Supplemental Material
Data S1.

Search Strategy:

PubMed

(Intermittent claudication[Title/Abstract] OR Peripheral arterial disease[Title/Abstract] OR Peripheral arterial disease[Title/Abstract] OR peripheral vascular disease[Title/Abstract] OR lower extremity arterial disease[Title/Abstract]) AND (SET[Title/Abstract] OR Exercise[Title/Abstract] OR Best medical therapy[Title/Abstract] OR BMT[Title/Abstract] OR Percutaneous angioplasty[Title/Abstract] OR PCA[Title/Abstract] OR Surgical intervention[Title/Abstract] OR Revascularization[Title/Abstract] OR Cilostazol[Title/Abstract])) AND (Maximum walking distance OR MWD OR treadmill OR walking distance OR quality of life OR walking capacity OR claudication distance OR claudication onset distance)
| Study reference | Intervention | MWD measurement method | QoL assessment | Type of exercise | Support/method |
|-----------------|--------------|------------------------|----------------|-----------------|----------------|
| Nylande 2007    | Control      | Graded treadmill test  | Short Form (SF-36) and Claudication Scale (CLAU-S) | -               | Smoking advice, exercise training, nutritional advice, prescribed statins and acetylsalicylic acid |
|                 | ER           |                        |                | -               | Percutaneous transluminal angioplasty |
| Mazari 2017      | ER           | Fixed load treadmill test | Short Form 36 (SF-36) and VascuQoL | Gym exercise included step-ups, bicycle exercise, knee extensions with weights, heel raises, knee bends and rest station to recover. | Conducted 3 times per week for 12 weeks. The session was supervised by a physiotherapist and conducted in the cardiac gym. For the first 6 weeks, patients complete one full circuit, followed by one extra station/week, thus by 12 weeks patients will complete 2 full circuits. Finally patients perform a series of gentle stretching and cooling down exercises. |
|                 | SET          |                        |                | -               | Combination of both the SET and ER strategies. |
|                 | SET+ER       |                        |                |                 | |
| Fakhry, 2013     | SET          | Standard treadmill test | Short Form 36 (SF-36) and VascuQoL | Treadmill walking | 24 weeks supervised treadmill exercise, 2x30 minute sessions/week. Patients were encouraged to walk at least 30 minutes 3 times/week + walk 1 hour per day |
|                 | ER           |                        |                | -               | Iliac revascularisation - self expanding nitinol stent (if initial balloon angioplasty not technically successful). Femoral revascularisation - self expanding nitinol stent if lumen diameter <50% after initial balloon angioplasty. All patients given general recommendations for lifestyle changes and strongly advised to walk regularly. |
| Djerf 2019      | ER           | Graded treadmill test  | Short Form 36 (SF-36) and VascuQoL | -               | TASC II A-C treated with endovascular intervention, TASC II D treated with surgical revascularisation. Procedures listed: Aortoiliac endovascular procedure, Percutaneous transluminal angioplasty/subintimal angioplasty with stent, Aortoiliac open procedure, Aortobifemoral bypass, Femoro-femoral bypass. |
|                  | Control                  | SR + SET                  | Greenhalgh 2008               |
|------------------|--------------------------|---------------------------|-------------------------------|
| ER               | Standard treadmill test  | Graded treadmill test     | SET consisted of 30 minutes of continuous exercise to a maximum pain threshold using walking circuit interspersed with 7 lower limb training stations (eg. stair climbing, heel raises, treadmill walking) supervised by physiotherapists or nursing staff. All participants underwent OMC which involved: assessment of BP measure, dyslipidaemia, serum glucose and anti-platelet treatments and drug therapy was commenced when necessary. |
| Control          | Short Form 36 (SF-36) and EuroQoL 5-dimensions (EQ5D) | SF36 short-form            | Stair climbing, heel raises and treadmill walking |
| Lindgren 2018    | -                        | -                         | Percutaneous transluminal angioplasty |
|                  | Modern nitinol bare metal stents (BMS) were used. Calibrated angiogram compared pre- and post-implant minimum lumen diameters. IV heparin bolus of 5000 units was administered. | -                          | SET patients received OMC + SET. Consisted of treadmill walking for up to 78 scheduled exercise sessions that were 1 hour long, 3 days a week for 6 months. Patients received quarterly contact by research coordinators during supervised phase - then participated in a telephone-based maintenance program (7-12 months) to promote exercise adherence. |
| Murphy 2015      | Both groups received daily antiplatelet therapy (75mg aspirin or 75mg clopidogrel), lipid lowering and antihypertensive drugs. Patients received a pedometer and were encouraged to exercise when readouts were recorded | Graded treadmill test       | EVR patients received OMC + stent revascularisation of hemodynamically significant stenoses in the aorta and iliac arteries in the symptomatic leg(s) |
| Control          | SF-12 (23), the Walking Impairment Questionnaire (WIQ) (10), and the Peripheral Artery Questionnaire (PAQ) | Treadmill walking          | -                             |
| Control Group    | Control group received OMC according to current guidelines - use of atherosclerosis risk factor management, cilostazol, home exercise counselling | -                          | Control group received OMC according to current guidelines - use of atherosclerosis risk factor management, cilostazol, home exercise counselling |
| SET              | SET patients received OMC + SET. Consisted of treadmill walking for up to 78 scheduled exercise sessions that were 1 hour long, 3 days a week for 6 months. Patients received quarterly contact by research coordinators during supervised phase - then participated in a telephone-based maintenance program (7-12 months) to promote exercise adherence. | -                          | SET patients received OMC + SET. Consisted of treadmill walking for up to 78 scheduled exercise sessions that were 1 hour long, 3 days a week for 6 months. Patients received quarterly contact by research coordinators during supervised phase - then participated in a telephone-based maintenance program (7-12 months) to promote exercise adherence. |
| ER               | EVR patients received OMC + stent revascularisation of hemodynamically significant stenoses in the aorta and iliac arteries in the symptomatic leg(s) | -                          | EVR patients received OMC + stent revascularisation of hemodynamically significant stenoses in the aorta and iliac arteries in the symptomatic leg(s) |
| Study            | Intervention | Outcomes | Summary |
|------------------|--------------|----------|---------|
| Gelin 2001       | Control      | Quality of life evaluation | All patients were advised to give up smoking. Control patients received no other specific advice or treatment apart from the general advice given to the two treatment groups. SET patients were referred to trained physiotherapists - 30 minute sessions of specific walking training per week during the initial 6 months with 10-12 patients participating in each training class as described. After 6 months 2 sessions per week were offered. EVR patients were referred for standard angiography. Based on these findings, endovascular or open surgical procedures were chosen. |
| Bo 2015          | ER           | Short Form 36 (SF-36) [26], as well as a disease-specific instrument, the Claudication Scale (CLAU-S) | Percutaneous transluminal angioplasty |
|                  | SET+ER       | Treadmill walking and high intensity exercises | SET two days per week for 12 weeks + one home based exercise session per week. After hospital based SET, participants conducted home based exercise sessions every week for an additional 12 weeks. Each session lasted 60 minutes (consisted of warm-up exercises, 3 high intensity intervals, two moderate intensity intervals and cool down exercises). Endovascular revascularisation was performed by an interventional radiologist. For iliac revascularisation: initial balloon angioplasty, if that failed then self-expanding nitinol stent was used. For femoral revascularisation: self-expanding nitinol stent was chosen based on angiography. |
| Spronk 2009      | ER           | Short Form 36 (SF-36) and VascuQoL | SET performed over 24 weeks on a walking treadmill - 30 minutes per session, twice weekly supervised by a vascular technologist. Treadmill exercise was initiated at a workload of 3.5km/h without a graded incline and decreased to 1km/h when perceived maximum claudication pain occurred, and increased after a few minutes after the pain subsided. |
| Crowther 2008    | Control      | NA       | Control |
|          | SET       | Graded treadmill test | Treadmill walking with progressive increase in intensity and duration | Exercise program initial consisted of treadmill walking 3 days per week for 25 minutes at 3.2 km/hr. Participants were required to walk until pain level was perceived as 3 or 4 on the CPS. Exercise intensity (treadmill grade and walking speed) and duration (25 to 40 minutes) was progressively increased. This was performed over a 12 month period |
|----------|-----------|-----------------------|-------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| Cheetham 2004 | HET       | Graded treadmill test | the Short-Form-36, the Charing Cross Symptom Specific Claudication Questionnaire (CCCQ) | All patients were given best medical treatment (antiplatelet therapy, antihypertensive therapy, cholesterol lowering agents and diabetic control. Each patient received verbal and written exercise advice - recommended a program of walking at least 3 times a week to near maximal pain for at least half an hour per session. Additional leg exercises were to be performed at home (stair climbing and tiptoe walking) |
| SET      | Gym exercise included stair climbing, low step climbing, high step climbing, tip toe walking, standing on tip toe from flat, standing on tip toe from ankle dorsiflexion and power-jogger walking | A 45 minute class was conducted under physiotherapy and medical supervision in a standard hospital gym. Commenced with a 5-10 minute talk on benefits of walking. Followed by half an hour of exercise consisting of a walking circuit and performing seven 2 minute exercise stations for lower limb strengthening. Stair climbing, low step climbing, high step climbing, tip toe walking, standing on tip toe from flat, standing on tip toe from ankle dorsiflexion and power-jogger walking. Each 2 minute station was interspersed with a 2 minute walking circuit | |
| Gardner 2002 | Control   | Self-reported Walking | -                                                        | Control                                                                                          |
| Study | SET | Graded treadmill test | NA | Treadmill exercise |
|-------|-----|-----------------------|----|-------------------|
| Baker 2017 | SET | Graded treadmill test | NA | Treadmill exercise |
| Control | - | - | Control |
| Brass 2012 | Cilostazol | Graded treadmill test | NA | - |
| Control | - | - | Placebo |

