# The clinical and cost-effectiveness of an evidence-based testing package to monitor long term conditions (LTC) in primary care: the "Test Smart" cluster randomised controlled trial

## Trial Protocol

| | |
|---|---|
| Short Title: | Test Smart study |
| Date: | 29/9/2026 |
| Version Number: | 1.9 |
| Sponsor: | University of Bristol |
| Funder: | NIHR Programme Grants for Applied Research<br><br>The Test Smart study is the fifth and final Workstream of the Optimal Testing NIHR Programme Grant for Applied Research<br><br>PGfAR Reference: NIHR201616 |
| Host: | BNSSG ICB |
| Trial Registration: | ISRCTN31106231 |

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# PLAIN ENGLISH SUMMARY

## What is the problem?

The number of blood tests performed in the NHS is increasing. Over half of these blood tests take place in general practice to monitor long-term conditions (LTC). Testing blood can be unnecessary, may cause distress and lead to further tests and treatments that are not be needed. However, not testing could miss important problems.

Patients aren't always told which blood tests they are having, and don't always understand what their test results mean. Current guidelines on which tests people with LTC should have are based on expert opinion rather than research evidence.

## What are we trying to find out?

We want to develop evidence-based testing strategies for people with high blood pressure, diabetes and kidney disease in general practice. This will let patients, doctors and nurses know which are the best tests for these conditions, how often to test patients, and how to use the results. It has the potential to free up resources from general practice, reduce unnecessary testing for patients and improve overall management of LTC.

## What have we done already?

We have developed evidence-based lists of tests for monitoring patients with diabetes, high blood pressure and kidney disease. We have also developed resources to help patients understand what their blood tests mean for their health. Together these make up the "*Test Smart*" intervention.

## What are we going to do?

We will implement the *Test Smart* intervention in ten GP practices and will compare rates of testing with ten practices following usual testing practice. We will monitor hospitalisations to see whether there are any risks of having less tests. We will also look at patient outcomes including 'patient activation', to see if patients feel more in control of their health when they are given more information to help them understand their monitoring tests.

## Patient and public involvement

Two patient representatives have been involved since the start of the programme and will continue to be involved in the *Test Smart* intervention development and testing. In addition, we have recruited a patient advisory group to provide project oversight.

