



**Title: Digital and remote 'health check' screening for cardiovascular disease in a workplace setting; a cohort study.**

Short title: ACHIEVE study (Assessment of Cardiovascular Health – Individual EValuative Exercise)

**RESEARCH PROTOCOL SUMMARY**

|                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>TITLE:</b>               | <b>Title: Digital and remote 'health check' screening for cardiovascular disease in a workplace setting; a cohort study.</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>Short title:</b>         | ACHIEVE study                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| <b>IRAS number</b>          | 360452                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| <b>Study design</b>         | Cohort study                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <b>Primary objective</b>    | Any change observed in cardiovascular health parameters, as measured with QRISK3 score, between baseline and 12 months follow-up PocDoc Healthy Heart Check tests.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <b>Secondary objectives</b> | <p>% of original baseline volunteers consenting to be participant in the ACHIEVE study, and % participants who will complete and report on the PocDoc Healthy Heart Check test.</p> <p>- Comparison of number of participants in three main QRISK3 categories at baseline and at 12-month follow-up (Low risk – QRISK3 score of less than 10%; Moderate risk – QRISK3 of 10-20%; High risk – QRISK3 score of more than 20%)</p> <p>-Any change observed in blood lipid and cholesterol markers, as outlined in Table 4 (including total cholesterol, HDL, non-HDL, total cholesterol : HDL ratio, total cholesterol : high density lipids ratio, total glycerides, LDL, between baseline and 12 months follow-up PocDoc Healthy Heart Check tests.</p> <p>-Number of significant (QRISK3 10% or higher) GP notifications indicated at baseline and 12 months follow-up PocDoc Healthy Heart Check tests respectively.</p> <p>-Review of Health Check Outcomes, ie an audit of what happened on the back of any significant findings when participants did the health check 12 months ago. Any actions and/or activities within 4 months of conducting that baseline PocDoc Healthy Heart test.</p> |

|                                           | <p>% participants who contacted and attended a GP consultation as a result.</p> <p>% GPs who contacted the participant, and invited them for a consultation (plus eventual attendance rate by participants).</p> <p>% participants where GP practice repeated blood lipid / cholesterol profile.</p> <p>% participants offered lipid modifying medication, ie statins, appropriately (plus eventual acceptance rate by participants).</p> <p>% participants investigated for high blood pressure and offered antihypertensives appropriately (plus eventual acceptance rate by participants).</p> <p>% participants offered weight loss advice or referral appropriately (eg NHS Digital Weight Management Programme for BMI ≥ 30).</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |               |                  |                 |       |                 |             |             |      |     |            |             |             |      |     |      |
|-------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------|------------------|-----------------|-------|-----------------|-------------|-------------|------|-----|------------|-------------|-------------|------|-----|------|
| <b>Inclusion &amp; Exclusion criteria</b> | <p>Inclusion criteria:</p> <ul style="list-style-type: none"><li>- Adults aged 25 – 80 years</li><li>- Participants in original workplace ‘baseline’ cardiovascular health check.</li><li>- Currently still employed by one of the original employers involved in the original cardiovascular health check initiative.</li><li>- Currently not absent from work long-term due to illness or for other reason (eg maternal leave, sabbatical; unless employee has explicitly indicated to employer that they can be contacted for non-work related reasons).</li></ul> <p>Exclusion criteria:</p> <ul style="list-style-type: none"><li>- No access to phone/tablet/computer to use the PocDoc App</li><li>- Any reasons for the person being unable to follow the protocol, including lack of mental capacity to consent to taking part in the study (examples include dementia, patient housebound, severe learning disability).</li><li>- The patient has concurrent (medical) conditions that in the opinion of the investigator may compromise patient safety or study objectives (examples include receiving palliative care, medical condition that contraindicates giving routine blood samples)</li></ul> |               |                  |                 |       |                 |             |             |      |     |            |             |             |      |     |      |
| <b>Sample size</b>                        | <p>The minimum number of participants for which baseline and 18-month data need to be collected is: <b>824</b>. To make the study more powerful, ideally as many as 2774 complete datasets are required. The following was applied for a priori sample size calculations: Wilcoxon test for paired samples.</p> <p>The sample size calculation is based on being able to detect a significant change in QRISK3 score, be it an increase or decrease in the average score over time within the cohort. From the baseline exercise information is known about the average QRISK3 score in the cohort for which the score was calculated. In our cohort, baseline average and its standard deviation (SD) for the QRISK3 score was 2.8% (SD 4.0).</p> <p><i>Table 6, Sample size calculation based on measured baseline average QRISK score and hypothetical change 12 months later.</i></p> <table><tr><th>Baseline (SD)</th><th>12-month FU (SD)</th><th>P-value</th><th>Power</th><th>Sample size (n)</th></tr><tr><td>2.8% (4.0%)</td><td>2.4% (4.0%)</td><td>0.05</td><td>80%</td><td><b>824</b></td></tr><tr><td>2.8% (4.0%)</td><td>2.5% (4.0%)</td><td>0.05</td><td>80%</td><td>1464</td></tr></table>       | Baseline (SD) | 12-month FU (SD) | P-value         | Power | Sample size (n) | 2.8% (4.0%) | 2.4% (4.0%) | 0.05 | 80% | <b>824</b> | 2.8% (4.0%) | 2.5% (4.0%) | 0.05 | 80% | 1464 |
| Baseline (SD)                             | 12-month FU (SD)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | P-value       | Power            | Sample size (n) |       |                 |             |             |      |     |            |             |             |      |     |      |
| 2.8% (4.0%)                               | 2.4% (4.0%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0.05          | 80%              | <b>824</b>      |       |                 |             |             |      |     |            |             |             |      |     |      |
| 2.8% (4.0%)                               | 2.5% (4.0%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0.05          | 80%              | 1464            |       |                 |             |             |      |     |            |             |             |      |     |      |

