Sheffield Hallam University

An updated systematic review and meta-analysis of home-based exercise programs for individuals with intermittent claudication

PYMER, Sean <http://orcid.org/0000-0003-1685-2091>, IBEGGAZENE, Said <http://orcid.org/0000-0001-9457-7887>, PALMER, Joanne, TEW, Garry A., INGLE, Lee, SMITH, George E., CHETTER, Ian C. and HARWOOD, Amy E.

Available from Sheffield Hallam University Research Archive (SHURA) at:

https://shura.shu.ac.uk/29350/

This document is the Accepted Version [AM]

Citation:

PYMER, Sean, IBEGGAZENE, Said, PALMER, Joanne, TEW, Garry A., INGLE, Lee, SMITH, George E., CHETTER, Ian C. and HARWOOD, Amy E. (2021). An updated systematic review and meta-analysis of home-based exercise programs for individuals with intermittent claudication. Journal of Vascular Surgery, 74 (6), 2076-2085.e20. [Article]

Copyright and re-use policy

See http://shura.shu.ac.uk/information.html

Sheffield Hallam University Research Archive
http://shura.shu.ac.uk

Review

An Updated Systematic Review and Meta-Analysis of Home-based Exercise Programmes for Individuals with Intermittent Claudication.

Authors:

Pymer, S.A. MSc[a]

Ibeggazene, S. PhD[b]

Palmer, J. MSc[a]

Tew, G.A. PhD[c]

Ingle, L. PhD[d]

Smith, G.E. MD[a]

Chetter, I.C. MD[a]

Harwood, A.E. PhD[d,e]

Institutions:

[a]Academic Vascular Surgical Unit; Hull York Medical School, Hull, UK.

[b] Department of Allied Health Professionals, Sheffield Hallam University, Sheffield, UK

[c]Department of Sport, Exercise and Rehabilitation, Northumbria University, Newcastle, UK.

[d]Department of Sport, Health & Exercise Science, University of Hull, Hull, UK.

[e]Centre for Sport, Exercise and Life Sciences, Coventry University, Coventry, UK.

Corresponding Author, pre and post publication:

Sean Pymer MSc

Academic Vascular Surgical Unit

Tower block

Hull Royal Infirmary

Hull

HU3 2JZ.

Email: sean.pymer@hey.nhs.uk;

Tel: 01482 674643

Running head: Home-based exercise for intermittent claudication

Declarations of interest: None.

Word Count: 3499

Key Words: Intermittent Claudication, Peripheral Arterial Disease, Exercise, Walking.

ARTICLE HIGHLIGHTS

Type of Research: Systematic Review and Meta-Analysis

Key Findings: Supervised exercise programmes are superior to structured home-based exercise programmes for patients with intermittent claudication (p = .004). However, when monitoring was used via pedometers or activity monitors, home-based exercise programmes were equivalent to supervised exercise programmes (p = .86).

Take home Message: When supervised exercise programmes are unavailable, home-based exercise programmes can be used. However, they must be appropriately structured and monitored to be effective.

Table of Contents Summary

In this meta-analysis, supervised exercise programmes were superior to structured home-based exercise programmes. However, home-based programmes with monitoring methods were equivalent. When supervised exercise programmes are unavailable, home-based exercise programmes can be used. However, they must be appropriately structured and monitored to be effective.

Abstract:

Objectives: Supervised exercise programmes (SEP) are effective for improving walking distance in patients with intermittent claudication (IC) but provision and uptake rates are sub-optimal. Access to such programmes has also been halted by the Coronavirus pandemic. The aim of this review is to provide a comprehensive overview of the evidence for home-based exercise programmes (HEP).

Data Sources: Medline, EMBASE, CINAHL, PEDro and Cochrane CENTRAL were searched for terms relating to HEP and IC.

Review Methods: This review was conducted in according with the published protocol and PRISMA guidance. Randomised and non-randomised trials that compared a HEP to SEP, basic exercise advice or no exercise controls for IC were included. A narrative synthesis was provided for all studies and meta-analyses conducted using data from randomised trials. The primary outcome was maximal walking distance. Sub-group analyses were performed to consider the effect of monitoring. Risk of bias was assessed using the Cochrane tool and quality of evidence via GRADE.

Results: 23 studies with 1907 participants were included. Considering the narrative review, HEPs were inferior to SEPs which was reflected in the meta-analysis (MD 139m, 95% CI 45 to 232m, p = .004, very-low-quality evidence). Monitoring was an important component, as HEPs adopting this were equivalent to SEPs (MD: 8m, 95% CI -81 to 97, p = .86; moderate-quality evidence). For HEPs versus basic exercise advice, narrative review suggested HEPs can be superior, though not always significantly so. For HEPs versus no exercise controls, narrative review and meta-analysis suggested HEPs were potentially superior (MD: 136m, -2-273m p = .05, very-low-quality evidence). Monitoring was also a key element in these comparisons.

