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#### Article:

Harwood, Amy E, Pymer, Sean, Ingle, Lee et al. (5 more authors) (2020) Exercise training for intermittent claudication: a narrative review and summary of guidelines for practitioners. BMJ Open Sport & Exercise Medicine. e000897. ISSN 2055-7647

https://doi.org/10.1136/bmjsem-2020-000897

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Review

BMJ Open Sport & Exercise Medicine

# Exercise training for intermittent claudication: a narrative review and summary of guidelines for practitioners

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To cite: Harwood AE, Pymer S, Ingle L, et al. Exercise training for intermittent claudication: a narrative review and summary of guidelines for practitioners. BMJ Open Sport & Exercise Medicine 2020;0: e000897. doi:10.1136/bmjsem-2020-000897

Received 14 July 2020 Revised 5 October 2020 Accepted 18 October 2020

#### **ABSTRACT**

Peripheral artery disease (PAD) is caused by atherosclerotic narrowing of the arteries supplying the lower limbs often resulting in intermittent claudication, evident as pain or cramping while walking. Supervised exercise training elicits clinically meaningful benefits in walking ability and quality of life. Walking is the modality of exercise with the strongest evidence and is recommended in several national and international guidelines. Alternate forms of exercise such as upper- or lower-body cycling may be used, if required by certain patients, although there is less evidence for these types of programmes. The evidence for progressive resistance training is growing and patients can also engage in strength-based training alongside a walking programme. For those unable to attend a supervised class (strongest evidence), home-based or 'self-facilitated' exercise programmes are known to improve walking distance when compared to simple advice. All exercise programmes, independent of the mode of delivery, should be progressive and individually prescribed where possible, considering disease severity, comorbidities and initial exercise capacity. All patients should aim to accumulate at least 30 min of aerobic activity, at least three times a week, for at least 3 months, ideally in the form of walking exercise to nearmaximal claudication pain.

## INTRODUCTION

Lower-limb peripheral artery disease (PAD) is an atherosclerotic cardiovascular disease in which the arteries that carry blood to the legs and feet become hardened, narrowed and/or obstructed by the build-up of atheroma. PAD is a common problem thought to affect over 200 million people worldwide. The total disease prevalence is approximately 13% of adults >50 years old, with major risk factors including smoking, diabetes and dyslipidaemia. The total disease prevalence is approximately 13% of adults >50 years old, with major risk factors including smoking, diabetes and dyslipidaemia.

The most classic symptom of PAD is intermittent claudication (IC). This is ischaemic muscle pain that usually presents in the calves (but can include the thighs or buttocks), is precipitated by exertion and relieved with rest (figure 1). This pain is thought to be due to a mismatch between the oxygen demand (of the working muscle) and an inadequate

# **Summary box**

# What is already known?

- Supervised exercise training promotes clinically meaningful benefit in patients with intermittent claudication.
- Walking as an exercise modality currently has the strongest level of evidence.

# What this study adds?

- ► A concise summary of evidence and practical recommendations for exercise implementation for practioners, including example protocols for exercise training.
- Progressive resistance training may be used as a supplement to walking programmes.

blood supply (due to the narrowed arterial pathway).<sup>5</sup>

Although PAD is progressive (in the pathological sense), the clinical course is relatively stable.<sup>6</sup> However, patients with PAD have a higher burden of cardiovascular disease and are at greater risk of major cardiovascular events.<sup>7</sup> Another major issue for many patients is the severe decline in functional capacity (VO<sub>2Peak)</sub> which are comparable to patients with heart failure and reduced ejection fraction.<sup>8</sup> The reduction in functional capacity is commonly caused by a decline in walking capacity, which may be up to less than 50% of healthy aged-matched controls. Factors influencing the walking distance or speed at which symptoms occur are multifactorial and include the site and severity of disease, walking pace, terrain, incline and footwear. 10 These physical constraints in turn have negative connotations on patient's mental health and there are strong associations with depression, poor quality of life (QoL) and further avoidance of physical activity. 11 12 This cycle of activity avoidance only leads to worsening functional ability and there is some evidence to suggest it also leads to an elevated mortality risk independent of disease severity and age. 13



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Figure 1 Intermittent claudication due to peripheral artery disease. Reproduced from Morlet et al<sup>3</sup> with permission from BMJ Publishing Group Ltd. Note: Iliac or femoral artery disease can cause symptoms at multiple distal muscle sites.

Treatment for patients with IC involves secondary prevention of cardiovascular disease risk, including smoking cessation, diet changes, lipid modification, statin therapy, antiplatelet therapy and management of diabetes and hypertension. In addition to therapeutic intervention and lifestyle modification, the primary treatment to address the functional impairment outlined earlier is for patients to engage in appropriate exercise training, best achieved through a supervised exercise programme (SEP).<sup>14</sup> This is supported by multiple consensus guidelines from various governing bodies. 15-17 18 However. they lack detail and consistency (between guidelines) as to the appropriate principles of exercise such as intensity and progression (table 1), which impacts upon effective implementation. In addition to inconsistencies in the recommendations for exercise, there is also variability in the delivery of exercise programmes globally with some clinicians reporting lack of expertise or support to guide the exercise delivery. 19–21

