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ORIGINAL ARTICLE

A prospective, randomized, controlled, multicentre trial for secondary prevention in patients with chronic coronary syndrome using a smartphone application for digital therapy: the CHANGE study protocol

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Aims Coronary artery disease (CAD) remains the leading cause of death worldwide. 'Stable' CAD is a chronic progressive condition, which recent European guidelines recommend referring to as 'chronic coronary syndrome' (CCS). Despite therapeutic advances, morbidity and mortality among patients with CCS remain high. Optimal secondary prevention in patients with CCS includes optimization of modifiable risk factors with behavioural changes and pharmacological therapy. The CHANGE study aims to provide evidence for optimization of secondary prevention in CCS patients by using a smartphone application (app).

Methods and results The CHANGE study is designed as a prospective, randomized, controlled trial with a 1:1 allocation ratio, which is currently performed in nine centres in Germany in a parallel group design. 210 patients with CCS will be randomly allocated either to the control group (standard-of-care) or to the intervention group, who will be provided the VantisTherapy* app in addition to standard-of-care to incorporate secondary prevention into their daily life. The study will be performed in an open design. Outcomes will be assessed using objective data from three in-person visits (0, 12, and 24 weeks). Primary outcomes will involve adherence to secondary prevention recommendations and quality of life (QoL). The recruitment process started in July 2022.

Conclusion The CHANGE study will investigate whether a smartphone-guided secondary prevention app, combined with a monitor function compared with standard-of-care, has beneficial effects on overall adherence to secondary prevention guidelines and QoL in patients with CCS.

Trial registration The study is listed at the German study registry (DRKS) under the registered number DRKS00028081.

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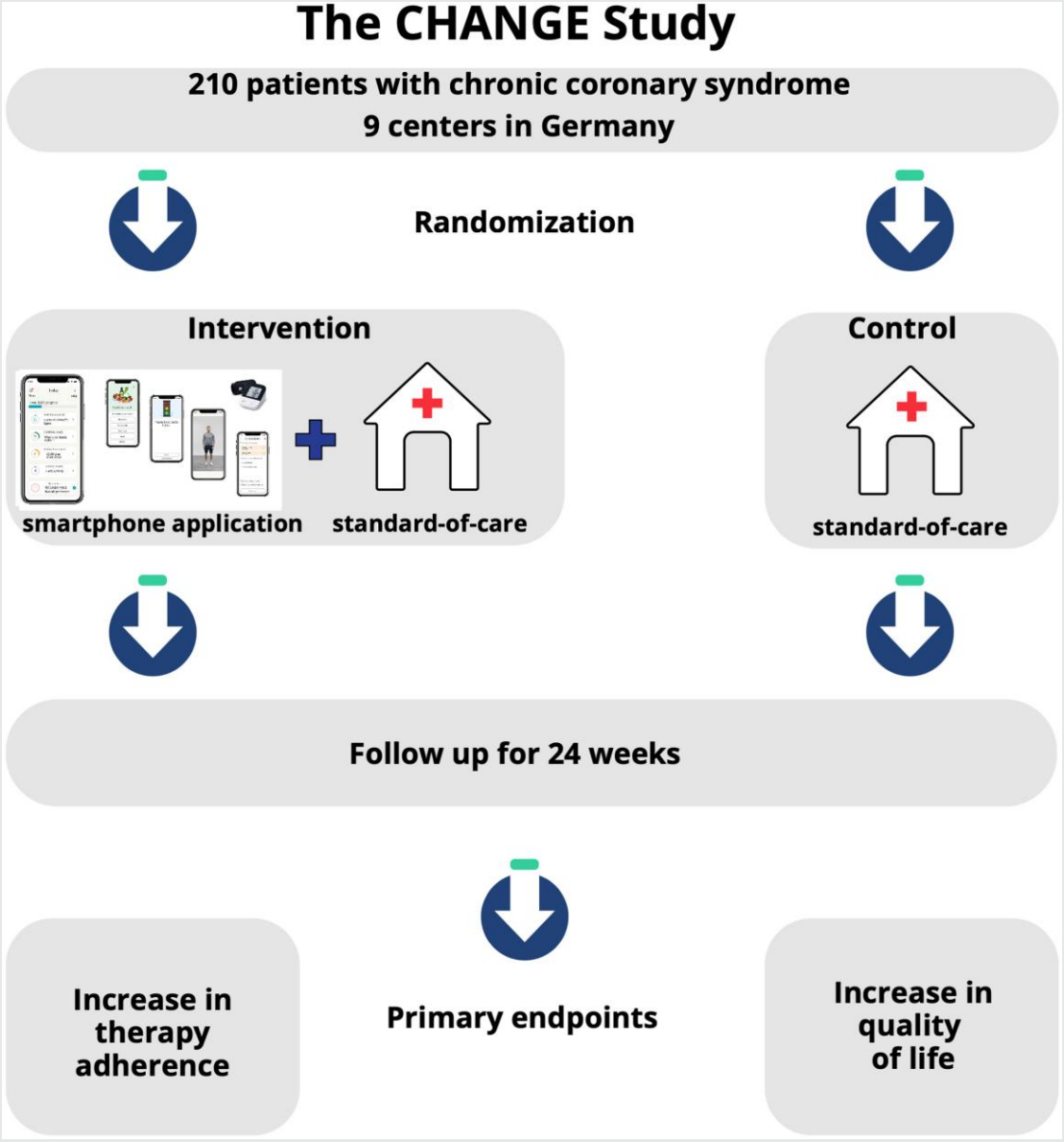
Graphical Abstract