Other elements such as appropriate frequency (≥3x a week), intensity (to moderate-maximum pain), duration (20 progressing to 60 minutes) and type (walking) of exercise were important, as was education, self-regulation, goal setting, feedback and action planning.

Conclusion: When SEPs are unavailable, HEPs are recommended. However, to elicit maximum benefit they should be structured, incorporating all elements of our evidence-based recommendations.

PROSPERO registration number: CRD42018091248

Introduction

Peripheral arterial disease (PAD) is categorised by stenotic or occlusive atherosclerotic lesions in the arteries that supply the legs, limiting blood flow[1]. Global estimates suggest that PAD affects 237 million people[2]. The classic symptom of PAD is intermittent claudication (IC); a reproducible ambulatory lower limb muscle pain, relieved by rest, caused by a muscle oxygen supply and demand imbalance[3,4]. IC can impede daily activities, functional capacity and quality of life (QoL) and carries an increased mortality risk[3-7]. First-line treatment for IC includes exercise therapy, ideally in the form of a supervised exercise programme (SEP)[8,9], with substantial evidence that SEPs significantly improve walking distance [10-12].

Despite this, only ~30% of patients with IC are eligible and willing to join a SEP and the majority of vascular units in the United Kingdom and United States do not have access to one, suggesting they are under-utilised and under-valued[13-15]. Patient-cited barriers include a lack of time and transport, whilst provider-cited barriers include a lack of funding, facilities or expertise[14,16]. Consequently, there has been an increased interest in home-based exercise programmes (HEP), with more recent evaluations including technological advancements such as wearable technology[17-19]. It is likely that interest in HEP provision has been increased further by the Coronavirus disease 2019 (COVID-19) pandemic, which meant that for some time, SEP access was not available, and this may still be the case in some countries.

A systematic review in 2013 demonstrated that there was low quality, preliminary evidence that HEPs can provide improvements in walking capacity and QoL[20]. The review concluded that more robust trials were required. Other reviews have attempted to consider the contemporary evidence base for HEPs[21,22], However, significant limitations included summating the evidence at the same time-points rather than the planned primary endpoint of each trial, including asymptomatic patients and combining exercise advice with no exercise controls, which limits their applicability Therefore, we aimed to update the aforementioned 2013 systematic review and provide a comprehensive overview of the evidence for HEPs versus SEPs, basic exercise advice or no exercise controls for improving walking distance in patients with IC. We also aimed to provide guidance for the most effective HEP elements which can aid healthcare professionals in the design and implementation of an evidence-based structured HEP for those with IC.

Methods

This systematic review was conducted in accordance with the PRISMA guidelines[23] and was prospectively registered on PROSPERO (CRD42018091248). Furthermore, our protocol outlining the full methodology, including search strategy, data management, outcome measures and the methods for assessing the risk of bias and rating the quality of evidence is published elsewhere[24].

Briefly, we included prospective non-randomised and randomised controlled trials (RCT's) that considered the effect of a HEP versus a comparator arm (SEP, basic exercise advice or no exercise control) on walking distance, QoL and/or physical activity for patients with IC. Searches were performed from database inception and completed in March 2020.

Data analysis and synthesis

Both RCT's and non-RCT's were included and a summary of findings table produced for each comparison including all studies. Where possible, a meta-analysis of RCT's was performed. Where data was not provided to allow entry into a meta-analysis, study authors were contacted, and relevant data requested. Meta-analysis was performed using Review Manager 5 (RevMan 2014), to produce forest plots with an overall effect estimate of mean difference and associated 95% confidence intervals. Random effects models were used for all meta-analyses to consider heterogeneity as interventions and outcomes differed between trials[25]. For meta-analyses, post-intervention mean and standard deviation was used unless only change scores were given. We have summated the results at the planned primary assessment point of each trial, rather than at designated time-points (e.g. six weeks) as this is the point at which the intervention is designed to have greatest effect[22].

A head-to-head analysis of the effectiveness of HEPs versus each comparator arm was conducted and sub-group analyses were performed based on the presence or absence of monitoring. Monitoring included either self-monitoring, using devices such as pedometers, or remote monitoring, using activity monitors. Other pre-specified sub-group analyses were not performed due to insufficient data. Furthermore, the robustness of the analyses was determined via sensitivity analysis. For this, we removed RCT's with a higher risk of bias assessment and repeated the analysis[26]. Further sensitivity analyses were also performed using change scores from baseline (where reported) instead of final measurement scores as has been recommended[27]. When certain studies reported only final measurement scores, these were used in conjunction with the change scores that were reported for the purpose of sensitivity analyses. All sensitivity analyses are presented in the supplementary material.