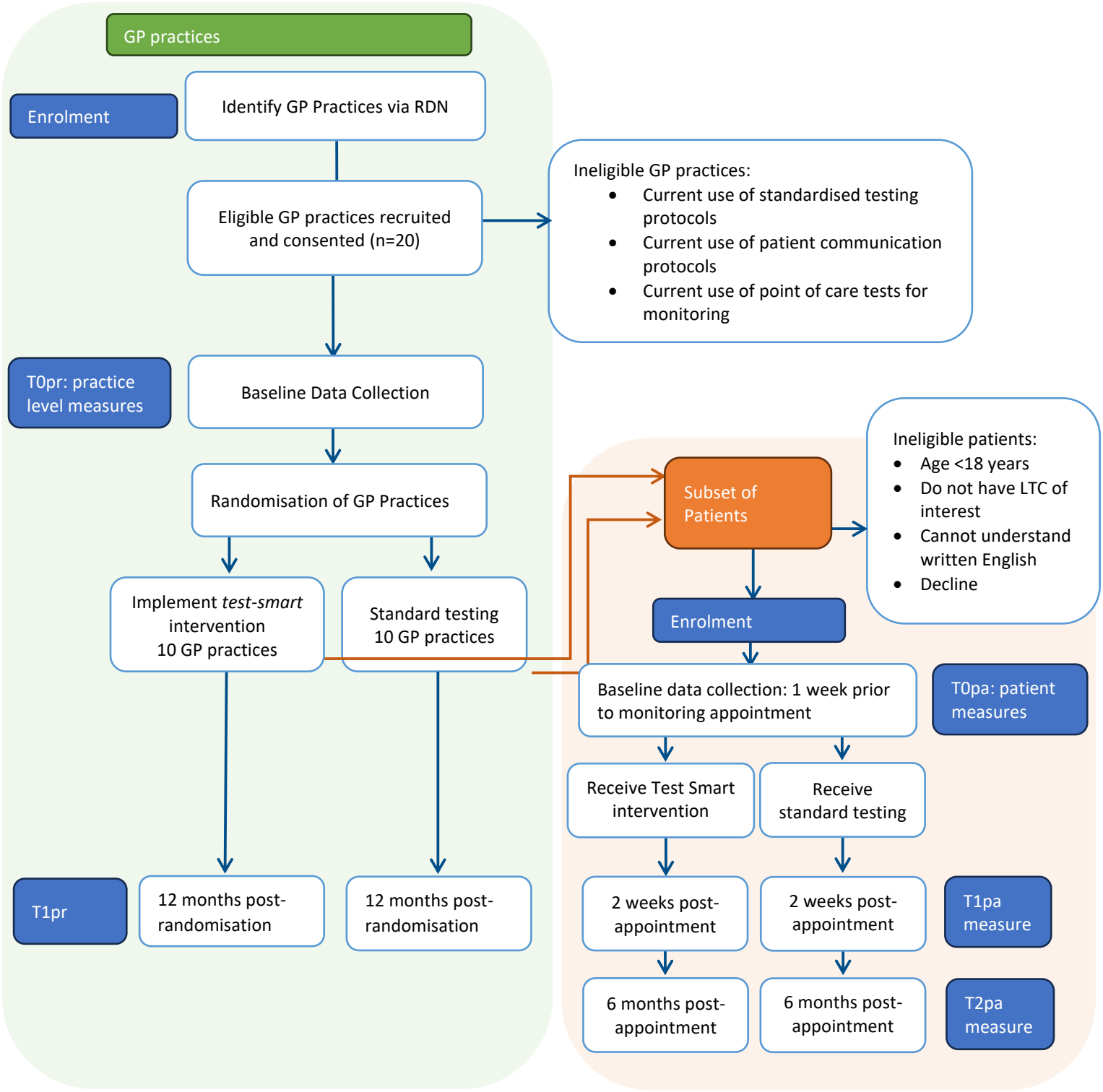
## Sharing our findings

All results will be reported in peer reviewed health care journals and a summary of findings will be disseminated to people involved in the delivery and organisation of health care for long term conditions. Relevant patient groups, and our patient advisors, will help us communicate our findings to patients.

## LIST OF ABBREVIATIONS

| | |
|---|---|
| BNSSG | Bristol, North Somerset and South Gloucestershire |
| BTC | Bristol Trials Centre |
| CKD | Chronic Kidney Disease |
| CPRD | Clinical Practice Research Datalink |
| CRN | Clinical Research Network |
| cRCT | Cluster Randomised Controlled Trial |
| DSA | Data Sharing Agreement |
| EBTS | Evidence Based Testing Strategies |
| GP | General Practitioner |
| HCP | Health Care Practitioner |
| HRA | Health Research Authority |
| ICB | Integrated Care Board |
| LTC | Long Term Condition |
| NHS | National Health Service |
| PAM | Patient Activation Measure |
| PMG | Programme Management Group |
| PoC | Point of Care |
| PPIE | Public and Patient Involvement and Engagement |
| PSC | Programme Steering Committee |
| RDN | Research Delivery Network |
| REC | Research Ethics Committee |
| RCT | Randomised Controlled Trial |
| SAE | Serious Adverse Event |
| T0pa | Baseline measure - patients |
| T0pr | Baseline measures – GP practices |
| T1pa | Follow-up 1 (2 weeks) – patients |
| T1pr | Follow-up 1 (12 months) – GP practices |
| T2DM | Type 2 Diabetes Mellitus |
| T2pa | Follow-up 2 (6 months) - patients |
| TMG | Trial Management Group |
| TSC | Trial Steering Committee |
| WP | Work package |

## STUDY FLOW CHART



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# 1. BACKGROUND AND RATIONALE

Over 15 million people in England have a long-term condition (LTC);[1] 13.8 million have hypertension, 4.1 million chronic kidney disease (CKD) and 6.5 million type-2 diabetes mellitus (T2DM), with considerable overlap between conditions.[2 3] Most patients are managed in primary care, where regular blood test monitoring is used to assess disease progression, adherence and response to treatment, early detection of complications, and development of associated diseases e.g. cardiovascular disease, and renal failure. There is currently no robust evidence to inform recommendations on the selection of tests, or test frequency for people with LTC.[4] Although guidance exists, this is based almost entirely on expert opinion.[4-8]

Primary care pathology testing cost the NHS £1.8bn in 2015/16, with the average GP estimated to spend 1.5 to 2 hours per day reviewing test results.[9] Monitoring of LTC accounts for around half of this pathology testing. [10] Numbers of tests are increasing, with significant implications for NHS costs and clinician workload.[9] There is substantial variation in testing rates between GP practices, suggesting clinical uncertainty in this area.[9 11] A review of chronic disease monitoring recommendations of 20 general practices in North Devon showed that no two practices recommended the same set of blood tests.[12]

## Summary of work completed to date

We are currently in year 4 of a 5-year NIHR Programme Grant for Applied Research project grant which started on 1 June 2021. The overall aim of this project is to optimise testing to monitor LTC (hypertension, T2DM and CKD) in primary care by developing an evidence-based testing package (the "*Test Smart* intervention") consisting of recommended testing panels and frequencies and accompanying patient and clinician materials to facilitate a better understanding of testing and test results for patients and clinicians. The first 3 years of this programme have focused on developing the *Test Smart* intervention; the next 2 years will be an implementation before-after study with the external control group. The programme of work involves 5 interlinked work packages: WP1 to 4 are expected to be completed by 31 August 2024.

### WP 1: DEVELOP EVIDENCE-BASED TESTING PANELS FOR PEOPLE WITH LTC*:*

Rapid reviews and clinical practice research datalink (CPRD) analysis to develop evidence-based recommendations on which tests people with LTC should have to monitor their condition. A consensus meeting of advisory panel members selected tests for inclusion, exclusion or further analysis.

### WP 2: DEVELOP EVIDENCE-BASED RECOMMENDATIONS ON FREQUENCY OF MONITORING

Following methods described by Glasziou et al 2008,[13] we will model the signal to noise ratio over time for each test included in the panel to estimate at what time point the signal is likely to exceed the noise. Model parameters will be determined through a combination of rapid reviews and CPRD

analyses and will feed into the health economics model. Value of information analysis will be used to assess the value of further research.

