ADMINISTRATIVE INFORMATION

***Title**: Telephone Health Coaching with Exercise Monitoring using Wearable Activity Trackers (TeGeCoach) for Improving Walking Impairment in Peripheral Artery Disease: study protocol for a randomized controlled trial and economic evaluation*

***Trial registration:** NCT03496948 (www.clinicaltrials.gov), initial release on 23 March 2018*

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ABSTRACT

Introduction: Peripheral artery disease (PAD) is the third most prevalent cardiovascular disease worldwide, with smoking and diabetes being the strongest risk factors. The most prominent symptom is leg pain while walking, known as intermittent claudication. To improve mobility, first line treatment for intermittent claudication are supervised exercise programs, but these remain largely unavailable and economically impractical, which has led to the development of structured home-based exercise programs. This trial aims to determine the effectiveness and cost advantage of TeGeCoach, a 12-month long home-based exercise program, compared with usual care of PAD. It is hypothesized that TeGeCoach improves walking impairment and lowers the need of health care resources that are spent on patients with peripheral artery disease. *Methods and analysis:* The investigators conduct a prospective, pragmatic randomized controlled clinical trial in a health insurance setting. 1760 patients diagnosed with peripheral artery disease at Fontaine stage II are randomly assigned to either TeGeCoach or Care-as-usual. TeGeCoach consists of telemonitored intermittent walking exercise with medical supervision by a physician and telephone health coaching. Participants allocated to the usual care group receive information leaflets and can access supervised exercise programs, physical therapy and a variety of programs for promoting a healthy lifestyle. The primary outcome is patient reported walking ability based on the Walking Impairment Questionnaire. Secondary outcome measures include quality of life, health literacy and health behavior. Claims data is used to collect total health care costs, healthcare resource use and (severe) adverse events. Outcomes are measured at baseline, 12 and 24 months. *Ethics and dissemination:* Ethical approval has been obtained from the Medical Association Hamburg. Findings are disseminated through peer-reviewed journals, reports to the funding body, conference presentations and media press releases. Data from this trial are made available to the public and researchers upon reasonable request.

Trial registration: NCT03496948 (www.clinicaltrials.gov)

INTRODUCTION

Peripheral Artery Disease (PAD) is the third most prevalent atherosclerotic cardiovascular disease with over 200 million people affected worldwide and has become one of the leading causes of disability and death.[1 2] It is characterized by the progressive narrowing of the peripheral arteries resulting in the reduction of blood supply, eventually leading to functional impairment and mobility loss.[3] If not intervened sufficiently early, the atherosclerotic processes can lead to ulcer formation and gangrenous necrosis (i.e. critical limb ischemia)[4], and may affect other vascular beds with potentially fatal consequences.[5 6] PAD is markedly more prevalent in the elderly population, estimating that 5.4% and 18.6% of individuals aged from 45 to 49 and 85 to 89 years are affected, respectively.[1 2] The amount of people with PAD has risen rapidly in recent years, with a sharp increase by nearly 25% between 2000 and 2010 in the general population.[2] Likewise, in Germany, the amount of PAD-related hospitalizations increased by 20.7% between 2005 and 2009, from 400 928 to 483 961. Meanwhile, hospital reimbursement costs for the treatment of PAD have grown nationwide from €2.14 billion in 2007 to €2.6 billion in 2009, a 21% increase within 2 years.[7] Major risk factors are tobacco smoking and diabetes, followed by high cholesterol, hypertension, history of cardiovascular disease (i.e. coronary heart disease, stroke) and chronic kidney disease.[1 2 8 9]