We also considered the components of effective HEP interventions, such as the frequency, intensity, time and type of exercise and the use of monitoring or dietary and lifestyle advice or psychological components. Effective HEP interventions were identified as those that induced a significantly greater change ($p<0.05$) for at least one outcome, when compared with the basic exercise advice or no exercise control comparator groups. For trials comparing a SEP and a HEP, without a no exercise control or basic exercise advice comparator group, the HEP intervention was considered effective if it induced a significant positive change from baseline (p<0.05). The effective individual components were then identified as those that were evident (and similar) within the majority of these HEPs.

Results

Search Results

The search yielded a total of 4,411 results. Twenty-six articles[17-19,28-50], reporting 23 studies, were included in this review, with 18 contributing to meta-analyses (Figure 1). Nine articles included in the previous review were excluded due to lack of an appropriate comparator arm and the inclusion of patients with atypical leg pain. Seventeen additional articles were identified. . The definition of HEPs was heterogenous with a number of studies referring to it as 'walking advice' or 'unsupervised exercise' when they were structured and included specific prescriptions.

Included trials

Of the included trials, three were non-randomised and compared HEPs with SEPs[33-35]. The remaining trials were RCT's, with nine comparing HEPs with SEPs[28,30,36,38,41-43,45,47], three comparing HEPs with basic exercise advice[31,32,48], two comparing HEPs with both these groups[18, 46] and six comparing HEPs to no exercise controls[17,19,29,39,49,50].

The total number of recruited patients was 1907. All studies used walking as the mode of exercise. The frequency of training was varied, with three sessions per week being the minimum prescription to a maximum prescription of three times per day. Duration of exercise was either prescribed as minutes per session or number of steps per day. Exercise intensity was not always specified but was often based on reaching a mild or near-maximal level of claudication pain. HEP duration and length of follow-up ranged from six weeks to 12 months.

All but one study[32] reported treadmill and/or six-minute walk test (6-MWT) MWD, whilst seven did not report PFWD[17,29,30,32,39,46,50]. There was a lack of consistency between studies with regards to how walking distances were reported; either in minutes or metres, or how they were measured; with 15 using a graded treadmill test, five a constant load treadmill test and two the 6-MWT. Three studies also reported both treadmill and 6-MWT MWD. One study, from 1966, was included, but not used in meta-analyses because the treadmill test was not standardised between patients. Generic and disease specific QoL was measured in 14 studies via the Walking Impairment Questionnaire (WIQ), the Medical Outcomes Study short form 36 (SF-36), 20 (SF-20), or 12 (SF-12), the Intermittent Claudication Questionnaire (ICQ), the World Health Organisation quality of life questionnaire, the Vascular Quality of Life Questionnaire and the Euroqol-5D.

Quality assessment and Risk of Bias

All outcomes were rated via GRADE as very low, low or moderate quality (supplementary-tables I-III). The most common reason for rating down was imprecision, based on wide confidence intervals and/or small sample sizes

Risk of bias summary is shown in Figure 2. All studies were rated as high risk for performance bias due to the nature of the interventions.. Across other domains, there was little evidence of a high risk of bias (other than for selective outcome reporting). However, there was often inadequate information to imply a low risk, resulting in several domains being rated as ‘unclear’.

HEP vs. SEP

Supplementary-table IV outlines the narrative findings of all studies that compared HEPs with SEPs[18,28,30,33-36,38,41-43,45-47]. Overall, these studies show that for MWD there were statistically significant improvements in half of the HEP groups, and in all of the SEP groups. For between-group analyses, there were significantly greater improvements following SEP in nine of the 14 studies. For PFWD, there were statistically significant improvements in half of the HEP groups and in 11 of the 14 SEP groups, with four of the SEP groups demonstrating significantly greater improvements than the HEP groups. For three studies that adopted monitoring for the HEP via pedometers or step-monitors, there were no differences between groups for improvements in PFWD[18,34,36]. For MWD, one study reported no differences between groups[36], another reported a significantly greater improvement in the SEP group[18] and the final study noted a significant improvement in the SEP group but not the HEP group (p = .06)[34]. The latter study also reported that individual increases were ‘much higher’ in the SEP group, though the difference in improvements between groups was 5% and it was not compared statistically.

For QoL outcomes, there were improvements in the WIQ and the physical functioning domain and physical component summary score of the SF-36 with improvements largely similar between groups.

Meta-analysis for MWD from eight studies including 334 participants showed an overall improvement favouring SEPs (MD 139m, 95% CI 45 to 232m, p = .004, very-low-quality evidence; Figure 2A). PFWD, including seven studies and 306 participants also favoured SEPs (MD 84m, 95% CI 25 to 143m, p = .005, very-low-quality evidence; Figure 2B). However, these differences were no longer significant in the sub-group analyses including only trials which included monitoring (moderate-quality evidence; Figure 2). 6-MWD was not significantly different between groups (very-low-quality evidence).