**WP 3: EXPLORE VIEWS ON TESTING TO MONITOR PEOPLE WITH LTC**

Following the person-based approach (PBA) to developing and implementing interventions, we used qualitative interviews to understand patient, clinician and commissioner views on testing.

**WP 4: PRODUCE INFORMATION MATERIALS FOR PATIENTS AND CLINICIANS**

Development of an intervention package, including patient and clinician resources, to support the implementation of the new testing strategy at a practice level.

**WP 5: THE FINAL WORK PACKAGE (WP5) OF OUR PROGRAMME GRANT WILL BE A CLUSTER RANDOMISED CONTROLLED TRIAL (CRCT) OF THE TEST SMART INTERVENTION IN PRIMARY CARE**. The Test Smart intervention consists of the evidence-based testing panel developed as part of WP1 and 2 and the accompanying clinician and patient educational and communication resources developed as part of WP4.

## 2. AIMS

The overall aim of this trial is to evaluate the clinical and cost-effectiveness of the *Test Smart* intervention to monitor LTC in primary care.

## 3. OBJECTIVES

### Primary Objectives:

1. Does the *Test Smart* intervention reduce rates of testing for monitoring of LTC in primary care?
2. Does the *Test Smart* intervention improve patient activation?

### Secondary Objectives:

3. Is there any evidence that the Test Smart intervention may cause harm through reduced testing?
4. Does the Test Smart intervention improve patients' satisfaction with their monitoring appointments?
5. Does the Test Smart intervention improve patient understanding of their test results?
6. What is the acceptability and fidelity of the Test Smart intervention?
7. What is the cost-effectiveness of the Test Smart intervention?
8. What are the barriers and facilitators to the widespread adoption, integration and sustainability of the Test Smart intervention?

# 4. DESIGN

The study will be a pragmatic, open-label, two-arm cluster RCT (cRCT) comparing the implementation of the *Test Smart* intervention against standard testing practice. The study incorporates a qualitative sub-study and economic evaluation.

## Setting and Population

We will recruit 20 GP practices from two integrated care boards (ICBs). We will select two ICBs in the South West and West Midlands regions, that do not currently have standardised testing protocols across the ICB. We anticipate approaching the following ICBs and will select two that are eligible:

- NHS South Staffordshire and Shropshire ICB
- NHS Black Country ICB
- NHS Birmingham and Solihull ICB

We will randomise 10 practices to implement the *Test Smart* intervention – these will be our intervention practices. A further ten practices will be randomised to usual care to serve as control practices.

At each intervention GP practice, we will encourage a GP, nurse, pharmacist, practice manager or practice data manager to take on the role of Site PI to help implement and monitor the use of the intervention. These champions will help set up the intervention and run monthly queries about implementing the evidence-based testing panels via GP electronic record systems.

### GP PRACTICE SELECTION CRITERIA

#### *Inclusion criteria*

**GP practices** in England will be eligible if they meet **all** the following criteria:

- Located in specified recruitment area
- Use Accurx text messaging software (98% of English practices use this system)
- Practice staff willing to take part in qualitative interviews
- Phlebotomy is conducted either at the practice level, or at an external hub, provided that all monitoring test decisions are made by a healthcare professional at the study site.

Practices that have existing LTC monitoring panels that include at least one additional test group beyond those in the Test Smart panels

#### *Exclusion criteria*

We will exclude practices meeting **any** of the following criteria:

- Practices that currently use standardised testing protocols for LTC, and have equivalent testing panels as those in the Test Smart study .Practices that currently use standardised communication protocols for LTC
- Practices that regularly use point of care (PoC) testing for LTC monitoring (eg PoC HbA1c testing). PoC tests would not be captured in our testing data and may replace laboratory testing and therefore data from these practices would not be comparable
- Practices that decline to provide a local Principal Investigator

## GP PRACTICE RECRUITMENT

Recruitment of practices within the three ICBs will be via Research Delivery Networks (RDNs) using established channels of communication. We will purposively recruit twenty GP practices with different demographics including both urban and rural practices, deprived and more affluent, and ethnically diverse populations. When GP practices are invited to participate, they will be advised on the general principles of the study, namely that the research will investigate methods to optimise the use of blood tests for monitoring LTC. Interested practices will be asked to complete a screening questionnaire to assess initial eligibility. We will seek agreement for them to provide a principal investigator as our primary contact.

GP practices will be considered to have been recruited once eligibility has been established and a contract consenting to take part has been signed.

### *Baseline questionnaire*

All eligible GP practices that consent to take part in the study will be asked to complete a baseline questionnaire to capture practice characteristics.