Supervised 6 months progressive exercise program followed by supervised, 12-month maintenance exercise program. The progressive program consisted of intermittent treadmill walking to near maximal claudication pain 3 days per week at a walking speed of approximately 2 mph. Walking duration began at 15 minutes for the first month of the program, and progressively increased by 5 minutes per month until a total of 40 minutes of walking was accomplished by the sixth month of rehabilitation. Walking intensity began at 50% of the maximal work load achieved during a maximal effort treadmill test, and progressively increased on an individual basis throughout the program to 80% by the sixth month of rehabilitation. Five minutes of cycling on a stationary bicycle ergometer served as both warm-up and cool-down exercise during each session. The final 12 months of the exercise program was considered the maintenance phase in which the frequency of exercise sessions was reduced to 2 days per week. Walking duration and intensity were maintained at 40 minutes and 80% of the maximal work load respectively.

Subjects performed three 60-minutes supervised exercise training sessions each week for a period of 3 months. Subjects walk on a treadmill at an initial speed of 2.0 mph to a mild to moderate pain level, stop and rest until the claudication pain has completely abated, and then resume walking. This pattern was repeated for a total of 60 minutes. If subjects can walk longer than 8 minutes without rest, the treadmill walking becomes more challenging via grade and speed increases in subsequent training sessions.

Patients were randomized to one of five study arms: placebo, K-134 at a dose of 25, 50, or 100 mg, or cilostazol at 100 mg, each twice daily.
All participants viewed a 7-minutes educational video about PAD and its clinical leg symptoms, life-threatening consequences of PAD (heart attack and stroke), other adverse outcomes (walking disability), and strategies for disease and risk factor management (smoking cessation, weight control, aerobic activity). After the video, each participant met face-to-face with the research coordinator. Participants were encouraged to ask questions about the video material. The coordinator queried participants regarding self-management behaviors (i.e., glucose monitoring, blood pressure monitoring) and gave them a calendar in which to document their daily glucose results, weekly blood pressures, and any routine lipid results provided by their primary care physician.

### HET

**Control**
- Graded treadmill test
- San Diego Claudication Questionnaire and Physical Activity Readiness Questionnaire (PAR-Q)

**HET**
- -

Intervention group subjects participated in a home-based walking program with three components: 1) A one-on-one interaction with the research coordinator at baseline; 2) Walking training and weekly group walking classes with an instructor; 3) Bi-weekly telephone calls for 6 months. Participants were then encouraged to walk 1 day per week with the study exercise instructor and other participants, as available, and to continue walking on their own at least 3 days per week for a minimum of 4 days of walking each week. Participants were advised to walk 50 minutes total for each session, and use their pedometers to increase the number of steps by 50 each session.

### Crowther 2012

**SET**
- Graded treadmill test
- Borg's Rating of Perceived Exertion (RPE) instrument and Claudication Pain Scale (CPS)

**Control**
- -

The exercise program initially consisted of intermittent supervised treadmill walking 3 days per week for a total time of 25 minutes at 3.2 km/hr (0.88 m/s). Participants were required to walk until the pain level was perceived as being 3 or 4 on the CPS. Exercise intensity (via treadmill grade and walking speed) and duration (25 minutes up to a maximum of 40 minutes) were progressively increased once the participant could walk continuously for 25 minutes at a level below 3 on the CPS pain scale. This exercise progression strategy was continued over the 6-month period.

### Dawson 2000

**Cilostazol**
- NA

**Cilostazol** taken 100 mg twice daily.
| Study | Group | Test | Outcome | Notes |
|-------|-------|------|---------|-------|
| Fakhry 2015 (ERASE trial) | Control | Graded treadmill test | - | Placebo taken daily |
| | SET + ER | Graded treadmill test | VascuQol and Short Form 36 Health Survey (SF-36) | Treadmill walking | ER performed by experienced interventional radiologist or vascular surgeon. For iliac and femoral revascularizations, a stent was used only if the initial balloon angioplasty was not successful (selective stenting). In addition, within 2 to 4 weeks after the procedure, patients were enrolled in the supervised exercise program described above. |
| | SET | Graded treadmill test | - | Treadmill walking |
| Gardner 2001 | SET | Graded treadmill test | Medical Outcomes Study Short Form 36 (MOS SF-36) | Treadmill walking | Exercise program consisted of treadmill walking to near maximum claudication pain. Physiotherapists were advised to start with a frequency of 2 to 3 sessions every week and approximately 30 to 45 minutes per session during the first 3 months. After this phase, the frequency was reduced to at least 1 session per week between months 3 and 6 and then to a frequency of 1 session every 4 weeks at 12 months depending on patients’ progress and preference. |
| | Control | Graded treadmill test | - | - |
| Gardner 2014 | SET | Graded treadmill test | Medical Outcomes Study Short Form 36 (MOS SF-36) | Treadmill walking with progressive increase in duration | Exercise sessions in our supervised exercise program were performed while wearing a step activity monitor as previously described. Briefly, the supervised program consisted of 3 months of intermittent treadmill walking to mild-to-moderate claudication pain 3 days per week at a speed of 2 mph and at a grade equal to 40% of the highest work load achieved during the baseline maximal treadmill test. Sessions progressively increased during the program from 15 to 40 minutes. |
This program consisted of 3 months of intermittent walking to mild-to-moderate claudication pain 3 days per week at a self-selected pace, in which exercise duration was progressively increased from 20 to 45 minutes per session. Patients wore the step activity monitor during each exercise session and returned the monitor and a logbook to the research staff at the end of week 1, 4, 8, and 12. During these brief 15-minute meetings, monitor data were downloaded, results were reviewed, and feedback was provided for the upcoming month of training.

**Control**

- Attention-Control, light resistance program. Light resistance training was performed 3 times per week, without any walking exercise, using a Pro-Form Fusion 6.0 LX weight system. On entry, the resistance that caused fatigue in various muscle groups after 15 repetitions (15-rep maximum) was established, and was reassessed each month. The resistance training phase consisted of performing upper extremity exercises that included the bench press, military press, butterfly, biceps curl, triceps press-down, and lat pulldown. Lower extremity exercises included the leg press, leg curl, and leg extension. One set of 15 repetitions was performed for each exercise. If the resistance from the exercise machine could not be lifted, resistance bands were used instead.

| Gardner 2012 | SET | Graded treadmill test | Walking Impairment Questionnaire | Treadmill walking with progressive increase in intensity and duration |
|--------------|-----|-----------------------|----------------------------------|---------------------------------------------------------------|
| HET          | -   | -                     | -                                | -                                                             |
| Control      | -   | -                     | -                                | -                                                             |

This program consisted of 6 months of supervised intermittent treadmill walking to near-maximal claudication pain 3 days per week. Walking duration and intensity of the sessions were progressively increased during the program. Walking duration began at 15 minutes for the first month of the program and increased by 5 minutes per month until 40 minutes of walking was accomplished by the sixth month of rehabilitation. Walking intensity began at an initial grade of 50% of the final workload attained during the baseline graded treadmill test and was increased by 10% every 6 weeks up to 80% during the final 6 weeks of the exercise program. During each exercise session, patients walked at approximately 2mph until their claudication pain reached a level of 3 on a 0 to 4 pain scale.

| Control | - | - | - |

This group were encouraged to walk more on their own but did not receive specific recommendations regarding an exercise program during the study.
| Study     | Group      | Test Type                        | Medical Outcomes Study Short-Form 36 (MOS SF-36) and Walking Impairment Questionnaire (WIQ) | Treadmill walking with progressive increase in intensity and duration | Notes |
|-----------|------------|----------------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|-------|
| Gardner   | HET        | Graded treadmill test            |                                                                                                 |                                                                   |       |
|           | SET        |                                  |                                                                                                 |                                                                   |       |
| Control   |            | NA                               |                                                                                                 |                                                                   |       |
| Hobbs     | Control    | Standard treadmill test          |                                                                                                 |                                                                   |       |
|           | ER         |                                  |                                                                                                 |                                                                   |       |

Home-based exercise program was designed to be as similar to the supervised exercise program as possible, and consisted of 12 weeks of intermittent walking to near maximal claudication pain three days per week at a self-selected pace. Walking duration began at 20 minutes for the first two weeks, and progressively increased five minutes bi-weekly until a total of 45 minutes of walking was accomplished during the final two weeks of the program. These exercise durations were five minutes longer throughout the program than in the supervised program in an attempt to better match the programs on total volume of exercise determined by multiplying the intensity and the duration of walking.