This guideline for practitioners aims to accompany these consensus guidelines to provide a succinct but more detailed overview of, and recommendations for, exercise prescription and training for IC. While we appreciate that delivery and provision will vary, the key exercise prescription components will remain and as such, this document will be relevant for exercise practitioners worldwide. In addition, we provide advice for the implementation of the exercise prescription guidelines into clinical practice (table 2), which also includes information on structured alternatives when SEPs are not available 19 23

#### Walking ability

Measures of walking ability include pain-free and maximum walking distance (or time) obtained during standardised treadmill testing and/or the distance covered in the 6-min 30-m corridor walk test. Several treadmill protocols have been reported, but the 'Gardner/Skinner' incremental protocol is most commonly used.<sup>26</sup> <sup>27</sup> This involves a constant speed of 3.2 km/hour at a 0% grade, increasing by 2% every 2 min. The advantage of using a treadmill test is that it can be standardised (ie, speed of treadmill, grade of treadmill), although it may not be as reflective of normal everyday walking (6-min walking distance). 28 29

# **Quality of life**

Several generic and condition-specific questionnaires have been used to assess OoL. The most validated, responsive and reliable questionnaires in the IC population are the Short-Form-36 (SF-36) and King's College Hospital's VascuQoL questionnaires, respectively. 30 31 Additional and commonly used questionnaires include the Walking Impairment Questionnaire<sup>32</sup> and the Peripheral Artery Questionnaire.<sup>33</sup>

# **EXERCISE TRAINING** Benefits of exercise training

A recent Cochrane review concluded that there is highquality evidence showing that SEPs (a variety of regimes) elicit important improvements in both pain-free and maximum walking distance compared with no-exercise control in people with IC.<sup>14</sup> A meta-analysis of nine trials (n=391) showed a mean between-group difference in pain-free walking distance at follow-up of 82 m (95% CI 72 to 92 m [follow-up ranging 6 weeks to 2 years]) and maximum walking distance of 120 m (95% CI 50.79 to 190 m). The most commonly tested mode of exercise was walking, with one cycling intervention. The corresponding difference for maximum walking distance was 120 m (95% CI 51 to 190 m; 10 trials, n=500). Improvements of this magnitude are likely to represent clinically meaningful changes in ambulatory function.<sup>34</sup>

The same review also reported that there was moderatequality evidence for improvements in physical and mental aspects of QoL, assessed using the SF-36. 14 A meta-analysis of data at 6 months of follow-up showed the physical component summary score to be 2 points higher in exercise versus control (95% CI 1 to 3; 5 trials, n=429). The corresponding difference for the mental component summary score was 4 points (95% CI 3 to 5; 4 trials, n=343). Such differences have the potential to be clinically meaningful. 14

## **Modes of exercise**

In most studies, SEPs have involved treadmill or track walking at an intensity that elicits moderate to maximal claudication pain.<sup>35</sup> There is a strong evidence-base for this type of training, and clinical guidelines cite it as the preferred modality (eg, The Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease II). 15 As of 2011, alternate exercise modalities had not been extensively studied.<sup>36</sup> In 2005, a randomised trial of 104 participants provided evidence that a 24-week intervention of either cycling or armcranking is viable alternatives for improving maximum walking distance (shuttle-walk) up to 29% and 31%, respectively.<sup>37</sup> These modalities may be most useful for patients who are unwilling/unable to walk because of severe pain or deconditioning.<sup>38</sup> Resistance training may also have a complementary role (eg, for improving muscular strength)<sup>39</sup>; however, at this point, international guidelines suggest it should not be used as a substitute for aerobic exercise because its impact on

Table 1 Vascular s	3	ine recommendations							Cupplementen
Recommendation	Frequency	Intensity	Туре	Time	Duration	Progression	Supervision	Location	Supplementary exercises
Guideline									
TASC II, 2007 <sup>15</sup>	3 × per week (typically)	Speed and grade that induces claudication within 3–5 min	Intermittent treadmill walking	30 min increasing up to 60 min	Not reported	Increase speed/ grade if patient can walk for more than 10 min	Not reported	Not reported	Not reported
AHA/ACC, 2016 <sup>17</sup>	3 × per week	Maximum- moderate claudication	Intermittent walking	30–45 min per session, with warm up and cool down	Minimum of 12 weeks	Not reported	Supervised by a qualified healthcare professional	Hospital/ outpatient facility	Not reported
ECS, 2017 <sup>18</sup>	Not reported	Not reported	Walking	Minimum 3 hours/week	At least 3 months	Not reported	Supervised	Not reported	Cycling, strength training and upper-arm ergometry
NICE 1472018 <sup>16</sup>	Not reported	Maximal pain	Walking	2 hours/week	3 months	Not reported	Supervised	Not reported	Not reported
RACGP, 2013 <sup>22</sup>	3–5 × p/w	Pain	Intermittent walking	30 min increasing to 60 min	Not reported	Not reported	Supervised	Not reported	Not reported

ACC; AHA; ECS; NICE; RACGP; TASC.