The most common clinical manifestation is leg pain while walking, known as *intermittent claudication* (IC), which reflects impaired hemodynamics and vascular dysfunction.[10 11] IC is associated with diminished mental health and lower quality of life, thus reducing symptom burden is the cornerstone of the comprehensive care for patients with PAD.[12-15] Besides pharmacotherapy, risk factor management and surgical revascularization procedures, exercise-based interventions provide substantial mental and physical health benefits for patients with IC.[16-19] Accordingly, formal *supervised exercise programs* (SEPs) are shown to be effective in the treatment of PAD with IC and are recommended as first-line therapy with the highest level of evidence in a variety of published clinical guidelines.[20-22] SEPs involve the use of intermittent walking exercise and are minimum three-month commitments, with at least three sessions per week (30-60 minutes per session) provided in a clinical setting (e.g. hospital outpatient setting, outpatient facility, or a physician's office). Although SEPs commonly form part of usual care, its use is hampered by low uptake and adherence rates, possibly due to copayment requirements and lack of reimbursement, lack of available local training centers and the burden of traveling.[23 24] These obstacles highlight the need for innovative models of care, which have led to the emergence of structured *home-based* exercise programs (HEPs) where SEPs are not available or impractical to deliver.[25] According to clinical practice guidelines, structured HEPs can serve as a useful alternative to SEPs[20 22] as they improve walking impairment[26] and are preferred by patients over SEPs.[27] Structured HEPs are performed independently by the patient but follow an exercise regimen similar to that of SEPs, with a duration of three to six months. Protocols of structured HEPs show considerable variation with regard to program

duration, form of exercise, exercise frequency and duration, and intervention components used (for an overview, see [28]). To achieve benefits, structured HEPs include psychological behavior change techniques (e.g. goal setting, barrier identification, motivational interviewing), regular follow-ups with a healthcare professional or coach (e.g. face-to-face, phone), activity monitoring and feedback (e.g. wearable activity trackers, logbooks), patient education, or any combination thereof.[28] Although inferior to SEPs[24 28-30], structured HEPs have been shown to improve performance-based[31-40], patient-reported[31-38 40] and cardiorespiratory fitness[39] outcomes with high adherence[31 37], whereas unstructured exercise giving merely "go home and walk" advice to patients with symptomatic PAD has proven ineffective.[41]

Given the promising results demonstrating the *efficacy* of structured HEPs in previous explanatory trials, pragmatic trials (i.e. with high external validity) are urgently warranted to establish the *effectiveness* of structured HEPs with the goal to inform clinical practice and to shape health care policies.[42] In response to the lack of effectiveness trials, while drawing on best available evidence and experience with previous telecoaching studies[43], three German statutory health insurance funds (*KKH Kaufmännische Krankenkasse, TK Techniker Krankenkasse, mhplus Krankenkasse*) launch TeGeCoach, a 12-month long structured HEP that involves telemonitored intermittent walking exercise using wearable activity trackers with medical supervision by a physician, and motivational interviewing-based telephone health coaching. TeGeCoach provides a streamlined, structured HEP approach based on current evidence using several components that have been shown to be beneficial; telephone health coaching have been shown to be a cost efficient and effective tool in the management of other chronic diseases[44-46], supporting physical activity and dietary behavior change.[47] Therefore, structured HEPs involving telephone health coaching may also offer great potential for patients with PAD, although the frequency of coaching conversations may play a critical role in whether telephone health coaching is beneficial.[48] With regard to the mode of exercise, intermittent walking exercise has been proven to be effective in patients with IC, which involves repeated bouts of exercise to maximally tolerable claudication pain alternated with recovery breaks.[49] Likewise, the use of activity trackers alone or as an intervention modality are considered a convenient way for facilitating physical activity[50 51] with long-term health benefits[52], while remote activity monitoring (e.g. by a coach) may improve walking impairment and significantly lower the costs of health care in PAD patients.[53] Among older adults, the use of activity trackers is well accepted and may be effective to encourage physical activity,[54 55] with behavioral change techniques such as social support and motivating feedback facilitating their (long-term) use.[56 57] Furthermore, adding some kind of counseling to the use of wearable activity tracker (e.g. activity monitor-based counseling) could allow the health coach to deliver behavior change techniques and to support sustained exercise. For example, using an activity tracker with regular feedback combined with access to SEPs has proven to improve functional walking performance and quality of life in PAD

patients.[58] Similarly, telephone health coaching combined with activity monitoring was found to increase physical activity and reduce sedentary behavior in elderly people.[59]

