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UNIVERSITY OF LEICESTER

PROTOCOL

Cardiovascular Risk reduction In the NHS abdominal aortic aneurysm (AAA) Screening Programme: a co-developed cardiovascular prevention intervention (the CRISP study)

Version 1.4 11/01/2023
IRAS: 273793

Sponsor: University of Leicester

TITLE OF THE STUDY

Cardiovascular Risk reduction In the NHS abdominal aortic aneurysm (AAA) Screening Programme: a co-developed cardiovascular prevention intervention (the CRISP study)

SHORT STUDY TITLE / ACRONYM

Cardiovascular risk reduction in patients with aneurysms / CRISP

PROTOCOL VERSION NUMBER AND DATE

Version: 1.4

Date: 11th January 2023

RESEARCH REFERENCE NUMBERS

IRAS Number:	273793
SPONSOR Number:	0746
FUNDERS Number:	NIHR Advanced Fellowship NIHR300059

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor (University of Leicester):

Signature:

Date:

11th January 2023

Name (please print): Yasmin Godhania

.....

Position: Research Governance Officer

Chief Investigator:

Signature:

Date:

11th January 2023

.....

Name: (please print):

Professor Matthew Bown

LIST of CONTENTS

KEY STUDY CONTACTS

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Funder(s)	National Institute for Health Research (NIHR) – Grant Code: NIHR300059 (awarded in 2019)
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STUDY SUMMARY

Study Title	Cardiovascular Risk reduction In the NHS abdominal aortic aneurysm (AAA) Screening Programme: a co-developed cardiovascular prevention intervention (the CRISP study)
Internal ref. no. (or short title)	CRISP
Study Design	Qualitative study with an additional quantitative feasibility study (mixed methodology)
Study Participants	Men with an abdominal aortic aneurysm identified through the existing NHS Abdominal Aortic Aneurysm (AAA) Screening Programme (NAAASP)
Planned Size of Sample (if applicable)	30
Follow up duration (if applicable)	Not applicable

Planned Study Period	4 years and 6 months (54 months; allowing for a 6 months' extension due to COVID-19 related pause in 2020)
Research Question/Aim(s)	The first research aim (**Stage 1** of this research) is to develop a cardiovascular-risk reduction programme specifically for men in AAA-surveillance that will address all aspects of cardiovascular-prevention based on current National Institute for Health and Care (NICE) guidance. The second aim (**Stage 2** of this research) is to test the feasibility of using the developed cardiovascular-risk reduction programme for men in AAA-surveillance in existing NHS AAA screening and surveillance programmes

FUNDING AND SUPPORT IN KIND

FUNDER(S)	**FINANCIAL AND NON FINANCIAL SUPPORT GIVEN**
National Institute for Health Research (NIHR) – Grant Code: NIHR300059 (awarded in 2019)	£ 906,093.00 This research is supported in whole by an NIHR Advanced Fellowship awarded to Mr Athanasios Saratzis (Chief Investigator). This funding covers all research costs.

Confidentiality Statement

ROLES OF STUDY SPONSOR & FUNDER

The **University of Leicester** acts as the **Sponsor** of this research and assumes overall responsibility for the initiation and management of the study.

Sponsor Standard Operating Procedures (SOPs)

Relevant SOPs will be followed to ensure that this study complies with all relevant legislation and guidelines

Declaration of Helsinki

The Investigator will ensure that this study is conducted in full conformity with the current revision of the Declaration of Helsinki (last amended October 2000, with additional footnotes added 2002 and 2004).

Guidelines for Good Clinical Practice (GCP)

The Chief Investigator will ensure that this study is conducted in full conformity with the Principles of GCP.

Approvals

Once Sponsor authorisation has been confirmed, the protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC), regulatory authorities, and host institution(s) for written approval.

Once Sponsor authorisation has been confirmed, the Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

Participant Confidentiality

The research staff will ensure that the participants' anonymity is maintained. The participants will be identified only by initials and a participants' identification number on any form and any electronic database used as part of this research. All documents will be stored securely and only accessible by trial staff and authorised personnel. The study will comply with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so.

Other Ethical Considerations

No vulnerable participants will be included and patients unable to provide informed consent will not be considered eligible for this research.

The funder (NIHR) is in no way involved in the conduct and delivery of this research.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Study Steering Group (SSG)

A SSG will convene on an at least a six monthly basis.

Patient & Public Involvement

All elements of this study have been developed with the help of 53 patients and their carers, between 2018-2019 (study development stage). Further, during Stage 1 of this research (qualitative study) a total of 20 patients are involved in creating the cardiovascular-risk reduction intervention alongside the study team; they regularly review all study documents and processes. Two patients will act as formal representatives on the Study Steering Group (SSG) and the core research/study team during Stage 2

of this research. The study involves several patient and public workshops and focus-groups, hence patients will have active involvement at all stages. Exhaustive information is provided in the relevant section of this protocol.

PROTOCOL CONTRIBUTORS

Main author: Mr Athanasios Saratzis, Associate Professor of Vascular Surgery, Chief Investigator

Contributors:

Professor Matthew Bown, Professor of Vascular Surgery (University of Leicester)

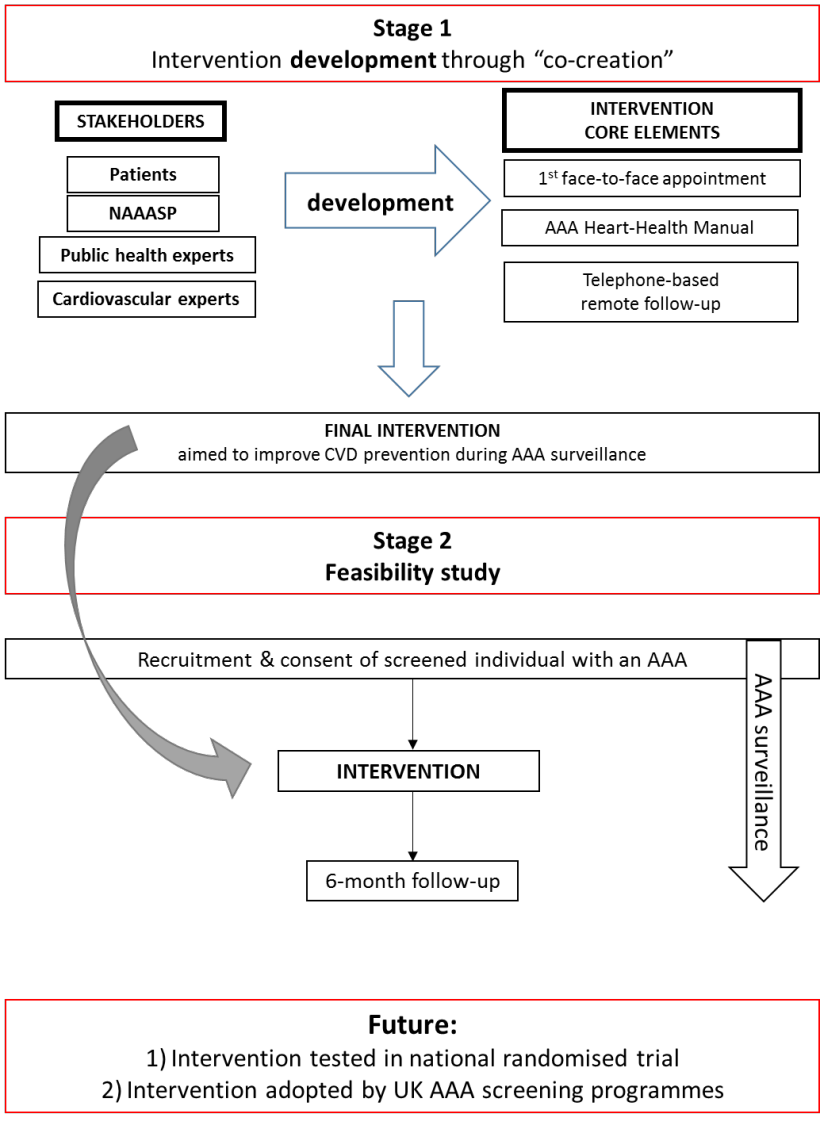
Dr Tom Withers Research Fellow (University of Birmingham)

Professor Colin Greaves, Professor of Psychology (University of Birmingham)

Mr Christopher Martin, Patient with an aneurysm (lay reviewer and contributor during study design).