Keywords Chronic coronary syndrome • Secondary prevention • Digital health

Introduction

Coronary artery disease (CAD) represents the manifestation of atherosclerosis in the coronary circulation and is characterized by chronic inflammation, endothelial dysfunction, and progressive atherosclerotic plaque formation.[1,2] The dynamic nature of CAD results in various clinical presentations, which can be categorized as either acute coronary syndromes (ACS) ranging from instable angina to sudden cardiac death or chronic coronary syndrome (CCS).[2,3] The latter condition used to be called 'stable CAD'. However, recent guidelines of the European Society of Cardiology (ESC) recommend to refer to this state as 'chronic coronary syndrome' to underline its chronic and dynamic character.[2]

Despite significant advances in therapeutic approaches, morbidity, mortality, as well as the readmission rate among patients with CCS remain high. Coronary artery disease remains the number one cause of death worldwide that contributes to 16% of total mortality.[4] Recently published data from 2021 report that CAD is the major driving force for cardiovascular mortality in European countries with 44 and 38% in male and female patients, respectively.[5] In Germany,

CAD ranks as the most common cause of death accounting for 7.8% of the total mortality in 2019.[3]

The causes are multifactorial, but insufficient behavioural change, inadequate medication adherence, and in short, a poor risk factor management in CAD patients play a major role.[6,7] Numerous epidemiological and interventional studies demonstrate that long-term survival of patients with cardiovascular disease is markedly diminished in the presence of cardiovascular risk factors such as dyslipidaemia and hypertension and that control of these risk factors is associated with a significantly improved prognosis.[8] In addition, striking evidence suggests an important role of lifestyle factors such as diet, abdominal obesity, and a lack of physical activity as well as smoking to increase cardiovascular risk.[9,10] These factors, together with dyslipidaemia, hypertension, and diabetes, are called 'standard modifiable risk factors'.[11] Previous studies have shown that adherence to behavioural advice regarding diet and exercise is capable of lowering the risk of major events 6 months after ACS by 50%.[10] As a consequence, evidence-based recommendations addressing lifestyle management are provided in several ESC guidelines.[2,12–14] These include advice regarding adherence to a Mediterranean diet, physical activity, smoking cessation, and strategies to reduce mental stress as well as home blood pressure monitoring.[2,14]

However, one of the core issues in the treatment of modifiable risk factors is poor adherence with pharmacological therapy and lifestyle advice.[15] Recent data indicate that after a cardiovascular event, 70% of patients fail to make the minimal behaviour adjustments needed for an effective risk reduction.[10,15] In one study, ~49% of patients who were smoking at the time of a cardiovascular event did not succeed in quitting smoking.[15] With respect to dietary habits, other investigations have provided evidence that only 40% of enrolled CAD patients reduced their consumption of saturated fats and only 35% increased their consumption of fruits and vegetables.[16]

Therefore, the lack of adherence to recommendations for lifestyle management is also considered in current guidelines. Physicians should advice their patients on lifestyle changes at every clinical appointment.[2] Furthermore, current ESC guidelines on lifestyle management in CCS recommend involvement of multidisciplinary healthcare professionals (e.g. cardiologists, general practitioners, nurses, dieticians, physiotherapists, psychologists, and pharmacists).[2] However, implementation of this practice into clinical routine is challenging due to the high workload for medical personnel in high-turnover patient settings.[17] In addition, prolonged gaps between brief clinical appointments between physician and patient further hamper regular enforcement of lifestyle advice and adherence to pharmacological therapy. Furthermore, the frequency of medical encounters may be reduced due to practical reasons such as reduced mobility. In this context, it has been shown that long distances to cardiac rehabilitation centres discourage patients from attending such activities.[17–19] Therefore, new strategies are needed to overcome these obstacles.