Baseline data will include:

I. Data about the practice staff composition (GP partners/salaried/sessional nurse practitioners and practice nurses and locums used in the last 12 months) and any other available characteristics (such as postcode).
II. Demographic data of participants with LTCs (CKD, HTN, T2DM) within each practice (including number, age distribution [median and IQR], ethnicity, sex, and IMD decile)
III. Data about systems of testing and monitoring for patients with hypertension, CKD and T2DM.
IV. Data about which clinician-types are responsible for testing and monitoring patients with hypertension, CKD and T2DM.
V. Data on baseline testing rates for LTC over the past 12 months

## GP PRACTICE RANDOMISATION

GP practices will be randomised to the *Test Smart* intervention or to control on a 1:1 basis, stratified on ICB, using a computer generated randomisation schedule by an independent statistician (Grace Young from the Bristol Trial Centre ,BTC). Randomisation will be at the practice level and will be stratified by ICB. All patients with LTC registered at a GP practice randomised to the intervention arm will receive the *Test Smart* intervention and those registered at a GP practice randomised to the "usual care" comparator arm will receive the standard testing protocol for that practice. Allocation concealment will be ensured, as the randomisation code will be held only by an independent statistician who will not be involved in recruiting GP practices and will be independent of the study team. The code will not be revealed until all practices have been recruited into the trial and randomisation is complete.

## PATIENT SELECTION CRITERIA

The study will seek to involve all adults (≥18 years) in participating practices diagnosed with T2DM, hypertension or CKD. A link to a patient information sheet with general information about the study will be shared by text message with patients with any of these LTCs in both intervention and control practices. We will seek to inform patients in the intervention practices about the study, using information posters, videos, and flyers in waiting rooms and phlebotomy rooms, information on practice websites, and proactive discussions with any patient groups associated with each practice. A subset of patients will be recruited to provide patient reported outcomes.

### *Inclusion criteria*

Patients will be eligible for recruitment to provide patient reported outcomes if they are:

- Aged≥18
- Registered at a participating practice and diagnosed with hypertension, and/or CKD and/or T2DM at the start of the study period.
- Attend for routine monitoring during the study period

### *Exclusion criteria*

Patients will be excluded if they are:

- Unable to understand written English or one of the two other study languages sufficiently to complete a questionnaire. The other study languages will be selected based on those most commonly spoken in the GP practices recruited to the study.
- Decline consent or are unable to consent
- Have previously declined to be contacted for research purposes

## PATIENT RECRUITMENT

Within each GP practice (both intervention and control practices) we will approach all participants that attend for monitoring for their LTC within the first 3 months of the study, with the aim of recruiting 30 patients per GP practice – at least 10 patients with each of our LTC of interest (some patients may have more than one of these LTC). Once our recruitment target of 30 patients per GP practice has been met, we will not recruit any additional patients. If we do not recruit sufficient patients during the first 3 months of the study, we will consider whether to extend the recruitment period and whether there are strategies to increase recruitment rates that could be implemented.

We consider that recruiting 30 patients per GP practice should be comfortably achievable. The average number of registered patients per practice in England is 9,803 thus we anticipate over 160 patients will have LTC blood tests per month so a target of 30 patients per practice over 3 months should be achievable.

In intervention practices, recruitment will occur via participant access to the Test Smart website. Eligible patients will receive a link to the Test Smart website through the automated messaging system at the time of booking or attending their long-term condition monitoring blood test. On

accessing the website landing page, patients will be asked to select their registered general practice from a drop-down menu. If the selected practice is actively recruiting for patient-reported outcomes, the landing page will present the option either to complete a questionnaire or to proceed directly to the Test Smart website. Individuals who choose to complete the questionnaire will be directed first to the participant questionnaire; upon completion, they will be redirected to the Test Smart patient website. This process ensures that baseline questionnaires are completed prior to exposure to the intervention materials. Once the recruitment target for an intervention practice has been reached, the questionnaire link will be removed and patients will proceed directly to the Test Smart website.
In the control practices, eligible patients will be sent a text message at the time of booking or attending their long-term condition monitoring bloods which will send them directly to the questionnaire platform (REDCap). The front page of the questionnaire will contain the patient information sheet and consent form. Participants will then complete eligibility screening questions and will be asked to indicate the date of their upcoming appointment for long-term condition monitoring, which will then be used to automate follow-up questionnaires.

Eligible patients who do not have a mobile phone number on their notes, or who have not consented to be contacted by text message, will be sent the study information and questionnaire by post at the time of booking their LTC monitoring blood tests, in order to reduce the risks of biases due to digital exclusion. Individuals receiving paper questionnaires will be asked to provide their name and address to allow the issuing of subsequent questionnaires.

### BLINDING

As this is a cluster randomised controlled trial and due to the nature of the intervention delivery, it will not be possible to blind the practices to their allocation of either control or intervention group. It will also not be possible to blind patients due to the nature of the intervention. The research team will be blinded to allocation apart from the trial manager, trial coordinator, trial administrator (for administrative purposes), the qualitative researchers (who are performing the interviews), the trial clinician and trial statistician (to report SAEs and communicate with the TSC), and the independent statistician who will perform the randomisation.

## Study Intervention

The Test Smart intervention consists of an evidence based testing panel and accompanying clinician and patient educational and communication resources.

### EVIDENCE BASED TESTING PANEL

The final evidence-based testing panel consists of a list of tests that patients should receive as part of their regular monitoring for each of the three LTCs of interest. We recommend annual testing for each included test. The evidence-based testing panel is shown in Table 1.