KEY WORDS: Cardiovascular; Abdominal Aortic Aneurysm; Screening; Prevention; Qualitative; Development

STUDY FLOW CHART



AAA: abdominal aortic aneurysm
NAAASP: NHS AAA screening programme
CVD: cardiovascular disease

STUDY PROTOCOL

Cardiovascular Risk reduction In the NHS abdominal aortic aneurysm (AAA) Screening Programme: a co-developed cardiovascular prevention intervention (the CRISP study)

1 BACKGROUND & RATIONALE

All men in the UK are invited for an ultrasound (US) scan to screen them for Abdominal Aortic Aneurysm (AAA) in the year of their 65th birthday. The vast majority of men diagnosed with AAA through screening do not require immediate surgery to treat the aneurysm. They are entered into a disease-surveillance programme to monitor AAA growth with repeat US measurements. Whilst screening reduces AAA-related mortality by providing an opportunity for timely surgical intervention, it has very minimal effect on all-cause mortality. The principal preventable cause of mortality in men under AAA-surveillance is cardiovascular disease. The regular attendance of these men at surveillance clinics represents an excellent opportunity to address their excess cardiovascular-risk within an existing, well defined and well attended clinical pathway. The national AAA-surveillance programme, however, was not specifically developed to deliver cardiovascular-risk modification and these individuals have very unique characteristics that make the adoption of cardiovascular-interventions developed in different clinical settings very challenging. Consequently, uptake of cardiovascular-risk management has been poor in AAA screening/surveillance, despite the fact that these individuals represent one of the highest cardiovascular-risk groups. Furthermore, no high-quality research has investigated the optimal interventions to reduce cardiovascular-risk in this clinical area.

Due to the long latent period between AAA development and rupture (which is deadly in 80% of patients) screening can detect AAA early and rupture can be prevented by surgical repair. Most deaths, however, in those with an AAA <5.4cm in diameter are due to cardiovascular-events(1). Since 2013, screening for AAA has been offered in England to men in the year of their 65th birthday through the NHS AAA Screening Programme (NAAASP). The NAAASP (England) invites 300,000 men for screening yearly (of which 80% attend) detecting around 2,300 AAAs. Similar programmes now exist across the UK and abroad. Eligible men are invited to attend a local clinic where a technician measures the maximal anteroposterior diameter of the infra-renal aorta with US. Those with a diameter <3cm are discharged. Those with a diameter between 3.0 and 5.4cm are offered regular US surveillance. Men with a diameter >5.4 cm are referred for surgery. In late 2017 there were 11,601 men in NAAASP surveillance. On average, men with a screen-detected AAA spend five years in surveillance before requiring surgical referral(2).

AAA and cardiovascular disease

Male-sex, smoking and hypercholesterolaemia are the main risk-factors associated with AAA(3). It is therefore logical to assume that men with AAA will be at high cardiovascular-risk. Our group has recently shown in a meta-analysis that 15% of men in AAA-surveillance will die due to a cardiovascular-event over five years(4). Based on my preparatory research for this fellowship using actual contemporary national data, men in AAA-surveillance in England suffer 348 preventable cardiovascular-deaths and 720 non-fatal major cardiovascular-events annually. I have also recently applied the SMART-REACH model(5), a validated cardiovascular-risk prediction tool designed for patients with existing cardiovascular disease, to assess the benefits of optimal cardiovascular-modification in AAA surveillance using data from NAAASP. Achieving a systolic blood pressure <140mmHg, stopping smoking and achieving a normal Low-Density Lipoprotein (LDL) leads to a 29% overall absolute risk reduction in 10-year predicted cardiovascular-events with seven cardiovascular-disease-free years of survival gained per patient.

Unfortunately, there are significant challenges in introducing cardiovascular-risk modification in AAA screening/surveillance:

Preliminary work for this study and concomitant interaction with men in AAA-surveillance has shown that these individuals have certain characteristics which make the implementation of cardiovascular-

management particularly challenging. These men typically suffer from multiple co-morbidities, avoid contact with primary or secondary healthcare (even though AAA-screening attendance consistently exceeds 80%), have poor medication adherence, and are often socio-economically deprived(6, 7).

Some risk-factors such as diabetes (which is protective against AAA development and growth(8)) or obesity are far less prevalent in these men compared to other individuals with similar cardiovascular-risk(9).

AAA screening/surveillance programmes were not specifically developed to facilitate cardiovascular-risk modification.

It is therefore unsurprising that our preliminary research has shown very poor delivery of cardiovascular-risk management during AAA-surveillance(6).

Given the excellent attendance and low dropout of AAA-surveillance, this is a major missed opportunity to offer better cardiovascular prevention in a very high-risk population(10, 11).

Literature supporting this research

The delivery of cardiovascular prevention in individuals with AAA is very poorly researched. We therefore sought to generate data and evidence to examine the exact association between aortic size and cardiovascular-risk, the current cardiovascular-health practices in screening/surveillance, and possible interventions to reduce cardiovascular-risk in this clinical setting. More specifically, we investigated: cardiovascular mortality in AAA-surveillance using meta-analysis(4) and linking NAAASP data with Hospital Episode Statistics (HES) and Office for National Statistics (ONS) datasets; precise associations between aortic diameter and cardiovascular-events using data from the Framingham Heart Study; the current uptake and characteristics of cardiovascular prevention in NAAASP; evidence on effective lifestyle behaviour change. We finally attempted to quantify the cardiovascular-benefits gained by introducing cardiovascular-risk management in NAAASP.

Key findings:

i. Cardiovascular mortality during AAA-surveillance is high.

In a meta-analysis of all published AAA cohorts with available cardiovascular data, the annual absolute risk of a non AAA-related major cardiovascular-event was 3%(4).

Consequently, we analysed outcomes of all men screened by the NAAASP in 2013/14. These men were linked to HES and ONS datasets, comparing cardiovascular and all-cause mortality for 2,320 individuals with AAA vs. 237,924 individuals without. Over two years, men with AAA in surveillance were twice as likely to die due to a cardiovascular-event (adjusted analysis, $p<0.001$) (data under publication).

ii. A large aorta is the best predictor of future cardiovascular-events.

To investigate the association between aortic size and cardiovascular-morbidity adjusted for relevant confounders, we obtained data from the Framingham Study (FHS); 1,383 individuals from the FHS(12) underwent Computed Tomographic (CT) measurements of their aorta in 2004 and were followed-up for 10 years. Based on multivariate analyses using the Framingham cardiovascular risk-score, an abdominal aortic diameter >2.5cm was independently associated with a 77% increase in cardiovascular-events over 10 years ($p<0.001$); this association was even stronger than the Framingham cardiovascular risk-score.

iii. Individuals in AAA surveillance receive poor cardiovascular-prevention(6, 7).

To assess the uptake of cardiovascular preventative medication during AAA-surveillance, we led a national audit of 1,053 men through the Vascular and Endovascular Research Network (VERN) in fifteen vascular centres. Only 43% of men with AAA in surveillance were prescribed a statin and an antiplatelet. To confirm this, we used data from the UK AAA Growth Study (UKAGS), a national cohort study investigating AAA growth; 4,871 men without AAA and 384 under AAA-surveillance were

followed up for 3 years. Men in AAA-surveillance were three times more likely to smoke (34% vs 11%, p<0.001) and had a higher prevalence of untreated hypertension (58% vs. 38%, p<0.001) and hypercholesterolaemia (53% versus 32%, p<0.0001). Only 48% were prescribed a statin and an antiplatelet.

iv. Several aspects of cardiovascular prevention during AAA surveillance should be improved.