In recent years, novel strategies have emerged that may be able to fill these gaps with 'eHealth' approaches using smartphone-based applications (apps). Digital approaches have been shown to be highly effective as diagnostic tools for the detection of cardiac arrhythmias. A recently published study provides evidence that a digital atrial fibrillation screening using a photoplethysmographic smartphone app increases the detection rate of patients requiring oral anticoagulation compared with routine symptom-based screening.[20] In the context of cardiovascular prevention, an early meta-analysis demonstrated a positive effect of eHealth approaches on behavioural realignment regarding diet and physical activity.[18] Another systematic review suggests a positive influence of digital interventions in CAD patients on physical activity, adherence to pharmacological therapy, and a healthy diet.[21] However, in this study, no reduction of unhealthy behaviour such as smoking was observed.[21] Yun *et al.*[22] were recently able to show a significant improvement of cardiovascular risk factors after 3 months of using a digital program (computer or app) in Korean patients with hypertension, hypercholesterolaemia, or diabetes in a dual centre, randomized, controlled trial. A recently published meta-analysis that includes randomized controlled trials that tested eHealth interventions compared with rehabilitation and/or usual care found a significant association of eHealth interventions with lower rehospitalization and cardiac events compared with non-intervention.[23] Furthermore, novel data demonstrate that complementing cardiac rehabilitation with a web-based app is able to improve blood pressure as well as dietary habits in patients that suffered from ACS.[24] Marvel *et al.*[25] reported that usage of the Corrie app was associated with lower risk of all-cause unplanned 30-day readmissions in patients after acute myocardial infarction. There is evidence available that supports the use of eHealth approaches for secondary prevention in CAD patients, however, systematic reviews identified differences between the mode of delivery of a digital intervention within the wide variability of options.[26] Thus, despite promising studies, there is the need for novel randomized controlled trials provide more evidence for the feasibility of digital approaches in treatment of heart patients. The recently published 'MyHeartMate study', a randomized controlled trial, which was conducted in Australia, investigated the influence of a game-based smartphone app on self-reported physical activity as primary endpoint in 390 CAD patients.[27] After 6 months, no improvement of risk factors or lifestyle behaviours other than triglyceride levels was reported.[27] A novel aspect of the present study is that it investigates a digital intervention combined with a monitor function in the secondary prevention of patients with CCS in a multicentre, prospective, and randomized design in a European patient cohort. Furthermore, the study investigates the impact of a multicomponent app on lifestyle changes by addressing a variety of central aspects in the secondary prevention such as physical activity, healthy diet, and adherence to pharmacological therapy combined with the evaluation of the impact on health-related quality of life (QoL). To date, there are no refundable cardiological digital health apps approved in Germany. Based on these results of the CHANGE study, the trial can build a basis for the first refundable, cardiological digital health app in Germany.

The aim of the multicentre, prospective, and randomized CHANGE study is to investigate if a smartphone-guided secondary prevention (SGSP) app combined with a monitor function compared with standard-of-care has beneficial effects on overall adherence to secondary prevention guidelines and QoL in patients with CCS. Recruitment of the study started in July 2022. At the time of submission of this manuscript, a total of 110 participants have been recruited.

The CHANGE study

Study rationale

Using the precursor product of the current app, our group was recently able to show in a cohort of 43 CAD patients that regular usage of the smartphone-based intervention leads to more physical activity, healthier dietary habits, and increased knowledge of cardiovascular risk factors, even after a short time period (28 days).[17] Therefore, we designed a study to investigate a more advanced, personalized app in a prospective, controlled, and randomized trial to validate the preliminary findings in CCS patients. Using a guideline-based smartphone app, the CHANGE study may be able to close a gap of knowledge regarding eHealth approaches in the secondary prevention of patients with CCS.

Hypothesis

Regular usage of a digital cardiac health programme in patients with CCS improves secondary prevention guideline adherence regarding physical activity, medication adherence, smoking cessation, healthier

diet, home blood pressure monitoring, and/or QoL compared with standard-of-care.

Methods

Smartphone-guided secondary prevention app (VantisTherapy*)

'VantisTherapy*' is a mobile SGSP app designed to support patients with CCS to accomplish recommended behaviour changes based on current ESC guidelines. Details about the development process have recently been published.[17] In a small monocentric pilot study, the beta version of VantisTherapy* was tested in CCS patients.[17] Changes were made based on the results and feedback given by the participants. To increase adherence with pharmacological therapy and lifestyle changes, the final version of the app covers more therapy areas, is personalized, integrates vital monitoring through connected devices (an upper arm blood pressure monitor is part of this study), and game design. Furthermore, patients can exchange questions and ideas in a forum.