Table 2 Summary of exercise prescription recommendations					
Exercise rationale	To improve walking capacity, claudication symptoms and quality of life, and for secondary prevention of cardiovascular disease				
Provider	The programme should have a designated clinical lead (eg, vascular surgeon, physician or nurse specialist). Exercise professionals who wish to work in this area should possess the essential competencies and minimum qualifications as per the country of work. Professional standards of accredited exercise physiologists should include detailed knowledge of pathophysiology, exercise physiology and exercise training for patients with IC. Some of these are specified in the following BACPR Position Statement (UK Based):http://www.bacpr.com/resources/51A_EPG_Position_Statement.pdf				
Mode of delivery	The exercise should ideally be delivered through an on-site supervised programme. The exercise prescription should be individually tailored based on an initial assessment; however, several patients may be supervised at the same time. A facilitated, self-managed exercise programme with embedded behaviour change techniques is a reasonable alternative for people who prefer this approach or are unable to access an on-site programme, or for longer-term benefit after a supervised programme is completed. Details of a structured education programme that promotes self-managed walking exercise can be found here. Additional information for home-based exercises can be found here: (https://circulationfoundation.org.uk/news/COVID-19-special)  Unstructured, unsupervised exercise approaches that consist solely of basic advice to walk or exercise more are not effective.				
Setting	On-site programmes can be delivered in various settings including hospital- or community-based exercise physiology or physiotherapy clinics or community exercise facilities. Self-managed programmes can be conducted in a setting that suits the individual.				
Materials	Assessment tools: Motorised treadmill with adjustable incline to allow incremental exercise testing (eg, 'Gardner' protocol) to determine pain-free and maximum walking distances or, if unavailable, procedures and instructions for an alternative functional capacity test (eg, 30 m 6-min corridor walk test); questionnaires for assessing patient-perceived ambulatory function (eg, WELCH questionnaire), and generic and condition-specific quality of life (eg, SF-36, VascuQoL and Walking Impairment uestionnaires, respectively). Optional—equipment to assess vascular status (eg, ankle-brachial index) and cardiovascular disease risk (eg, blood pressure, lipid profile).  Exercise equipment: Motorised treadmills with adjustable incline or space for over-ground walking (preferably indoor and air-conditioned). Optional for aerobic exercise—upper and lower limb ergometers. Optional for resistance exercise—weights machines, dumbbells.  Intensity-monitoring equipment: Five-point claudication pain scale, exertion scale (eg, 6–20point Borg Rating of Perceived Exertion Scale), heart rate monitors, manual sphygmomanometer and stethoscope.				
Walking exercise guidelines	Programme duration: At least 3 months Frequency: ≥3 times/week Claudication pain endpoint: Based on current evidence, patients should be advised to walk to the point of near-maximum leg pain (ie, 4–5 on claudication pain scale); however, preliminary evidence suggests that walking only to the onset of ischaemic leg pain may also be beneficial for patients reluctant to walk at higher levels of pain Pattern: Following a warm-up period, the patient should walk at a speed and grade that induces claudication pain within 3–5 min. The patient is instructed to stop walking and rest when his or her claudication pain reaches a moderate-to-strong level. When the claudication has abated, the patient resumes walking until a moderate-to-strong claudication pain recurs. This cycle of exercise and rest is ideally repeated for at least 30 min. In subsequent visits, the speed or grade of walking is increased if the patient is able to walk for ≥10 min without reaching moderate claudication pain. For those patients who start at a lower level of claudication pain (1–3/5), as the patient tolerates it, they should be encouraged to increase the intensity of pain achieved as a progression tool.  Duration per session: Many patients with IC may need to start with just 10–15 min of walking exercise per session. In this situation, the duration of exercise should be increased by 5 min each week, until the patient is walking for at least 30 min per session. Patients who can walk for more than 30 min per session should be encouraged to increase the exercise duration to 45–60 min. They should also be encouraged to include other modes of exercise to work on improving cardiorespiratory fitness and muscular strength				
	Continued				

Table 2 Continued				
Exercise rationale	To improve walking capacity, claudication symptoms and quality of life, and for secondary prevention of cardiovascular disease			
Upper and lower limb ergometry	May be considered as alternative aerobic exercise strategies for improving walking ability and quality of life. May also have the potential to provide a greater cardiorespiratory stimulus than walking exercise in individuals with severe claudication.  Example protocol: Ten sets of 2 min of upper or lower extremity ergometry conducted twice weekly for at least 3 months. Intensity should be moderate or Borg RPE 13–14 (6–20 scale)			
Resistance exercise	Though evidence is increasing, resistance exercise is yet to be included in international guidelines as a sole therapy, it is purely recommended as an adjunct for now. It therefore should be considered as complementary (eg, for targeting improved strength or reduced falls risk), but not as a replacement for aerobic exercise because its impact on walking ability appears modest at best. <b>Example protocol:</b> Moderate-to-high intensity (Borg exertion rating of 14–16), 6–8 exercises (leg press, Knee flexion, knee extension, calf press, chest press, seated row) targeting the major muscle groups of the upper and lower body, 2–4 sets of 10–15 repetitions per set, 2–3 sessions per week.			
Other	Circuit-based training may be a practical way of delivering a combination of aerobic and resistance exercises when circumstances necessitate group-based training and is an effective tool for improving both muscle strength and cardiorespiratory fitness, which are both related to reduced cardiovascular and all-cause mortality. <sup>25</sup>			
Safety issues	An initial risk assessment should occur as per Appendix E of the following ACPICR Standards document https://www.acpicr.com/data/Page_Downloads/ACPICRStandards.pdf . Exercise is contraindicated by foot ulcers and limb pain at rest (ie, critical limb ischaemia). As patients increase their walking ability, there is the possibility that cardiac signs and symptoms may appear (eg, dysrhythmia, angina). These events should prompt further clinical assessment to ensure safety continuing. Clinical assessment should also be considered when a patient undertakes a mode of exercise that is not limited by claudication pain.			