According to National Institute for Health and Care Excellence (NICE) guidance (CG181) men in AAA-surveillance should be offered blood pressure control, antiplatelet medication, statin therapy, lifestyle advice, and support to stop smoking, given that their risk of cardiovascular-events exceeds 10% over 10 years(6, 7, 13).

We completed a formal national survey of all NAAASP screening units in 2017 to assess how they approach cardiovascular-prevention. Most units (82%) suggest an antiplatelet and statin should be added to the individual's prescription after diagnosing an AAA by writing to their GP; however, they do not check whether these are prescribed. Only 36% of NAAASP units refer smokers to a smoking-cessation clinic.

v. Improving cardiovascular-health in AAA-surveillance confers significant survival benefits.

The SMART-REACH model(5) was recently developed and validated as a risk-prediction tool specifically for patients with prevalent cardiovascular disease. Using the model and data from the national VERN audit described above, we predicted the potential benefits of cardiovascular-modification in 443 men undergoing AAA-surveillance. Achieving a systolic blood pressure <140mmHg, stopping smoking and achieving normal LDL-levels leads to a 29% overall absolute risk reduction in 10-year predicted cardiovascular-events with seven cardiovascular-disease-free years of survival gained.

2 THEORETICAL FRAMEWORK

Through the use of intervention mapping(32), an evidence-informed cardiovascular-risk reduction intervention grounded in the needs of patients and caregivers will be developed, through extensive stakeholder involvement. This process builds on the already completed preliminary work and follows MRC intervention-development guidance(33).

Intervention mapping will identify: i) targets for change (e.g. changes in diet or lifestyle); ii) determinants of change (barriers and facilitators); iii) intervention components to modify each determinant. This will be followed by compilation of the components into a coherent framework and evaluation-with-feedback (the feasibility study) to identify further improvements.
The final choice of intervention components will be guided by existing evidence and theory and selected from a range of sources, including taxonomies of behaviour change techniques(34, 35). The intervention will draw on existing tools and facilitation methods, including intervention components developed by Professor Greaves for promoting physical activity in older adults at increased cardiovascular-risk(28-30), or which have been associated with effectiveness for dietary/lifestyle change(21, 26, 27, 36). Co-creation is an important principle for optimisation of intervention design and will be used in this research(37). The patient/carers groups will help identify patient and caregiver needs, refine intervention objectives/strategies and deliver training to the intervention facilitators. Service providers including representatives from all those involved in AAA screening/surveillance will provide extensive formal feedback to fine-tune the intervention.

3 RESEARCH QUESTION /OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

3.1 Objectives

Main objectives:

This study is delivered in two stages.

Objective 1: To develop (**Stage 1**) a cardiovascular-risk reduction programme specifically for men in AAA-surveillance that will address all aspects of cardiovascular-prevention based on current NICE-guidance(13).

Objective 2: To feasibility test the finalised intervention (**Stage 2**) in existing AAA screening and surveillance centres in the NHS.

Specific aims:

Aim 1; Stage 1 – Develop a cardiovascular-risk reduction intervention that is grounded in evidence and co-created with service users and providers

Aim 2; Stage 2 –To test the feasibility of using the aforementioned cardiovascular-risk reduction intervention in patients who have an AAA and are being seen regularly seen in NHS screening and surveillance centres. .

3.2 Outcomes

The main outcome **Stage 1** of this study is a purpose-built cardiovascular risk reduction intervention for patients with AAA.

The main outcome measure of **Stage 2** is to assess the feasibility of using the purpose-built cardiovascular risk reduction intervention developed in Stage 1 in patients who have an AAA and who are being seen regularly in existing NHS AAA screening and surveillance centres.

Secondary outcome measures of interest for Stage 2 will include:

Proportion of patients agreeing to take part out of all patients invited (intervention recruitment rate); proportion of patients recruited who provide data at the end of the study period (intervention retention rate); all cardiovascular events; mortality; quality of life using the EuroQol-5D (EQ-5D) questionnaire; weight and other relevant anthropometric information including Body Mass Index (BMI); blood-pressure levels; self-reported medication adherence; smoking status (self-reported); uptake of smoking-cessation services; reason for dropout; low-density and high-density lipoprotein levels as well as routine biochemistry.

4 STUDY DESIGN and METHODS

4.1 STAGE 1 (Development of the cardiovascular-risk reduction intervention with patients and experts/stakeholders)

Completed preliminary work

Identification of the intervention objectives with Patient and Public Involvement (PPI) and expert input

Based on NICE guidance(1), Medical Research Council (MRC) complex-intervention guidance, a systematic literature review, and consultation with patients, GPs as well as cardiovascular experts, we have established the five key intervention targets:

i. Smoking cessation: A clear and easy to follow pathway should be in place, including patient-centred discussion of barriers and referral to existing expert-services.

ii. Lifestyle modifications: physical activity and diet should be assessed and individuals should (if needed) be supported in setting and achieving specific targets for change.

iii. Antiplatelet agents: Aspirin 75mg (or Clopidogrel 75mg if Aspirin is contra-indicated) should be offered to all individuals.

iv. Lipid control: High-intensity statin-therapy should be offered to all individuals regardless of baseline lipid levels

The antiplatelet and statin strategy are supported by NICE (document CG147) and European Society of Cardiology guidance(2, 3).

v. BP-control: A target of 140/90mmHg should be achieved using the NICE CG127 treatment-algorithm.

Given the low prevalence of diabetes in men with AAA and its potential protective role against AAA growth, glucose control is not part of the proposed intervention(4, 5).

Interaction with patients to identify barriers to change and suitable intervention processes

We convened two formal focus-groups in 2017 attended by 56 men undergoing AAA-surveillance. We also involved primary care doctors through a national online survey (194 responses by GPs across the UK) and interviewing members of the UK GP research collaborative. Based on the framework for complex intervention development by Wight et al.(6), we focussed on the following:

- Which are the main barriers or facilitators in engaging with cardiovascular-risk modification during AAA-surveillance?
- Which of these causal or contextual factors are modifiable and have greatest scope for change?

We identified the following key barriers:

- Lack of initial structured discussion of cardiovascular-health
- Poor prescription practices (e.g. antiplatelet not prescribed on repeat prescription) by both primary and secondary care
- Lack of specific cardiovascular-health or lifestyle targets (e.g. specific BP level targets) communicated to patients
- Poor medication adherence and patient lack of understanding of the importance of cardiovascular-risk control(7-9)
- Patient loss to follow-up by their GP and secondary care
- Extremely poor uptake of NHS vascular checks

- Stress and anxiety(10). This was a recurring common theme in the PPI-sessions; my recent research(11) shows that AAA diagnosis through screening may lead to health-related stress and anxiety. Psychosocial interventions aiming to reduce stress have been shown to improve cardiovascular-outcomes in similar populations(12).

We then proceeded to identify appropriate strategies to support change and identify how to deliver cardiovascular-prevention using existing pathways.

To ensure the intervention is based on the best available evidence, the evidence-base on lifestyle intervention components and behaviour change strategies associated with effectiveness for reducing cardiovascular-risk were reviewed. This included updating a prior review on this topic(13) as part of a commissioned "state of the art" review(14). The CI also reviewed cardiovascular-interventions developed for high-risk populations with similar characteristics, such as male long-distance truck drivers and patients with psoriasis(15-17). This included recent work by Gray et al.(18) focussing on overweight men and Macleod/Anderson et al. who developed a cardiovascular-intervention within cancer screening(19). Each strategy identified was discussed with all PPI and experts participants. Digital health interventions were explored in great length (e.g. mobile phone apps). Almost all patient participants were against the use of digital technologies.

