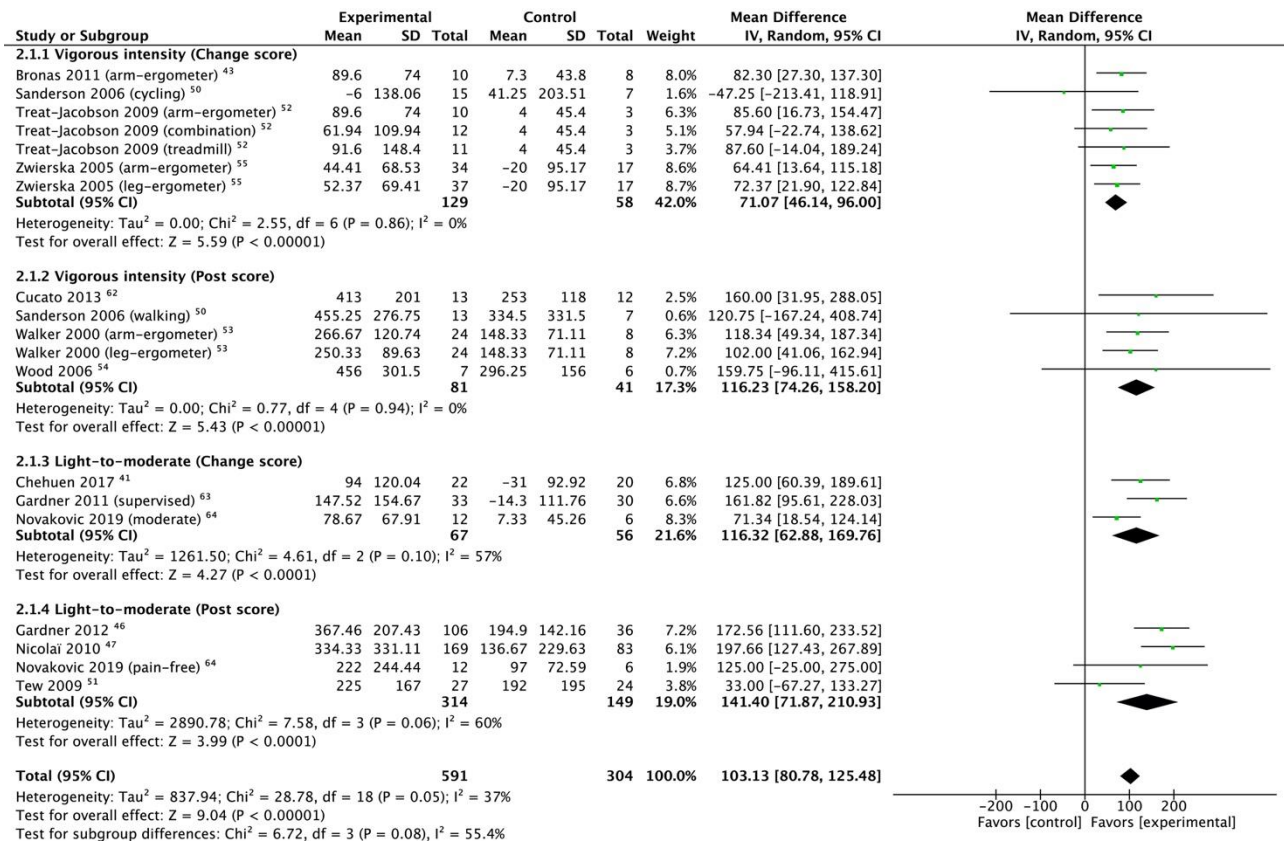
*According to American College of Sports Medicine (Garber et al. ³²) or Hansen et al. ⁴⁰

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.