The SF-36 measures of pain (p = .006, low-quality evidence) and social functioning (p = .04, low-quality evidence) significantly favoured SEPs. The WIQ domain of distance also significantly favoured SEPs (p = .01, very-low-quality evidence). The remaining QoL measures showed no significant mean difference between groups, which was also the case for daily steps (very-low to moderate-quality evidence). (very-low to moderate-quality evidence).

HEP vs. basic exercise advice

Supplementary-table V outlines the narrative findings of the five studies that compared HEPs with basic exercise advice[31,32,36,46,48]. Three studies reported change from baseline with two noting significant improvements in MWD and PFWD for the HEP groups. Two studies, which included monitoring, demonstrated significantly greater improvements in MWD for the HEP group compared to basic exercise advice.

For QoL, there were statistically significant improvements in the WIQ and the physical functioning domain of the SF-36, with the improvements in the WIQ being significantly greater than the basic exercise advice group in one study. For two of the three studies that reported physical activity measures, there were significantly greater improvements in daily steps and maximum 20-, 30- and 60-minute cadence for the HEP group in comparison to the basic exercise advice group[32,36].

Meta-analysis for MWD from four studies including 137 participants showed no significant difference between groups (MD 39.0m, 95% CI -123.1 to 201.1m, p = .64, very-low-quality evidence; Figure 3A). For sub-group analysis, findings were not altered for studies adopting monitoring. However, monitoring appeared important as there was a trend (p = .05) for HEPs without it to be inferior to basic walking advice (very-low-quality evidence, Figure 3A). For PFWD, including 3 studies and 109 participants, there was a significant between group difference, favouring HEPs (MD 64.5m, 95% CI 14.1 to 114.8m, p = .01, very-low-quality evidence; Figure 3B). Two of the three studies in this analysis adopted monitoring, precluding sub-group analysis. There was also a significant between group difference for the ICQ, favouring HEPs (p = <.01, low-quality-evidence). There were no significant mean differences for daily steps or the WIQ (very-low-quality evidence).

HEP vs. no exercise controls

Supplementary table VI outlines the narrative findings of all 6 studies that compared HEPs with no exercise controls[17, 19,29,39,49,50]. Three studies provided statistical comparisons and there were significant improvements in MWD and PFWD for the HEP groups, which were generally, significantly greater than the control groups. Two studies provided statistical comparisons for the 6-MWD with one demonstrating significant improvements in the HEP group, whilst the other showed no significant difference compared to baseline or control.

For QoL outcomes, there were improvements in the WIQ though they were not analysed statistically. The SF-12 and SF-36 outcomes were variable between studies.

For two studies that reported physical activity measures, only one provided statistical comparison and reported no significant improvements in either group[19,48]. For the three studies that adopted monitoring via an activity monitor or pedometer, two reported significant improvements in MWD for the HEP group and one also reported a greater improvement compared to the control group[19]. Meta-analysis including three studies and 100 participants revealed a mean difference in MWD of 136m, favouring HEPs, though it was not significant (95% CI -2 to 273m, p = .05, very-low-quality evidence; figure 4). There were insufficient studies to perform a meta-analysis of PFWD or sub-group analysis for MWD. There were no significant mean differences for daily steps, 6-MWD, the WIQ or the physical and mental component summaries of the SF-12/36 (moderate to very-low-quality evidence).

HEP adherence

HEP adherence was poorly reported, stated in only seven studies[18,19,29,30,32,33,36] and assessed via self-reported methods in four[29,30,32,33]. Three studies were able to receive quantified adherence information via their remote monitoring methods[18, 19, 36].

Four studies reported an adherence of >80%[18,29,32,36], and the lowest reported was 67%. The HEP prescribed on the basis of step count, reported poor adherence to the prescribed steps, but did not report adherence to frequency of exercise[19].

Discussion

The aim of this systematic review and meta-analysis was to provide an up-to-date comprehensive overview of the evidence for HEPs versus SEPs, basic exercise advice and no exercise controls for patients with IC. Comparable to a recent review[51], the overall findings indicated that HEPs are inferior to SEPs for improvements in PFWD and MWD. However, HEPs may be more effective than basic exercise advice, and certainly more effective than no exercise at all. One novel finding is that for all comparisons, monitoring appeared to be an important contributing factor to an effective HEP.