ACPICR; BACPR; IC; RPE; SE-36, Short-Form-36; VascuQoL; WELCH.

walking distance appears modest (eg, McDermott *et al* 2009). Nevertheless, there is emerging evidence to support its efficacy, and it should no longer be a mode of exercise that is ignored. A recent systematic review and meta-analysis (n=826; 363 resistance trained) demonstrated that resistance training (in comparison to control) can significantly improve both maximum walking distance via constant treadmill testing (standardised mean difference (SMD) 0.51 [95% CI 0.23 to 0.79]) and maximum walking distance via progressive treadmill testing (SMD 0.45 [95% CI 0.08 to 0.83]). Only 6-min claudication onset time (not pain-free treadmill distance) was significantly improved with resistance training (mean difference (MD) 82 m [95% CI 40.91 to 123.54). 39

#### Frequency of exercise

A comparison of different training frequencies for patients with IC has not been investigated in a single study. The 1995 meta-analysis of Gardner and Poehlman suggested that an exercise frequency of ≥3 sessions per week was associated with better outcomes compared with <3 times per week, although it should be noted that it pooled data from randomised controlled trials and uncontrolled studies. In addition, the 2004 review of Bulmer and Coombes also identified three sessions per week as the optimal frequency for maximum improvements in walking distance. Conversely, a meta-analysis in 2012 including 1054 patients did not identify an optimal frequency for programmes. The authors of the 2012 meta-analysis do note, however, that a SEP with

three sessions per week (in combination with duration of programme and session) 'would give the best results'. <sup>42</sup> Therefore, frequency of SEPs should aim to be at least three times per week, which is in line with common physical activity guidelines for the general population. <sup>17</sup>

#### **Duration of programme**

No standardised duration of programme for patients with IC has been identified, with exercise programme length ranging from as little as 2 weeks to as many as 18 months. Sardner *et al* (2012) measured outcomes at 2, 4 and 6 months (n=80) and demonstrated that exercise-mediated improvements in pain-free and maximum walking distances were largely achieved in the first 2 months. Additional meta-analysis has also demonstrated that improvements in treadmill walking occur following 3 months of supervised exercise. It may be likely that the optimal prescription is difficult to elucidate due to heterogeneity of studies, including differences in frequency, intensity and type of the exercise. Currently, we recommend that programmes should be at least a minimum of 12 weeks in duration.

#### **Intensity of exercise**

Exercise intensity is commonly prescribed on the basis of heart rate, rating of perceived exertion, or  $\dot{V}O_{2peak}$  obtained via exercise stress testing, <sup>46</sup> and may be classified as low, moderate or vigorous based on the American College of Sports Medicine guidelines. <sup>47</sup> There is limited information on the appropriate intensities of exercise

programmes for patients with PAD. 17 48 However, a metaanalysis by Parmenter et al (2015) investigated the relationship between exercise intensity,  $\dot{V}O_{2peak}$  (ie, aerobic capacity) and maximal walking distance, and demonstrated that the greatest improvements occurred when exercise intensity was between 70% and 90% HRmax (ie, vigorous according to the American College of Sports Medicine guidelines). 49 A further systematic review by Pymer et al (2019) focusing on high-intensity exercise identified four studies that prescribed exercise on the VO<sub>2peak</sub> or HRmax achieved during baseline testing. Overall, six studies demonstrated significant improvements in treadmill maximum walking distances compared with a control group (generally consisting of exercise advice alone). 50 However, further research is required to establish the relationship between intensity (moderate vs vigorous) and walking improvements and compare those findings to SEPs.

## **Claudication pain scale**

Relatively few trials have used classically defined measures of exercise intensity as described earlier, and for patients with PAD, there is a common misconception between exercise 'intensity' and severity of leg pain or discomfort.<sup>51</sup> Most reported trials in the literature use the claudication pain scale to instruct patients when to stop exercising and not exercise intensity markers such as heart rate. The claudication pain scale is a continuous scale from 1, indicating no pain, to 5 indicating severe pain, 49 with trials often instructing patients to walk to near-maximal pain levels.

Three studies have specifically investigated the relationship between 'intensity' (based on pain) and walking outcomes. 52-54 Mika et al (2013) used different intensities corresponding to scores on the pain scale and matched exercise duration in 60 patients.<sup>53</sup> Gardner et al (2005) prescribed intensity as 'high—80%' or 'low—40%' based on the maximal grade achieved at baseline in 31 patients.<sup>52</sup> Finally, Novakovic et al (2019) randomised 36 patients to either moderate or pain-free walking, with moderate training prescribed on 70% of the patients predicted HRmax.<sup>54</sup> For all studies, outcomes including pain-free and maximum walking distance did not differ between the intensities prescribed. This may highlight that the volume of exercise (and not intensity prescribed) is perhaps the most important factor for improving walking distance in patients with IC.<sup>36</sup> <sup>49</sup> <sup>55</sup> With regard to pain, overall the current evidence seems to favour patients walking near maximal pain for beneficial outcomes. However, walking to no pain, or minimal pain, may also been shown to be effective for this cohort. 54 55 Indeed, a meta-analysis by Parmenter et al (2011) showed that walking without inducing claudication pain produced significant improvements in initial claudication distance and also improved absolute claudication distance. 36 Additionally, a meta-analysis (six studies) in 2015 demonstrated that improvements in cardiorespiratory fitness were obtained when walking to mild pain (MD

0.79 mL/kg/min [95% CI 0.45 to 1.14]).49 Current recommendations are if patients can tolerate, then walking to moderate pain (i.e 4–5 on the claudication scale) may be suitable. If patients are unable to tolerate higher levels of pain on the claudication scale, then they can walk to low levels of pain, provided the volume of exercise is sufficient, <sup>47</sup> which may improve adherence levels.