This standardized program consisted of three months of supervised intermittent treadmill walking, three days per week at a speed of approximately two mph. Walking duration began at 15 minutes for the first two weeks of the program, and progressively increased by 5 minutes biweekly until a total of 40 minutes of walking was accomplished during the final two weeks of the program. Because we have previously shown that changes in COT and MWT are similar for patients who train at a relatively high exercise intensity (80% of peak work load) and patients who train at a lower intensity (40% of peak work load) for longer duration.

This group were encouraged to walk more on their own but they did not receive specific recommendations regarding an exercise program during the study.

Control

Percutaneous transluminal angioplasty
| Study | Group | Test Type | Notes |
|-------|-------|-----------|-------|
| Hobbs 2007 | SET | Standard treadmill test | The supervised exercise comprised a 3-month, twice weekly, 1-hour physiotherapist-led exercise program. In addition to the supervised sessions, subjects were provided with a videotape of the exercise program and encouraged to undertake the exercises at home and complete an exercise log on the days that they did not attend the classes. Cilostazol was prescribed at a dose of 100 mg twice daily. If side effects were encountered (most commonly headache and diarrhoea), the dosing regimen was halved for 1 week. Programs were as followed in both SET and Cilostazol groups. |
| | Cilostazol | - | Control |
| | SET + Cilostazol | - | Control |
| Hodges 2008 | SET | Graded treadmill test | Patients in the supervised group visited the hospital twice weekly for a period of 12 weeks. During the session patients were encouraged to walk on a treadmill (3.2 km/h) and 75% of the initial grade achieved during the exercise test) until they reached stage three or four on the PAD pain scale. Repeated until each patient had accrued 30 minutes of exercise per session. |
| | | Self-reported rating of perceived exertion | Treadmill exercise |
The patients in the control group were given normal treatment. These patients were told to walk as often as possible, but given no exercise regime to follow.

All patients received the following: Current smokers were advised to stop smoking, antiplatelet therapy, preferably 75mg aspirin once daily, was commenced if the patient was not already on it and lipid-lowering agents (statins) were prescribed and titrated to reduce LDL serum levels below 2.5–3 mmol/L, if necessary. Patients allocated to unsupervised exercise (control group) were advised to exercise daily by walking as much as possible to near maximal pain, for a period of at least 45 minutes.

Patients attended the physiotherapy department for exercise therapy three times per week for the first 6 months. Compliance was assessed with logbooks. Supervision was provided on an individual or group basis and each session lasted for about 60 minutes. A session consisted of 5 minutes warm up activities, 50 minutes of intermittent exercise and ended with 5 minutes of cool-down activities. Walking treadmill exercise was started at a low treadmill workload of 2 mph, 0% grade. Patients walked until claudication pain become moderately severe, at which time they step off the treadmill and rest until claudication pain subsides. After the patient had walked 8–10 minutes at the initial workload, either the grade was increased by 1–2%, or the speed was increased by 0.5 mph as tolerated.
| Kruidenie r 2011 | ER | Graded treadmill test | Medical Outcomes Study Short-Form 36 (MOS SF-36) and Euroqol-5D questionnaire | - |
|-----------------|----|-----------------------|-----------------------------------------------------------------|-----|
| SET+ER          |    | Treadmill walking, , Cycle ergometer, Indoor walking space, Small group exercise room | Treadmill walking, , Cycle ergometer, Indoor walking space, Small group exercise room | - |

All patients received cardiovascular risk factor modification, including therapy with a platelet inhibitor and a statin and treatment of hypertension or diabetes or both as required. All patients who smoked were repeatedly advised to quit smoking and were offered a smoking cessation program. All patients were advised concerning lifestyle changes (eg, physical activity, weight, diet) according to the Dutch standard for cardiovascular risk management. The choice for a primary PVI for the individual patient was based on the results of imaging with duplex ultrasound or magnetic resonance angiography or both as discussed in a multidisciplinary meeting of interventional radiologists and vascular surgeons. Mainly iliac lesions generally were treated with a PVI, and depending on lesion classification, femoropopliteal lesions also were treated. Not all lesions were necessarily treated. All PVIs were performed by an experienced interventional radiologist and consisted of iliac angioplasty with selective stent placement for iliac stenoses, angioplasty with primary stent placement for superficial femoral artery stenoses, or recanalization with primary stent placement for iliac and femoral occlusions.

Patients in the PVI SET group, the SET program was scheduled to start within 3 weeks after the PVI. The SET program was performed in a community-based setting, meaning that patients followed exercise therapy by a trained physiotherapist in proximity to their homes. Organization and results of community-based SET have been described previously. SET was administered according to the guidelines of the Royal Dutch Society for Physiotherapy. The main goal of SET is to increase a patient’s walking distance by interval training with short (3–5 minutes) walking intervals up to submaximal pain (distraction not possible). Secondary goals are increasing endurance and strength and improving walking patterns. Patients generally started with a frequency of two to three sessions of 30 minutes a week. Frequency of the sessions was phased down according to the patient’s progress. Patients were encouraged to walk on a daily basis.
| Authors       | SET | Graded treadmill test | Medical Outcomes Study Short-Form 36 (MOS SF-36) | Treadmill walking with progressive increase in duration | Treadmill walking followed by recovery on an exercise bike with no resistance |
|--------------|-----|-----------------------|-----------------------------------------------|-----------------------------------------------------|-----------------------------------------------------------------------------|
| Lamberti 2016 | HET | Standard treadmill test | -                                            | -                                                   | -                                                                           |
| ER           |      |                        |                                               |                                                     |                                                                             |
| Novaković 2018 | SET | Standard treadmill test | 36-Item Short Form Survey (SF-36)              | Treadmill walking                                    | Interventions consisted of 36 training sessions, two or three times per week, according to the patient’s preferences. If patients could not attend prescheduled sessions, they were offered a new rescheduled session in the same week. A single training session lasted around 60 minutes and consisted of walking on a treadmill, followed by active recovery on an exercise bike with no resistance. |
| Control      |      |                        |                                               |                                                     |                                                                             |
| Mauer 2015   | SET | Graded treadmill test  | Baltimore Activity Scale for Intermittent Claudication (BASIC) questionnaire | Treadmill walking                                    | Supervised exercise rehabilitation program that was designed to elicit increases in COT and PWT as previously described. This standardized program consisted of 3 months of supervised treadmill walking sessions 3 days per week. Walking duration began at 15 minutes for the first 2 weeks of the program and progressively increased by 5 minutes bi-weekly until a total of 40 minutes of walking was accomplished during the final 2 weeks of the program. Patients walked at a grade equal to 40% of the final workload from the baseline maximal treadmill test to the point of near-maximal claudication pain at which point they stopped to relieve their leg pain. |