The apparent superiority of SEPs compared to HEPs, could be due to differences in the exercise dose between the two programme types. SEPs are, within reason, clearly defined as structured exercise with recommended frequency, intensity, time and type (FITT) principles[8,52-54]. HEPs are much less established, have varied utilisation and suffer greater heterogeneity, especially in older studies. Indeed, three studies included SEPs that had (up to 40 minute) longer individual sessions than the HEP[28,38,43], whilst two SEP groups were also told to complete the HEP in conjunction with the SEP[34,38], meaning they received at least one extra exercise session per week, compared to the HEP only group. Conversely, three HEPs prescribed daily walking[33,38,41], up to a maximum of three times a day, versus a frequency of two to three times a week in the SEP group. This HEP prescription may be too intense and discourage engagement, especially given the reduced functional capacity evident in these patients[1]. As such, heterogeneity may be greater for HEPs than it is for SEPs, especially with regards to dose, contributing to their inferiority.

Additionally, the terminology used to describe HEPs may also be a contributing factor. HEP descriptions included ‘exercise advice’ or ‘unsupervised exercise’, which for patients can either be too vague, or even perceived as optional (in the case of exercise advice). It is therefore important that patients are made aware that exercise therapy, including HEPs when appropriate, constitutes part of their treatment regime and should be adhered to, as well as being provided in a way that is structured and multifaceted, rather than simple advice. This problem is compounded by recent guidelines which identify that home-based walking is a useful alternative to SEPs, but refer only to simple ‘unsupervised’ or ‘non-supervised’ exercise with no specific recommendations[9].

Evidence from our sub-group analyses suggests that HEPs may not always be inferior to SEPs. Specifically, HEPs adopting remote or self-monitoring, via pedometers and/or activity monitors were equivalent to SEPs, or at least reduced their superiority by half for improvements in MWD. Furthermore, the results also suggest that HEPs without monitoring may be inferior to basic exercise advice. One possible explanation for the apparent benefit of monitoring is that it can provide a form of remote supervision, with four of the seven monitoring studies having the facility to regularly feedback data to the study team, potentially improving adherence[17-19,36]. For SEPs, the intensity of supervision is associated with the level of improvement in walking distance[51]. It would therefore be reasonable to assume that this remote supervision will be more effective than little or no supervision (or monitoring) at all. However, based on the findings of three studies included in this review[17,18,36], for remote monitoring to be most effective, and to add specificity to feedback, the device should only be worn during exercise sessions, rather than at all times during the day.

In addition to remote monitoring, self-monitoring, with the use of pedometers and exercise diaries, also appeared effective. This is not surprising given that pedometer use is associated with a reactive effect, with the greatest reactivity seen in those who are asked to record their daily step count in an activity diary[55]. This process of recording daily step count may increase awareness of activity levels, leading to effective goal-setting and greater confidence for walking. Monitoring via exercise diaries (without step-monitors) or telephone calls is ineffective. Clearly, given the variety of possible monitoring, standardisation is required. However, we recommend pedometers in conjunction with an exercise diary as the minimum.

In addition to monitoring, a number of HEP components were identified in studies which, in isolation, appeared to provide similar benefits to SEPs[18,34,36,47], or superior benefits to basic exercise advice or no exercise controls[19,29,36,48]. As such, we have created an example supported home-based exercise programme (SHEP), outlined in table I. Our programme is structured and includes a detailed prescription based on the FITT principle, and incorporates support including regular feedback (ideally in real-time), goal setting and patient education with appropriate theoretical underpinning. These elements also demonstrated good patient adherence, have recently been highlighted as important from the PAD patient perspective[56] and provide a holistic, patient-centred approach.

Only one study has combined these components into a deliverable structured HEP[48], though it was not an adequately powered RCT, meaning it is currently untested. Future, larger, longer-term studies adopting this SHEP structure in a way that is accessible and pragmatic to patients, such as via telehealth (alongside other monitoring), which has shown promise in other clinical populations[57,58], are required. These studies should report the intervention in full to aid replication in clinical practice[59]. In addition, they should also report clinical and cost-effectiveness and the patient eligibility, recruitment, adherence and completion rates. This important information is required to build an appropriate evidence base for the effectiveness of a standardised, structured SHEP, whilst identifying if it is an acceptable alternative to SEPs.

However, in the absence of such an evidence base, HEPs should currently only be considered when SEPs are unavailable or impractical. HEPs should also be considered in exceptional circumstances, such as the COVID-19 pandemic, which suspended SEP availability and practicality. Under these normal and exceptional circumstances, we recommend that a structured SHEP, based on the components outlined in table I, is likely most effective, and should be provided to engage more patients in appropriate lifestyle and exercise behaviour change.

Such a programme could also be recommended to aid continued engagement for those who do complete a SEP, as currently, there is limited provision of long-term exercise recommendations.