**TABLE 1 EVIDENCE-BASED TESTING PANEL**

| Test purpose | Type 2 diabetes | Chronic kidney disease | Hypertension |
|---|---|---|---|
| **Disease progression/ treatment response** | HbA1c | eGFR | |
| **Secondary conditions** | eGFR | Haemoglobin (FBC)<br>HbA1C | eGFR<br>HbA1C |
| **Drug monitoring** | Potassium – ARB and ACEi<br>Vitamin B12 – metformin | Potassium – ARB and ACEi | Potassium – ARB and ACEi<br>Sodium – Thiazide type diuretics<br>HbA1c – Thiazide type diuretics |

Patients in the intervention practices with T2DM, hypertension or CKD who attend for annual monitoring bloods will receive the tests specified in Table 1, and will not receive additional tests (unless requested for another reason e.g. intercurrent illness or co-morbidities).

The evidence-based testing panel will be implemented using the following methods:

1. **Automated popups** integrated into the electronic health records which will flag when eligible patients with LTC have a code for chronic disease monitoring added to their notes.
2. **Test ordering panels** integrated by local clinical teams into test ordering systems, allowing clinicians to click on '*Test Smart* diabetes annual review panel bloods', rather than being required to select each relevant test individually.
3. **Posters in phlebotomy rooms** with lists of the recommended evidence-based testing panels for T2DM, hypertension and CKD monitoring.

## EDUCATIONAL AND COMMUNICATION RESOURCES

### *Intervention components for GP practice staff*

1. **Information website** (hcp.test-smart.co.uk) for clinicians which will:
   a. Link to training videos (see details below)
   b. Explain evidence supporting the testing panels
   c. Summarise test panels for each LTC
   d. Explain how multimorbidity will be managed
   e. Explain why tests were removed from the testing panels with hyperlinks to published evidence from WP1 and WP2
   f. Explain patient centred test communication
   g. Answer FAQs about the intervention
2. **Introductory training video** of 3-5 minutes duration made using PowerPoint and screenshots, aimed at all HCPs in the practice. Training videos will cover the science behind the change to test lists, the test list for each LTC, introduce the automated test ordering system , explain patient preferences for test result communication, and explain how to send text messages to patients with information resources .
3. **Training video for staff taking bloods** of 3-5 minutes duration made using PowerPoint and screenshots, aimed at phlebotomists (and those HCAs/Nurses involved in taking LTC monitoring bloods). Training to cover in more depth test ordering systems, content of

~~Accurx~~ text template, including hyperlinks to study website, introducing the study Intervention website contents for clinicians and patients

### *Intervention components for patients*

1. **Information website**: There will be an introduction page, linking to the animation (see below). There will be a section for each LTC, each one will explain the following information:
    - These are the tests you've had
    - This is what they can tell us
    - This is what a normal range is
2. **Patient information leaflets** will briefly summarise the information on the website and will be available as a printable PDF, so they can be offered to all patients in paper format at the time of their monitoring blood tests. The leaflets will direct patients to the website for additional information. The leaflets will be translated and made available in up to 2 other commonly spoken languages in England. Languages will be selected based on those most commonly spoken in the GP practices recruited to the study.
3. **Automated message templates** which will be sent to all eligible patients at the time of their monitoring blood test appointment with embedded hyperlinks to the study website
4. **Patient focused animation** using VideoScribe, lasting 2-3 minutes to explain improvements to test lists and test communication/demonstrate how to navigate the study webpage and signpost the resources available there. The animation will be available in up to 2 other commonly spoken languages in England. The animation can be used to share information about the study on the screen in the practice waiting room, on participating GP practice websites and on the study information website.

## Implementation Strategy

The Site PIs will oversee the setup of the intervention and support its implementation at the intervention practices. Site PIs at intervention practices will receive remuneration to cover the time required for this oversight. There will be a 1-month run-in period to allow the intervention to be embedded in practice systems before data collection commences.

## Outcomes

We will collect data on the following service, patient, economic and implementation outcomes:

### SERVICE (PRACTICE) OUTCOMES:

- Monthly practice level blood testing rates in the 12 months prior to implementation and 12 months post 1 month run-in period (objective 1; co-primary outcome)
- Monthly practice level hospitalisation rates amongst patients with LTC in the 12 months prior to implementation and 12 months post 1 month run-in period (objective 3)

- Practice level acute and new prescriptions rate amongst patient with LTC in the 12 months prior to implementation, 6 months and 12 months post-implementation.
- Practice level referral rate amongst patient with LTC in the 12 months prior to implementation, 6 months and 12 months post-implementation.

### PATIENT OUTCOMES (SEE APPENDIX 3):

- Patient Activation Measure (PAM) (objective 2; co-primary outcome)
- Patient satisfaction (NHS Friends and Family test) (objective 4)
- Patient understanding of their test results (objective 5)

### ECONOMIC OUTCOME

- NHS costs of primary care consultations for routine monitoring; blood tests and hospital-based care (objective 7)

### INTERVENTION FIDELITY OUTCOMES:

- Proportion of patients with LTC who receive all the tests listed in the testing panels in the 12 month period post implementation (objective 6)
- Proportion of patients with LTC who receive additional tests not listed in the testing panels in the 12 month period post implementation (objective 6)
- Proportion of patients with LTC who receive a text message telling them about the study information website *(*objective 6*)*
- Website analytics, including page views and downloads per practice *(*objective 6*)*

We will also conduct a process evaluation to explore the following outcomes in qualitative interviews with staff and patients, data from practice records systems and website usage *(*objectives 4, 5, 6 and 8*)*:

- Clinician and patient views on the intervention experience
- Patient satisfaction
- Patient understanding of test results
- Blood test related anxiety
- Experience of receiving blood test results
- Satisfaction in communication during a blood test monitoring appointment
- Experience of monitoring consultations
- Barriers and facilitators to implementation in practice
- Recommendations for optimisation of the intervention to support future rollout

Appendix 2 provides a detailed overview of how each outcomes maps to the study objectives and provides details on data collection and analysis for each outcome.