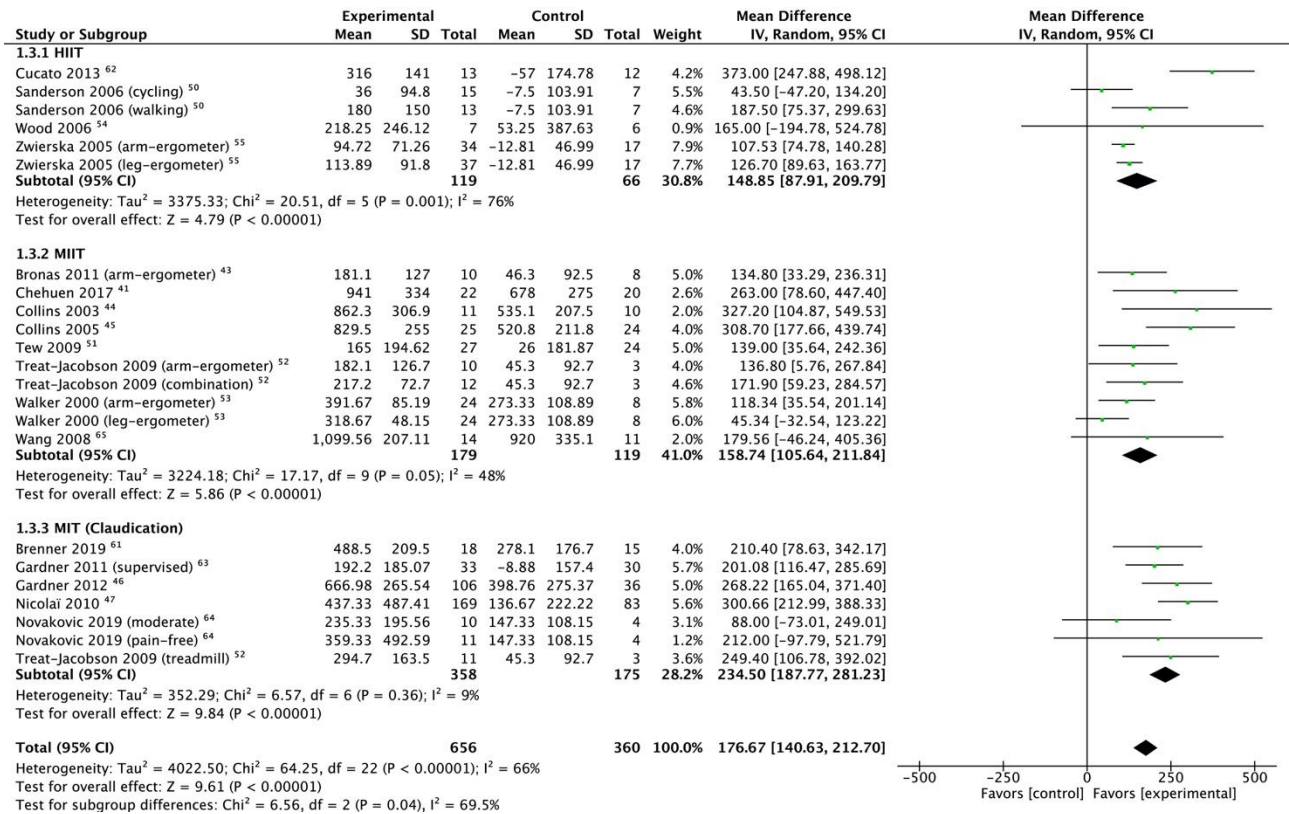
Suppl 4. Maximal walking distance (m) following vigorous and light-to-moderate exercise intensity (post and change score) CI: confidence interval; IV: inverse variance; SD: standard deviation of change.