|                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |             |      |     |      |
|----------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|------|-----|------|
|                                                                | 2.8% (4.0%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 2.4% (4.0%) | 0.01 | 90% | 1562 |
|                                                                | 2.8% (4.0%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 2.5% (4.0%) | 0.01 | 90% | 2774 |
| <b>Chief Investigator</b>                                      | Dr Stacey Fisher, Research GP, North Cumbria Integrated Care NHS Foundation Trust, <a href="mailto:stacey.fisher@ncic.nhs.uk">stacey.fisher@ncic.nhs.uk</a>                                                                                                                                                                                                                                                                                                                                                                                                                           |             |      |     |      |
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| <b>Sponsor and organisation where research will take place</b> | <p>Sponsor: North Cumbria Integrated Care NHS Foundation Trust, R&amp;D department, Cumberland Infirmary, Carlisle, CA2 7HY</p> <p>Location of research: Cumbria Health, and 15 GP practices in North Cumbria (see Table 2 for list).</p>                                                                                                                                                                                                                                                                                                                                             |             |      |     |      |
| <b>Planned timeline</b>                                        | <p>Study start date: 1 Dec 2025</p> <p>Patient Recruitment start date: 1 Jan 2026</p> <p>Recruitment end date (last patient, consent/screen visit): 30 Nov 2026</p> <p>Follow-up end date (last patient, last outcome data): 31 Dec 2026</p> <p>Study end date: 27 Feb2027</p>                                                                                                                                                                                                                                                                                                        |             |      |     |      |
| <b>Protocol version, date</b>                                  | Version 2.1, dd 13August 2026                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |             |      |     |      |

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## Lay Summary

"Prevention is better than cure" is an old saying which continues to apply today. For this purpose, the National Health Service (NHS) introduced the NHS Health Check for patients aged 40-74 back in 2009. The intention is to detect any health conditions early, like high blood pressure or high cholesterol, to then tackle them with lifestyle advice and medication. In recent years initiatives have looked at improving patient attendance rates and reduce costs, both of which are an issue in the NHS. One example, proven to be successful outside the UK, is to introduce a Health Check in the workplace. To make the health check process more cost effective and quicker, others have looked at an at-home rather than in-person check-up.

There is a lack in evidence concerning the effectiveness of a digital, remote approach of people / patients conducting health checks via the workplace route. If participation rates are high, and appropriate follow-up of cases - where (medical) intervention is indicated - takes place, then this could potentially be an alternative to the traditional in-person NHS Health Check. This present ACHIEVE study looks to recruit from a cohort of 4,500 people who, as employees, had a health check-up in a remote and digital manner using a point-of-care test to measure their heart health. By repeating the health check process a year later, the impact of the initial scheme can be determined. The PocDoc Healthy Heart check that is used gives information on blood lipids/cholesterol and the risk of heart attack and stroke. The safety of how any initial significant baseline findings was acted on a year ago during testing (for example, if someone was found to have really high cholesterol levels) will also be evaluated.

## 1 BACKGROUND AND RATIONALE

In the UK, the NHS introduced the NHS Health Check for patients aged 40-74 back in 2009. Initiatives akin to the NHS Health Check have been appraised as early as the 1990s (Wood et al, 1994). The programme has managed to identify many high risk patients and has contributed to a reduction in early deaths (Debiec et al, 2023; Robson et al, 2016). However, there is a debate regarding its cost effectiveness and whether sufficient patients take up the opportunity to attend for a health check (Patel et al, 2020; Martin et al, 2018).

In more recent years initiatives have looked at improving attendance rates. One successful example is to introduce the NHS Health Check, or equivalent type of health screening, in the workplace (Summerton, 2015; Kwak et al, 2009). This is already commonplace in some other countries, notably South Korea. To make the health check process more cost effective, others have looked at remote rather than in-person check-ups and also by utilising point-of-care testing rather than use of a central laboratory for processing and analysing samples. The latter has been proven to be more economical (El-Osta et al, 2017; Jain et al, 2011).

There is paucity in evidence concerning the effectiveness of a digital, remote, point-of-care approach of conducting health checks in people via the workplace route. If participation rates are high, and appropriate follow-up of cases - where (medicinal) intervention is indicated - takes place then this could potentially be a genuine alternative to the traditional in-person NHS Health Check. This study looks to follow-up a cohort of people who as employees had a health check-up in a remote and digital manner using a point-of-care test to measure their lipid profile. For this they used the PocDoc Healthy Heart Check point-of-care test kit, which can be conducted by the patient / subject themselves (Roest et al, 2024). The PocDoc kit also measures the QRISK3 score, which gives an indication of the risk of heart attack or stroke in the next decade in an individual (Hippisley-Cox et al, 2017). At the baseline exercise, a subset of volunteers also measured their own blood pressure (BP), but this was done initially in the workplace and then follow-up with continuous BP monitoring for one week; this is not considered for this present ACHIEVE study due to the logistical implications. By repeating the process ~12 months later, the effectiveness of the initial scheme can be determined. The impact of any initial baseline findings will also be evaluated by auditing participants' GP medical records; this will determine if any findings were acted upon (appropriately).

## 2 OBJECTIVES

### 2.1 PRIMARY OBJECTIVE AND OUTCOME MEASURES

- Any change observed in cardiovascular health parameters, as measured with QRISK3 score, between baseline and 12 months follow-up PocDoc Healthy Heart Check tests.

### 2.2 SECONDARY OBJECTIVES AND OUTCOME MEASURES

- % of original baseline volunteers consenting to be participant in the ACHIEVE study, and % participants who will complete and report on the PocDoc Healthy Heart Check test.