The app provides a daily plan for the patients (*Figure 1*), which includes video-guided home exercises depending on the patient's capabilities, medication tracking, and educational units in brief texts. In addition, a digital nutrition coaching provides information about a healthy diet according to guidelines. Furthermore, the patients can perform home blood pressure measurements and record their bodyweight, food intake, or specific symptoms. The app tracks specific symptoms (e.g. angina pectoris) and vital parameters (e.g. elevated blood pressure) and gives the patient more information regarding these parameters. This may include the recommendation to address this topic during the next doctor appointment, visit a doctor immediately, or call an ambulance. Therefore, the software uses data either provided by the patients themselves or connected devices, such as a Bluetooth blood pressure measuring device (e.g. Omron HEM-7155T-D or similar). The progress made by the patients is summarized for behavioural inputs such as exercise levels or medication adherence and health outputs such as blood pressure, weight, or resting pulse. The overall therapy progress is summarized in a simulated 'heart age'. All activity is also available as a PDF download, which patients may bring to clinical appointments with their physicians. The surface of the app is optimized to enhance adherence including elements from game design. By dividing therapy objectives into small attainable goals and presenting them as action-oriented steps that can be implemented immediately, the patient's involvement in their therapy and their self-efficacy is reinforced.[28] A cornerstone of the app is positive reinforcement by rewarding positive behaviour such as completing activities within the app.

Study design

The CHANGE study is designed as a prospective, randomized, and controlled trial with a 1:1 allocation ratio, that will be performed in nine centres in Germany in a parallel group design. 210 patients with CCS will be randomly allocated to either the control group or to the intervention group, who will be provided the VantisTherapy* app in addition to standard-of-care to implement secondary prevention into their daily life. The control group will receive standard-of-care alone based on current ESC guidelines on CCS.[2] This involves appropriate pharmacological therapy, periodical assessment by a cardiovascular caregiver (cardiologist, internist, general practitioner, or cardiovascular nurse) and lifestyle interventions based on ESC guideline recommendations. The study will be performed in an open design. Outcomes will be assessed using objective data from three in-person visits (0, 12, and 24 weeks) and the data withdrawn from the app. The data will be collected and compared between groups.

Recruitment and population

Enrolled patients are required to be diagnosed with CCS (I25, ICD-10) and to be older than 18 years of age (*Table 1*). Exclusion criteria are divided into two groups, study related and device related. Study-related exclusion criteria are participation in another clinical trial, conflict of interest to the sponsor of the study or investigator and a planned or completed participation in a CAD-related rehabilitation programme in the past two months. Device-related exclusion criteria are as followed: no access to a compatible