Eventually, through a consensus building process involving PPI, GPs and experts, the following components were identified as the core-elements of the future intervention, which will be fully developed during stage 1 of this research:

i) One initial face-to-face consultation (e.g. to assess and discuss risk-factors, address motivation and barriers and decide actions/targets)

ii) Telephone-based remote follow-up (potentially with further face to face catch-up meetings)

iii) A structured "Aneurysm Heart-Health Manual".

Intervention development process (Stage 1)

The content of the core elements which were identified during the preliminary PPI work (face-to-face consultation, remote follow-up and "aneurysm heart-health manual") will be developed and finalised during this research, to ensure that the final intervention can: i) assess and address the specific needs and concerns of each individual; ii) provide a tailored interaction between individuals with AAA and healthcare providers to develop individual plans and strategies for self-care; iii) appropriately address all of the individual's medical needs. To achieve this, the following principles will be adopted:

- Integration of behaviour change techniques and theory in the initial consultation and follow-up
- Patient-centred and empathic delivery style
- Balancing multiple patient behaviours
- Matching intervention components to individual needs (tailored-support)
- Ensuring the intervention addresses all five clinical-care target areas identified in the preliminary work (smoking, lifestyle, antiplatelet-therapy, lipids, BP-control)
- Ensuring the intervention can be delivered by nurses or other trained staff involved in delivering the NAAASP
- Creating a training package for intervention delivery that can be adopted nationally.

In total three groups will be involved in the development of the intervention:

- Patient and public involvement (PPI) group.

- Health service delivery group.
- Cardiovascular expert group.

A summary of the intervention development is shown below. All formal meetings will be recorded to ensure that an accurate record is kept of what is discussed, with recordings deleted after detailed meeting notes (not full transcripts) have been made.

***Table 1**: Summary of intervention development. GREEN are PPI activities, AQUA service delivery group, RED cardiovascular expert group, GREY academic group.*

<table>
<tr><th colspan="7">2020</th></tr>
<tr><td>Pre-start</td><td>April</td><td>May</td><td>June</td><td>July</td><td>August</td><td>Sept -Oct</td></tr>
<tr><td>1. Form and train PPI group (project orientation).
2. Develop and distribute ‘scaffolding questionnaire’ to cardiovascular expert group, programme delivery group and PPI group.
3. Reviewing of guidelines.</td><td>1. Analysis of the scaffolding questionnaire.
2. First PPI group meeting, Review behaviour change targets, discuss acceptability, barriers /enablers for each target.</td><td>1. Development of potential intervention ideas.
2. Second PPI meeting. More on barriers /enablers if needed. Discuss intervention formats / support needed from NHS? Discuss initial intervention idea.</td><td>1. Presentation to and discussion of the change targets, barriers and enablers to delivery with the service delivery group.
2. Further development of the intervention based on feedback from PPI and service delivery group.</td><td colspan="2">1. Presentation to and discussion of initial intervention ideas with the cardiovascular expert group.*
2. Potential Delphi study with the aim of prioritising the key elements of the intervention.
3. Third PPI group meeting: Review ideas /initial intervention materials. Address any specific questions arising.
4. Second service delivery group meeting: Review ideas /initial intervention materials. Address any specific questions arising.</td><td>1. Development of training materials.</td></tr>
<tr><td colspan="3">2020</td><td colspan="4">2021</td></tr>
<tr><td>November</td><td colspan="2">December</td><td>January</td><td>February</td><td>March</td><td>April-May</td></tr>
<tr><td>1. Joint service delivery and PPI group meeting to fine tune elements of the intervention.</td><td colspan="2">Final development of intervention before talk through activities.</td><td colspan="2">Talk through activities with intervention delivered to a separate group of patients in ‘condensed mode’ /over a 2 week period (2-4 small-group meetings)</td><td colspan="2">Final modification of intervention before feasibility study or further research.</td></tr>
</table>

* NB: There will be ongoing individual contact with the CVD experts during intervention development; specific questions will address issues arising during this process.

Data collection and intervention development methods for Stage 1

Scaffolding questionnaire (Stage 1)

Initially a 'scaffolding questionnaire' (see separate files) will be used for all groups involved in the development of the intervention. The aim of this questionnaire will be to inform our ideas on the scope and delivery of the intervention. The service delivery and cardiovascular group will be given the same questionnaire and the PPI an amended version due to the differing perspective that this group will bring to the development of the intervention (e.g. we would ask cardiovascular experts and service providers who would be best qualified to provide the intervention, but this question would have to be amended for the PPI group). The questionnaire (see separate file) will include both discrete choice questions and open-ended questions. The open-ended questionnaire responses will be analysed within and between sub-groups for common and/or contrasting themes. Discrete choice questions will be summarised by respondent group and compared using a triangulation protocol (42).

Patient and Public Involvement (PPI) focus groups (Stage 1)

At least twenty individuals with AAA in surveillance will take part in the PPI group. There will be a maximum of six meetings of the PPI group (five are represented in Table 1 and one additional meeting may be needed, depending on the rate of progress and data completion/saturation). Following an initial meeting that will focus on the training of the group on the aims of the study, the tasks expected of them and how PPI works. The meetings will follow a semi-structured format and be a maximum of two hours long, with up to two hours of pre- or post- meeting activities (e.g. reading and commenting on documents). The broad content of the meetings is indicated in Table 1, but will include exploring the optimum duration, format and content of the initial consultation, the telephone follow-ups the structure and content of the "aneurysm heart-health manual" and the facilitation process. They will specifically explore barriers to and enablers of the behaviour changes identified as intervention targets by the scaffolding questionnaire, evidence reviewing and discussions with cardiovascular experts.

If following these two initial meetings and consultation with both the cardiovascular expert and service delivery group, there are disagreements or choices to be made regarding how the intervention is delivered and the contents, a Delphi study will be undertaken with all groups. This will be followed by a joint meeting between the PPI and service delivery group to ensure that the intervention being delivered is both practical to deliver and palatable to patients.

Following the final writing of the intervention materials and training course, a group of five patients (separate to the PPI group) and five service providers will be asked to try out a condensed (2-week) version of the intervention. Each interaction with providers and a simulated 'at home' session with the intervention will be recorded, with the patient (and provider if present) asked at each step (multiple times during each session) to reflect on their thoughts and concerns. The aim of this "talk-through" phase is to fine tune the intervention and identify any potential challenges in respect to delivery, engagement with and sequencing of the intervention. It is envisaged that the patient group will be asked to take home elements of the intervention for two weeks, then a further review meeting (with further talk-through feedback will be conducted. The intervention and its training course will then be appropriately modified.

Developing the intervention with experts (Stage 1)

Two expert groups will be involved in the development of this intervention. The cardiovascular care expert group will consist of experts in cardiovascular and vascular medicine and care for example cardiovascular specialist nurses, cardiologists and vascular surgeons; we will also invite exercise physiologists and individuals with prior experience in designing exercise programmes. The service delivery group will consist of service delivery specialists, for example ultrasound scientists, ultrasound assistants, screening unit managers and public health consultants.

Initially both expert groups will be asked to undertake the 'scaffolding questionnaire' and we may seek to have individual or group meetings with selected specialists to address specific topics (e.g. how to

specify a safe exercise regime for people with AAA; what options are likely to be commissionable). Following the initial two PPI meetings the service delivery group will meet to discuss the initial intervention ideas (see schedule in Table 1). The service delivery group meetings will focus on the deliverability and skills or training needed to deliver of the proposed intervention. This information will then feed into both the development of the intervention and be shared with the PPI group.

This will be followed by a meeting of the cardiovascular expert group who will ensure that the intervention being developed is as evidence-based as possible, safe and compatible with principles of clinical care for people with AAA. Following this, the PPI group and service delivery group will meet jointly to help finalise the intervention.

4.2 STAGE 2 (Feasibility study of the developed intervention)

This is a prospective cohort study of individuals with an AAA using the intervention developed in Stage 1.

Following development of the cardiovascular-risk reduction intervention for patients with an AAA, we will commence a prospective cohort study in several NHS AAA screening and surveillance centres We will prospectively recruit consecutive individuals with an AAA from NHS sites and ask them to use the intervention over a period of six months.