The aim of this study is to explore the effectiveness of TeGeCoach, a structured HEP for patients with PAD. A randomized controlled trial of 1760 patients with PAD is conducted to determine whether TeGeCoach improves patient-reported walking impairment while lowering health care costs at 12-and 24-month follow-up, compared to the usual care of PAD. It is hypothesized that TeGeCoach improves walking impairment and lowers the costs of health care that are spent on patients with PAD. Given the size and remote nature of the study (i.e. no personal contact to research staff), as well as the pragmatic trial approach (i.e. measurement of outcomes should be patient relevant and should not interfere with the usual care[60]), it was opted to use only patient-reported outcome measures (PROMs), while collecting healthcare utilization and costs from claims data. PROMs emphasize the patient perspective by collecting information that are directly relevant to the patients; with growing interest in comparative effectiveness research, PROMs are commonly used in clinical trials to measure treatment effects.[61] If effective, TeGeCoach could be widely integrated into PAD usual care with the potential to provide health benefits for patients with PAD while reducing health care costs.

METHODS

Trial design

This is a two-arm, parallel-group, open-label, pragmatic, randomized, controlled superiority trial embedded within three German statutory health insurance funds (*KKH Kaufmännische Krankenkasse, TK Techniker Krankenkasse, mhplus Krankenkasse*). It is designed to compare the effects of TeGeCoach (intervention arm) to the usual care of PAD (Care-as-usual, CAU), conducted in a health insurance system-based setting (Figure 1). Trial initiation was in 04/2018 and ends in 02/2021. The recruitment period was 9 months (04/2018 - 12/2018). TeGeCoach has been registered at www.clinicaltrials.gov (NCT03496948, Table 1); protocol modifications will be added to the trial registry. Ethical approval has been obtained at the ethics committee of the Medical Association Hamburg (Ärztekammer Hamburg; reference number: PV5708). The study is conducted in full compliance with Good Clinical Practice quality standards and in accordance with the Declaration of Helsinki of 2008. It is expected that final results are reported after study completion in 2021.

This study protocol is reported in accordance with the CONsolidated Standards Of Reporting Trials (CONSORT) statement [62]; the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement [63]; the SPIRIT Patient-Reported Outcome (PRO) extension [64]; and the Template for Intervention Description and Replication (TIDieR) checklist.[65]

Table 1. *Trial registration data*

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov (NCT03496948)

Date of registration in primary registry	23 March, 2018
Source(s) of monetary or material support	Innovation Fund, Federal Joint Committee (G-BA)
Trial sponsor	KKH Kaufmännische Krankenkasse
Contact for public queries	FB (frank.bienert@kkh.de), KKH Kaufmännische Krankenkasse
Contact for scientific queries	FR (f.rezvani@uke.de), University Medical Center Hamburg-Eppendorf
Public title	TeGeCoach – a home-based exercise program using telephone health coaching with telemonitoring for patients with peripheral artery disease
Scientific title	Telephone Health Coaching with Exercise Monitoring using Wearable Activity Trackers (TeGeCoach) for Improving Walking Impairment in Peripheral Artery Disease: study protocol for a randomized controlled trial
Countries of recruitment	Germany
Health condition(s) or problem(s) studied	Peripheral Artery Disease (PAD)
Intervention(s)	Active comparator: Telemonitored intermittent walking exercise with medical supervision by a physician and telephone health coaching (TeGeCoach)
	Active comparator: Care-as-usual (CAU)
Key inclusion and exclusion criteria	Ages eligible for study: ≥35 years & ≤80 years Sexes eligible for study: both Accepts healthy volunteers: no
	Inclusion criteria: ≥35 years & ≤80 years, insured at one of the participating statutory health insurance funds, access to a telephone, primary or secondary diagnosis of PAD at Fontaine stage IIa/b within the last 36 months, no primary or secondary diagnosis of PAD at Fontaine stage I within the last 12 months, no diagnosis of Fontaine stage III/IV within the last 36 months
	Exclusion criteria: immobility that goes beyond claudication, inability to carry out intervention, (chronic) physical conditions that interfere with the intervention, cognitive disorders, severe and persistent mental disorders, suicidality, life-threatening illnesses, active or recent participation in any other PAD intervention trial, ongoing hospitalization, alcoholism and/or other drug dependency, heart failure graded NYHA class III and IV
Study type	Interventional
	Allocation: randomized Intervention model: parallel assignment masking: analysis blinding
	Primary purpose: Prevention
Date of first enrolment	April 2018
Target sample size	1760
Recruitment status	Completed
Primary outcome(s)	**PROM:** Walking impairment *Time points: baseline, 12 and 24 months*
Key secondary outcomes	**PROMs:** Generic health-related quality of life, PAD-specific quality of life, depression, generalized anxiety disorder, alcohol use, nicotine dependence, health literacy, patient activation **Claims data:** Total health care costs, healthcare resource use, (severe) adverse events *Time points: baseline, 12 and 24 months*