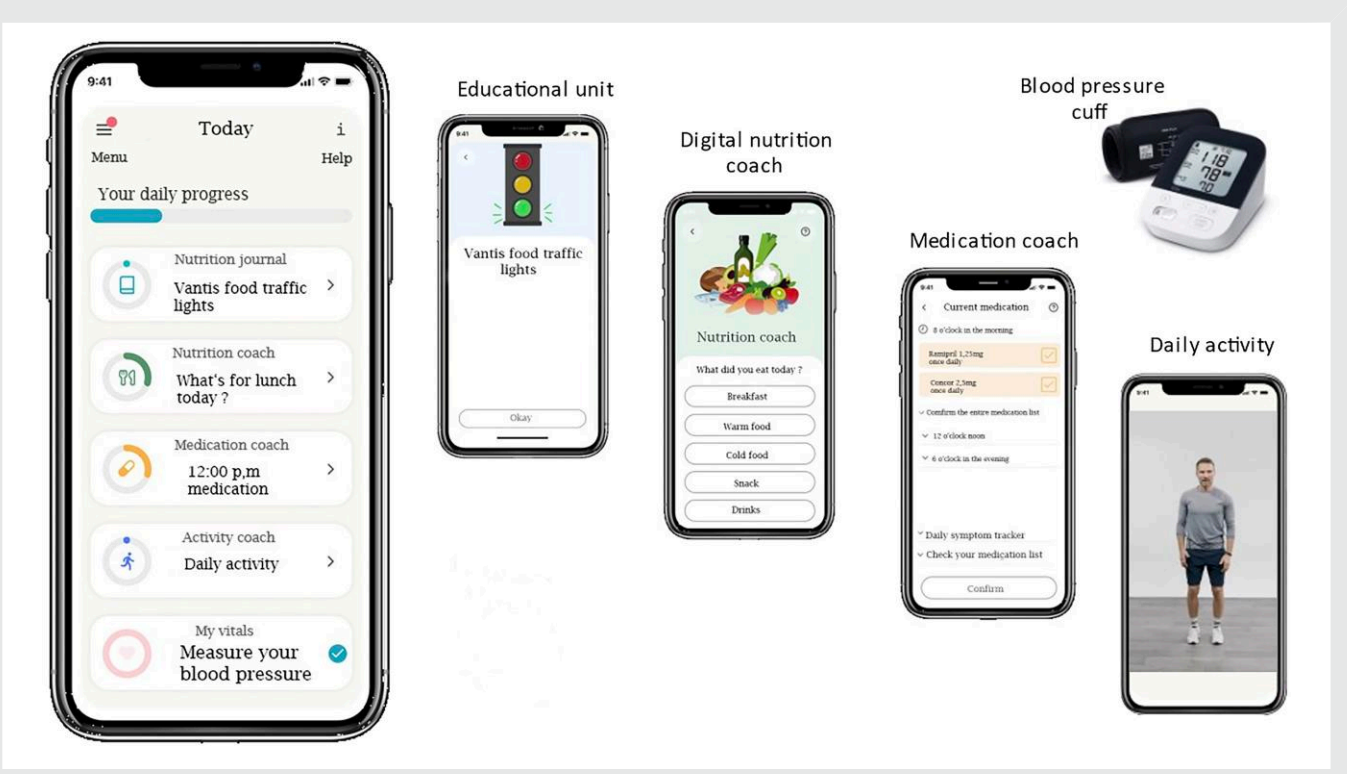


Figure 1 Overview of the VantisTherapy* interface and a selection of specific functions.

smartphone or no capability to use it and insufficient language proficiency, as the VantisTherapy* app is available only in German language. Potential candidates are screened for inclusion and exclusion criteria at each centre. If the criteria are met, the patient is approached personally to gather written informed consent. During this initial visit by a physician, a brief discussion of CAD, modifiable risk factors, and secondary prevention measures is performed before the randomization of each patient. Afterwards, patient data are entered in the eCRF, and patients are allocated in one of the two study groups. After enrolment, patients are visited by the study staff and Visit 0 is completed (*Table 2*).

Participating study centres

Patients will be recruited in nine centres in Germany. These centres include two university hospitals located in a metropolitan region of Germany (Bonn and Düsseldorf). In addition, a large non-university tertiary care hospital (Trier) and a secondary care hospital (Cologne) as well as five specialist practices in cardiology in Kaiserslautern, Bonn, Leverkusen, Bad Neuenahr-Ahrweiler, and Cologne recruit patients in an outpatient setting. With this distribution, the whole spectrum cardiology care of Germany including inpatients and outpatients is represented in the CHANGE study.

Table 1 Inclusion and exclusion criteria for the CHANGE study

Inclusion criteria
Patients ≥18 years diagnosed with CCS (ICD-10: I25)
Patients understanding the study protocol and giving written consent
Exclusion criteria
Device related
Patient does not own a compatible smartphone or is not able to use the app/smartphone
Insufficient proficiency of German language
Study related
Participation in another clinical trial after inclusion in the present study
Planned or current (<2 months ago) participation in a CAD-related rehabilitation programme
Conflict of interest to the sponsor of this study or the investigator

CAD, coronary artery disease; ICD, International Statistical Classification of Diseases and Related Health Problems.

Study endpoints and data source

Primary study endpoints will be overall adherence to secondary prevention guidelines (physical activity, dietary habits, smoking cessation, medication adherence, and home blood pressure monitoring) and changes in QoL after 24 weeks of treatment.

Overall adherence with recommended measures will be evaluated using validated questionnaires separately assessing adherence regarding physical activity, diet, and adherence to pharmacological therapy. Patient data will be collected at three in-person visits (V0: baseline, V1: 12 weeks, and V2: 24 weeks) (*Table 2*). Data will include self-reported information collected from the patients during a brief interview (e.g. smoking habits and home blood pressure measurements), the results of questionnaires, and physical findings such as office blood pressure and heart rate.

Measurements

The questionnaires are handed out to the patients after inclusion and completed by the patients in private following the requirements of each questionnaire. According to current recommendations, participants are advised to be physically active for at least 150 min/week, distributed over at least 5 days. Patients will be asked to report the time (in minutes) with moderate and high-intensity physical activity using the 'Physical Activity Questionnaire—Short Form'.[29] The questionnaire uses seven questions to assess physical activity distributed over the past 7 days in minutes. Minutes with high-intensity activity will be counted twice in this setting. Adherence to a Mediterranean diet will be measured with the 'Mediterranean Diet Adherence Screener' questionnaire (MEDAS), which includes consumption of fruit and vegetables, seafood and healthy fats.[30] The German version of the questionnaire has recently been validated.[31] In a total of 14 questions, patients can achieve 0–1 point per question, patients who achieve 8 points in the MEDAS questionnaire will be considered adherent to guideline recommendations. Regarding adherence to pharmacological therapy, the goal is to achieve four points in the 'Morisky Medication Adherence Scale' questionnaire (MMAS-4).[32–34] This questionnaire contains four items that require a 'yes' or 'no' answer regarding adherence to pharmacological therapy. Patients who answer all questions with 'no' will be considered adherent to pharmacological therapy. In total, patients can achieve a score of 0–4 or 0–4.5 points (if home blood pressure monitoring is indicated) depending on how many modifiable risk factors they have improved during follow-up (*Table 3*). Quality of life after 24 weeks will be measured by the HeartQoL, which has previously been validated for patients with CAD in Germany.[35]