5 STUDY SETTING

The study will recruit participants from the abdominal aortic aneurysm screening and surveillance programmes for both Stage 1 and Stage 2.

For Stage 1, they will be invited to a number of focus-groups and workshops, alongside experts in cardiovascular health care from England, to create a package which will address cardiovascular risk reduction in men who have an AAA.

For Stage 2, they will be invited to use the purpose-built cardiovascular risk-reduction programme to improve their heart health, taking part in a prospective cohort study.

All research activities will take place in England and the NHS (in existing NHS AAA screening and surveillance programmes).

6 PARTICIPANT ELIGIBILITY CRITERIA

Patients:

Adult men (>18 years of age) who have been identified to have an AAA through participation in the NHS screening programmes will be invited to take part in the relevant study workshops/focus-groups/interviews (for Stage 1) or use the purpose-built cardiovascular risk reduction programme (for Stage 2).

Stakeholders:

As far as expert participants are concerned, any adult stakeholder who is in some way involved in providing care for individuals with an AAA will be invited to take part. The pool of participants will be drawn from online resources of stakeholder groups and societies relevant to the care of individuals

with aneurysms (e.g. the Vascular Society of Great Britain and Ireland, Society for Vascular Nursing, the British Heart Foundation, the Circulation Foundation).

6.1 Inclusion criteria

PATIENTS in either Stage of the study:

Adult men with an abdominal aortic aneurysm (defined as maximal infrarenal aortic diameter above 3.0cm)detected via the existing NHS aneurysm screening programme, who are able to provide written informed consent.

Adult relatives or care givers of men with an abdominal aortic aneurysm, who are also able to provide written informed consent.

EXPERTS & STAKEHOLDERS in either Stage of the study:

Doctors, nurses and healthcare providers with experience in providing care for men with aneurysms, who are also able to provide written informed consent.

6. 2 Exclusion criteria

The following will not be able to take part in the study (either Stage 1 or Stage 2):
Individuals who cannot provide written informed consent.
Individuals who cannot speak/write in English.

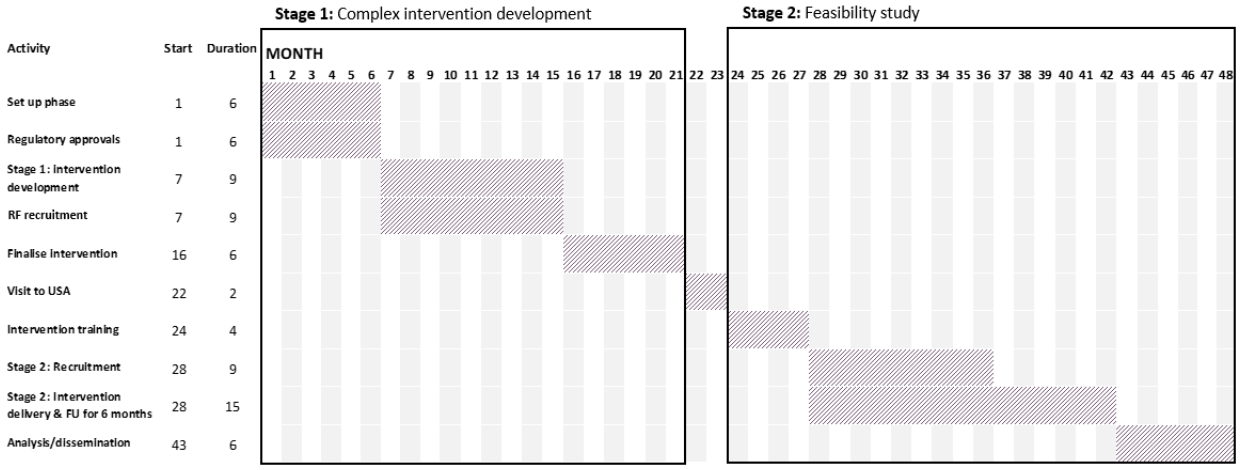
For stage 2 only: patient who are underweight or currently serving a custodial sentence

7 STUDY PROCEDURES

Schedule of procedures (Gantt chart)

After a six-month set-up period, **Stage 1** will commence, lasting for nine months and followed by a six-month analysis period used to finalise the intervention and four months to train the nurses in intervention-delivery.

A feasibility study will then commence (**Stage 2**) to test the fully-developed intervention. Recruitment will last nine months and follow-up another six months. Analysis and dissemination will last six months.



Schedule of procedures table for Stage 2 (feasibility study)

Procedures	**Visits (insert visit numbers as appropriate)**				
	Screening	**Baseline**	**Treatment Phase**		**Follow Up 6 months**
Invitation	Visit 1				
Informed consent		Visit 2			
Demographics		Visit 2			
Medical history		Visit 2			
Physical examination		Visit 2			
Vital signs		Visit 2			
Concomitant medications		Visit 2			
Quality of life assessment		Visit 2			
AAA size (ultrasound)		Visit 2			
Commencement of cardiovascular-risk intervention		Visit 2			
Nurse assessment		Visit 2	Visit 3	Visit 4	Visit 5
Adverse event assessments		Visit 2	Visit 3	Visit 4	Visit 5
Physician's Withdrawal Checklist					

7.1 Recruitment

Stage 1: At least ten (10) individuals with AAA in surveillance will take part in the service-development workshops (as outlined above). We aim to have at least 45 responses to the scaffolding questionnaire from each stakeholder group (patient groups and expert groups). Further, at least five (5) expert stakeholders involved in the care of patients with an AAA in screening and surveillance programmes will also be asked to take part in focus-groups and interviews, to refine and finalise the cardiovascular-risk reduction intervention.

Stage 2: At least thirty (30) individuals with an AAA in the AAA screening and surveillance programme will be recruited and they will be followed-up over a minimum of six months. This will allow us to assess the primary outcome of interest (feasibility and acceptability). Participants that consent will be interviewed to further explore the feasibility of the intervention.

Further, at least five (5) expert stakeholders will be recruited to take part in interviews to assess the acceptability and fidelity of the intervention delivery by healthcare-staff in the participating NHS AAA screening and surveillance programmes.

7.1.1 Participant identification, screening, and recruitment

Potential participants will be identified by reviewing the list of men in aneurysm surveillance within the local aneurysm screening programmes. This will be overseen by the CI who is a clinician (vascular surgeon) who provides clinical care for patients with aneurysm in Leicestershire and already has access to the Leicestershire aneurysm screening programme lists as an NHS care provider.

Potential participants will then be contacted during their surveillance appointment at the aneurysm screening programme and via mail correspondence. A Participant Information Sheet (PIS) will be given to the potential participants and they will have the chance to ask questions. A minimum period of one day will be given to the potential participants to consider taking part in the study prior to signing a written informed consent formed. Posters and leaflets will also be used at the aneurysm screening programme clinics and vascular imaging departments at NHS hospital sites.

The potential participants will all be under the care of a regional aneurysm screening programme

A list of men who have consented to be contacted about taking part in future research is already available in local aneurysm screening units. This consent for future contact is established at the time of screening for aneurysm in all men who attend for screening. These individuals will then be contacted by the CI and/or the study team and will be given a PIS, either in one of their clinic appointments (secondary care), when they attend their surveillance scan in the screening/surveillance programme (community), via post/email, or via telephone invitation. A minimum of one day (24 hours) will be given to the patients in order to consider their participation after they have received their PIS. They will be allowed as much time as they wish in order to consider taking part and they will be given ample time to discuss their queries regarding the study (in both Stage1 and Stage 2) with the CI and the study team at each study site.

For Stage 1, the potential participants will be asked to fill in the scaffolding questionnaire first and then attend (potentially) the focus groups and/or interviews in the future (once they have signed written informed consent).