Patient and public involvement statement

This research was planned without patient involvement. Patients were not invited to comment on the study design and were not consulted to develop patient relevant outcomes. Patients were not invited to contribute to the writing or editing of this document for readability or accuracy.

Participants

Participants have to meet the following criteria: registered with one of the participating statutory health insurance funds (*KKH Kaufmännische Krankenkasse, TK Techniker Krankenkasse, mhplus Krankenkasse*); aged between 35 and 80; German-speaking; access to a telephone (landline or mobile); and a primary or secondary diagnosis of PAD at Fontaine stage IIa (> 200 m, Fontaine stage IIa) or IIb (< 200 m, Fontaine stage IIb) within the last 36 months (corresponding ICD-10-GM-codes: I70.21, I70.22, I73.9). Participants should have no primary or secondary diagnosis of PAD at Fontaine stage I (asymptomatic) within the last 12 months, and no diagnosis of Fontaine stage III (ischemic rest pain) or IV (ulcer, gangrene) within the last 36 months to increase diagnostic accuracy (corresponding ICD-10-GM codes: I70.23, I70.24, I73.25).

Exclusion criteria for participants are: immobility that goes beyond claudication (Fontaine stage III or IV; inability to carry out intervention); (chronic) physical conditions that interfere with the intervention (e.g. COPD); cognitive disorders (inability to carry out intervention); severe and persistent mental disorders (adherence reasons); suicidality (safety reasons); life-threatening illnesses (safety reasons); active or recent participation in any other PAD intervention trial; ongoing hospitalization; (self-reported) alcoholism and/or other drug dependency (adherence reasons); and heart failure graded NYHA class III and IV (inability to carry out intervention and competing risks).

Recruitment

Participants

Recruitment of participants is managed by three statutory health insurance funds in Germany: *KKH Kaufmännische Krankenkasse, TK Techniker Krankenkasse* and *mhplus Krankenkasse*. Eligible participants are retrospectively identified using ICD-10-GM diagnosis codes from inpatient and outpatient encounters, which are routinely collected for reimbursement purposes (claims data). Due to the high number of diagnostic errors and poor coding habits in outpatient settings, exclusion criteria are only checked using inpatient diagnosis codes.

An iterative recruitment process was developed, as substantial challenges to the recruitment of clinical trials have been shown in the PAD population.[66] Eligible participants are contacted by their health insurance fund to explain the purpose of the study and to confirm their PAD diagnosis by questioning them about their symptoms. Eligible participants receive a study information letter that is supplemented with consent and permission forms (i.e. authorization for release of medical reports by the contracted physician to the health coach). If interested to participate, they are asked to sign all documents and send them back to their health insurance fund. Eligible non-responders that are still interested in the study but have not given written consent are followed up by phone to be reminded of the trial. Once the

written consent has been received, a query is submitted to the data warehouse of the respective health insurance fund which automatically assigns a pseudonym to the participant. No participant will be enrolled without full, written informed consent.