## **Supervision**

Despite consistent evidence demonstrating the clinical effectiveness of SEPs, a European survey conducted in 2012 demonstrated that approximately 30% of the respondents had access to a supervised programme, <sup>56</sup> with similar availability in the UK. 19 Similar evidence has recently emerged from the USA with 54% of the respondents stating no exercise to a SEP.<sup>20</sup> These low provision rates may be attributed to several factors including funding provision, facilities, referral pathways, resources and a lack of trained staff. 19 23

A 2014 review noted uncertainty regarding the benefits of SEPs over unsupervised exercise, especially regarding QoL.<sup>51</sup> Despite the apparent superiority of SEPs, there is still a need to develop alternative programmes, given that supervised programmes may be 'unpopular' with patients due to financial, time or transport limitations, 57 58 or simply because they are looking for a 'quick fix'. 59 As supervised programmes may be unavailable to a large proportion of patients, the development of alternative home-based or 'self-facilitated' programmes have been increasingly trialled. These types of interventions have in content but include psychological interventions, <sup>60</sup> such as cognitive behavioural changes, <sup>61</sup> step-monitoring<sup>62</sup> and patient education.<sup>24</sup>

## Home exercise programmes

Evidence for home-based or self-managed programmes is currently conflicting. In 2013, a systematic review reported that there was low-level evidence to suggest home-based programmes can improve walking distance and OoL in comparison to walking advice or nonexercise. <sup>63</sup> In 2018, a Cochrane review including 21 studies and 1400 patients, reported that there was high-quality evidence showing greater improvements in maximum walking distance (measured via treadmill testing) at 3 months among patients enrolled in a SEP versus a homebased programme (95% CI 0.12 to 0.65), or in patients who received walking advice only (95% CI 0.53 to 1.07).<sup>64</sup> This translates to walking distance improvements of between 120 and 210 m in favour of supervised exercise, respectively, with similar improvements maintained at 6 and 12 months. However, the prescription of exercise may influence the magnitude of effect, possibly due to training specificity. 49 Conversely, the meta-analysis of QoL outcomes showed no marked differences between supervised exercise and home exercise programmes. In a recent randomised trial, McDermott et al (2018) considered the efficacy of home-based exercise (n=99) with wearable technology and telephone coaching versus no



exercise advice and found no difference home exercise and control.<sup>65</sup> Therefore, further research is required to evaluate the specific components of home-based interventions to maximise patient benefit (ie, wearable technology, on-site visits, etc).

## Safety

There may be a misconception that exercise training may be unsafe in patients with PAD. Indeed, 70% of the vascular surgeons in one survey thought that cardiovascular comorbidities or aorto-iliac stenosis or occlusions were relative contraindications to exercise. 66 Gommans et al (2015) explored the safety of supervised exercise training (via any exercise modality) and reviewed adverse event data from clinical trials.<sup>67</sup> Seventy-four trials were included, representing 82 725 hours of training in 2876 patients with a mean age of 64 years (range 54–76 years). Nine adverse events were reported, six of cardiac, two of non-cardiac origin and one fatal adverse event (myocardial infarction). This resulted in an all-cause complication rate of one event per 10 340 patient-hours. The total noncardiac and cardiac event rate was 1 per 13 788 patients and 1 per 41 363 hours. The study concluded that supervised exercise training is safe for people with IC due to a low all-cause complication rate, and routine cardiac prescreening is not required.<sup>67</sup> However, it should be noted that patients participating in clinical trials might not be a true representation of the overall population. This may be due to strict exclusion/inclusion criteria screening out patients with extensive comorbidities. It would be beneficial to have observational data for adverse events in routine SEPs, to fully elucidate the all-cause complication rates. In addition, it is important to note, that as a patient's exercise tolerance, pain tolerance and walking ability improve, this may begin to unmask underlying signs and symptoms of coronary artery disease. While not routine practice, cardiac screening may also be considered when patients are engaging in an exercise modality that may not elicit claudication pain such as cycling or when they are engaging in higher-intensity exercise programmes. In general, contraindications to participation in an exercise programme include uncontrolled hypertension, unstable angina or other uncontrolled arrhythmias. Relative contraindications include known obstructive coronary disease, acquired or advance heart block. A comprehensive list of both absolute and relative contraindications can be found in the 'American College of Sports Medicine Guidelines for Exercise Testing and Prescription . 47 68