- Comparison of number of participants in three main QRISK3 categories at baseline and at 12-month follow-up (Low risk – QRISK3 score of less than 10%; Moderate risk – QRISK3 of 10-20%; High risk – QRISK3 score of more than 20%)
- Any change observed in blood lipid and cholesterol markers, as outlined in Table 4 (including total cholesterol, HDL, non-HDL, total cholesterol : HDL ratio, total cholesterol : high density lipids ratio, total glycerides, LDL, between baseline and 12 months follow-up PocDoc Healthy Heart Check tests.
- Number of GP notifications indicated at baseline and 12 months follow-up PocDoc Healthy Heart Check tests respectively.
- Review of Health Check Outcomes, ie an audit of what happened on the back of any significant findings when participants did the health check 12 months ago. Any actions and/or activities within 4 months of conducting that baseline PocDoc Healthy Heart test.
  - % participants who contacted and attended a GP consultation as a result.
  - % GPs who contacted the participant, and invited them for a consultation (plus eventual attendance rate by participants)
  - % participants where GP practice repeated blood lipid / cholesterol profile.
  - % participants offered lipid modifying medication, ie statins, appropriately (plus eventual acceptance rate by participants)
  - % participants investigated for high blood pressure and offered antihypertensives appropriately (plus eventual acceptance rate by participants)
  - % participants offered weight loss advice or referral appropriately (eg NHS Digital Weight Management Programme for BMI  $\geq$  30)

### 3 INVESTIGATIONAL PLAN

#### 3.1 TRIAL DESIGN AND TIMELINE

Cohort study; Table 1 shows the anticipated timeline for the study.

*Table 1, Anticipated study timeline*

| Month           | Setup                      | Cohort                 | Analysis                   |
|-----------------|----------------------------|------------------------|----------------------------|
| <b>Nov 2025</b> | Submission to NRES and HRA |                        |                            |
| <b>Dec 2025</b> | HRA and Trust approval     |                        |                            |
| <b>Jan 2026</b> |                            | Start recruitment      |                            |
| <b>Nov 2026</b> |                            | Finish all recruitment |                            |
| <b>Dec 2026</b> |                            | Last research activity |                            |
| <b>Feb 2027</b> |                            |                        | Finalise analysis & report |

## 4 PARTICIPANTS

### 4.1 TRIAL PARTICIPANTS & LOCATIONS

Patients will be recruited from an existing cohort of people who previously undertook a workplace-based PocDoc Healthy Heart Check. This happened in and around late 2024 to early 2025. At the time, a number of organisations / companies consented for the employees to be approached to do the health screening exercise. We intend to re-approach those employers, to them to consent for us to re-approach those employees who took part previously. We will ask the employers to distribute an Invite Letter / email, which contains instructions on how to express an interest in participating, so that those who wish to take part in the ACHIEVE study can inform the study team of this. Therefore, the potential participant will be approached initially by their employer; this avoids the ACHIEVE study team trying to access potential participants directly. Furthermore, Pocdoc App users previously signed a privacy policy terms & conditions with PocDoc. This allows PocDoc to send notifications to users (see Appendix 1); however, this is only to individuals who have given explicit consent to be contacted for PocDoc news and announcements. The researchers will obtain digital informed consent from the participants using MS Forms, and will countersign a copy of the completed informed consent form and return a copy to the participant (along with the PocDoc Healthy Heart Check kit). The participant can do the test themselves at their own home.

As outlined in the Participant Information Sheet and Appendix 1 of this Protocol, the aim is to complete a 'Review of Health Check Outcomes', ie an audit of what happened on the back of any significant findings when participants did the health check ~12 months ago. The ACHIEVE team will check if appropriate actions were taken as a result of the significant findings (in the 4 months after the GP was made aware of the test result). This will be done for participants who are registered with one of the 15 GP practices listed below in Table 2. The Chief Investigator and research delivery team already have a Honorary Contract or letter of Access to work in said GP practices (see Appendix 2).

*Table 2, List of participating GP practices*

| ODS<br>CODE | name                            | POSTCODE | patient list (Jan2023) |
|-------------|---------------------------------|----------|------------------------|
| A82016      | Carlisle Healthcare             | CA1 3UB  | 37516                  |
| A82047      | James Street Group Practice     | CA14 2DL | 32999                  |
| A82044      | Fellview Healthcare             | CA28 7QE | 24021                  |
| A82020      | Eden Medical Group              | CA2 7AJ  | 16330                  |
| A82041      | Lowther Medical Centre          | CA28 7RG | 14343                  |
| A82045      | Wigton Group Medical Practice   | CA7 9QD  | 8980                   |
| A82654      | Warwick Square Group Practice   | CA1 1LB  | 7777                   |
| A82055      | Aspatia Medical Group           | CA7 3HH  | 6869                   |
| A82013      | Upper Eden Medical Practice     | CA17 4RB | 6680                   |
| A82024      | Seascale Health Centre          | CA20 1PN | 5878                   |
| A82038      | Temple Sowerby Medical Practice | CA10 1RW | 4882                   |
| A82037      | Silloth Group Medical Practice  | CA7 4AH  | 4328                   |
| A82631      | Court Thorn Surgery             | CA4 0HP  | 3690                   |
| A82029      | The Croft Surgery               | CA7 5JH  | 3479                   |
| A82004      | Alston Medical Practice         | CA9 3QX  | 2236                   |
| A82620      | Glenridding Health Centre       | CA11 0PD | 932                    |

## 4.2 INCLUSION & EXCLUSION CRITERIA

### Inclusion criteria:

- Adults aged 25 – 80 years
- Participants in original workplace 'baseline' cardiovascular health check.
- Currently still employed by one of the original employers involved in the original cardiovascular health check initiative.
- Currently not absent from work long-term due to illness or for other reason (eg maternal leave, sabbatical; unless employee has explicitly indicated to employer that they can be contacted for non-work related reasons).