The program included two 10-minute sessions/day (6 days/week) of intermittent walking (1-minute work and 1-minute rest while seated) at a prescribed speed converted into a walking cadence and followed at home using a metronome. A semipersonalized training program was proposed according to the patient’s baseline exercise capacity (ICD less than or greater than 50 metres). The walking sessions were preferably performed indoors at home (e.g., in a hallway or a heated garage) to avoid the influence of weather on a treadmill. Open surgery or endovascular revascularization or both were planned. The team included highly experienced vascular surgeons and interventional radiologists. For each patient, the team performed the option that was most likely to yield the best hemodynamic improvement. After intervention, the patients received general recommendations regarding lifestyle changes and standardized advice to be physically active at home. The control group was advised to continue with secondary preventive activities including regular walking as recommended by the treating vascular specialist.
| Control | - | - | Patients randomized to this group \( n = 7 \) participated in supervised light resistance training over the 3-month study period. Light resistance training was performed three times per week, without any walking exercise, using a Pro-Form Fusion 6.0 LX weight system. On entry, the resistance that caused fatigue in various muscle groups after 15 repetitions (15-rep maximum) was established and was reassessed each month. The resistance training phase consisted of performing upper extremity exercises that included the bench press, military press, butterfly, biceps curl, triceps press down, and lat pull-down. Lower extremity exercises included the leg press, leg curl, and leg extension. One set of 15 repetitions was performed for each exercise. If the resistance from the exercise machine could not be lifted, resistance bands were used instead. |
|--------|---|---|---|
| HET    | - | - | Home-based exercise rehabilitation program that was designed to be as similar to the supervised Exercise program as possible and consisted of 12 weeks of intermittent walking to near-maximal claudication pain 3 days per week at a self-selected pace. Walking duration began at 20 minutes for the first 2 weeks and progressively increased 5 minutes bi-weekly until a total of 45 minutes of walking was accomplished during the final 2 weeks of the program. |
| Mays 2015 | Control | - | Patients assigned to the control group received verbal advice to exercise but no other formal training. |
| HET    | Graded treadmill test | Walking Impairment Questionnaire and SF-36 | Patients in the intervention group received in-hospital exercise training on a treadmill for an initial 2 weeks (3 days/week). Patients then completed 12 weeks of community-based walking exercise training. Patients instructed to walk/rest on treadmill for 35 minutes progressing to 50 minutes as tolerated. Intensity enough to induce moderate leg pain in 3-5 minutes for patients with IC. Attempts were made to increase exercise intensity weekly. |
| Mika 2005 | SET | Standard treadmill test | NA | Treadmill walking | Patients in the treatment group participated in 12 weeks of supervised treadmill training. The exercise training sessions were conducted three times a week on a treadmill during the morning hours. Treadmill speed was set at 3.2 km/hr and at an inclination on 12 degrees. The session consisted of intermittent walking to 85% of the previously individually determined pain-
| Study         | Group       | Test                           | Intervention                                                                 | Notes                                                                                                                                 |
|--------------|-------------|-------------------------------|-----------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|
| Miika 2011   | Training    | Graded treadmill test         | Treadmill walking with progressive increase in inclination, cycling exercise | Patients in the training group participated in a 12-week supervised treadmill training programme. The sessions were conducted in the morning, three times per week and consisted of repetitive walking exercise with 3-minutes resting intervals. During each session, after 5 minutes of warm-up activities (free cycling on a stationary cycle ergometer), subjects walked on the treadmill at a speed of 3.2 km/h and a grade that induced claudication pain within approximately 3 to 5 min. Walking was continued until onset of claudication pain (level 2 on pain scale). The main goal of this protocol was to approach but not continue walking beyond the claudication pain. Patients stopped exercise when the pain level 2 was reached. Both the duration and intensity of sessions were progressively increased during the programme. |
|              | Control     | NA                            |                                                                             | Control patients were instructed to maintain their usual level of activity. All study participants were encouraged to stop smoking. Their diet was neither controlled nor modified throughout the study period. |
| O'Donnell 2009 | Placebo    | Standard treadmill test       | Short form 36 (SF-36), Disease-Specific Walking Impairment Questionnaire (WIQ), and Vascular Quality of Life (VascuQoL) | Cilostazol 100 mg twice daily                                                                                                                                                                  |
|              | Control     | NA                            |                                                                             | Placebo twice daily                                                                                                                                                                          |
| Sandercock 2007 | Training  | Graded treadmill test         | Walking instructions with diary to complete                                  | The SET group were given an exercise diary to complete and instructed to undertake one additional weekly 30 minutes walking session. |

The goal of such a workload was not to produce a claudication pain.
| Study  | Group  | Test | Protocol | Results |
|--------|--------|------|----------|---------|
| HET 2011 | HET | - | - | HET group were given an exercise diary to complete and instructed to undertake three 30 minutes walking sessions per week at a RPE of 12 - 14. This group was also contacted weekly by telephone and given support and encouragement in adhering to the protocol. |
| Control | - | - | - | The control group were given verbal information regarding the safety and efficacy of walking exercise but no specific instructions were given regarding exercise duration, intensity or frequency. |
| Schlager 2011 | SET | Standard treadmill test | Incremental exercise training | Patients underwent a standardized training program twice a week for six months. SET was based upon the current guidelines for patients with intermittent claudication and was guided by physiotherapists. After a warm up period of 5–10 min, the initial duration included 35 minutes of intermittent walking which was increased by 5 minutes each session until 50 minutes of intermittent walking was accomplished. The workload of exercise training was set to a walking speed that elicited claudication symptoms within 3–5min. Patients were trained at this workload until they achieved moderate claudication followed by a brief resting period to allow symptoms to resolve. |
| Control | - | - | - | |
| Stewart 2008 | SET | Standard treadmill test | Circuit format with no treadmill walking | Supervised exercise program comprised 5 different exercises in a circuit format. Patients were advised to rest when symptoms of claudication became intolerable and to recommence exercise when the pain subsided. After 8 minutes, the patients moved on to the next exercise. Two 1 hour classes were run each week, each with a maximum exercise time of 40 minutes with 10 minutes warm-up and cool down periods. The exercises were mainly based on calf muscle and could be continued at home without the need for specialized equipment. Treadmill exercises were not included to avoid the potential bias between the groups. |
| HET | - | - | - | Control group that received exercise advice alone. |
| Strandness 2002 | Cilostazol Medical Outcomes | - | - | Cilostazol 100 mg twice daily |
| Study (Year)  | Group 1 | Group 2 | Outcome Measures | Placebo | Notes |
|--------------|---------|---------|------------------|--------|-------|
| Tew 2015     | Controls | Graded treadmill test | EuroQoL | - | Control |
| HET          | Controls | Graded treadmill test | Walking Impairment Questionnaire (WIQ), and Claudication Outcome Measures | - | The intervention was modelled on the structured education self-management programmes used in diabetes care |
| Tsai 2002    | SET     | Graded treadmill test | Medical Outcomes Study Short-Form 36 (MOS SF-36) Chinese version, Walking Impairment Questionnaire | Treadmill walking with progressive increase in inclination | Patients in the exercise group performed the treadmill exercise three times each week until 12 weeks. Exercise training began with 5 minutes of warm up and ended with 5 minutes of cool down. During exercise, patients’ heart rate and 12-lead electrocardiogram were continuously monitored to detect any exercise-induced dysrhythmias. Arm blood pressure values and claudication pain scores were collected every 5 minutes Exercise intensity started from 2 mph, 0% grade, with 1% grade increase every 10 minutes if patients reported a claudication pain score below 2. Patients were encouraged to exercise up to 30 minutes with their claudication pain scores between 2 and 3 (pain levels between mild and moderate). |
| Control      | SET     | Incremental shuttle walk | NA | - | Control - usual care |
| Zwierska 2005 | SET     | Incremental shuttle walk | NA | Cycling exercise | SET twice a week for 24 weeks. For each of the supervised training sessions, patients exercised in cycles of 2 minutes exercise at a crank rate of 50 rev/min, followed by 2 minutes rest, for a total exercise time of 20 minutes in a 40-minute session. For the upper limb aerobic exercise training, the arm-crank ergometer was placed on a table in front of the seated patient with the mid-point of the sprocket set at shoulder height. |
| Study               | SET/Control | Activity                                      | Description                                                                                                                                                                                                 |
|---------------------|-------------|-----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Duscha 2018         | SET         | Cycling exercise                              | For lower limb aerobic exercise training, the seat height was adjusted to allow slight knee flexion at bottom dead centre. Up to eight patients exercised together in the same session.  |
|                     | Control     | -                                             | Patients in the control group were given lifestyle advice, including encouragement to undertake regular exercise.                                                                                           |
|                     | HET         | PAD-specific maximal treadmill cardiopulmonary exercise | Patients wore the Fitbit device for 2 weeks, and were told to continue normal activities without purposely increasing or decreasing exercise.                                                                      |
|                     | Control     | -                                             | Control                                                                                                                                                                                                    |
| Bulinska 2016       | SET (treadmill) | Graded treadmill test                          | The program of supervised walk training was carried out for three months (36 training sessions), three times a week from 30 (first week) up to 50 min. Each training began with a short warm-up (5–10 min) which consisted of flexibility exercises for upper and lower extremities and spine. Training was ended with stretching and breathing exercises (3–5 min). Treadmill training was conducted on a treadmill HX-100 with the constant workload protocol based on TASC II guidelines. Speed and slope were constant, amounted to 3.2 km/h (2.0 mph) and 12% grade. Patients walked up to the reach of submaximal level of pain (ACSM – level 4) and next rested in standing position when the level of pain decreased to 1 (no pain) but no longer than 2 min. |
|                     | Control     | -                                             | Control                                                                                                                                                                                                    |
| SET (Nordic Pole Walking) | NA | Nordic pole walking                            | NPW was performed by a qualified physiotherapist using the NW technique according to the guidelines of the International Nordic Walking Federation (INWA) with the KV+ poles. The pole length was adopted for each subject based on body height (0.7 × height). Patients trained under the same conditions as in TT. During the rest period, patients monitored HR individually. NPW was conducted in a group (max 12 participants) generally in outdoor. |
|        | SET (Nordic Pole Walking) | Nordic pole walking | Before Nordic walking sessions, all NWG patients received individual training for 30 minutes on the handling of poles and the technique of Nordic walking, to discover the activity and become familiar with the most effective movements. |
|--------|--------------------------|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Girolf 2017 | SET (Walking group) | Graded treadmill test | Walking on flat surface                                                                                                                                                                           |
|        |                          | NA                  | Walking sessions for both groups started after a 10-minutes warm-up to stimulate and effectively prepare the cardiorespiratory and muscular system for the effort. Then, each patient performed a 45-minutes session of walking at a pace dictated by the training heart rate. |
| Spafford 2014 | HET (NPW) | Modified shuttle walking test | -                                                                                                                                                                                                         |
|        |                          | NA                  | The HEP group was given written instructions to walk at their normal pace for at least 30 minutes three times per week.                                                                                       |
|        |                          | -                   | Patients in the NPW group were given a pair of LEKI Nordic walking poles adjusted for height (height × 0.7) and asked to walk using the poles for at least 30 minutes three times per week. |