## **APPLICATION TO PRACTICE**

#### **Recommendations for exercise training**

All prospective patients should be clinically assessed, and risk stratified to ensure that they do not have any contraindications to the exercise therapy, and to document comorbidities that may need to be accounted for, in order to individualise the exercise programme. Patient ability and preference should also be taken into account

when prescribing the exercise programme. Clinical assessment should be repeated as exercise tolerance improves to ensure that the training intensity is sufficient to ensure ongoing patient safety. Any exercise programme should ideally be delivered through an on-site supervised programme with clinical oversight. However, a facilitated, self-managed exercise programme involving behaviour change techniques is a reasonable alternative for patients who prefer this approach or are unable to access supervised exercise.<sup>24</sup> The core modality for SEPs should be walking; however, other modes are also efficacious for those who cannot tolerate walking programmes, as outlined in table 2. Alternative modes include arm cranking, cycling, pole-striding and progressive resistance training. A structured programme should involve walking at an intensity that elicits moderate-to-strong claudication pain and should be conducted for a minimum of 3 months, involving at least three sessions of 30–45 min/ week. Initial exercise prescription should be based on actual baseline maximum walking distance. Further evidence-based recommendations for exercise training are provided in table 2. However, if patients struggle with the maximum intensity of pain prescribed, then walking at lower pain levels will also lead to improvements in walking ability/distance. 36 55

During exercise training sessions, acute responses to exercise should be monitored to inform the exercise prescription, including heart rate, blood pressure (in the first few exercise sessions), perceived exertion and claudication pain. The continuous monitoring of blood pressure is not recommended but should be revaluated if the intensity or mode of exercise changes. It is recommended that heart rate may be continuously monitored, and blood pressure, perceived exertion and claudication pain are recorded intermittently when the patient stops exercises (if interval walking) or if any signs or symptoms (such as dizziness are present). Finally, programme entry and exit assessments should be performed to determine changes in patient outcomes, including walking distance (primarily 6-min walk test) and QoL.

To support the provision and uptake of exercise, alongside this guideline an infographic of key messages has been developed that may be used as a poster or handout in clinic; particularly where patients cannot access a supervised programme.<sup>69</sup>

## **SUMMARY**

Exercise training is a safe, effective and low-cost intervention for improving walking ability in patients with IC. Additional benefits may include improvements in QoL, muscle strength and cardiorespiratory fitness. Clinical guidelines advocate supervised exercise training as a primary therapy for IC, with walking as the primary modality. However, evidence is emerging for the role of various other modes of exercise including cycling and progressive resistance training to supplement walking training. In addition, there is emerging evidence for home-based exercise programmes. Revascularisation or

drug treatment options should only be considered in patients if exercise training provides insufficient symptomatic relief.

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**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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#### **REFERENCES**

- 1 McDermott MM. Peripheral arterial disease: epidemiology and drug therapy. Am J Geriatr Cardiol 2002;11:258–66.
- 2 Fowkes FG, Rudan D, Rudan I, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *Lancet* 2013;382:1329–40.
- 3 Morley RL, Sharma A, Horsch AD, et al. Peripheral artery disease. BMJ 2018;360:j5842.
- 4 Rose G. The diagnosis of ischaemic heart pain and intermittent claudication in field surveys. *Bull World Health Organ* 1962;27:645. Available https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2555832/
- 5 Hamburg NM, Balady GJ. Exercise rehabilitation in peripheral artery disease: functional impact and mechanisms of benefits. *Circulation* 2011;123:87–97.
- 6 Norgren L, Hiatt WR, Dormandy JA, et al. Inter-society consensus for the management of peripheral arterial disease (TASC II). Eur J Vasc Endovasc Surg 2007;33:S1–75.
- 7 van Haelst STW, Koopman C, den Ruijter HM, et al. Cardiovascular and all-cause mortality in patients with intermittent claudication and critical limb ischaemia. Br J Surg 2018;105:252–61.
- 8 Harwood AE, Totty JP, Pymer S, et al. Cardiovascular and musculoskeletal response to supervised exercise in patients with intermittent claudication. J Vasc Surg 2019;69:1899–1908 e1891.
- 9 Hou XY, Green S, Askew CD, et al. Skeletal muscle mitochondrial ATP production rate and walking performance in peripheral arterial disease. Clin Physiol Funct Imaging 2002;22:226–32.
- 10 Gorely T, Crank H, Humphreys L, et al. "Standing still in the street": experiences, knowledge and beliefs of patients with intermittent claudication: a qualitative study. J Vasc Nurs 2015;33:4–9.