For Stage 2, the participants will be given the intervention documents and leaflets which are relevant to their personalised risk factors and they will continue with their standard NHS care outside the CRISP study. Participation in the study will not alter their AAA screening and surveillance scans or attendance to any other NHS service. The intervention is based on existing NICE guidance (best medical and surgical therapy) and NHS principles.

The cardiovascular expert sample will be drawn from the CI and the research team via interrogating the following lists of potential participants: existing national research groups (NIHR and MRC websites), Public Health England (PHE) groups and committees (online lists), NIHR funding panels (online lists), personal contacts of the CI and research team from their clinical environment, NHS AAA screening committees (online lists), Society for Vascular Nursing committees (online lists), the Vascular Society of Great Britain and Ireland (online lists) and the British Heart Foundation (online lists). Potential participants will be invited to take part by the CI via a formal email which will include a letter invitation and an expert PIS. Furthermore, Professor M Bown (part of the research team), who is currently chair of the AAA Specialist Interest Research Group (part of the Vascular Society of Great Britain and Ireland), will invite those who sit on this committee to join the research. General Practitioners from primary care in the wider Midlands area will also be approached via email (as above) which will include the formal invitation letter and an expert PIS. Finally, academics with an interest in cardiovascular sciences and public health will be invited in an identical fashion from three institutions: University of Leicester, University of Birmingham, and King's College London.

7.1.2 Payments

Participants will not be paid for taking part in either Stage 1 or Stage 2 of this research. Travel costs will be reimbursed to those attending the qualitative workshops/focus-groups/interviews.

7.2 Consent

Informed consent will be obtained prior to the participant undergoing any activities that are specifically for the purposes of the study.

A discussion will take place between the potential participant or his/her legally acceptable representative and a member of the research team about the nature and objectives of the study and possible risks associated with their participation.

All participants will have the opportunity to ask questions regarding takin part and withdrawing from this research.

A Patient Information Sheet (PIS) which has been approved by a REC will be given to all potential participants.

An assessment of capacity will take place prior to obtaining written informed consent. For consent to be ethical and valid in law, participants must be capable of giving consent for themselves. A capable person has to:

- understand the purpose and nature of the research
- understand what the research involves, its benefits (or lack of benefits), risks and burdens
- understand the alternatives to taking part
- be able to retain the information long enough to make an effective decision.
- be able to make a free choice
- be capable of making this particular decision at the time it needs to be made (though their capacity may fluctuate, and they may be capable of making some decisions but not others depending on their complexity)
- where participants are capable of consenting for themselves but are particularly susceptible to coercion, it is important to explain how their interests will be protected

The participant must personally sign and date the latest approved version of the informed consent form before any study specific procedures are performed.

Written and verbal versions of the participant information and Informed consent will be presented to the participants detailing no less than: the exact nature of the study; the implications and constraints of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal.

The participant will be allowed as much time as wished to consider the information, though no less than 24 hours, and the opportunity to question the Investigator, their GP or other independent parties to decide whether they will participate in the study. Written Informed Consent will then be obtained by means of participant dated signature and dated signature of the person who presented and obtained the informed consent. The person who obtained the consent must be suitably qualified and experienced, and have been authorised to do so by the Chief/Principal Investigator as detailed on the Delegation of Authority and Signature log for the study. The original signed form will be retained at the study site within the Investigator Site File (ISF). A copy of the signed Informed Consent will be given to participants and a copy retained in the participant medical notes.

All informed consent processes will follow the HRA guidance available at:
http://www.hra.nhs.uk/resources/before-you-apply/consent-and-participation/consent-and-participant-information/

Informed consent will be checked at all visits.

We will allow participants at least 24 hours to consider their participation in the research and ask questions, once a PIS has been given to them. The original written informed consent forms will be kept safely in a study master file at Glenfield Hospital, University Hospitals of Leicester NHS Trust, Groby Road, LE39QP.

7.3 Baseline data

Stage 1: For the focus-groups and intervention development sessions (qualitative research) we will record the age and size of AAA for patients taking part and the profession of expert stakeholders taking part.

Stage 2: For patients taking part in the prospective cohort study we will record their baseline data (anonymised) based on the "Study Assessments" schedule below (7.4).

7.4 Study Assessments for Stage 2

Each participant in Stage 2 (feasibility study) will be assigned an anonymised participant identification study number once signing a consent form. The following are to be recorded at baseline (day of written informed consent). Demographic information (age and sex/gender)

- Medical and surgical history
- Smoking history, including e-cigarettes/vaping
- Alcohol intake
- Weight
- Height
- Blood pressure
- Full blood count
- Routine biochemistry including lipid profile
- List of medications
- Quality-of-life using the EQ5D5L tool.

7.5 Follow-up assessments for Stage 2

All participants will be followed-up for a minimum of six months. We will record the following information every time they come into contact with the NHS AAA screening and surveillance service and also at six months (final follow-up appointment):

- Medical and surgical history, change since consent
- Change in smoking history, including e-cigarettes/vaping
- Change in alcohol intake
- How many components of the intervention they have received
- Date(s) of last appointment with the NHS AAA screening and surveillance service(s).

7.6 Qualitative and fidelity assessments for Stage 2

Semi-structured interviews will be conducted with patients receiving the intervention who consent to interview and with all intervention-provider staff. Topic guides will be developed and piloted/refined across the first few interviews. Interview content will explore participants' and providers' experiences of receiving and delivering the intervention, including barriers to engagement or delivery, acceptability and ideas for improving the intervention. Both patient and healthcare professional interviews will stop when data saturation is reached, which maybe before all participants and healthcare professionals have been interviewed.

All intervention sessions will be audio-recorded and the audio files will be scored independently by the intervention design-team and the person who delivered the intervention, using an intervention fidelity (IF) checklist to assess quality of intervention delivery and the presence or absence of intervention components. The checklist will use a Dreyfus competence-rating scale(20). This method has been used successfully to identify areas of good practice and ideas for intervention refinement in several prior projects including three large-scale NIHR-funded trials.

7.7 Withdrawal criteria

Any participant is free to withdraw from the study at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal. We will no longer contact the participant, but may with the participant's permission retain and use information provided previously, obtain and use information from the participant's health records or interview them about their study experience.

7.8 Assessment and management of risk

This study does not impact on routine NHS care and follows existing NICE guidance for all aspects of care provided to patients. This study will not use any investigational medicinal products. We therefore do not expect patients to come to harm.

7.9 End of study (Stage 2)

The end of the study is defined as when the last participant has attended their sixth month (final) follow-up assessment.

8. SAMPLES

No clinical samples will be obtained as part of this research outside usual NHS care.

9. Recording and reporting of SAEs

9.1 Definitions

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a patient or clinical investigation participants, which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the the study, whether or not considered related to the study.

Adverse Reaction (AR)	An untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant. The phrase "response to an investigational medicinal product" means that a causal relationship between a trial medication and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out. All cases judged by either the reporting medically qualified professional or the Sponsor as having a reasonable suspected causal relationship to the trial medication qualify as adverse reactions. It is important to note that this is entirely separate to the known side effects listed in the SmPC. It is specifically a temporal relationship between taking the drug, the half-life, and the time of the event or any valid alternative etiology that would explain the event.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences. NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.
Serious Adverse Reaction (SAR)	An adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to one of the trial treatments, based on the information provided.
Expected Serious Adverse Events/Reactions	This study does not impact on routine NHS care and follows existing NICE guidance for all aspects of care provided to patients. This study will not use any investigational medicinal products. We therefore do not expect patients to come to harm.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	A serious adverse reaction, the nature and severity of which is not consistent with the information about the medicinal product in question set out in the reference safety information: • in the case of a product with a marketing authorisation, this could be in the summary of product characteristics (SmPC) for that product, so long as it is being used within it's licence. If it is being used off label an assessment of the SmPCs suitability will need to be undertaken. • in the case of any other investigational medicinal product, in the investigator's brochure (IB) relating to the trial in question

9.2 Reporting procedures for All Adverse Events

All AEs occurring during the study observed by the investigator or reported by the participant, whether or not attributed to study, will be recorded on the CRF.