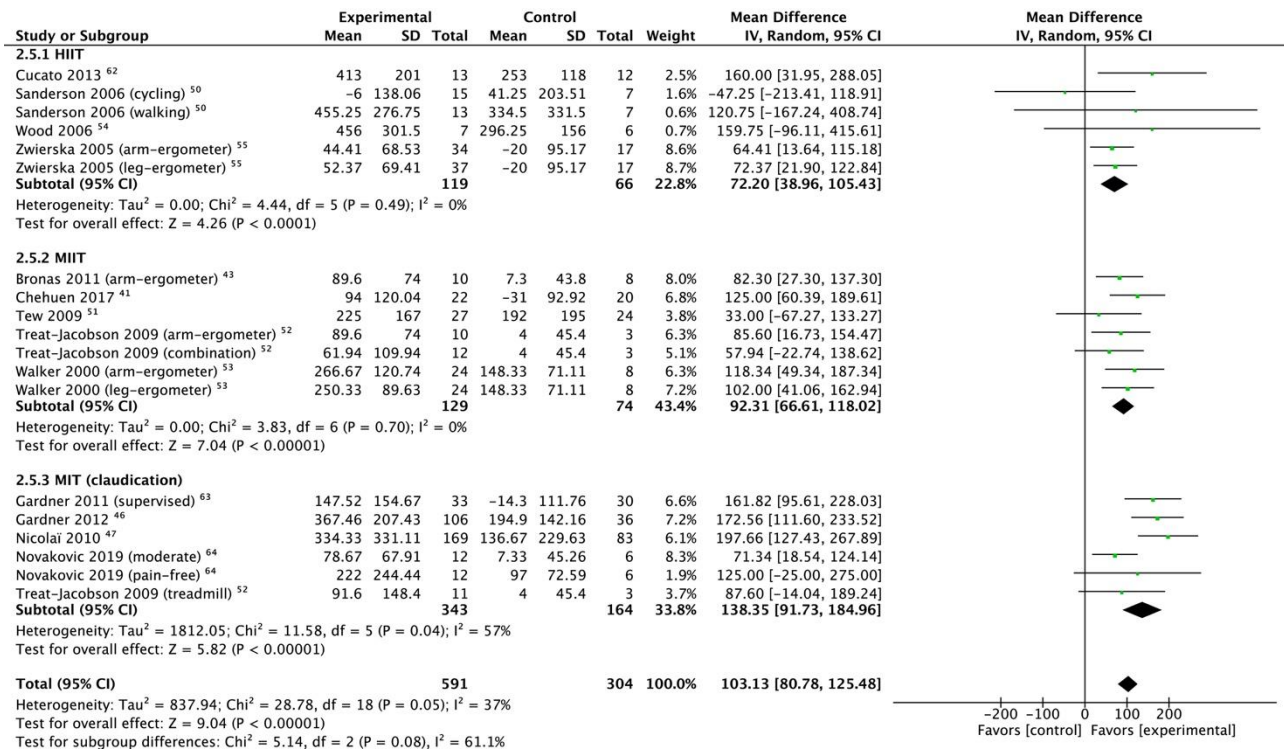
Suppl 5. Pain-free walking distance (m) following vigorous and light-to-moderate exercise intensity (post and change score) CI: confidence interval; IV: inverse variance; SD: standard deviation of change.



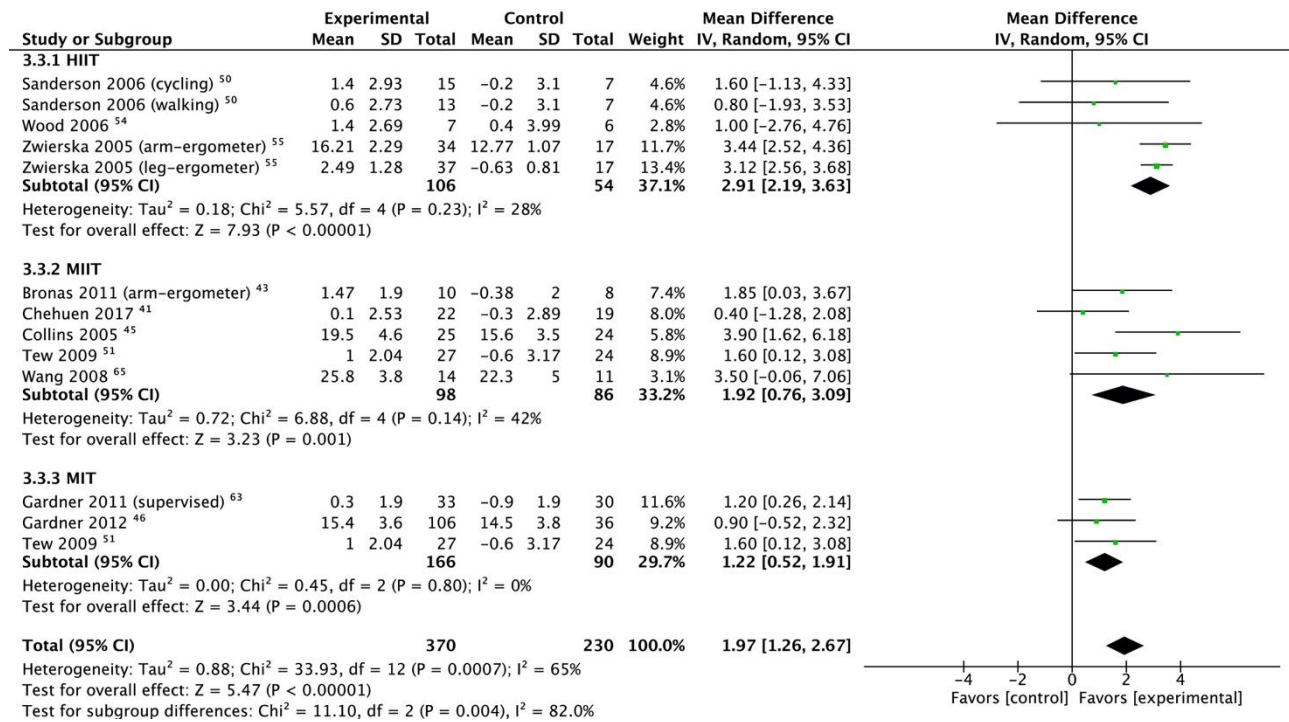
Suppl 6. Maximal walking distance (m) following high-intensity interval training (HIIT), moderate-intensity interval training (MIIT), and moderate-intensity training (MIT). CI: confidence interval; IV: inverse variance; SD: standard deviation of change.