### Exclusion criteria:

- No access to phone/tablet/computer to use the POCDOC App
- Any reasons for the person being unable to follow the protocol, including lack of mental capacity to consent to taking part in the study (examples include dementia, patient housebound, severe learning disability).
- The patient has concurrent (medical) conditions that in the opinion of the investigator may compromise patient safety or study objectives (examples include receiving palliative care, medical condition that contraindicates giving routine blood samples)

## 5 STUDY PROCEDURES

### 5.1 INFORMED CONSENT

Before being recruited to this study, participants must have consented to participate, after the nature, scope and possible consequences of the evaluation have been explained in an understandable form. For all eligible employees, an initial invite letter and patient information leaflet will be provided via their employer (see also Section 4.1). They'll also get a notification via PocDoc (see Appendix1). If patients are interested, they then complete an online MS forms Informed Consent Form. The link to this ICF is on the invite letter and Participant Information Sheet.

Although the informed consent process is done remotely, the research staff will be trained in obtaining informed consent as part of professional development, members of research staff involved in the consent process are encouraged to have current ICH Good Clinical Practice training (even though this officially does not fall under the remit of Good Clinical Practice requirements), and the study will be conducted in line with ICH GCP principles.

### 5.2 STUDY ACTIVITIES

See Table 3 for an overview of the participant-related activities conducted for the ACHIEVE study. See also Appendix 1.

*Table 3, Overview of study activities for study participants.*

|                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Informed consent</p> <p>(takes ~10 minutes in total)</p>                   | <p>After reading this Participant Information Sheet, employee completes the online Informed Consent Form via MS Forms.</p> <p>If they have any questions, can contact ACHIEVE research team via tel. 01228 602173 (has answerphone) or email research.edc@ncic.nhs.uk</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <p>Health Check activities</p> <p>(take ~30 minutes in total)</p>             | <p>Study team sends PocDoc Healthy Heart Check kit in the post to participant (along with paper copy of signed ICF).</p> <p>Within 4 weeks of receiving the kit, participant undertakes the health checks.</p> <p>After participant has completed the test, their results will be automatically copied to their medical record by PocDoc (using NHS App).</p> <p>The ACHIEVE team will also be able to see your PocDoc Healthy Heart Check test results. They will inform participant's GP practice in the case of raised results (lipids, cholesterol or QRISK3 score, see Table 4). This is to safeguard for any serious medical condition that may be identified.</p> <p>Any follow-up care that patient may seek or receive after the PocDoc testing does not form part of this ACHIEVE research study</p>                                |
| <p>Review of Health Check Outcomes</p> <p>(done by ACHIEVE research team)</p> | <p>This is an optional item for participants who are registered with a selection of GP practices (see Table 2 for list). Participant does not have to do anything themselves for this part of the study.</p> <p>ACHIEVE team reviews participant's GP medical records to check if appropriate actions were taken on the back of any findings made by doing the health check. We only do this review exercise for the results from the tests the last time round (when participant volunteered in late 2024 to early 2025)</p> <p>This means we assess:</p> <ul style="list-style-type: none"> <li>- Did participant or the GP make contact to consult about the findings</li> <li>- Was the relevant test repeated in a central laboratory</li> <li>- Was any treatment, medication or otherwise, indicated and – if so - offered.</li> </ul> |

### 5.3 Description of study tests and procedures

It should be stressed that this study does not aim to evaluate the diagnostic performance (eg sensitivity and specificity) of the screening / diagnostic tests. These have been established and have been reported on previously (see Roest et al, 2024).

The PocDoc Healthy Heart Check will give the following test results:

- Cholesterol Profile: This includes levels of HDL ("good" cholesterol), LDL/Non-HDL ("bad" cholesterol), and triglycerides.
- BMI: Body Mass Index, a measure of body weight relative to height.
- NHS Heart Age: A comparison of your heart health to that of someone your actual age, based on NHS guidelines.
- 10-Year Risk Assessment (QRISK3): An estimate of your likelihood of experiencing a heart attack or stroke in the next decade. This score takes into account factors like age, sex, ethnicity, cholesterol, BMI, and lifestyle

An abnormal test result for any of the above parameters will be based on nationally agreed cut-off values (the NHS uses those same cut-off points). See also Section 6 of this Protocol.

The way that the PocDoc Healthy Heart Check works is:

- Participant downloads the free PocDoc Pro App and follow the registration steps.
- Disinfect subject's fingertip
- Collection of a small finger prick of blood (~ 3 drops of blood), using a finger prick and a capillary tube.
- Apply the blood to the PocDoc lateral flow test
- Once the subject has scanned the lateral flow device, the App will analyse the test results.
- Wait 7 minutes to allow review of results.

In addition, the participant will be asked to measure your height and weight, so that this information can be added to the PocDoc App and all the test results can be calculated (notably QRISK3 score).

#### 5.4 DEFINITION OF END OF STUDY

For participants the study involves the Pocdoc Healthy Heart Check test and weight / height measurement. Thereafter, all study involvement is complete; some participants may potentially be undergoing clinical follow-up as a result of the screening exercise, but this does not form part of the ACHIEVE study. The study itself therefore ends as soon as we receive notification through the PocDoc App system that the last participant has done their health screen and scanned the lateral flow device via the PocDoc App.

#### 5.5 DISCONTINUATION OR WITHDRAWAL OF PARTICIPANTS

Each participant has the right to withdraw from the study at any time. All data already collated as part of the study – or as part of the baseline exercise - will be destroyed if a subject withdraws from the study. Participants do not need to give a reason for study withdrawal and their normal clinical care and their relationship with their employer will not be affected should they decide to discontinue participating in the study. This will also be outlined in the Participant Information Leaflet.