ACSM – The American College of Sports Medicine; BMS – Bare metal stent; BP – Blood pressure; COT – Claudication onset time; CPS – Composite pain scale; d – Day; ER – Endovascular revascularization; HET – Home exercise therapy; HR – Heart rate; ICD – Intermittent claudication distance; IC – Intermittent claudication; INWA – International Nordic walking federation; km/h – Kilometer/hour; mg – Milligram; m/s – meters/second; mph – Miles per hour; MWD – Maximum walking distance; MW – Maximum walking time; NR – Not reported; NPW – Nordic pole walking; OMC – Optimal Medical Care; PAD – Peripheral artery disease; PTA – Percutaneous transluminal angioplasty; PVI – Percutaneous vascular intervention; PWT – Peak walking time; RPE – Ratings of perceived exertion; SET – Supervised exercise therapy; TASC – Transatlantic Inter-Society Consensus; TT – Treadmill testing; Wk – Week; % - Percentage.
Table S2. Ranking probability percentage of each treatment arms.

### Ranking probability (%) - Short term follow-up

|          | Rank1 | Rank2 | Rank3 | Rank4 | Rank5 | Rank6 |
|----------|-------|-------|-------|-------|-------|-------|
| Control  | 0     | 0     | 0     | 0.09  | 6.62  | 93.28 |
| HET      | 0     | 0.28  | 13.93 | 47.83 | 37.23 | 0.73  |
| ER       | 0.02  | 13.79 | 54.79 | 22.43 | 8.75  | 0.2   |
| Cilostazol | 0.03  | 3.18  | 14.83 | 28.79 | 47.37 | 5.78  |
| SET      | 0.25  | 82.45 | 16.42 | 0.85  | 0.01  | 0     |
| SET_ER   | 99.68 | 0.29  | 0.02  | 0     | 0     | 0     |

### Ranking probability (%) - Moderate term follow-up

|          | Rank1 | Rank2 | Rank3 | Rank4 | Rank5 |
|----------|-------|-------|-------|-------|-------|
| Control  | 0     | 0.03  | 1.86  | 18.48 | 79.63 |
| ER       | 0.03  | 1.62  | 43.96 | 50.54 | 3.83  |
| HET      | 1.1   | 10.70 | 41.60 | 30.68 | 16.52 |
| SET      | 0.95  | 86.53 | 12.24 | 0.26  | 0     |
| SET_ER   | 97.9  | 1.73  | 0.33  | 0.03  | 0     |

### Ranking probability (%) - Long term follow-up

|          | Rank1 | Rank2 | Rank3 | Rank4 |
|----------|-------|-------|-------|-------|
| Control  | 2.97  | 9.65  | 22.6  | 64.72 |
| ER       | 41.56 | 41.93 | 15.51 | 1     |
| SET      | 3.01  | 16.59 | 49.59 | 30.49 |
| SET_ER   | 52.46 | 31.82 | 12.28 | 3.43  |
Table S3. Quality of life outcomes as reported at different follow-up periods from eligible trials.