Physicians

Each participant allocated to TeGeCoach must be medically supervised by a physician, which is a prerequisite for receiving the TeGeCoach intervention; participants can elect their preferred physician prior to program start, or are alternatively referred to an already contracted physician by their health coach. To encourage physicians to participate, they enter into an integrated care contract with the respective health insurance fund that provides financial incentives for the delivery of special medical services throughout the intervention.[67] The enrolment and reimbursement of contracted physicians is coordinated by medicalnetworks (Kassel, Germany), a company that is specialized on the management of integrated care programs (ICPs) within the § 140a volume V of the German Social Security Code (SGB V). If the physician of choice refuses to participate, the participant is referred to a nearby contracted physician that has already entered into the integrated care contract. Once enrolled, the health coach contacts the contracted physician to discuss their tasks during the course of the study. Due to recruitment barriers, it is possible that no suitable physician can be found for the patient by the end of the recruitment phase. For safety reasons, participants for whom no physician can be appointed do not receive TeGeCoach.

Treatment allocation and blinding

Participants are allocated in a 1:1 ratio to either the TeGeCoach or CAU group, stratified by health coaching center using a permuted block method within each stratum. In order to prevent selection bias and to eliminate any predictability (allocation concealment), participants are randomly allocated via Sealed Envelope (London, United Kingdom), a secure internet-based randomization service including concealment, stratification and blocking for each health coaching site.

Blinding of care providers (health coaches and contracted physicians) and participants is not possible because of obvious differences between the TeGeCoach intervention and CAU. However, as supported by the CONSORT guidelines, blinding of the analysis is achieved by engaging an independent data analyst and by withholding information about how the groups were coded before analytical decisions have been completed.[68]

Interventions

TeGeCoach

TeGeCoach is a 12-month long structured HEP that is designed to inspire healthy habits in patients with PAD based on the transtheoretical model of behavior change. The main strategies used to improve

health outcomes include patient-centered motivational interviewing, shared decision making and active listening, aiming to help patients to enhance their individual motivation for exercise and receive the support needed to improve their condition.

Telemonitored intermittent walking exercise: Patients are instructed to continuously wear an activity tracker device (i.e. from getting up to going to bed; not while showering, bathing and swimming). Two different brands of activity tracker are used that record the number of steps (*KKH Krankenkasse* and *mhplus Krankenkasse*: AS 95 Pulse by Beurer; *TK Techniker Krankenkasse*: Mi Band 2 by Xiaomi). The data from the activity tracker is transmitted automatically to the health coaching platform once per day over the internet using a SIM card modem (econnect, IEM GmbH). A 60-minute baseline assessment is initially taken to evaluate the patient's individual walking capacity whereby patients are instructed to walk at a brisk pace (defined as >50 steps/minute) until maximal tolerable claudication pain is reached, followed by breaks and continued walking when the pain subsides (intermittent walking). The net brisk walking time (>50 steps/minute) during the 60-minute baseline assessment is used to assign patients to one of three intermittent walking plans of increasing duration; the patient is assigned to level A (15 minutes exercise, including breaks) if he/she is able to walk less than 15 minutes during the baseline assessment, level B (30 minutes exercise, including breaks) if he/she is able to walk 15-30 minutes, and level C (60 minutes exercise, including breaks) if he/she is able to walk 30-60 minutes. Patients are instructed to walk intermittently at a brisk pace (>50 steps/minute) on at least five days per week. The assignment to one of the training levels is not conclusive; the coach regularly reviews, and if necessary, adjusts the walking plan after every coaching session. The goal is to progressively increase walking intervals and shortening breaks until painless walking exercise (or bearable pain) without breaks needed has been achieved by the patient, suggesting to switch to the next training level. In addition to exercise sessions, the health coach also sees the absolute number of steps per day as a measure of overall physical activity. To ensure patient safety, the contracted physician initially reviews the proposed exercise plan, checks if any contraindications to exercise exist, and whether all important comorbidities such as high blood pressure, diabetes and coronary heart disease are sufficiently treated. Furthermore, they receive three health reports from the health coach during the course of the program, which are important for the joint exchange of information to provide collaborative care.