#### 5.6 SOURCE DATA

Source data will include patient's GP records, the original 'baseline' PocDoc Healthy Heart Test results, and the Case Record Form for the results of the testing. The funder of the study, Vital Signs

Solutions Ltd (manufacturer and distributor of PocDoc Healthy Heart Check point-of-care test), will have no access to patient data other than pseudo-anonymised data.

All documents will be stored safely in confidential conditions. On all study-specific documents, other than the signed consent, the participant will be referred to by their pseudo-anonymous study ID number.

## 6 SAFEGUARDING REPORTING TO GP

### 6.1 CRITERIA FOR SAFEGUARDING REPORTING

The PocDoc Healthy Heart Check kit and the accompanying App will show whether a result is out of the normal reference range. The cut-off values are based on NICE guidance (NG238).

This means for the QRISK3 a value of >10% (for those aged 25-85 years). For the blood lipid and cholesterol markers, Table 4 gives overview of value cut-offs.

*Table 4, Overview of normal value cut-offs for blood lipid and cholesterol markers, and QRISK3*

| Blood marker                                                | NHS guideline healthy limit (mmol/l) |
|-------------------------------------------------------------|--------------------------------------|
| TC, total cholesterol                                       | ≤ 5                                  |
| HDL, high density lipids                                    | ≥ 1 (men) / ≥ 1.2 (women)            |
| Non-HDL, non-high density lipids                            | ≤ 4                                  |
| TC:HDL ratio, total cholesterol : high density lipids ratio | ≤ 6                                  |
| TG, total glycerides                                        | ≤ 2.3                                |
| LDL, low density lipids                                     | < 3                                  |
|                                                             |                                      |
| Risk score for cardiovascular disease                       | NHS / NICE healthy limit             |
| QRISK3                                                      | < 10%*                               |

\*Without presence of known risk factor that recommends against using QRISK3 (such as type 1 diabetes, chronic kidney disease, familial hypercholesterolaemia)

### 6.2 NOTIFICATION OF GP FOR SAFEGUARDING REPORTING

A GP notification letter / task message (via EMIS medical records system) will be sent to the participant's GP.

## 7 SAFETY

### 7.1 SAFETY DEFINITIONS

For the purpose of this study, the only safety reporting that is indicated is strictly only when there is an adverse event during the diagnostic testing, ie when the participant takes a finger-prick blood sample for the purpose of the PocDoc Healthy Heart Check or when . Over the course of patient involvement in the study, any other clinic incidents (eg hospital admissions, falls and other emergencies) are not considered part of the research study and will not be reported on.

*Table 5, Description of different adverse event reporting definitions.*

|                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Adverse Event (AE)    | <p>Any untoward medical occurrence in a patient or other clinical investigation participant taking part in a trial of a medical device, which does not necessarily have to have a causal relationship with the device under investigation.</p> <p>An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of the device, whether or not considered related to the device.</p>                                                                                                                                                                                                                                                                                                                                                                           |
| Serious Adverse Event | <p>A serious adverse event is any untoward medical occurrence that:</p> <ul style="list-style-type: none"> <li>- results in death</li> <li>- is life-threatening</li> <li>- requires inpatient hospitalisation or prolongation of existing hospitalisation</li> <li>- results in persistent or significant disability/incapacity</li> <li>- consists of a congenital anomaly or birth defect.</li> </ul> <p>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.</p> <p>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.</p> |

## 7.2 PROCEDURES FOR RECORDING ADVERSE EVENTS

All SAEs need to be reported to the sponsor/host Trust R&D immediately and within no more than 24 hours of the investigator team becoming aware of them.

The only devices to be in contact with the patient are a PocDoc-provided pin-prick (lancet) for taking a small blood sample of about 5 drops maximum (equivalent to circa 0.25 ml maximum) and a capillary tube to collect the blood into. The pin-prick is invasive, but only makes a very small pierce into the skin of a finger. It should not lead to extensive bleeding or significantly increase the risk of infection. Cross contamination risk is also minimal because the participant themselves can take the sample.

## 7.3 CAUSALITY

The relationship of each adverse event to the trial must be determined by a medically qualified individual according to the following definitions:

**Related:** The adverse event follows a reasonable temporal sequence from Medipin device application. It cannot reasonably be attributed to any other cause.

**Not Related:** The adverse event is probably produced by the participant's clinical state or by other modes of therapy administered to the participant.

## 8 Statistical consideration and data analysis plan

### 8.1 GENERAL AND BASELINE CHARACTERISTICS

The numbers of employees who are invited will be recorded, provided the employers can give information on how many of the original 'baseline' volunteers are still employed by them and how many are suitable for an invite. The number of informed consents (ie participants entering the study) will be recorded, as will be number of participants who actually conduct the PocDoc Healthy Heart Check, and any study withdrawals. Adverse events will also be recorded – adverse events are only included if the event occurs during the actual PocDoc Healthy Heart Check, (see Section 7). Any preceding, interim, or subsequent events will not be considered an adverse event.

In order to describe the sample and facilitate analysis of objectives, the following characteristics and parameters will be collated, mostly from the PocDoc App: Patient demographics, including age, sex, weight, height, and body mass index. QRISK3 related information, which includes: smoking status; diabetes status; existing cardiovascular disease (e.g. heart failure, heart attack, angina, stroke); rheumatoid arthritis status; severe mental illness status; already on blood pressure medication; chronic kidney disease status; history of atrial fibrillation; migraines or not; currently taking cholesterol-lowering medication (e.g. statins).