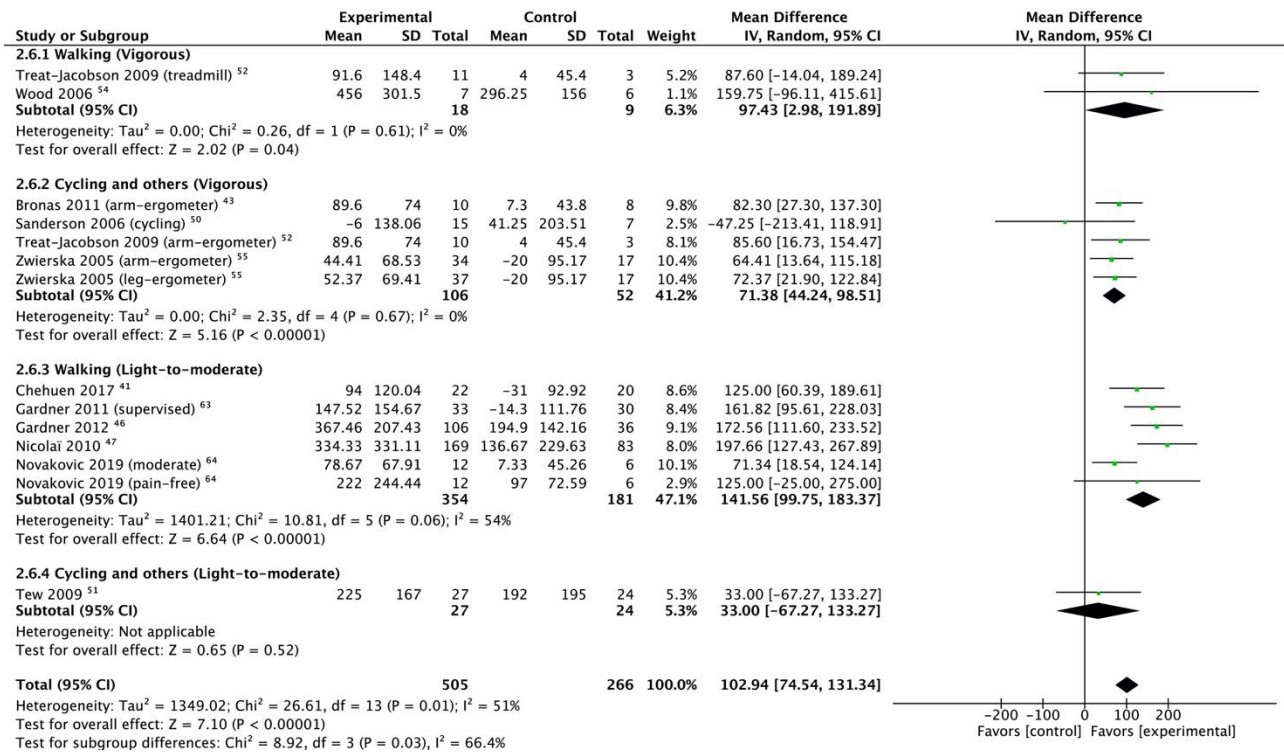
Suppl 7. Pain-free walking distance (m) following high-intensity interval training (HIIT), moderate-intensity interval training (MIIT), and moderate-intensity training (MIT). CI: confidence interval; IV: inverse variance; SD: standard deviation of change.



Suppl 8. Cardiorespiratory fitness ($V'O_{2peak}$, $mL O_2 \cdot kg^{-1} \cdot min^{-1}$) 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.



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.



Suppl 10. Cardiorespiratory fitness ($\dot{V}O_{2peak}$, $mLO_2 \cdot kg^{-1} \cdot min^{-1}$) 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.