- 11 Gardner AW, Montgomery PS, Killewich LA. Natural history of physical function in older men with intermittent claudication. *J Vasc Surg* 2004;40:73–8.
- 12 Brostow DP, Petrik ML, Starosta AJ, et al. Depression in patients with peripheral arterial disease: a systematic review. Eur J Cardiovasc Nurs 2017;16:181–93.
- 13 Gardner AW, Montgomery PS, Parker DE. Physical activity is a predictor of all-cause mortality in patients with intermittent claudication. J Vasc Surg 2008;47:117–22.
- 14 Lane R, Harwood A, Watson L, et al. Exercise for intermittent claudication. Cochrane Database Syst Rev 2017;12:CD000990.
- 15 Norgren L, Hiatt WR, Dormandy JA, et al. Inter-society consensus for the management of peripheral arterial disease (TASC II). J Vasc Surg 2007;45:S:S5–67.
- 16 NICE. The National Institute of Health and Care Excellence. Peripheral arterial disease: diagnosis and management clinical guideline [CG147]. National Institute for Health and Care Excellence, 2012.
- 17 Gerhard-Herman MD, Gornik HL, Barrett C, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: executive summary: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. Circulation 2017; 135: e686–e725.
- 18 Aboyans V, Ricco JB, Bartelink ML, et al. 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS). Kardiol Pol 2017;75:1065–160.
- 19 Harwood A, Smith G, Broadbent E, et al. Access to supervised exercise services for peripheral vascular disease patients. Bull R Coll Sur Engl 2017;99:207–11.
- 20 Dua A, Gologorsky R, Savage D, et al. National assessment of availability, awareness, and utilization of supervised exercise therapy for peripheral artery disease patients with intermittent claudication. J Vasc Surg 2019;69:e55–e56.
- 21 Hageman D, Fokkenrood HJP, Essers PPM, et al. Improved adherence to a stepped-care model reduces costs of intermittent claudication treatment in The Netherlands. Eur J Vasc Endovasc Surg 2017;54:51–7.
- 22 Au TB, Golledge J, Walker PJ, et al. Peripheral arterial disease diagnosis and management in general practice. Aust Fam Physician 2013;42:397–400.
- 23 Dua A, Gologorsky R, Savage D, et al. National assessment of availability, awareness, and utilization of supervised exercise therapy for peripheral artery disease patients with intermittent claudication. J Vasc Surg 2020;71:1702–7.
- 24 Tew GA, Humphreys L, Crank H, et al. The development and pilot randomised controlled trial of a group education programme for promoting walking in people with intermittent claudication. Vasc Med 2015;20:348–57.
- 25 Steell L, Ho FK, Sillars A, et al. Dose-response associations of cardiorespiratory fitness with all-cause mortality and incidence and mortality of cancer and cardiovascular and respiratory diseases: the UK Biobank cohort study. Br J Sports Med 2019;53:1371–8.
- 26 Gardner AW, Skinner JS, Cantwell BW, et al. Progressive vs single-stage treadmill tests for evaluation of claudication. Med Sci Sports Exerc 1991;23:402–8.
- 27 McDermott MM, Guralnik JM, Criqui MH, et al. Six-minute walk is a better outcome measure than treadmill walking tests in therapeutic trials of patients with peripheral artery disease. Circulation 2014;130:61-8
- 28 Hiatt WR, Rogers RK, Brass EP. The treadmill is a better functional test than the 6-minute walk test in the rapeutic trials of patients with peripheral artery disease. *Circulation* 2014;130:69–78.
- 29 McDermott MM, Ades PA, Dyer A, et al. Corridor-based functional performance measures correlate better with physical activity during daily life than treadmill measures in persons with peripheral arterial disease. J Vasc Surg 2008;48:1231–1237, 1237 e1231.
- 30 Chetter IC, Spark JI, Dolan P, et al. Quality of life analysis in patients with lower limb ischaemia: suggestions for European standardisation. Eur J Vasc Endovasc Surg 1997;13:597–604.
- 31 Gulati S, Coughlin PA, Hatfield J, et al. Quality of life in patients with lower limb ischemia; revised suggestions for analysis. *J Vasc Surg* 2009;49:122–6.
- 32 Regensteiner JG. Evaluation of walking impairment by questionnaire in patients with peripheral arterial disease. J Vasc Med Biol 1990;2:142–52.
- 33 Spertus J, Jones P, Poler S, *et al.* The peripheral artery questionnaire: a new disease-specific health status measure for patients with peripheral arterial disease. *Am Heart J* 2004;147:301–8.
- 34 Gardner AW, Montgomery PS, Wang M. Minimal clinically important differences in treadmill, 6-minute walk, and patient-based outcomes



- following supervised and home-based exercise in peripheral artery disease. *Vasc Med* 2018;23:349–57.
- 35 Tew GA, Brabyn S, Cook L, et al. The completeness of intervention descriptions in randomised trials of supervised exercise training in peripheral arterial disease. PLoS One 2016;11:e0150869.
- 36 Parmenter BJ, Raymond J, Dinnen P, et al. A systematic review of randomized controlled trials: walking versus alternative exercise prescription as treatment for intermittent claudication. Atherosclerosis 2011:218:1–12
- 37 Zwierska I, Walker RD, Choksy SA, et al. Upper- vs lower-limb aerobic exercise rehabilitation in patients with symptomatic peripheral arterial disease: a randomized controlled trial. J Vasc Surg 2005;42:1122–30.
- 38 Sanderson B, Askew C, Stewart I, et al. Short-term effects of cycle and treadmill training on exercise tolerance in peripheral arterial disease. J Vasc Surg 2006;44:119–27.
- 39 Parmenter BJ, Mavros Y, Ritti Dias R, et al. Resistance training as a treatment for older persons with peripheral artery disease: a systematic review and meta-analysis. Br J Sports Med 2019.
- 40 Gardner AW, Poehlman ET. Exercise rehabilitation programs for the treatment of claudication pain. A meta-analysis. *JAMA* 1995;274:975–80.
- 41 Bulmer AC, Coombes JS. Optimising exercise training in peripheral arterial disease. Sports Med 2004;34:983–1003.
- 42 Fakhry F, van de Luijtgaarden KM, Bax L, et al. Supervised walking therapy in patients with intermittent claudication. J Vasc Surg 2012;56:1132–42.
- 43 Gardner AW, Montgomery PS, Parker DE. Optimal exercise program length for patients with claudication. *J Vasc Surg* 2012;55:1346–54.
- 44 Gommans LN, Saarloos R, Scheltinga MR, et al. Editor's choice: the effect of supervision on walking distance in patients with intermittent claudication: a meta-analysis. Eur J Vasc Endovasc Surg 2014;48:169–84.
- 45 Fokkenrood HJ, Bendermacher BL, Lauret GJ, et al. Supervised exercise therapy versus non-supervised exercise therapy for intermittent claudication. *Cochrane Database Syst Rev* 2013; CD005263.
- 46 Beltz NM, Gibson AL, Janot JM, et al. Graded exercise testing protocols for the determination of VO2max: historical perspectives, progress, and future considerations. J Sports Med (Hindawi Publ Corp) 2016;2016:3968393.
- 47 American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. Wolters Kluwer: Philadelphia, 2018.
- 48 Treat-Jacobson D, McDermott MM, Bronas UG, et al. Optimal exercise programs for patients with peripheral artery disease: a scientific statement from the American Heart Association. Circulation 2019; 139: e10–e33.
- 49 Parmenter BJ, Dieberg G, Smart NA. Exercise training for management of peripheral arterial disease: a systematic review and meta-analysis. Sports Med 2015;45:231–44.
- 50 Pymer S, Palmer J, Harwood AE, et al. A systematic review of high-intensity interval training as an exercise intervention for intermittent claudication. J Vasc Surg 2019;70:2076–87.
- 51 Gardner AW, Afaq A. Management of lower extremity peripheral arterial disease. *J Cardiopulm Rehabil Prev* 2008;28:349–57.
- 52 Gardner AW, Montgomery PS, Flinn WR, et al. The effect of exercise intensity on the response to exercise rehabilitation in patients with intermittent claudication. J Vasc Surg 2005;42:702–9.