| Study reference | Intervention | QoL type | QoL | Short term summary                                                                 | Moderate term summary                                                                 | Long term summary                                                                 |
|-----------------|--------------|----------|-----|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Nylande 2007    | Control      | Generic  | SF-36| Significant improvements were seen in physical functioning and reported health transition. | Bodily pain and reported health transition were significantly improved               | Only reported health transition domain was significantly improved                |
|                 | ER           |          |     | Only physical functioning domain was significantly improved. Remaining domains did not change | Bodily pain and reported health transition were significantly improved               | Only reported health transition domain was significantly improved                |
|                 | Control      | Disease specific | CLAU-S | None of the domains significantly improved                                      | Only severity of pain was significantly improved                                      | Only pain during activity was significantly improved                             |
|                 | ER           |          |     | Pain during activity and severity of pain significantly improved. Other domains including everyday life, pain related to sleep, social life, specific fears related to illness and psychological well-being did not change | Only pain during activity was significantly improved                                      | Only pain during activity was significantly improved                             |
| Mazari 2017     | ER           | Generic  | SF-36| NA                                                                                 | NA                                                                                   | None of the domains significantly improved                                       |
|                 | SET          |          |     | NA                                                                                 | NA                                                                                   | None of the domains significantly improved                                       |
|                 | SET+ER       |          |     | NA                                                                                 | NA                                                                                   | None of the domains significantly improved                                       |
|                 | ER           | Disease specific | Vascu QoL | NA                                                                                 | NA                                                                                   | None of the domains significantly improved                                       |
|                 | SET          |          |     | NA                                                                                 | NA                                                                                   | None of the domains significantly improved                                       |
|                 | SET+ER       |          |     | NA                                                                                 | NA                                                                                   | None of the domains significantly improved                                       |
| Study          | Measure                  | Domain                                                                 | Improvement                                                                 |
|---------------|--------------------------|------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Fakhry, 2013  | SET Generic SF-36        | Physical function, bodily pain and general health significantly improved | General health domain significantly decreased                              |
|               | ER                       | Physical function, role physical and bodily pain significantly improved | Physical functioning, role physical and bodily pain significantly improved  |
|               | SET Disease specific Vascu QoL | VascuQoL and rating score significantly improved                     | Only VascuQoL score significantly improved                                 |
|               | ER                       | VascuQoL and rating score significantly improved                      | Only VascuQoL score significantly improved                                 |
| Djerf 2019    | ER Generic SF-36         | Physical functioning and bodily pain significantly improved compared to baseline and control group | Domains including physical functioning, role physical and bodily pain significantly improved |
|               | Control                  | None of the domains significantly improved                             | None of the domains significantly improved                                 |
|               | ER Disease specific Vascu QoL | Domains including activities, symptoms, and emotional were significantly increased | All domains significantly improved                                          |
|               | Control                  | None of the domains significantly improved                             | None of the domains significantly improved                                 |
| Lindgren 2018 | ER Generic SF-36        | NA                                                                      | NA                                                                         |
|               | Control                  | NA                                                                      | NA                                                                         |
|               | ER Generic EQSD         | NA                                                                      | EQSD did not significantly improve                                         |
|               | Control                  | NA                                                                      | EQSD did not significantly improve                                         |
|               | ER WIQ                   | NA                                                                      | WIQ scores significantly improved                                          |
| Control       | Disease specific | NA | NA | WIQ scores significantly improved |
|---------------|------------------|----|----|-----------------------------------|
| Control       | Specific         | NA | NA | No significant improvement in SF-12 physical score |
| SET           | Generic          | NA | NA | SF-12 physical score was significantly improved compared to control but no difference within intragroup |
| ER            | Disease specific | NA | NA | SF-12 physical score was significantly improved compared to control but no difference within intragroup |
| Control       | Disease specific | NA | NA | No significant improvement in pain severity and walking distance |
| SET           | Disease specific | NA | NA | Pain severity and walking distance were significantly improved compared to control and baseline but no significance reported |
| ER            | Disease specific | NA | NA | Pain severity and walking distance were significantly improved compared to control and baseline but no significance reported |
| Control       | Disease specific | NA | NA | No significant improvement in physical limitation, symptoms, QoL and summary |
| SET           | Disease specific | NA | NA | Only PAQ summary was significantly improved compared to baseline and control |
| Study          | Intervention | Tool       | Baseline | SET | ER | Physical limitation, symptoms, QoL and summary improved compared to baseline and control. Physical limitation, QoL and summary were significantly improved compared to SET | NA                  |
|---------------|--------------|------------|----------|-----|----|--------------------------------------------------------------------------------|---------------------|
| Greenhalgh 2008a | ER+SET       | Generic SF-36 | NA       | NA  | NA | None of the domains significantly improved                                      | None of the domains significantly improved |
|               | SET          |             | NA       | NA  | NA |                                                                                |                     |
| Greenhalgh 2008b | ER+SET       | Generic SF-36 | NA       | NA  | NA | Physical score domains significantly improved compared to SET, but no significance reported comparing with baseline |                     |
|               | SET          |             | NA       | NA  | NA |                                                                                |                     |
| Gelin 2001    | Control      | Generic NA  | NA       | NA  | NA |                                                                                | NA                  |
|               | SET          |             | NA       | NA  | NA |                                                                                | NA                  |
|               | ER           |             | NA       | NA  | NA |                                                                                | NA                  |
| Bo 2013       | ER           | Generic SF-36 | NA       | NA  | NA | Physical function, bodily pain and vitality were significantly different between the groups, but not reported against baseline. | NA                  |
|               | SET+ER       |             | NA       | NA  | NA |                                                                                | NA                  |
|               | ER           | Disease specific CLAU-S | NA | NA | Daily life domain showed a trend towards improvement but not statistically different. Other domains did not change. | NA                  |
| Spronk 2009   | ER           | Generic SF-36 | None of the domains significantly improved | None of the domains significantly improved | NA | None of the domains significantly improved | NA                  |
|               | SET          |             | None of the domains significantly improved | None of the domains significantly improved | NA | None of the domains significantly improved | NA                  |
|               | ER           | Disease specific Vascu QoL | None of the domains significantly improved | None of the domains significantly improved | NA | None of the domains significantly improved | NA                  |
| Study          | Group 1 | Group 2 | Measurement | Outcome 1 | Outcome 2 | Outcome 3 |
|---------------|---------|---------|-------------|-----------|-----------|-----------|
| Crowther 2008 | Control | NA      | NA          | NA        | NA        | NA        |
|               | SET     | NA      | None of the domains significantly improved | None of the domains significantly improved | NA        | NA        |
| Cheetah 2004  | HET     | Generic | SF-36       | NA        | Physical functioning was significantly improved in SET compared to HET group | NA        |
|               | SET     | Disease specific | ICQ | Scores improved but not significant | Scores significantly improved | NA        |
| Gardner 2002  | Control | Disease specific | WIQ | Scores did not change between pre and post intervention | Scores did not change between pre and post intervention | NA        |
|               | SET     | Disease specific | WIQ | Scores did not change between pre and post intervention | Scores did not change between pre and post intervention | NA        |
| Baker 2017    | SET     | NA      | NA          | NA        | NA        | NA        |
|               | Control | NA      | NA          | NA        | NA        | NA        |
| Brass 2012    | Cilostazol | NA      | NA          | NA        | NA        | NA        |
|               | Control | NA      | NA          | NA        | NA        | NA        |
| Collins 2011  | Control | Generic | SF-36       | Only mental health domain significantly improved in HET compared to control group | NA        | NA        |
|               | HET     | Disease specific | WIQ | Walking speed domain significantly improved in HET compared to control group | NA        | NA        |
| Crowther 2012 | SET     | NA      | NA          | NA        | NA        | NA        |
|               | Control | NA      | NA          | NA        | NA        | NA        |
| Dawson 2000   | Cilostazol | Generic | MOS SF-36 | None of the domains significantly improved | NA        | NA        |
| Study               | Intervention | Domain          | Measure     | Improvement                                                                 |
|---------------------|--------------|-----------------|-------------|-----------------------------------------------------------------------------|
| Fakhry 2015         | SET+ER       | Generic         | SF-36       | Physical functioning, bodily pain, physical role functioning score and general health perceptions were significantly improved |
|                     | SET          | Disease specific| VascuQoL    | VascuQoL and rating score significantly improved                            |
|                     | HET          | Generic         | SF-36       | Physical function significantly increased compared to baseline              |
| Gardner 2001        | SET          | Generic         | MOS SF-36   | None of the domains significantly improved                                  |
|                     | Control      | Disease specific| WIQ         | None of the domains significantly improved                                  |
|                     | SET          | Disease specific| WIQ         | None of the domains significantly improved                                  |