### 8.2 SAMPLE SIZE CALCULATION

#### For primary outcome measure (QRISK3)

The sample size calculation is based on being able to detect a significant change in QRISK3 score, be it an increase or decrease in the average score over time within the cohort. From the baseline exercise information is known about the average QRISK3 score in the cohort for which the score was calculated. Already during the baseline exercise, those employees aged under 25 years did not have their QRISK3 calculated (and these will not be included in this ACHIEVE study either).

In our cohort, baseline average and its standard deviation (SD) for the QRISK3 score was 2.8% (SD 4.0). In a population the variation of the QRISK3 score can differ wildly, and in another study involving patients with learning disabilities the average score was 6.31 (SD 8.95) (Ho et al, 2021).

The minimum number of participants for which baseline and 18-month data need to be collected is: **824**. To make the study more powerful, ideally as many as 2774 complete datasets are required. The following was applied for a priori sample size calculations: Wilcoxon test for paired samples. See also Table 6.

It must be recognised that simply by ageing one year, the QRISK3 score for all participants will increase if all other parameters remain unchanged. Therefore, it is harder to achieve an average significant improvement in QRISK3 score than it is to observe a significant increase in average QRISK3 score.

*Table 6, Sample size calculation based on measured baseline average QRISK score and hypothetical change 12 months later.*

| Baseline (SD) | 12-month FU (SD) | P-value | Power | Sample size (n) |
|---------------|------------------|---------|-------|-----------------|
| 2.8% (4.0%)   | 2.4% (4.0%)      | 0.05    | 80%   | 824             |
| 2.8% (4.0%)   | 2.5% (4.0%)      | 0.05    | 80%   | 1464            |

|             |             |      |     |      |
|-------------|-------------|------|-----|------|
| 2.8% (4.0%) | 2.4% (4.0%) | 0.01 | 90% | 1562 |
| 2.8% (4.0%) | 2.5% (4.0%) | 0.01 | 90% | 2774 |

### For secondary objective, Review of Health Check Outcomes

For auditing the outcomes of what happened with significant findings at baseline exercise, the aim is to audit at least n = 272 (or as close to this if that minimum number of cases is not available). This gives sufficient power at a confidence level of 90% and margin of error of 5%. The a priori calculation is based on sample size requirements for surveys, see eg <https://www.calculator.net/sample-size-calculator.html?type=1&cl=90&ci=5&pp=50&ps=100000&x=Calculate> .

### 8.3 PRIMARY OUTCOME STATISTICS

Any change observed in cardiovascular health parameters, as measured with QRISK3 score, between baseline and 12 months follow-up PocDoc Healthy Heart Check tests.

- As mentioned in Section 8.2, Wilcoxon test for paired samples will be applied.

### 8.4 SECONDARY OUTCOME STATISTICS

% of original baseline volunteers consenting to be participant in the ACHIEVE study, and % participants who will complete and report on the PocDoc Healthy Heart Check test.

- Only analysed with descriptive statistics. Depending on outcomes and participation levels, binary logistic regression can be applied to determine what kind of patient profile did or did not volunteer to participate again.

Comparison of number of participants in three main QRISK3 categories at baseline and at 12-month follow-up (Low risk – QRISK3 score of less than 10%; Moderate risk – QRISK3 of 10-20%; High risk – QRISK3 score of more than 20%).

- Chi-squared test analysis

Any change observed in blood lipid and cholesterol markers, as outlined in Table 4 (including total cholesterol, HDL, non-HDL, total cholesterol : HDL ratio, total cholesterol : high density lipids ratio, total glycerides, LDL, between baseline and 12 months follow-up PocDoc Healthy Heart Check tests.

- Wilcoxon test for paired samples

Number of GP notifications indicated at baseline and 12 months follow-up PocDoc Healthy Heart Check tests respectively.

- Descriptive statistics.

Review of Health Check Outcomes, ie an audit of what happened on the back of any significant findings when participants did the health check 12 months ago. Any actions and/or activities within 4 months of conducting that baseline PocDoc Healthy Heart test.

- As mentioned in Section 8.2, only descriptive statistics will be used.

No identifiable data will be presented in reports or articles; only averages and totals will be used. Analysis will be performed on available data only; there will be no process to account for any missing data. Data will first be collated in Microsoft Excel, followed by analyses performed using SPSS v24.

## 9 Data handling and Monitoring

Data arising from this study is confidential. Identifiable information can only be accessed by delegated members of the study team. Anyone in the research team who will work on Trust premises and see patients, and does not have a substantive contract with NCIC, will need to apply for a letter of access via the NIHR research passport scheme. Relevant employees of our partner organisation for this study, Cumbria Health, will work with NCIC under the Research Passport scheme (ie they will be issued with a Letter of Access). See also Appendix 2.

Participants will be pseudoanonymised by allocating a study ID to each of them. Patient / subject identifiable data will only be used within Cumbria Health and North Cumbria Integrated Care NHS Foundation Trust by staff on the study delegation log; if applicable, only pseudoanonymised data are shared with the wider members of the study team. All identifiable data is stored on password protected NHS computer systems (this includes Cumbria Health, vetted provider of NHS services). Anonymised data will be shared and stored using security-enabled systems such as password-protection and encryption of e-mails and files. The requirements of the Data Protection Act and NHS Code of Confidentiality will be followed at all times. All researchers will be fully trained in NHS Confidentiality and GCP training. The final pseudoanonymised dataset will be shared with the funder of this project, Vital Signs Solutions Ltd (manufacturer and distributor of PocDoc Healthy Heart Check point-of-care test). Subjects will be made aware of this during the consent process.