# 5. SAMPLE SIZE

We have two co-primary outcomes. Testing rates (measured at the practice level) and patient activation (measured at the individual patient level). We have therefore conducted two sample size calculations to ensure that the study is powered to detect a clinically important difference in both outcomes, each calculation is based on 2.5% significance to account for the co-primary outcomes.

We estimate that 14 GP practices (7 intervention and 7 control practices) would provide 90% power to detect a reduction in tests from 7 to 6 per patient per year (assuming a conservative SD of 3.0) at the 2.5% significance, assuming around 1800 eligible patients per practice, an intraclass correlation coefficient (ICC) of 0.03 and a coefficient of variation (CoV) of 1.16. The reduction from 7 to 6 tests per patient per year is a conservative estimate based on an early implementation study in Devon that reported a decrease of between 14 and 22% in testing rates,[12] combined with more recent data on current testing rates that we calculated using CPRD data. To provide information from a broad range of practices with different demographic features we will expand this to 20 practices - 10 intervention and 10 control practices.

At the patient level, we estimate that 70 patients would provide 90% power to detect an improvement in PAM score of 5 points, assuming a baseline score of 60 (SD=15)[14] and within patient correlation of 0.7. Whilst this number of patients could be recruited from a single practice we will aim to recruit patients from all 20 practices – this will be to ensure consistency of effect across GP practices with different patient cohorts. We will recruit 30 patients (10 with each LTC) from each GP practice giving a total of 300 patients in intervention practices and 300 patients in control practices.

# 6. TIMELINES AND DATA COLLECTION

The study will run for 24 months from May 2026. The study Gantt chart is provided in Appendix 1. Ethical and sponsorship approval will be sought prior to the study start between September and November 2024. Once ethical approval has been obtained, 3 months will be spent recruiting practices via the ICBs, appointing Site PIs and developing the study tools and database. Intervention implementation will take place between March 2025 and May 2025. Patients will be recruited from March 2025, after the intervention has been implemented in intervention practices. Practices will be involved in the study for a period of 15 to 18 months post recruitment.

## Data collection

Table 2 provides an overview of how data will be collected for each of the quantitative study outcomes. Appendix 2 provides a detailed overview of how each outcomes maps to the study objectives and provides details on data collection and analysis for each outcome. Further details of each method of outcome collection are provided below.

**TABLE 2 OVERVIEW OF QUANTITATIVE OUTCOMES AND PROPOSED DATA COLLECTION METHODS**

| Outcome | Details | Data collection method | | | |
|---|---|---|---|---|---|
| | | GP records | Laboratory records | Patient questionnaire | Website usage |
| Testing rates | • Average number of tests per patient with each LTC per year (CKD, HTN, T2DM).<br>• We will define one 'test' as being a cluster of analytes which is requested as a single panel, for example full blood count would be counted as a single 'test'. | x | x | | |
| Cohort Characteristics | • Demographic profile of eligible participants with long term conditions (T2DM, HTN, CKD) including age (reported as median, IQR and stratification ), sex (counts), and ethnicity (counts).<br>• Socioeconomic status, derived from patient postcodes converted to Index of Multiple Deprivation (IMD) deciles. | x | | | |
| Describe wider impact of testing panels | • Proportion of patients with LTC who receive acute or new prescriptions in the 12 months before implementation, and 6 and 12 month period post implementation.<br>• Proportion of patients with LTC who get referred in the 12 months before implementation, and 6 and 12 month period post implementation. | x | | | |
| Adherence to the testing panels | • Proportion of patients with LTC who receive all the tests listed in the testing panels in the 12 month period post implementation.<br>• Proportion of patients with LTC who receive additional tests not listed in the testing panels in the 12 month period post implementation. | x | | | |
| Access to web-based communication tools (HCPs and patients) | • Number of downloads of HCP training videos<br>• Number of text messages with link to study website sent to patients<br>• Number of patient animation downloads<br>• Number of patient website visits<br>• Number of HCP website visits | | | | x |

| Outcome | Details | Data collection method | | | |
|---|---|---|---|---|---|
| | | GP records | Laboratory records | Patient questionnaire | Website usage |
| Serious Adverse Events:<br>• Hospital admissions<br>• Significant harm events attributed to lack of testing | • Unplanned hospital stay<br>• A&E visits<br>• Fatal or serious AND potentially related to study participation | x | | X | |
| Patient Activation | Patient Activation Measure (PAM) questionnaire[15] | | | X | |
| Overall patient satisfaction | NHS Friends and Family test[16] (*Appendix 3*) | | | X | |
| Patient understanding of test results | Questionnaire adapted from the BALLETs study[17] (*Appendix 3*) | | | X | |
| NHS costs of care | • primary care consultations for routine monitoring<br>• blood tests<br>• hospital-based care | x | | | |

## GP ELECTRONIC RECORDS

Baseline anonymised data (T0pr) on monthly blood testing rates amongst patients with LTC will be collected using automated searches of the GP records for the 12 months prior to the intervention being implemented. There will be a 1 month period while the intervention is implemented and then outcome data on monthly testing rates and unplanned hospitalisation rates amongst patients with LTC will be collected 12 months after the end of the intervention implementation period (T1pr).