|                     | Control      | Disease specific| WIQ         | None of the domains significantly improved                                  |
| Gardner 2014        | SET          | Generic         | MOS SF-36   | Physical function significantly increased compared to baseline              |
|                     | HET          | Generic         | MOS SF-36   | Physical function significantly increased compared to baseline              |
|                  | Disease specific | WIQ          | None of the domains significantly improved | NA   | NA   |
|------------------|-----------------|--------------|---------------------------------------------|------|------|
| Control          |                 |              |                                             |      |      |
| SET              | Disease specific |              | Walking economy and fractional utilization increased significantly from baseline in the supervised exercise group | NA   | NA   |
|                  |                 |              |                                             |      |      |
| HET              |                 |              | Walking economy and fractional utilization increased significantly from baseline in the supervised exercise group | NA   | NA   |
| Control          |                 |              | None of the domains significantly improved | NA   | NA   |
| Gardner 2012     | SET             | Disease specific | Walking distance and speed significantly improved | NA   | NA   |
|                  |                 |              | None of the domains significantly improved | NA   | NA   |
| Control          |                 |              |                                             |      |      |
|                  | HET             | Generic      | Physical function score significantly improved | NA   | NA   |
|                  |                 | MOS SF-36    | Physical function score significantly improved | NA   | NA   |
| Control          |                 |              | None of the domains significantly improved | NA   | NA   |
| Gardner 2011     | HET             | Disease specific | Fractional utilization, walking distance, speed and stair climbing scores significantly increased | NA   | NA   |
|                  |                 |              |                                             |      |      |
| SET              | Disease specific |              | Walking economy, fractional utilization, walking distance, speed and stair climbing scores significantly increased | NA   | NA   |
|                  |                 |              |                                             |      |      |
| Control          |                 |              | Fractional utilization significantly improved | NA   | NA   |
| Control          | NA              | NA           |                                             | NA   | NA   |
| Study            | Treatment | Generic Measure | Improvement                                                                                      | ER Only | SET+ER Only | ER Only | SET+ER Only |
|------------------|-----------|-----------------|-------------------------------------------------------------------------------------------------|---------|-------------|---------|-------------|
| Hobbs 2006       | ER        | NA              | NA                                                                                              | NA      | NA          | NA      | NA          |
|                  | SET       | NA              | NA                                                                                              | NA      | NA          | NA      | NA          |
|                  | Cilostazol| NA              | NA                                                                                              | NA      | NA          | NA      | NA          |
|                  | SET + Cilostazol | NA            | NA                                                                                              | NA      | NA          | NA      | NA          |
|                  | Control   | NA              | NA                                                                                              | NA      | NA          | NA      | NA          |
| Hobbs 2007       | SET       | NA              | NA                                                                                              | NA      | NA          | NA      | NA          |
|                  |            | NA              | NA                                                                                              | NA      | NA          | NA      | NA          |
| Hodges 2008      | SET       | NA              | NA                                                                                              | NA      | NA          | NA      | NA          |
|                  | Control   | NA              | NA                                                                                              | NA      | NA          | NA      | NA          |
| Kakkos 2005      | HET       | Generic SF-36   | None of the domains significantly improved                                                     | Only mental health sub-domain significantly improved | NA      | NA      | NA          |
|                  | SET       | Disease specific WIQ | None of the domains significantly improved                                                    | None of the domains significantly improved | None of the domains significantly improved | None of the domains significantly improved | NA          |
|                  |            | Generic MOS SF-36 | Domains including mental health, vitality and mental summary score were significantly improved in SET+ER as compared to ER only | NA      | NA          | NA      | NA          |
| Kruidenier 2011  | ER        | Generic MOS SF-36 | Both total score and general health were similar in both treatment strategies                 | NA      | NA          | NA      | NA          |
|                  | SET+ER    | Disease specific EuroQoL | Both total score and general health were similar in both treatment strategies                 | NA      | NA          | NA      | NA          |
|                  | ER        | Generic MOS SF-36 | Both total score and general health were similar in both treatment strategies                 | NA      | NA          | NA      | NA          |
|                  | SET+ER    | Disease specific EuroQoL | Both total score and general health were similar in both treatment strategies                 | NA      | NA          | NA      | NA          |
| Lamberti 2016    | HET       | Generic MOS SF-36 | physical component summary, bodily pain, emotional role, general health, mental component summary, mental health, physical functioning, physical role, social functioning and vitality were significantly improved | NA      | NA          | NA      | NA          |
| Study      | Type  | Group   | Measure | Results                                                                 |
|------------|-------|---------|---------|-------------------------------------------------------------------------|
| Novakovic 2018 | SET   | Generic SF-36 | physical component summary, bodily pain, emotional role, physical functioning, physical role and vitality were significantly improved |
|             | Control | NA | NA | NA |
| Mauer 2015 | SET   | Disease specific BASIC-Q | Physical functioning, bodily pain and physical component summary significantly improved |
| HET        | Disease specific BASIC-Q | None of the domains significantly improved |
| Control    | Disease specific BASIC-Q | None of the domains significantly improved |
| Mays 2015  | Control | Generic SF-36 | None of the domains significantly improved |
| HET        | Generic SF-36 | None of the domains significantly improved |
| HET        | Disease specific WIQ | Distance, speed and combined percentage significantly improved with intervention compared to control group |
| Control    | Disease specific WIQ | None of the domains significantly improved |
| HET        | Disease specific WIQ | None of the domains significantly improved |
| Miika 2005 | SET   | NA | NA | NA |
| HET        | NA | NA | NA | NA |
| Miika 2011 | SET   | NA | NA | NA |
| Control    | NA | NA | NA | NA |
| O'Donnell 2009 | Cilostazol | Generic SF-36 | Physical function and physical component summary were significantly improved. Physical function was significantly improved compared to control |
| Control    | NA | NA | NA | NA |
| Study               | Group    | Domain     | Measure     | Improvement                                                                 |
|---------------------|----------|------------|-------------|-----------------------------------------------------------------------------|
| Control             |          |            | Vascu QoL   | None of the domains significantly improved                                 |
| Cilostazol         | Disease  |            | Vascu QoL   | Pain domain significantly improved                                          |
| Control             |          |            | Vascu QoL   | None of the domains significantly improved                                 |
| Sandercock 2007     | SET      | NA         | NA          | NA                                                                           |
| Control             |          |            |             | NA                                                                           |
| Schlager 2011       | SET      | NA         | NA          | NA                                                                           |
| Control             |          |            |             | NA                                                                           |
| Stewart 2008        | SET      | NA         | NA          | NA                                                                           |
| Control             |          |            |             | NA                                                                           |
| Strandness 2002     | Cilostazol| Generic   | SF-36       | Significant improvement in physical function, and a trend towards improvement in bodily pain, role-physical and general health perception compared to placebo |
| Control             |          |            |             | NA                                                                           |
| Cilostazol         | Disease  |            | WIQ         | Walking distance score improved but significance not reported              |
| Control             |          |            | WIQ         | NA                                                                           |
| Tew 2015            | Control  | Disease    | WIQ         | Superior improvement in WIQ speed, distance and stair-climbing scores compared to control, but significance not reported |
| HET                 |          | specific   |             | NA                                                                           |
| Control             |          | Generic    | EQSD        | None of the domains significantly improved                                 |
| HET                 |          |            | EQSD        | NA                                                                           |
| Study          | Intervention                      | MOS SF-36 | Significance                                                                 | Control |
|---------------|-----------------------------------|-----------|-----------------------------------------------------------------------------|---------|
| Tsai 2002     | SET                               | Generic   | Significant improvement was seen in physical function, role limitations/physical, bodily pain, general health and vitality as compared to baseline and control | NA      |
|               | Control                           |           | None of the domains significantly improved                                  | NA      |
|               | SET                               | Disease   | Significant improvement was seen in WIQ distance, speed and stairs walking compared to baseline. Only speed and stairs improved against control | NA      |
|               | Control                           | specific  | None of the domains significantly improved                                  | NA      |
| Zwierska 2005 | SET                               | NA        | NA                                                                          | NA      |
|               | SET                               | NA        | NA                                                                          | NA      |
|               | Control                           | NA        | NA                                                                          | NA      |
| Duscha 2018   | HET                               | NA        | NA                                                                          | NA      |
|               | Control                           | NA        | NA                                                                          | NA      |
| Bulinska 2016 | SET (treadmill)                   | NA        | NA                                                                          | NA      |
|               | SET (NPW)                         | NA        | NA                                                                          | NA      |
|               | Control                           | NA        | NA                                                                          | NA      |
| Girold 2017   | SET (NPW)                         | NA        | NA                                                                          | NA      |
|               | SET (Walking group)               | NA        | NA                                                                          | NA      |
|               | HET                               | NA        | NA                                                                          | NA      |
| Spafford 2014 | HET (NPW) | NA | NA | NA |
|--------------|-----------|----|----|----|