Table 2 Overview about the three timepoints, collected data, and parameters

Week	V0 0	V1 12 ± 7 days	V2 24 ± 7 days
Inclusion and exclusion criteria	√		
Basic data, medical history, risk factors, and cardiovascular medication	√		
Written informed consent	√		
Four questionnaires (physical activity, diet, medication, and QoL)	√	√	√
Smoking status	√	√	√
Regularity and documentation of blood pressure measurement	√	√	√
Measurement of blood pressure, heart rate, and BMI	√	√	√
CAD-related laboratory parameters (if available due to clinical routine)	√	√	√
Changes in medication		√	√
Adverse events and product defects		√	√

BMI, body mass index; CAD, coronary artery disease; QoL, health-related quality of life.

Table 3 Modifiable risk factors and guideline-based recommendations for improvement

Modifiable risk factor	Requirements	Points (0–1)
Physical activity	Physical activity for ≥150 min/week (over ≥5 days)	
Diet	≥8 points in the 'MEDAS' questionnaire	
Smoking	Smoking cessation in the past 14 days	
Home blood pressure monitoring (if indicated)	Blood pressure home measurements for ≥8 days in the past 14 days	
Adherence to pharmacological therapy	Four points in the MMAS-4 questionnaire	
Total (0–4.5 or 0–4 points if blood pressure measurement is indicated)		

Patients who meet the minimal requirements can receive 1 point per risk factor and 0.5 points for adherence to home blood pressure monitoring if indicated. In total, patients can achieve a score from 0 to 4.5 or 0 to 4.
MEDAS, Mediterranean Diet Adherence Screener; MMAS-4, Morisky Medication Adherence Scale.

Data collection

Information about smoking cessation in the past 14 days will be self-reported by the patients during an interview with the study staff. As the study is designed as a post-market clinical follow-up study that is classified as non-invasive and without burden for the patient, no additional invasive procedures are allowed to measure specific biomarkers. However, whenever available, blood results from routine tests as standard-of-care outside of the study will be analysed during follow-up visits. Patients are asked to keep a blood pressure journal and to perform home blood pressure monitoring for at least 8 out of 14 days if indicated.[14] Home blood pressure monitoring is indicated if 'white-coat hypertension' or masked hypertension is suspected and to evaluate blood pressure control in hypertensive patients with high cardiovascular risk.[14] Furthermore, every patient with suspected hypertension during baseline is asked to keep a blood pressure journal. Patients with an indication for home blood pressure monitoring will achieve 0.5 points for performing home measurements for ≥8 days within the past 14 days. In addition, two blood pressure measurements according to study protocol will be performed in all patients during study Visits 0–2.[36]

Secondary endpoints of the study are an increase in overall adherence with recommended measures and QoL after 12 weeks compared with baseline, which will be measured in analogy to the primary endpoint. Another secondary endpoint will be a 'change in health status' after 12 and 24 weeks, which is estimated by multiple independent parameters. Change in systolic/diastolic blood pressure in patients with a systolic blood pressure >139 mmHg (or >89 mmHg diastolic) at baseline will contribute to this endpoint as well as a change in LDL-cholesterol in patients with baseline LDL-levels >55 mg/dL. Furthermore, changes in heart rate in patients with a heart rate >50 b.p.m. at baseline and changes in body mass index (BMI) in patients with a BMI >25 kg/m^2 will be evaluated (*Figure 2*). Finally, app usage will be quantified by frequency of app usage in 'dropouts' (0/14 days), 'irregular users' (1–6/14 days) and 'regular users' (≥7/14 days). Furthermore, app usage will be investigated depending on completed activities in the app daily. Activities might be amongst others blood pressure measurements or monitoring of medication intake. Extracurricular doctor visits will be documented during study visits and compared between control and intervention groups.

Data management

Data management will be performed using the study software 'SecuTrial' (iAS interActive Systems GmbH). Using this software, an eCRF is created for each patient. The database system automatically generates a code for each patient to protect their identity. After this pseudonymization, the database software performs randomization in a 1:1 manner. Entered data are audited from a monitor of a clinical research organization (CRO Dr. med. Kottman GmbH & Co. KG). Raw data will be published together with study results.