All paper data will be held in secure locked environments in the office of Cumbria Health and Research & Development department of North Cumbria Integrated Care NHS Foundation Trust. Electronic data will be saved on the patient management system such as EMIS, and also a password protected research database. Data released (e.g. by publication) will contain no information that could lead to the identification of an individual participant. Upon completion of the study the site files will be archived for a period of 10 years in line with local archiving policy and procedures. Final research data will be available to other researchers/NHS staff in a pseudoanonymised form. Direct access to source data will only be available to authorised representatives from the sponsor and national regulatory authorities to permit study related monitoring, audit and inspection.

## 10 Governance of study

### 10.1 APPROVALS AND LEGAL BASIS

This study will be conducted in compliance with the protocol approved by the Health Research Authority, National Research Ethics Service, and local Trust R&D Approval, and according to Good Clinical Practice standards including the Declaration of Helsinki (1964, Amended Oct 2013). No deviation from the protocol will be implemented without the prior review and approval of the aforementioned review bodies, except where it may be necessary to eliminate an immediate hazard to a research subject. In such case, the deviation will be reported according to policies and procedures.

The legal basis that underpins this work is covered by General Data Protection Regulation (GDPR), Article 6 Lawfulness of processing. The processing is lawful because the following applies: (a) the data subject has given consent to the processing of his or her personal data for one or more specific purposes.

## 10.2 SPONSOR & INDEMNITY

North Cumbria Integrated Care NHS Foundation Trust is the sponsor of this study and therefore NHS indemnity applies for design, conduct and management of the study. Vital Signs Solutions Ltd (manufacturer and distributor of PocDoc Healthy Heart Check point-of-care test) has provided a grant for this study.

Patients will not be given financial incentives for taking part in the study. Travel expense reimbursement is not applicable for this study, since participants do not have to travel anywhere to participate in the study.

## 11 Publication and data-sharing policy

The results of this study are planned to be disseminated through:

- Peer-reviewed scientific journal publication
- Internal report

A summary of the main findings can be supplied to participants on request and this will be stated in the patient information leaflet.

## 12 References and Further Reading

Chan LS. Minimal clinically important difference (MCID)—adding meaning to statistical inference. *American journal of public health*. 2013 Nov;103(11):e24-5.

Debiec R, Lawday D, Bountziouka V, Beeston E, Greengrass C, Bramley R, Sehmi S, Kharodia S, Newton M, Marshall A, Krzeminski A. Evaluating the clinical effectiveness of the NHS Health Check programme: a prospective analysis in the Genetics and Vascular Health Check (GENVASC) study. *BMJ open*. 2023 May 1;13(5):e068025.

El-Osta A, Woringer M, Pizzo E, Verhoef T, Dickie C, Ni MZ, Huddy JR, Soljak M, Hanna GB, Majeed A. Does use of point-of-care testing improve cost-effectiveness of the NHS Health Check programme in the primary care setting? A cost-minimisation analysis. *BMJ open*. 2017 Aug 1;7(8):e015494.

Hippisley-Cox J, Coupland C, Brindle P. Development and validation of QRISK3 risk prediction algorithms to estimate future risk of cardiovascular disease: prospective cohort study. *bmj*. 2017 May 23;357.

Jain A, Persaud JW, Rao N, Harvey D, Robertson L, Nirmal L, Nirmal D, Thomas M, Mikhailidis DP, Nair DR. Point of care testing is appropriate for National Health Service health check. *Annals of clinical biochemistry*. 2011 Mar;48(2):159-65.

Kwak W, Won JU, Rhie J, Lee MS, Kang EJ, Roh J. A workplace cardiovascular health promotion program and its short-term health effects. *Annals of Occupational and Environmental Medicine*. 2009 Mar 1;21(1):46-52.

Martin A, Saunders CL, Harte E, Griffin SJ, MacLure C, Mant J, Meads C, Walter FM, Usher-Smith JA. Delivery and impact of the NHS health check in the first 8 years: a systematic review. *British Journal of General Practice*. 2018 Jun 19.

Patel R, Barnard S, Thompson K, Lagord C, Clegg E, Worrall R, Evans T, Carter S, Flowers J, Roberts D, Nuttall M. Evaluation of the uptake and delivery of the NHS Health Check programme in England, using primary care data from 9.5 million people: a cross-sectional study. *BMJ open*. 2020 Nov 1;10(11):e042963.

Robson J, Dostal I, Sheikh A, Eldridge S, Madurasinghe V, Griffiths C, Coupland C, Hippisley-Cox J. The NHS Health Check in England: an evaluation of the first 4 years. *BMJ open*. 2016 Jan 1;6(1):e008840.

Roest KN, Lee M, Rees J, Gubala V. Smartphone-based digital point-of-care panel assay with enzymatic catalytic reaction. *Biosensors and Bioelectronics: X*. 2024 Aug 1;19:100504.

Summerton N. Heart health: why the workplace is a great environment for screening. *Occupational Health & Wellbeing*. 2015 Nov 1;67(11):18.