The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to study, other suspect device and action taken. Follow-up information should be provided as necessary.

AEs considered related to the study as judged by a medically qualified investigator or the sponsor will be followed until resolution or the event is considered stable. All related AEs that result in a participant's withdrawal from the study or are present at the end of the study, should be followed up until a satisfactory resolution occurs.

It will be left to the investigator's clinical judgment whether or not an AE is of sufficient severity to require the participant's removal from treatment. A participant may also voluntarily withdraw from treatment due to what he or she perceives as an intolerable AE. If either of these occurs, the participant must undergo an end of study assessment and be given appropriate care under medical supervision until symptoms cease or the condition becomes stable.

The severity of events will be assessed on the following scale: 1 = mild, 2 = moderate, 3 = severe.

The relationship of AEs to the study will be assessed by a medically qualified investigator.

9.3 Reporting Procedures for Serious Adverse Events

All SAEs occurring from the time of written informed consent until the end of the study must be reported to the Sponsor immediately and within 24 hours of becoming aware of the event. The SAE will be reported using appropriate forms and according to the Sponsor SOP for reporting serious adverse events. Additional information will be provided if requested to the Sponsor and main Research Ethics Committee (REC). The Principal Investigator or another delegated physician (as agreed by the Sponsor) is responsible for the review and sign off of the SAE and the assessment of causality (i.e. whether an event is related to a study procedure or intervention).

The Sponsor will perform an initial check of the information and ensure that the SAE line listing is reviewed by the Director of Research & Innovation. All SAE information must be recorded on an SAE form and sent to the Sponsor. Additional information received for a case (follow-up or corrections to the original case) needs to be detailed on a new SAE form and sent to the Sponsor.

Copies of all documentation and correspondence relating to SAEs will be stored in the TMF and / or ISF.

The Sponsor will report all SUSARs to the Research Ethics Committee concerned. Fatal or life-threatening SUSARs must be reported within 7 days and all other SUSARs within 15 days. The CI will inform all investigators concerned of relevant information about SUSARs that could adversely affect the safety of participants.

In addition to the expedited reporting above, the CI shall submit once a year throughout the study or on request an Annual Report to the Ethics Committee which lists all SAEs / SUSARs that have occurred during the preceding 12 months.

9.4 Responsibilities

All individual SAEs, AEs, ARs and trends in events and reactions will be independently reviewed in addition to usual study safety monitoring procedures by the SSG, which will convene at least every 3 months.

9.5 Reporting urgent safety measures

If any urgent safety measures are taken the CI/Sponsor shall immediately and in any event no later than 3 days from the date the measures are taken, give written notice to the Sponsor and the relevant REC of the measures taken and the circumstances giving rise to those measures.

10 STATISTICS AND DATA ANALYSIS

10.1 Sample size calculation

A total of at least 10 patients will be taking part in the **Stage 1** development focus-groups alongside a minimum of 10 experts / stakeholders, to allow a sufficient sample for qualitative analysis and development of the intervention.

For Stage 2, assuming that 30% of invitees will be recruited and in order to estimate the recruitment rate with a precision of +/- 8%, 30 participants will have to be recruited. Assuming a dropout rate of 25% and having recruited 30 individuals, the precision of the estimated retention rate during six months would be +/- 14%. This will also provide an ample sample size to draw on for qualitative interviewing. The decision to proceed to a definitive multicentre trial will be made on the basis of acceptable rates and time for recruitment and retention, as well as participant satisfaction. Detailed progression criteria will be drawn up in collaboration with an independently chaired Study Steering Committee upon completion of recruitment and follow-up.

10.2 Statistical analysis plan

Recruitment, retention, measures-completion rates and participant satisfaction scores will be reported using descriptive statistics with 95% confidence intervals. Qualitative data will be transcribed verbatim and analysed. Intervention fidelity scores will be presented as mean scores and ranges for each intervention component and also broken down by facilitator to examine variation between provider staff. During fidelity scoring, examples of good practice will be extracted to use in training intervention providers for the main trial.

11. DATA MANAGEMENT

11.1 Data handling and record keeping

All study data will be entered on a REDCap based data collection form, created specifically for the study by the National Institute for Health Research Leicester Biomedical Research Centre Bioinformatics Hub staff. As per ICH GCP (Section 5.5), all electronic data entry systems are validated and Standard Operating Procedures are maintained by the National Institute for Health Research Leicester Biomedical Research Centre.

The participants will be identified by a study specific participant number and/or code in any database. The patient's name and any other identifying detail will NOT be included in any study data electronic file. No identifiable information will be shared between study sites at any point. Consent forms (signed) will be kept in study-specific site files at the NHS institutions taking part in this research in a locked safe NHS office as per standard Good Clinical Practice guidance and NHS policies.

Voice recordings will be transferred to the University of Leicester servers securely. Once transferred, recordings will be deleted from the voice recorder. The voice recorder will be stored securely in a locked cabinet within a locked room with limited access to the CI. Participant ID will be stated at the beginning of the recording. Transcribing will be conducted either by the CI or a transcribing company who will have a confidentiality agreement in place.

11.2 Access to Data

Direct access will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections- in line with participant consent.

11.3 Archiving

Research data will stored for 6 years and storage will comply with the University of Leicester archiving Standard Operating Procedure. Details can be found at: http://www2.le.ac.uk/offices/ias.

12. MONITORING, AUDIT & INSPECTION

Direct access will be granted to authorised representatives from the Sponsor and host institutions for monitoring and/or audit of the study to ensure compliance with regulations. Sponsor operates a risk based monitoring programme with this study will be subject to.

13. ETHICAL AND REGULATORY CONSIDERATIONS

13.1 Research Ethics Committee (REC) review & reports

Once the initial sponsor review process is complete and a sponsor reference number has been allocated, and all requested documentation has been received and checked, authorisation from the University of Leicester's Research Governance Office will be issued to book further review of the proposed research. The University of Leicester's Ethics Committee or NHS Research Ethics Committee and the Health Research Authority will then review the proposal. Agreement in principle is subject to the research receiving all relevant regulatory permissions. Submission for regulatory approvals will be submitted via Integrated Research Application System (IRAS). The Chief Investigator will ensure that all regulatory approvals, confirmation of capacity and capability from NHS sites and sponsor greenlight are in place before participants are approached.

For any required amendment to the study, the Chief Investigator, in agreement with the sponsor will submit information to the appropriate body in order for them to issue approval for the amendment. Amendments will be implemented upon receiving Sponsor Green Light.

The Research Governance Office's Standard operational procedures will be followed for the duration of the trial.

Amendments will be submitted to the sponsor in the first instance for review and approval.

Annual progress reports will be submitted to the Ethics Committee annually on the anniversary date of when favourable opinion is given by the Chief Investigator.

The Chief Investigator will notify the REC when the study has ended by completing the end of study notification form and will submit a final report of the results within one year after notifying REC.

A study master file will be maintained for the duration of the study and will be stored for 6 years after the study has ended. The only time this could be exceeded, is if samples are being retained beyond the scope

of the original study i.e. there is consent for future research. In this circumstance ICFs would have to be retained for as long as the samples are in existence, as we have a legal requirement to prove the samples were obtained with consent.

13.2 Peer review

This study has been externally and internally peer-reviewed, including a thorough review from an NIHR funding committee.

13.3 Public and Patient Involvement

Identifying the research question, aims and objectives

Since 2015 we have led the research component of an annual education forum for individuals with Abdominal Aortic Aneurysm (AAA), their families and carers. Fifty individuals have attended these events on average. Vascular nurse specialists and NHS AAA Screening Programme staff (the key stakeholders in this clinical area), also took part. During these events we discussed areas for improvement in the clinical management of AAA. The dominant themes identified by those with AAA were fear of losing independence, mobility and the ability to meet caring responsibilities. Individuals with AAAs and their carers identified that these concerns predominantly related to the risk of heart attacks and strokes, rather than the risk of AAA rupture per se. Using a structured survey at the 2018 event, we identified that the majority of individuals were in favour of formal cardiovascular-risk modification being included as part of their AAA surveillance. A common theme amongst them was that that they highly value regular contact with a small team of healthcare professionals who are committed to improving their health. They unanimously identified that their relationships with the AAA surveillance team are strong, with high levels of engagement and trust, hence AAA surveillance would be a good platform upon which to build general health improvement.