- 53 Mika P, Konik A, Januszek R, et al. Comparison of two treadmill training programs on walking ability and endothelial function in intermittent claudication. *Int J Cardiol* 2013;168:838–42.
- 54 Novakovic M, Krevel B, Rajkovic U, et al. Moderate-pain versus pain-free exercise, walking capacity, and cardiovascular health in patients with peripheral artery disease. J Vasc Surg 2019;70:148–56.
- 55 Parmenter BJ, Dieberg G, Phipps G, et al. Exercise training for health-related quality of life in peripheral artery disease: a systematic review and meta-analysis. Vasc Med 2015;20:30–40.
- 56 Makris GC, Lattimer CR, Lavida A, et al. Availability of supervised exercise programs and the role of structured home-based exercise in peripheral arterial disease. Eur J Vasc Endovasc Surg 2012;44:569–75.
- 57 Harwood AE, Smith GE, Cayton T, et al. A systematic review of the uptake and adherence rates to supervised exercise programs in patients with intermittent claudication. Ann Vasc Surg 2016;34:280–9.
- 58 Abaraogu U, Ezenwankwo E, Dall P, et al. Barriers and enablers to walking in individuals with intermittent claudication: a systematic review to conceptualize a relevant and patient-centered program. PLoS One 2018;13:e0201095.
- 59 Popplewell MA, Bradbury AW. Why do health systems not fund supervised exercise programmes for intermittent claudication? Eur J Vasc Endovasc Surg 2014;48:608–10.
- 60 Cunningham MA, Swanson V, O'Carroll RE, et al. Randomized clinical trial of a brief psychological intervention to increase walking in patients with intermittent claudication. Br J Surg 2012;99:49–56.
- 61 McDermott MM, Liu K, Guralnik JM, et al. Home-based walking exercise intervention in peripheral artery disease: a randomized clinical trial. JAMA 2013;310:57–65.
- 62 Gardner AW, Parker DE, Montgomery PS, et al. Step-monitored home exercise improves ambulation, vascular function, and inflammation in symptomatic patients with peripheral artery disease: a randomized controlled trial. J Am Heart Assoc 2014;3:e001107.
- 63 Al-Jundi W, Madbak K, Beard JD, et al. Systematic review of home-based exercise programmes for individuals with intermittent claudication. Eur J Vasc Endovasc Surg 2013;46:690–706.
- 64 Hageman D, Fokkenrood HJ, Gommans LN, et al. Supervised exercise therapy versus home-based exercise therapy versus walking advice for intermittent claudication. Cochrane Database Syst Rev 2018;4: CD005263.
- 65 McDermott MM, Spring B, Berger JS, et al. Effect of a home-based exercise intervention of wearable technology and telephone coaching on walking performance in peripheral artery disease: the HONOR randomized clinical trial. JAMA 2018;319:1665–76.
- 66 Lauret GJ, van Dalen HC, Hendriks HJ, et al. When is supervised exercise therapy considered useful in peripheral arterial occlusive disease? A nationwide survey among vascular surgeons. Eur J Vasc Endovasc Surg 2012;43:308–12.
- 67 Gommans LN, Fokkenrood HJ, van Dalen HC, et al., Safety of supervised exercise therapy in patients with intermittent claudication. *J Vasc Surg* 2015; 61: 512–8e512.
- 68 Association of Chartered Physiotherapists in Cardiac Rehabilitation. ACPICR standards: Standards for physical activity and exercise in the cardiovascular population. Association of Chartered Physiotherapists in Cardiac Rehabilitation, 2015.
- 69 Tew GA, Allen L, Askew CD, et al. Infographic. Exercise for intermittent claudication. *Br J Sports Med* 2020.