Limitations

A number of studies provided inadequate data to allow for meta-analysis, meaning the meta-analyses provided herein do not encompass the full evidence base. In addition, a number of meta-analysable outcomes were restricted by moderate to very-low-quality evidence, small sample sizes and a lack of robustness to sensitivity analyses, meaning their interpretation is limited. Finally, due to the limited number of studies included in the meta-analysis, publication bias could not be excluded via funnel plot.

Conclusion

HEPs still appear inferior to SEPs. However, with remote- and self-monitoring this inferiority is markedly reduced. Compared to basic exercise advice, HEPs generally provided a benefit, though this was not always significantly greater. However, HEPs did appear to demonstrate superiority compared to no exercise controls for improvements in MWD, though with very-low-quality evidence. As such, evidence for HEPs suggests they should only be recommended when SEPs are unavailable or impractical. When HEPs are appropriate, they should be structured and personalised, taking into account the specific FITT (and other) principles, provided in the recommendations outlined above. Larger, longer-term studies combining all of these elements into one accessible, pragmatic SHEP, potentially via telehealth, should provide the future direction of HEP-based research for patients with IC.

Acknowledgements

The authors would like to thank Professors Mary McDermott, Professor Jason Allen, Professor George Geroulakos and Associate Professor Stavros Kakkos for providing unpublished data.

Funding

Sean Pymer and Joanne Palmer are funded by a University of Hull PhD Scholarship. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

References:

1. Hiatt WR. Medical treatment of peripheral arterial disease and claudication. N Engl J Med 2001;344(21):1608-21.
2. Song P, Rudan D, Zhu Y, Fowkes FJ, Rahimi K, Fowkes FGR, et al. Global, regional, and national prevalence and risk factors for peripheral artery disease in 2015: an updated systematic review and analysis. The Lancet Global Health 2019;7(8):e1020-e1030.
3. Harwood A-E, Broadbent E, Totty JP, Smith GE, Chetter IC. "Intermittent claudication a real pain in the calf"—Patient experience of diagnosis and treatment with a supervised exercise program. Journal of Vascular Nursing 2017;35(3):131-135.
4. Meru AV, Mittra S, Thyagarajan B, Chugh A. Intermittent claudication: an overview. Atherosclerosis 2006;187(2):221-237.
5. Golomb BA, Dang TT, Criqui MH. Peripheral arterial disease. Circulation 2006;114(7):688-699.
6. Pell J. Impact of intermittent claudication on quality of life. European Journal of Vascular and Endovascular Surgery 1995;9(4):469-472.
7. Criqui MH, Langer RD, Fronek A, Feigelson HS, Klauber MR, McCann TJ, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. New England Journal of Medicine 1992;326(6):381-386.
8. NICE. Peripheral arterial disease: diagnosis and management. Clinical guidance 147.; 2012.
9. Aboyans V, Ricco J-B, Bartelink M-LE, Björck M, Brodmann M, Cohnert T, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS) Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteries Endorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). European heart journal 2017;39(9):763-816.
10. Lane R, Harwood A, Watson L, Leng GC. Exercise for intermittent claudication. The Cochrane database of systematic reviews 2017;12:CD000990.
11. Gardner AW, Montgomery PS, Flinn WR, Katzel LI. The effect of exercise intensity on the response to exercise rehabilitation in patients with intermittent claudication. Journal of vascular surgery 2005;42(4):702-9.
12. Lauret GJ, Fakhry F, Fokkenrood HJ, Hunink MG, Teijink JA, Spronk S. Modes of exercise training for intermittent claudication. Cochrane Database Syst Rev 2014(7):CD009638.
13. Harwood A-E, Smith GE, Cayton T, Broadbent E, Chetter IC. A systematic review of the uptake and adherence rates to supervised exercise programs in patients with intermittent claudication. Annals of vascular surgery 2016;34:280-289.