Statistical considerations

The CHANGE study will be evaluated by an intention-to-treat analysis. Calculations for both primary endpoints, increase of overall adherence with recommended measures and QoL after 24 weeks will be performed separately postulating the null hypothesis of no difference between intervention group (VantisTherapy*) and control group (standard of care). Estimation of effect sizes was performed based on app data as well as available research data.[7,35,37] With alpha = 0.025 (two-sided), a power of 80% and a 1:1 allocation ratio a sample size of 92 patients was calculated for the overall adherence endpoint and 210 patients for the QoL endpoint to detect statistically significant differences regarding changes in overall adherence and QoL, respectively. Based on prior studies, an increase of 0.073 points of overall adherence and an increase of 0.12 points in QoL can be considered as clinically relevant in the present study.[7,35,37]

Primary endpoints of the study are changes in overall adherence with recommended measures after 24 weeks (*Table 3*) and QoL after 24 weeks compared with baseline. Data for the evaluation of primary endpoints will be collected by using validated questionnaires (physical activity, diet, adherence to pharmacological therapy, and QoL) or self-reported information during three in-person visits (smoking, home blood pressure measurements). Both endpoints will be analysed separately by analysis of variance with repeated measures considering the initial value as a covariate. Differences will be tested by factor 'group' and interaction 'group*time'.

Missing data regarding both primary endpoints will be replaced in accordance with maximum likelihood estimation. In addition, three sensitivity analyses will be performed: (i) *t*-test using the Last-Observation-Carried-Forward method for replacement of missing data; (ii) *t*-test using baseline-observation-carried-forward for replacement of missing data; and (iii) *t*-test considering only the patients that completed the study according to the study protocol with V2. We further aim to perform subgroup analyses for primary endpoints such as prior participation in a CCS-related rehabilitation programme. Effect of frequency in app usage will be compared by dropout app users (0/14 days) vs. irregular users (1–6/14 days) vs. regular users (≥7/14 days). In addition, subgroup analyses regarding the difference of men vs. women, age >65 vs. ≤65 years, completion of the study and assessment of the presence of relevant comorbidities such as hypertension, diabetes, and heart failure will be performed. Subgroup analyses will include changes in medication vs. stable medication with respect to changes in blood pressure as secondary endpoint.

An interim analysis of primary endpoints and other obligatory parameters will be performed after 70 patients have completed V1 or dropped out of the study. The interim analysis only uses regular planned visits and thus does not bias the results of the study.

The statistical analysis will be performed using the current version of SAS (Statistical Analysis Software), SAS Institute Inc., Cary, NC, USA.

Early stopping

The principal investigator can terminate the trial prematurely if a continuation of the trial appears to disagree with ethical or medical standards or if resources for continuation of the study are no longer available. Patients can actively quit their participation in the trial at any time. Furthermore, the investigators can exclude patients from the study in case of major complications, which will interfere with the study protocol or a violation of inclusion or exclusion criteria.

Ethics

The study complies with local legal requirements and has been evaluated by the ethics committees of the University of Bonn (479/21), University of Düsseldorf (2022-1868), Medical Chamber North-Rhine (Ärztekammer