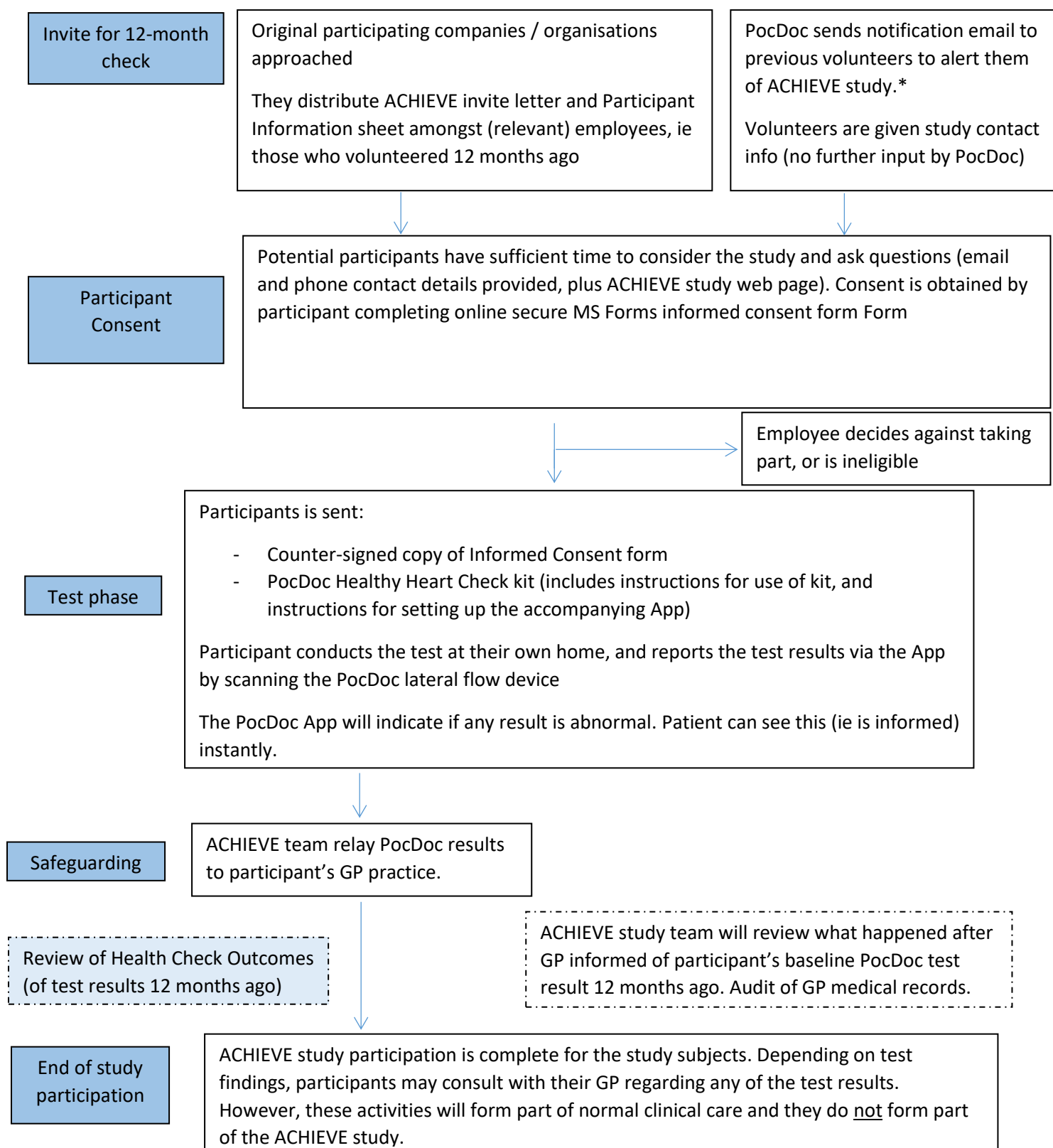
Wood DA, Kinmonth AL, Davies GA, Yarwood J, Thompson SG, Pyke SD, Kok Y, Cramb R, Le Guen C, Marteau TM, Durrington PN. Randomised controlled trial evaluating cardiovascular screening and intervention in general practice: principal results of British family heart study. *Bmj*. 1994 Jan 29;308(6924):313-20.

NICE Guideline. Cardiovascular disease: risk assessment and reduction, including lipid modification, NG238, 14 December 2023, <https://www.nice.org.uk/guidance/ng238/chapter/Recommendations>

Ho JS, Rohra V, Korb L, Perera B. Cardiovascular risk quantification using QRISK-3 score in people with intellectual disability. *BJPsych Open*. 2021 Jun;7(S1):S52-3.

Williams E, Round T, Jones NR. Cardiovascular disease—risk assessment and reduction: NICE 2023 update for GPs. *British Journal of General Practice*. 2024 Nov 1;74(748).

## APPENDIX 1. STUDY (PARTICIPANT) FLOWCHART



\*If they have given explicit consent to be contacted for PocDoc news and announcements during sign up to PocDoc privacy policy.

## APPENDIX 2. STUDY (TEAM / DATA) OVERVIEW

### Team:

Dr Stacey Fisher (Chief Investigator): paid employment as GP with Cumbria Health and NCIC. Honorary contract with 15 GP practices and access to medical records for research purposes (per Table 2).

Mr Richard McGregor: paid employment with Cumbria Health

Ms Lucy Brown: paid employment with Cumbria Health

Dr Leon Jonker: paid employment with NCIC, Letter of Access to primary care NHS via NIHR Research Passport scheme (including 15 GP practices, Table 2, and access to medical records for research purposes)

NCIC RRDN (regional research delivery network) delivery staff: paid employment with NCIC, Letter of Access to primary care NHS via NIHR Research Passport scheme (including 15 GP practices, Table 2, and access to medical records for research purposes)

### Data:

#### Baseline PocDoc / QRISK3 data

- Retrieved from PocDoc / Cumbria Health with participant's permission

#### Review of Health Check Outcomes (ie on significant Baseline PocDoc / QRISK3 results)

- Conducted by Dr Stacey Fisher and above NCIC research team

#### 12-month PocDoc / QRISK3 data

- Retrieved from PocDoc and transferred to Cumbria Health with participant's permission

#### GP practice notification

- Done electronically as a task notification in the GP practice's EMIS medical records system via Cumbria Health (who themselves use EMIS medical records system)

#### Electronic data and paper data

- Stored on Cumbria Health and NCIC computers (password protected, periodic back-ups made). Identifiable data restricted to delegated ACHIEVE research study staff
- Stored on Cumbria Health and NCIC premises (locked cabinets, locked offices)
- Archived by NCIC in accordance with NCIC SOP/policy