Telephone health coaching: Over the course of 12 months, patients regularly receive health information leaflets and have up to nine structured 30-60 minute phone calls with their health coach. During these structured phone calls, the health coach and the patient jointly discuss the progress towards exercise goals and review the activity tracker data to check whether the patient adheres to the walking plan. For this purpose, exercise sessions (i.e. intermittent walking represented as changes between walking and break intervals) are visualized and automatically identified as an exercise session by the health coaching platform. Additional phone calls are warranted when no data has been received,

no steps were taken or when coaches are alerted that the amount of exercise days has fallen below an individual threshold. During these calls, barriers like lack of motivation, exercise intolerance or technical issues are discussed and how they can be overcome through behavioral support. Along with the walking exercise, patient-tailored topics of interest that are relevant to the management of PAD are discussed in order to improve health literacy, to facilitate patient empowerment and to adopt a proactive stance in dealing with their disease. The health coaching curriculum includes: Knowledge of PAD, PAD medication, comorbidities of PAD and other related health topics (e.g. tobacco use, nutrition). The health coaches use an electronic documentation system to monitor the coaching process (*KKH Kaufmännische Krankenkasse* and *mhplus Krankenkasse*: Picama® Managed Care, Trustner GmbH; *TK Techniker Krankenkasse*: Philips GmbH Market DACH). The telephone health coaching is carried out by three health coaching centers that are located throughout Germany, each affiliated to one of the three statutory health insurance funds (Health Coaching Center of *KKH Kaufmännische Krankenkasse*, Telemedical Center at Robert-Bosch-Hospital on behalf of *TK Techniker Krankenkasse*, Health Coaching Center of *mhplus Krankenkasse*), and are staffed with licensed health workers (e.g. nurses, physical therapists, medical assistants, etc.). To ensure high-quality health coaching, health coaches are regularly supervised by a team of experts and receive 51 hours of training, including 19 hours of program training, seven hours of medical training, eight hours of group supervision and one hour of individual supervision. Compliance to coaching guidelines are continuously monitored and reviewed. In addition to the structured TeGeCoach intervention, participants have regular access to usual care (CAU) as described below.

After 12 months, there is an additional 12 months of unstructured follow-up in which patients have no interaction with their health coach but still have access to their activity tracker device, which they may continue to use to self-monitor their physical activity.

Care as usual (CAU)

Patients allocated to CAU receive usual medical care through the regular statutory health care system. Additionally, participants receive PAD patient information leaflets from their statutory health insurance fund, with each health insurance fund providing its own leaflets. These leaflets provide information about course offerings of the respective health insurance fund to encourage regular exercise and to promote lifestyle changes, including SEPs (vascular and cardio exercise), physical therapy, nutritional assistance programs, smoking cessation programs, weight loss programs, as well as patient education programs for obesity and diabetes. It is thereby ensured that participants allocated to CAU receive genuine usual care as supplied in everyday practice.

Outcome Measures

Outcome measures are listed in Table 2 along with timing of assessment; the effectiveness of TeGeCoach is measured based upon PROMs, claims data, activity tracker data. PROMs are collected at baseline (t0), at 12 (t1) and 24 (t2) months.

Primary Outcomes

- *PROM:* Walking impairment (Walking Impairment Questionnaire, WIQ) [69-72]

Secondary Outcomes

- *PROMs:* Generic health-related quality of life (EQ5D-5L & SF-12 questionnaires) [73-76] ; PAD-specific quality of life (VascuQoL-25 questionnaire) [77 78]; depression (PHQ-9 questionnaire) [79]; generalized anxiety disorder (GAD-7 questionnaire) [80 81]; alcohol use (AUDIT-C questionnaire) [82-84]; nicotine dependence (FTND) [85]; health literacy (HLQ) [86 87]; patient activation (PAM-13 questionnaire) [88 89]
- *Claims data:* Total health care costs, i.e. inpatient hospital care costs; outpatient (ambulatory) services and primary care costs, costs for drugs and other medical supplies, sick pay costs; healthcare resource use, i.e. time period until hospitalization, probability of hospitalization, number and duration of inpatient hospitalization, outpatient medical treatment, drug dose (defined daily dose, DDD); (severe) adverse events, i.e. death, amputation, and revascularization (see supplementary file)