14. Harwood A, Smith G, Broadbent E, Cayton T, Carradice D, Chetter I. Access to supervised exercise services for peripheral vascular disease patients. The Bulletin of the Royal College of Surgeons of England 2017;99(6):207-211.
15. Dua A, Gologorsky R, Savage D, Rens N, Gandhi N, Brooke B, et al. National assessment of availability, awareness, and utilization of supervised exercise therapy for peripheral artery disease patients with intermittent claudication. Journal of vascular surgery 2019.
16. Harwood AE, Hitchman LH, Ingle L, Doherty P, Chetter IC. Preferred exercise modalities in patients with intermittent claudication. Journal of Vascular Nursing 2018.
17. McDermott MM, Spring B, Berger JS, Treat-Jacobson D, Conte MS, Creager MA, 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(16):1665-1676.
18. Gardner AW, Parker DE, Montgomery PS, Blevins SM. Step-monitored home exercise improves ambulation, vascular function, and inflammation in symptomatic patients with peripheral artery disease: a randomized controlled trial. Journal of the American Heart Association 2014;3(5):e001107.
19. Duscha BD, Piner LW, Patel MP, Crawford LE, Jones WS, Patel MR, et al. Effects of a 12-week mHealth program on FunctionalCapacity and physical activity in patients with peripheralArtery disease. The American journal of cardiology 2018;122(5):879-884.
20. Al-Jundi W, Madbak K, Beard JD, Nawaz S, Tew GA. Systematic review of home-based exercise programmes for individuals with intermittent claudication. European journal of vascular and endovascular surgery : the official journal of the European Society for Vascular Surgery 2013;46(6):690-706.
21. Hageman D, Fokkenrood H, Gommans L, van den Houten M, Teijink J. Supervised exercise therapy versus home-based exercise therapy versus walking advice for intermittent claudication. The Cochrane database of systematic reviews 2018;4:CD005263.
22. Golledge J, Singh T, Alahakoon C, Pinchbeck J, Yip L, Moxon J, et al. Meta-analysis of clinical trials examining the benefit of structured home exercise in patients with peripheral artery disease. British Journal of Surgery 2019;106(4):319-331.
23. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS medicine 2009;6(7):e1000100.
24. Pymer S, Tew GA, Palmer J, Ingle L, Smith GE, Chetter IC, et al. Home-based exercise programmes for individuals with intermittent claudication: A protocol for an updated systematic review and meta-analysis. SAGE open medicine 2018;6:2050312118818295.
25. Ryan R. Heterogeneity and subgroup analyses in Cochrane Consumers and Communication Group
reviews: Planning the analysis at protocol stage. http://cccrg.cochrane.org. In; 2016.

26. Bown M, Sutton A. Quality control in systematic reviews and meta-analyses. European Journal of Vascular and Endovascular Surgery 2010;40(5):669-677.
27. Fu R, Holmer HK. Change score or followup score? An empirical evaluation of the impact of choice of mean difference estimates. 2015.
28. Allen JD, Stabler T, Kenjale A, Ham KL, Robbins JL, Duscha BD, et al. Plasma nitrite flux predicts exercise performance in peripheral arterial disease after 3 months of exercise training. Free Radical Biology and Medicine 2010;49(6):1138-1144.
29. Brenner IK, Brown CA, Hains SJ, Tranmer J, Zelt DT, Brown PM. Low-Intensity Exercise Training Increases Heart Rate Variability in Patients With Peripheral Artery Disease. Biological research for nursing 2020;22(1):24-33.
30. Cheetham D, Burgess L, Ellis M, Williams A, Greenhalgh R, Davies A. Does supervised exercise offer adjuvant benefit over exercise advice alone for the treatment of intermittent claudication? A randomised trial. European journal of vascular and endovascular surgery 2004;27(1):17-23.
31. Christman SK. Intervention to slow progression of peripheral arterial disease. 2003.
32. Cunningham M, Swanson V, O'Caroll R, Holdsworth R. Randomized clinical trial of a brief psychological intervention to increase walking in patients with intermittent claudication. British journal of surgery 2012;99(1):49-56.
33. Degischer S, Labs K-H, Hochstrasser J, Aschwanden M, Tschoepl M, Jaeger KA. Physical training for intermittent claudication: a comparison of structured rehabilitation versus home-based training. Vascular Medicine 2002;7(2):109-115.
34. Dopheide JF, Geissler P, Rubrech J, Trumpp A, Zeller GC, Daiber A, et al. Influence of exercise training on proangiogenic TIE-2 monocytes and circulating angiogenic cells in patients with peripheral arterial disease. Clinical Research in Cardiology 2016;105(8):666-676.
35. Fakhry F, Spronk S, de Ridder M, den Hoed PT, Hunink MM. Long-term effects of structured home-based exercise program on functional capacity and quality of life in patients with intermittent claudication. Archives of physical medicine and rehabilitation 2011;92(7):1066-1073.
36. Gardner AW, Parker DE, Montgomery PS, Scott KJ, Blevins SM. Efficacy of quantified home-based exercise and supervised exercise in patients with intermittent claudication: a randomized controlled trial. Circulation 2011;123(5):491-8.
37. Imfeld S, Singer L, Degischer S, Aschwanden M, Thalhammer C, Jaeger K. Quality of life improvement after hospital-based rehabilitation or home-based physical training in intermittent claudication. VASA Zeitschrift fur Gefasskrankheiten 2006;35(3):178-184.
38. Kakkos S, Geroulakos G, Nicolaides A. Improvement of the walking ability in intermittent claudication due to superficial femoral artery occlusion with supervised exercise and pneumatic foot and calf compression: a randomised controlled trial. European journal of vascular and endovascular surgery 2005;30(2):164-175.