Developing the research proposal

After identifying the research aims and objectives in the PPI fora, we convened two PPI focus-groups attended by 56 individuals with AAA, families and carers to develop the proposal. This was supported by the BRC's PPI facilitator and existing PPI links with ethnic and religious community leaders. Prior to this, potential barriers and enablers to lifestyle change or engagement with cardiovascular risk factor management were identified in a systematic review. These were discussed in the focus-groups, alongside possible intervention features (e.g. including an online component was not a popular option). This process led to the identification of the three core elements of the complex intervention which will be finalised during the first stage of the research. This also informed the structure and duration the proposed feasibility study.

Patients and the public will be actively involved in developing/co-creating the complex intervention (stage 1), managing the research (stages 1 and 2), and dissemination.

Individuals with AAA in surveillance will be invited to take part in stage 1 research activities ("co-creation"); an independent PPI advisory group of 8-10 individuals with AAA (identified from our AAA-specific PPI groups and AAA education events) will convene regularly and, alongside two lay members of the research team, will support intervention development, research delivery, management and dissemination.

1) Co-creation with PPI to finalise the core elements of the intervention.

i. Our PPI advisory group will take part in a series of service-development workshops. The workshops will be semi-structured and will systematically explore the duration, frequency and content of the core elements, identify further barriers to, and enablers of each of the intervention targets.

ii. Following similar interactions with service providers (especially NHS AAA Screening Programme staff), the findings will be synthesised and taken back to our PPI advisory group, who will review all intervention procedures to reach consensus and finalise the intervention.

2) Management and dissemination.

Two lay research team members will support research delivery, by participating in study management meetings, providing feedback on recruitment documents and data collection tools, discussing interpretation of findings, and acting as co-authors on publications. Study updates and lay summaries upon completion will be prepared with the help of these two team members prior to lay dissemination online (through social media, study webpage, NIHR Leicester BRC online resources) and via traditional routes (patient leaflets, posters, NIHR resources).

PPI training

The advisory PPI group will be trained in principles of intervention development and understanding research data. This will be undertaken as an initial one-hour training and subsequent ad-hoc sessions (as part of the advisory group meetings) by the research team (Professor Greaves, the research fellow and I). Furthermore, we will deliver lay lectures to the ten participants of the PPI workshop and the advisory PPI group, relating to AAA diagnosis, management, treatment options and current NHS care strategies.

13.4 Regulatory Compliance

The study will not commence until Favourable REC opinion and until all relevant regulatory approvals are in place. Before any site can enrol patients into the study, the Chief Investigator/Principal Investigator or designee will ensure that appropriate approvals from participating organisations are in place. For any amendment to the study, the Chief Investigator or designee, in agreement with the sponsor will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments at NHS sites as well as the study delivery team) so they can put the necessary arrangements in place to implement the amendment to confirm their support for the study as amended.

13.5 Protocol compliance

If a protocol breach occurs, then the CI will document this in adherence to the University's Standard Operational Procedure SOP Identifying and Reporting Deviations and Serious Breaches of GCP and/or the Protocol for Trials. The CI will seek advice from the research supervisors and the sponsor.

13.6 Data protection and patient confidentiality

All information collected in the study will be kept strictly confidential.

The Chief Investigator will have access to the study documentation and will be the data custodian.

The investigator will comply with the requirements of the General Data Protection Regulation (and other applicable regulations) with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

Analysis of the generated will be undertaken by the chief investigator on University of Leicester premises. All collected data and electronic confidential information will be saved on a secure drive at the University of Leicester. Any printed confidential material will be kept in a folder in a locked drawer in a secured room in a secure office environment office at the University of Leicester.

Anonymised research data will be stored for six years after the study has ended, unless there is explicit consent for the data to be retained beyond the scope of the original research project, then it should be defined how long the data would be retained for i.e. indefinitely, or for as long as the samples are to be retained. If the study is a data only study, then the duration of the data retention timelines should be made clear in the PIS and ICF. Long-term storing will comply with the University of Leicester archiving Standard Operating Procedure. Details can be found at: http://www2.le.ac.uk/offices/ias.

13.7 Financial

This research is funded in whole by the National Institute for Health Research.

13.8 Indemnity

The University of Leicester insurance applies for this study.

13.9 Post trial care

Not applicable.

13.10 Access to the final trial dataset

The Chief Investigator will have access to the full dataset.

Direct access will be granted to authorised representatives from the Sponsor and host institutions for monitoring and/or audit of the study to ensure compliance with regulations.

14. DISSEMINATION POLICY

The data arising from the study will be owned by the University of Leicester (Sponsor).

On completion of the study, the data will be analysed and tabulated and a Final Study Report will be prepared as per Sponsor SOPs and HTA guidance.

A full study report will be submitted to the NIHR and will be available online on the relevant NIHR website. A full study report will also be submitted to the NAAASP and the Sponsor; it will be available on NAAASP and University of Leicester websites.

As per NIHR policy (funder) the data will be open access and so will any resulting publications.

Funding by the NIHR will be acknowledged within the publications.

The participants will receive lay summaries relating to the outcome of the study via a newsletter (mail).

The study protocol, full study report, anonymised participant level dataset, and statistical code for generating the results will be made publicly on the NIHR website.

To ensure appropriate dissemination, the scientific community will receive regular updates; the CI will personally attend the Vascular Society of Great Britain and Ireland (VSGBI), European Society of Vascular Surgery (ESVS) and NHS AAA Screening Programme (NAAASP) meetings annually to provide a progress synopsis. Public Health England (PHE) will receive a report upon completion of each research stage. A study website will be maintained, including three-monthly updates in the form of an online blog (lay and expert language). All updates will be linked to study-specific social media feeds managed by the NIHR Leicester BRC. The findings of the study, once completed, will be submitted for publication in a medical journal with broad international readership across disciplines. Wherever possible, data will be published in open-access format. Anonymised open data will be shared on appropriate platforms (ClinicalStudyDataRequest and "Supporting Open-Access for Researchers" initiative).

14.1 Authorship eligibility guidelines and any intended use of professional writers

No professional writers will be used. The criteria for individually named authors or group authorship will follow the guidance of The International Committee of Medical Journal Editors.

Authorship will based on the following criteria:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

15. REFERENCES

1. Glover MJ, Kim LG, Sweeting MJ, Thompson SG, Buxton MJ. Cost-effectiveness of the National Health Service Abdominal Aortic Aneurysm Screening Programme in England. The British journal of surgery. 2014;101(8):976-82.

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16. Appendix 1 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1	1.1	18/10/2021	Mr Athanasios Saratzis Dr Tom Withers	Addition of details for Stage 2 of the research.
2	1.2	17/03/2021	Professor Matt Bown Dr Tom Withers Mrs Ann Elsworth	Amendment to CI, removal of Warwickshire for Stage 2 and inclusion of more sites
3	1.3	13/09/2022	Mr Athanasios Saratzis Dr Tom Withers Mrs Ann Elsworth	Minor amendments to patient follow up details for Stage 2, study steering group
4	1.4	11/01/2023	Mr Athanasios Saratzis Dr Tom Withers Mrs Ann Elsworth	Amendment to increase patient numbers to be interviewed for stage 2

11. APPENDICES

11.1 Appendix 1- Required documentation

- Curriculum vitae (CV) or research team members
- Participant Information Sheets (PISs) for both lay and expert participants
- Consent Forms (CFs) for both lay and expert participants on headed sheet
- Scaffold Questionnaire