## PATIENT QUESTIONNAIRES

Baseline patient questionnaires will be collected prior to the first LTC monitoring appointment after the intervention has been implemented at the practice level (T0), with patient questionnaire recruitment occurring in intervention practices via the study website as detailed previously ("Patient Recruitment"). A recognised risk of this approach is that participants may access the website and view intervention materials before completing the baseline questionnaire, potentially influencing responses and affecting the validity of baseline data. To mitigate this, clear instructions are provided informing participants that the questionnaire should be completed before accessing any Test Smart materials. Eligibility screening questions will be completed prior to the questionnaire and will include an item asking whether the participant has already viewed the website. Following completion of the baseline questionnaire, participants will receive a thank-you message that reiterates the importance of reviewing the Test Smart website before their monitoring appointment and before completing any follow-up questionnaires. In the baseline questionnaires, patients will be asked to consent to participate in the study and to allow direct contact to complete follow-up questionnaires. They will also be asked to provide basic demographic details and complete all patient level outcome questionnaires to provide a baseline measurement. These questionnaires will be repeated 2-weeks after their LTC monitoring appointment and again 6 months after their LTC monitoring appointment. Participants will receive a small shopping voucher to recompense their time participating after completing the 2-week and 6-month follow up questionnaires. Table 23 provides an overview of the patient level outcomes, data to be collected and timings for outcome collection; Appendix 3 provides a draft patient questionnaire.

### TABLE 23 OVERVIEW OF OUTCOMES TO BE COLLECTED THROUGH PATIENT QUESTIONNAIRES AND TIMINGS OF OUTCOME COLLECTION

| Outcome | 1 week prior to appointment (T0) | 2 weeks post-appointment (T1 – primary) | 6 months post-appointment (T2 – secondary) |
|---|---|---|---|
| Patient consent | x | | |
| Patient demographics | x | | |
| Patient Activation Measure (PAM) | x | X | x |
| Patient satisfaction | x | X | x |
| Website use/experience | | X | |
| Serious Adverse Events | | | x |

## QUALITATIVE INTERVIEWS

We will conduct between 44 and 50 semi-structured interviews with patients and healthcare professionals recruited from 4 intervention practices. Practices will be selected to ensure we capture different patient populations and practices. We will use social deprivation scores, percentage of ethnically diverse patients and patient list size as sampling criteria. We will aim to recruit 5 HCPs (2 GPs, 1 practice nurse, 2 phlebotomists: N=20) and 6 patients (2 patients per LTC, including some patients living with multimorbidity: N=24) from each practice. Patients completing the study questionnaire will be asked to indicate whether they would also be willing to take part in an interview. Interview participants will primarily be recruited via this route, but recruitment directly by HCP in intervention practices will also be used if needed in order to ensure the sample includes a range of age, gender, ethnicity, educational attainment and whether English is their primary language.

Interviews will follow a topic guide, co-developed with PPI and based on issues identified in WP3 as part of a Person Based Approach to developing an intervention.

Interviews with HCPs will explore:

- views on current testing practices for LTC
- the acceptability of the intervention
- views on any changes in workload during the period of the study
- experiences of LTC monitoring consultations and delivery of care pre and post intervention.
- barriers and facilitators to integration of the intervention in the practice
- views on intervention optimisation and sustainability to support a possible future widescale rollout.

Interviews with patients will explore:

- patient experience of their LTC monitoring consultations during the study, including their experience of getting test results
- patient information processing style and their levels of activation
- patient experience of receiving automated messages with additional links to the website with further information
- patient experience of using the intervention website (how many times, what information they accessed and whether it was helpful or not)
- patients understanding and knowledge of blood tests-why they are done, what test results mean
- experiences of blood test related anxiety
- acceptability of the intervention

Interviews will be conducted face to face at the GP practice or online depending on the interviewee preference. Interviews will be recorded using an encrypted digital recorder and transcribed verbatim.

### WEBSITE ANALYTICS

Website analytics will be built into the website design to allow us to collect information on the following for each intervention practice:

- Number of views of the HCP training videos
- Number of views of the patient animation
- Number of visits to each page of the website
- Number of downloads of the patient information leaflets

# 7. ANALYSIS

## Quantitative analysis

All analyses and reporting will be in line with CONSORT guidelines and its extension for cluster randomised trials. Primary analyses will be conducted on an intention-to-treat (ITT) basis. A full *Test Smart* statistical analysis plan will be developed and agreed by the Trial Steering Committee prior to undertaking analyses of the main trial. Descriptive statistics (means and standard deviations or medians and IQRs for continuous data dependent on distribution, and numbers and percentages for categorical data) will be presented to describe the characteristics of the participants and the flow of GP practices and patients throughout the study.