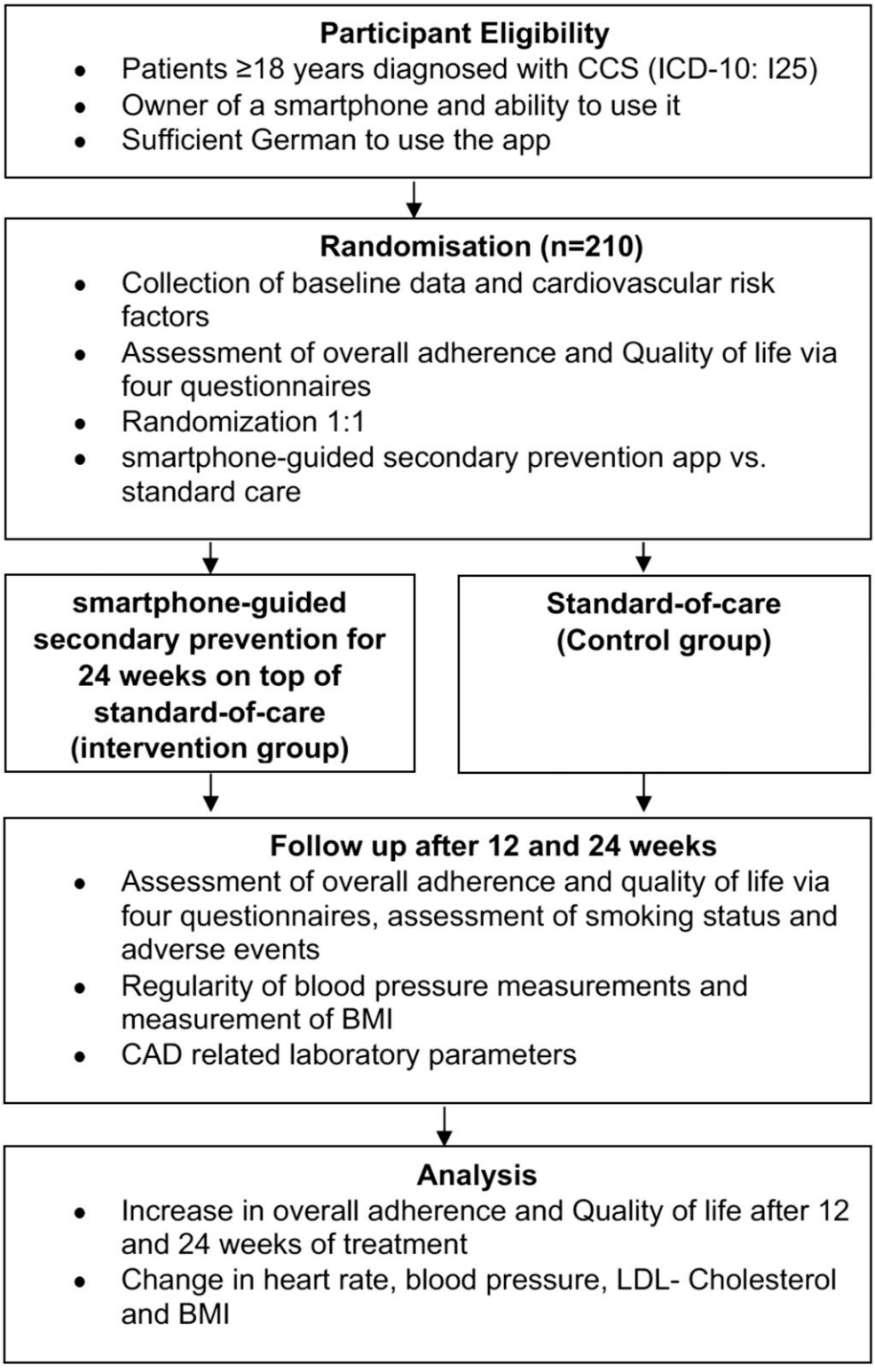


Figure 2 Flow chart of the CHANGE study.

Nordrhein, 2022049), and Medical Chamber Rhineland-Palatinate (Ärztekammer Rheinland-Pfalz, 2022-16378). The study will be performed in accordance with the Declaration of Helsinki, and all patients must provide written informed consent to participate. The trial is approved by the local ethics committee.

Registration

The study is registered at the German study registry number DRKS00028081.

Discussion

Management of modifiable cardiovascular risk factors is a major cornerstone in secondary prevention for patients with CCS.[2] Improving adherence of patients with lifestyle changes and pharmacological therapy is a highly potent therapeutic approach to decelerate disease progression and improve prognosis.[10] In this context, eHealth approaches that use apps have been shown to positively influence behavioural realignment.[17,22,25,38]

The multicentre, prospective, and randomized CHANGE study will investigate whether an SGSP app, combined with a monitor function compared with standard-of-care, has beneficial effects on overall adherence to secondary prevention guidelines and QoL in patients with CCS. The study will test the hypothesis that using a smartphone app is a feasible approach to close existing gaps between clinical appointments of physicians and patients. There are possible limitations of the proposed approach. First, the control group does not receive a 'placebo-app' without interventions. An ideal placebo-app would engage the patient in daily activity without transmitting any health-related content. For an application of which a key feature is to remind the patient of medication and other healthy lifestyle behaviour, it is difficult to imagine an app that engages the patient at a similar level without indirectly reminding him of the study and thereby of his cardiovascular risk and lifestyle. Consequently, we refrained from using a 'placebo-app' because applicable standards and necessity are uncertain. Second, despite existing evidence that 12–24 weeks are an adequate time to establish sustained behavioural changes, we are unable to exclude that long-term effects of the intervention may vanish over the time.[39] In addition, effects could be terminated after trial conclusion. Current ESC guidelines on CCS recommend a multidisciplinary approach in secondary prevention.[2] In our study, patient recruitment as well as delivering the VantisTherapy* app is performed only by cardiologists and the study staff. However, the app represents a multicomponent intervention that goes beyond physical activity and includes smoking habits, nutrition, blood pressure, and adherence to medication as additional therapeutic elements.[27] The strengths of the study are the differentiated primary endpoints that contain an evaluation of several highly relevant behavioural changes in addition to QoL. Furthermore, compared with other studies, it is important to point out that patients who have recently completed a cardiac rehabilitation programme will be excluded from the study to extrapolate the effects of app usage.[24] In addition, the multicomponent app is based on ESC guidelines and aims to emphasize the multidisciplinary approach in lifestyle management that is proposed by current ESC guidelines and addresses a variety of risk factors with a special focus on involving the patients themselves in their secondary prevention.[2] Further, the study design provides a sufficient size of participants and covers the whole spectrum of cardiological care of Germany. Taken together, the results of the CHANGE study will provide evidence for optimization of secondary prevention in patients with CCS.

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Conflict of interest: A.Z. received a lecture fee from Vantis GmbH on one occasion. The authors declare no conflicts of interest. The authors are not employees or beneficiaries of the Vantis GmbH.

Data availability

All data are made available by the corresponding author upon reasonable request.

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