39. McDermott MM, Liu K, Guralnik JM, Criqui MH, Spring B, Tian L, et al. Home-based walking exercise intervention in peripheral artery disease: a randomized clinical trial. Jama 2013;310(1):57-65.
40. McDermott MM, Guralnik JM, Criqui MH, Ferrucci L, Zhao L, Liu K, et al. Home-based walking exercise in peripheral artery disease: 12-month follow-up of the GOALS randomized trial. Journal of the American Heart Association 2014;3(3):e000711.
41. Nicolaï SP, Teijink JA, Prins MH. Multicenter randomized clinical trial of supervised exercise therapy with or without feedback versus walking advice for intermittent claudication. Journal of vascular surgery 2010;52(2):348-355.
42. Parmenter BJ, Raymond J, Dinnen P, Lusby RJ, Fiatarone Singh MA. High-Intensity Progressive Resistance Training Improves Flat-Ground Walking in Older Adults with Symptomatic Peripheral Arterial Disease. Journal of the American Geriatrics Society 2013;61(11):1964-1970.
43. Patterson RB, Pinto B, Marcus B, Colucci A, Braun T, Roberts M. Value of a supervised exercise program for the therapy of arterial claudication. Journal of Vascular Surgery 1997;25(2):312-319.
44. Pinto BM, Marcus BH, Patterson RB, Roberts M, Colucci A, Braun C. On-Site Versus Home Exercise Programs: Psychological Benefits for Individuals With Arterial Claudication. Journal of Aging & Physical Activity 1997;5(4).
45. Regensteiner JG, Meyer TJ, Krupski WC, Cranford LS, Hiatt WR. Hospital vs home-based exercise rehabilitation for patients with peripheral arterial occlusive disease. Angiology 1997;48(4):291-300.
46. Sandercock GR, Hodges LD, Das SK, Brodie DA. The impact of short term supervised and home-based walking programmes on heart rate variability in patients with peripheral arterial disease. Journal of sports science & medicine 2007;6(4):471.
47. Savage P, Ricci MA, Lynn M, Gardner A, Knight S, Brochu M, et al. Effects of home versus supervised exercise for patients with intermittent claudication. Journal of Cardiopulmonary Rehabilitation and Prevention 2001;21(3):152-157.
48. Tew GA, Humphreys L, Crank H, Hewitt C, Nawaz S, Al-Jundi W, et al. The development and pilot randomised controlled trial of a group education programme for promoting walking in people with intermittent claudication. Vascular Medicine 2015;20(4):348-357.
49. Larsen A, Lassen N. Effect of daily muscular exercise in patients with intermittent claudication. The Lancet 1966;288(7473):1093-1095.
50. Galea-Holmes M, Weinman J, Bearne L. A randomized controlled feasibility trial of a home-based walking behavior-change intervention for people with intermittent claudication. Journal of vascular nursing: official publication of the Society for Peripheral Vascular Nursing 2019;37(2):135-143.
51. Gommans L, Saarloos R, Scheltinga M, Houterman S, de Bie R, Fokkenrood H, et al. The effect of supervision on walking distance in patients with intermittent claudication: a meta-analysis. Journal of Vascular Surgery 2014;60(2):535-536.

52. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, 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. Journal of the American College of Cardiology 2017;69(11):1465-1508.
53. Tew GA, Harwood AE, Ingle L, Chetter I, Doherty PJ. The BASES Expert Statement on Exercise Training for People with Intermittent Claudication due to Peripheral Arterial Disease. The Sport and Exercise Scientist 2018.
54. ACSM. ACSM's Guidelines for Exercise Testing and Prescription. 9th ed. Baltimore: Lippincott, Williams, & Wilkins.; 2014.
55. Clemes SA, Parker RA. Increasing our understanding of reactivity to pedometers in adults. Medicine & Science in Sports & Exercise 2009;41(3):674-680.
56. Lortz J SJ, Kuether T, Kreitschmann-Andermahr I, Ullrich G, Steinmetz M, Rammos C, Jánosi RA, Moebus S, Rassaf T, Paldán K. Needs and requirements of patients with peripheral arterial disease: Questionnaire study to design patient-centred mobile interventions. JMIR Formative Research (pre-print) 2020.
57. Rawstorn JC, Gant N, Direito A, Beckmann C, Maddison R. Telehealth exercise-based cardiac rehabilitation: a systematic review and meta-analysis. Heart 2016;102(15):1183-1192.
58. Maddison R, Rawstorn JC, Stewart RA, Benatar J, Whittaker R, Rolleston A, et al. Effects and costs of real-time cardiac telerehabilitation: randomised controlled non-inferiority trial. Heart 2019;105(2):122-129.
59. Tew GA, Brabyn S, Cook L, Peckham E. The completeness of intervention descriptions in randomised trials of supervised exercise training in peripheral arterial disease. PloS one 2016;11(3):e0150869.

636