Additional outcomes (intervention arm only)

- *PROM:* Patient satisfaction (ZAPA questionnaire) [90]
- *Activity tracker data:* Exercise adherence, e.g. number of alerts and corresponding phone calls made when step frequency or the duration of exercise sessions fall below an individual threshold range; amount of steps/net walking time (>50 steps/minute) per day/week

Table 2. *Participant timeline: Time schedule of enrolment (eligibility screen, informed consent, pseudonymization and allocation), study arms (TeGeCoach or CAU) and measurements (questionnaires and claims data).*

	Study period			
	Enrollment	Allocation	Postallocation	
Time point *[1]	**-t1**	**t0**	**t1**	**t2**
Enrollment				
Eligibility screening (claims data)	x			
Informed consent	x			
Pseudonymization		X		
Allocation		X		
Study arms				
TeGeCoach (intervention)		◆———	◆- - -	- - -◆
CAU (control)		- - -	- - -	- - -▶
Measurements				

Intervention and control arm				
PROMs (questionnaires) *2		X	x	x
Cost and medical outcomes (claims data) *3		◆———	◆———	◆———
Intervention arm only				
ZAPA questionnaire			x	
Walking exercise parameters (activity tracker data) *4		◆———	◆———	

*1 -t1: ~1 month before patient in, t0: baseline; t1: 12 month follow-up t2: 24 month follow-up
*2 WIQ, EQ5D-5L, SF-12, VascuQoL-25, PHQ-9, GHD-7, AUDIT-C, FTND, HLQ, PAM-13
*3 Health care costs, healthcare resource use, (severe) adverse events
*4 Exercise adherence, amount of steps/net walking time (>50 steps/minute) per day/week

Sample size

To find a 'meaningful' effect that is clinically relevant, practicable and economically feasible, the sample size is calculated based on the distribution-based minimal clinically relevant difference (MCID) for small changes on the WIQ following three months of a structured HEP that have been determined in previous studies (WIQ speed MCID: 6%; WIQ distance MCID: 5%; WIQ stair climbing MCID: 5%).[91] As TeGeCoach is more intensive and longer, a small-to-moderate group difference was estimated (f=0.15), while accounting for the inherited heterogeneity of this pragmatic trial that could lead to a dilution of the treatment effect. Assuming a response rate of 30% (TeGeCoach) and 20% (CAU) from baseline 24-month follow-up (t2) [43 92], a sample size of 1760 (880 per group) is required to have 176 and 264 participants at t2 in the CAU and intervention arm, respectively, which is sufficient to detect the estimated small-to-moderate effect with 80% power and a 5% level of significance (Gpower v.3.1.9.2).

Data collection and management

Data management and storage are carried out in compliance with the General Data Protection Regulation (GDPR) in the European Union and Good Scientific Practice guidelines by the German Research Foundation.[93] To ensure confidentiality, all data are collected, processed, analyzed and stored in de-identified form by replacing personally identifying information of each participant with a unique patient identification number (i.e. by pseudonymization), which allows to combine data from multiple sources and to merge longitudinal data. Linkage to an identity (depseudonymization) is not possible without a separately stored pseudonymization key, which is protected by technical and organizational measures.

At each study point, the data coordinators of the health insurance funds send out a set of paper-based questionnaires (PROMs) to the participants. Participants are asked to send them back to the Department of Medical Psychology at the University Medical Center Hamburg-Eppendorf. To maximize response rates, participants who have not send their questionnaire back in time receive a postal reminder after 2-4 weeks. All participants are followed up at t1 and t2, irrespective of whether questionnaires have been returned at previous study points. Questionnaire data are entered into an

electronic database, with only authorized personnel being allowed to retrieve, enter or change data. For data quality and monitoring purposes, validation checks regarding out of range data, illogical and invalid responses and data entry errors are performed.

Claims data are routinely collected for the purpose of billing and contains information on all contacts with the health care system including ICD codes, operations and procedure key (OPS) codes (the German equivalent to the American procedure coding system, PCS), medication prescriptions and amount of sick leaves. After study completion, the health insurance funds assemble and pseudonymize the claims data and send it to the study team (University Medical Center Hamburg-Eppendorf). No individual insurance information can be identified from this data.