* Data compares intergroup only. Intragroup comparing against baseline not available.

BASIC-Q – Baltimore Activity Scale for Intermittent Claudication questionnaire; CLAU-S – Claudication scale; ICQ – Intermittent Claudication Questionnaire; ER – Endovascular revascularization; EQ5D – EuroQol-5D; HET – Home exercise therapy; MOS-SF36 – Medical Outcomes Study; NA – Not available; PAQ – Peripheral artery questionnaire; QoL – Quality of life; SET – Supervised exercise therapy; SF – Short Form; NPW – Nordic pole walking; VascuQoL – Vascular QoL
Table S4. Adverse events reported in all included trials.

| Study reference | Treatment | Sample size | Follow-up (months) | MI | Stroke | Any hospital admissions | Lower limb revascularization procedures | Any other vascular procedures | Amputation | All-cause mortality |
|-----------------|-----------|-------------|--------------------|----|--------|------------------------|----------------------------------------|-------------------------------|------------|-------------------|
| Nylande 2007    | Control   | 28          | 24                 | NR | NR     | NR                     | NR                                     | NR                            | NR          | 0                 |
| Nylande 2007    | ER        | 28          | 24                 | NR | NR     | NR                     | NR                                     | NR                            | NR          | 1                 |
| Mazari 2017      | ER        | 60          | 60                 | 4  | 2      | NR                     | 14                                     | NR                            | 1           | 14                |
| Mazari 2017      | SET       | 60          | 60                 | 2  | 1      | NR                     | 10                                     | NR                            | 0           | 13                |
| Mazari 2017      | SET_ER    | 58          | 60                 | 3  | 5      | NR                     | 6                                      | NR                            | 0           | 12                |
| Fakhry, 2013     | SET       | 75          | 84                 | NR | NR     | NR                     | 32                                     | NR                            | 2           | 17                |
| Fakhry, 2013     | ER        | 75          | 84                 | NR | NR     | NR                     | 17                                     | NR                            | 3           | 15                |
| Djerf 2020       | ER        | 79          | 60                 | NR | 2      | NR                     | 22                                     | NR                            | 0           | 13                |
| Djerf 2020       | Control   | 79          | 60                 | NR | 2      | NR                     | 20                                     | NR                            | 1           | 7                 |
| Lindgren 2018    | ER        | 45          | 24                 | 3  | 2      | NR                     | 10                                     | NR                            | 1           | 1                 |
| Lindgren 2018    | Control   | 47          | 24                 | 2  | 0      | NR                     | 7                                      | NR                            | 0           | 1                 |
| Murphy 2015      | Control   | 22          | 18                 | 1  | NR     | NR                     | 0                                      | NR                            | 0           | 1                 |
| Murphy 2015      | SET       | 43          | 18                 | 0  | NR     | NR                     | 0                                      | NR                            | NR          | 1                 |
| Murphy 2015      | ER        | 46          | 18                 | 0  | NR     | NR                     | 1                                      | NR                            | NR          | 0                 |
| Gelin 2001^      | Control   | 89          | 12                 | NR | NR     | NR                     | NR                                     | NR                            | 2           | 4                 |
| Gelin 2001^      | SET       | 88          | 12                 | NR | NR     | NR                     | NR                                     | NR                            | 0           | 5                 |
| Gelin 2001^      | ER        | 87          | 12                 | NR | NR     | NR                     | NR                                     | NR                            | 1           | 5                 |
| Bo 2013          | ER        | 21          | 12                 | NR | NR     | NR                     | 0                                      | NR                            | 0           | 6                 |
| Bo 2013          | SET_ER    | 29          | 12                 | NR | NR     | NR                     | 6                                      | NR                            | NR          | 0                 |
| Spronk 2009      | ER        | 75          | 12                 | 1  | NR     | NR                     | 2                                      | NR                            | 0           | 5                 |
| Spronk 2009      | SET       | 75          | 12                 | 0  | NR     | NR                     | 4                                      | NR                            | 3           | 3                 |
| Crowther 2008    | Control   | 11          | 12                 | NR | NR     | NR                     | NR                                     | NR                            | NR          | NR                |
| Crowther 2008    | SET       | 10          | 12                 | NR | NR     | NR                     | NR                                     | NR                            | NR          | NR                |
| Gardner 2002     | Control   | 14          | 18                 | NR | NR     | NR                     | NR                                     | NR                            | 0           | 2                 |
| Study            | Design   | Week 1 | Week 4 | Week 6 | Week 8 | Week 10 | Week 12 | Week 14 | Week 16 | Week 18 |
|------------------|----------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Gardner 2002     | SET      | 17     | 18     | NR     | NR     | NR     | NR     | NR     | 1      | 1      |
| Baker 2017       | SET      | 29     | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Baker 2017       | Control  | 35     | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Brass 2012       | Cilostazol | 89  | 6.5   | NR     | 1      | NR     | NR     | NR     | 1      |
| Brass 2012       | Control  | 87     | 6.5    | NR     | 0      | NR     | NR     | NR     | 0      |
| Collins 2011     | Control  | 73     | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Collins 2011     | HET      | 72     | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Crowther 2012    | SET      | 11     | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Crowther 2012    | Control  | 11     | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Spafford 2014    | SET      | 28     | 3      | 0      | NR     | NR     | NR     | NR     | 0      |
| Spafford 2014    | HET      | 24     | 3      | 1      | NR     | NR     | NR     | NR     | 1      |
| Dawson 2000      | Cilostazol | 227 | 6     | NR     | NR     | NR     | NR     | NR     | 2      |
| Dawson 2000      | Control  | 239    | 6      | NR     | NR     | NR     | NR     | NR     | 1      |
| Fakhry 2015      | SET_ER   | 106    | 12     | NR     | NR     | NR     | NR     | NR     | 0      | 1      |
| Fakhry 2015      | SET      | 106    | 12     | NR     | NR     | NR     | NR     | NR     | 2      | 3      |
| Gardner 2001     | SET      | 31     | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Gardner 2001     | Control  | 30     | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Gardner 2014     | SET      | 60     | 3      | NR     | 1      | NR     | 0      | NR     | NR     | NR     |
| Gardner 2014     | HET      | 60     | 3      | NR     | 0      | NR     | 1      | NR     | NR     | NR     |
| Gardner 2014     | Control  | 60     | 3      | 1      | 1      | NR     | 0      | NR     | NR     | NR     |
| Gardner 2012     | SET      | 106    | 6      | 1*     | 3*     | NR     | NR     | 1*     | 1*     | NR     |
| Gardner 2012     | Control  | 36     | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Gardner 2011     | HET      | 40     | 3      | 1      | 1      | NR     | 1      | NR     | NR     | NR     |
| Gardner 2011     | SET      | 40     | 3      | 0      | 1      | NR     | 0      | NR     | NR     | NR     |
| Gardner 2011     | Control  | 39     | 3      | 0      | 1      | NR     | 1      | NR     | NR     | NR     |
| Hobbs 2006       | Control  | 7      | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Hobbs 2006       | ER       | 9      | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Hobbs 2006       | SET      | 7      | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Hobbs 2007       | SET      | 9      | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Study Year  | Intervention  | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 | Item 9 |
|------------|---------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Hobbs 2007 | Cilostazol    | 9      | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Hobbs 2007 | Control       | 9      | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Hodges 2008| SET           | 14     | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Hodges 2008| Control       | 14     | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Kakkos 2005| HET           | 10     | 12     | NR     | NR     | NR     | NR     | NR     | NR     | 0      |
| Kakkos 2005| SET           | 12     | 12     | NR     | NR     | NR     | NR     | NR     | NR     | 1      |
| Kruidenier 2011 | ER | 35     | 6      | NR     | NR     | NR     | NR     | 2      | NR     | NR     |
| Kruidenier 2011 | SET_ER | 35     | 6      | NR     | NR     | NR     | NR     | 0      | NR     | NR     |
| Lamberti 2016 | HET | 18     | 4      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Lamberti 2016 | ER | 9      | 4      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Novakovic 2019 | SET | 12     | 4.5    | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Novakovic 2019 | Control | 12     | 4.5    | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Mauer 2015  | SET           | 16     | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Mauer 2015  | Control       | 7      | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Mays 2015   | Control       | 10     | 3.5    | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Mays 2015   | HET           | 10     | 3.5    | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Mika 2005   | SET           | 49     | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Mika 2005   | HET           | 49     | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Mika 2011   | SET           | 34     | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Mika 2011   | Control       | 34     | 3      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Sandercock 2007 | SET | 13     | 3      | NR     | NR     | NR     | 1      | NR     | NR     | NR     |
| Sandercock 2007 | HET | 15     | 3      | NR     | NR     | NR     | 0      | NR     | NR     | NR     |
| Sandercock 2007 | Control | 15     | 3      | NR     | NR     | NR     | 0      | NR     | NR     | NR     |
| Schlager 2011 | SET | 20     | 12     | 0      | NR     | NR     | NR     | NR     | NR     | 0      |
| Schlager 2011 | Control | 20     | 12     | 1      | NR     | NR     | NR     | NR     | NR     | 1      |
| Stewart 2008 | SET           | 30     | 6      | NR     | 1      | NR     | 1      | NR     | NR     | 1      |
| Stewart 2008 | HET           | 30     | 6      | NR     | 1      | NR     | 0      | NR     | NR     | 0      |
| Zwierska 2005 | SET | 37     | 6      | NR     | NR     | NR     | NR     | NR     | NR     | 3      |
| Zwierska 2005 | Control | 33     | 6      | NR     | NR     | NR     | NR     | NR     | NR     | NR     |
| Source               | Type       | Group | Exercise | NR | 2* | NR | NR | 2* | NR | 2 |
|----------------------|------------|-------|----------|----|----|----|----|----|----|----|
| Greenhalgh 2008a     | SET_ER     | 48    | 24       | NR | 2* | NR | NR | 2* | NR | 2 |
| Greenhalgh 2008a     | SET        | 45    | 24       | NR | 2* | NR | NR |     |     |    |
| Greenhalgh 2008b     | SET_ER     | 19    | 24       | NR | 2* | NR | NR | 0  | NR | 1 |
| Greenhalgh 2008b     | SET        | 15    | 24       | NR | 2* | NR | NR | 0  | NR | 2 |
| Cheetham 2004        | HET        | 30    | 12       | NR |     | NR | NR |     |     |    |
| Cheetham 2004        | SET        | 29    | 12       | NR |     | NR | NR |     |     |    |
| O'Donnell 2009^      | Cilostazol | 39    | 6        | NR |     | NR | NR |     |     |    |
| O'Donnell 2009^      | Control    | 41    | 6        | NR |     | NR | NR |     |     |    |
| Strandness 2002      | Cilostazol | 133   | 6        | NR |     | NR | NR |     |     |    |
| Strandness 2002      | Control    | 128   | 6        | NR |     | NR | NR |     |     |    |
| Tew 2015             | Control    | 9     | 1.5      | NR | 0   | NR | NR |     |     |    |
| Tew 2015             | HET        | 14    | 1.5      | NR | 1   | NR | NR |     |     |    |
| Tsai 2002            | SET        | 27    | 3        | NR |     | NR | NR |     |     |    |
| Tsai 2002            | Control    | 26    | 3        | NR |     | NR | NR |     |     |    |
| Duscha 2018          | HET        | 10    | 3        | NR |     | NR | NR |     |     |    |
| Duscha 2018          | Control    | 9     | 3        | NR |     | NR | NR |     |     |    |
| Bullinska 2016       | SET        | 31    | 1.5      | NR |     | NR | NR |     |     |    |
| Bullinska 2016       | HET        | 21    | 1.5      | NR |     | NR | NR |     |     |    |
| Girolod 2017         | SET        | 21    | 1        | NR |     | NR | NR |     |     |    |
| Girolod 2017         | HET        | 21    | 1        | NR |     | NR | NR |     |     |    |

* Group-wise data not available; ^ Cardiovascular adverse events reported together with other events, but individual event numbers were not provided; * Cerebral vascular accidents was considered as stroke; ER – Endovascular revascularization; HET – Home exercise therapy; SET – Supervised exercise therapy; NR – Not reported; MI – Myocardial infarction.
Figure S1. Markov Chain Monte Carlo simulation showing the trace plots and corresponding density plots during short-term follow-up.

Convergence was achieved with higher iterations (100,000) and was suitable for the network model. HET – Home exercise therapy, SET – Supervised exercise therapy, ER – Endovascular revascularization, SD – Standard deviation
Figure S2. Markov Chain Monte Carlo simulation showing the trace plots and corresponding density plots during moderate follow-up.

Convergence was achieved with higher iterations (100,000) and was suitable for the network model. HET – Home exercise therapy, SET – Supervised exercise therapy, ER – Endovascular revascularization, SD – Standard deviation.
Figure S3. Markov Chain Monte Carlo simulation showing the trace plots and corresponding density plots during long-term follow-up.

Convergence was achieved with higher iterations (100,000) and was suitable for the network model. SET – Supervised exercise therapy, ER – Endovascular revascularization, SD – Standard deviation.