Activity tracker data are automatically uploaded to the electronic documentation system via SIM card modem (econnect, IEM GmbH) once per day. The statutory health insurance funds share the activity tracker data with the study team in pseudonymized form.

All data are stored for a maximum of 10 years, securely locked in cabinets and saved on password-protected computers in areas with restricted access. Personally identifiable information of participants and pseudonymization keys are only accessible to the data coordinators at each health insurance fund. The pseudonymization keys are deleted two years after study completion so that virtually from this point all data is fully anonymized. Regarding dissemination, all publicly available data are fully anonymized and do not disclose identities. Participants have the right to be informed about their data. If a participant decides to withdraw from the trial prematurely, the data already collected may be used, unless revoking their informed consent. Deletion of the data cannot be requested if the data has already been anonymized.

Statistical analysis

Analyses are by intention-to-treat in accordance with the CONSORT guidelines, i.e. participants who do not adhere to or withdraw from the prescribed TeGeCoach intervention and for whom no doctor could be appointed (see *recruitment* section) are included in the analyses as randomized. For questionnaire data, changes from baseline to follow-up measurements are compared between study arms using linear mixed models.[94] Single imputation using the Expected-Maximization algorithm are applied for item-level missing data. Scale-level imputation of missing data is not necessary since this is fully handled by estimating mixed models with full information maximum likelihood (FIML).[95 96] In order to take correlation between the observations into account, models are adjusted for participant and health coaching center characteristics. For claims data, changes over time between groups are compared between study arms using random-effects regression models (difference-in-differences method) after eliminating differences in observable baseline characteristics between groups with the use of entropy balancing[97]. Entropy balancing allows a better balancing compared to conventional

processes such as propensity matching. Tests of treatment effects are conducted at a two-sided significance level of 0.05. In order to check the robustness of the results, subgroup analyses are performed to determine the influence of baseline characteristics (e.g. degree of walking impairment), health insurance fund (i.e. *KKH Kaufmännische Krankenkasse, TK Techniker Krankenkasse, mhplus Krankenkasse*) and type of analysis (i.e. intention-to-treat and per-protocol).

Data monitoring and harms

This trial is not monitored by a data monitoring committee, and no interim analyses are performed as TeGeCoach is a low risk, non-invasive intervention with no identifiable risks. Over the course of the intervention, participants allocated to TeGeCoach are medically monitored by their treating physician while having regular access to the usual care of PAD. The risks from the use of wearable activity trackers is low; all devices have been certified and conform to health, safety, and environmental protection standards for products sold within the European Union (CE certificate).

Ethics and Dissemination

The study protocol, the informed consent forms and all other documents that are handed out to the participants have been reviewed and approved by the ethical review bodies (Medical Association Hamburg; reference number: PV5708). The ethics committee will be informed in case of any amendments made to the study protocol or informed consent forms.

Findings are disseminated widely through peer-reviewed manuscripts published in scientific journals, reports to the funding body, international conference presentations and media press releases. Furthermore, the study team realizes the value of open science and feels committed to information exchange through data being accessible to the research community. Therefore, in an attempt to tackle the problem of hidden data, deidentified participant data from this trial are made available to the public and the medical research community upon reasonable request to the corresponding author.

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for the implementation of the technical infrastructure of the study; Y.G., S.B., J.P., F.R., F.K., C.N., F.L., L.B., C.S. and C.S. are responsible for the actual conduct of the study by working out study processes and materials; F.R. wrote the initial draft of the manuscript with support from J.D; all authors substantially contributed to the final manuscript and provided critical feedback; all authors have agreed to be accountable for their own contributions and to ensure that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Competing Interests: None.

Data sharing statement: Data are available upon reasonable request to the corresponding author.

[Figure 1]

Figure 1. Prospective flow chart of the study design. TeGeCoach: telemonitored intermittent walking exercise with medical supervision by a physician and telephone health coaching; CAU: usual care of PAD.

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