The co-primary outcomes will be the mean number of tests per patient with LTC at each practice over a 12-month period, and the Patient Activation Measure (PAM). Significance will be at the 2.5% level for these two co-primaries. Formal comparisons between intervention and control arms (all combined as well as each individual setting) will be made as follows: binary outcomes will be analysed using logistic regression and presented as odds ratios with corresponding 95% confidence intervals (CIs) and p-values; continuous outcomes will be analysed using linear regression and presented as mean differences with corresponding 95% CIs and p-values.

All quantitative data will be analysed using R.

## Qualitative analysis

Analysis will be informed by reflexive thematic approaches and will use NVIVO to manage the data set. 10% of the dataset will be double coded and a coding framework agreed before the remaining data is coded. Analysis will involve a thematic analysis and will initially separate the HCP data set to the patient data set before bringing them together to make comparisons. Codes in the qualitative data set will be compared across HCP roles, and then across patients in terms of practice and LTC. In the final phase of analysis comparisons will then be made between the HCP and patient data sets to look for overlap in emerging themes and determine where there are differences. Themes will be developed based on an analysis of patterns in the coded data. We will triangulate qualitative data from the process evaluation with questionnaire responses.

## Economic Analysis

We will record the resources used in developing and implementing the intervention (e.g. developing training packages, educational materials). We will use national (e.g. National cost collection for the NHS) and local (e.g. laboratory estimates of testing costs) to value the resources used in monitoring the LTCs and hospitalisations. We will provide descriptive statistics on resource use and cost by category of resource before and after implementation in the intervention and control practices. As cost data are likely to be non-normal and positively skewed due to a small number of patients with high NHS costs, we will consider using Generalised Linear Modelling (GLM) with appropriate link function and distribution to estimate the incremental cost/saving of the intervention. This will be presented alongside key primary and secondary outcomes in a cost-consequence table to provide information about the likely value of wider implementation across NHS GPs.

# 8. PATIENT AND PUBLIC INVOLVEMENT AND ENGAGEMENT

The *Test Smart* intervention has been developed collaboratively with our PPIE panel and our two patient co-applicants. Their comments and suggestions about the format of the intervention and parent/carer materials have informed both the design of the intervention and the planned patient reported outcomes. They have made significant contributions to the development of website content, and the design of the patient questionnaire (Appendix 2). Our two patient co-applicants have contributed to the content of this protocol and have reviewed the plain language summary.

Our PPIE panel will meet four times throughout the study, allowing the investigators to report on progress of the study and discuss issues that arise during the study. The PPIE group will input into all the materials for parents/carers as they are further developed including any patient-facing tools and patient information sheets. Our two co-applicants will continue as active members of the PMG and will participate in PMG meetings for the duration of the study. We will discuss the study findings with our PPIE group once the study is complete and work collaboratively with our PPIE group and patient co-applicants to communicate our findings with patients, including the development of patient accessible outputs such as animations and infographics. We will continue the programme patient collaboration log to record all PPIE events, summarise the discussions, and record outcomes and actions. At the end of the study, we will use the CUBE Framework questionnaire[18] to evaluate our PPIE throughout the programme of work.

# 9. KNOWLEDGE MOBILISATION AND IMPACT

We will present the final *Test Smart* intervention at a stakeholder event, to which we will invite:

- NHS Commissioners
- Commercial and non-profit companies such as
    - ARDENS who produce templates and popups for chronic disease monitoring
    - LabTestsOnline who produce patient facing resources for testing
    - Accurx who produce template text messages used by 98% of UK general practices
- Representatives from the Royal College of General Practitioners (RCGP)
- Representatives from the Royal College of Pathologists (RCPath)

- Representatives from NHS England Getting It Right First Time (GIRFT) Pathology programme
- Patient charities and patient groups such as Diabetes UK, Kidney Care UK and British Heart Foundation

Our existing stakeholder group already includes representatives from the RCGP, RCPath, GIRFT, commissioners and patients, and through these links we will be able to reach out to this wider stakeholder network. At these stakeholder events we will explore innovative approaches to integrating, scaling up and sustaining our intervention for monitoring LTC. We will share our methods for developing standardized testing panels for T2DM, CKD and HTN and explore whether similar methods could be used to standardise monitoring testing for other relevant LTC and drug monitoring.

We have been working closely with GIRFT throughout the Optimal Testing programme grant, and they have expressed an interest in integrating our testing panels into their national 'care sets' to reduce variation in testing pathways. We will make our *Test Smart* tools and guidance freely available and will work closely with the GIRFT team to disseminate these via their National Networks with the aim of embedding these test panels into national test ordering systems. This aligns with the GIRFT Pathology agenda as outlined in their 2021 Report.[19] We will also explore options of embedding our patient facing resources into the LabTestOnline website. Watson (co-PI) works as an editor for LabTestOnline and has experience of developing new resources for them during the covid-19 pandemic. If we are unable to maintain the website and ensure that all materials are kept up to date, the website will be taken down at the end of the study (Aug 2026).

We will work in close collaboration with the implementation team of the BNSSG Impact Accelerator Unit (IAU). The IAU is overseen by a Professor of Knowledge Mobilisation and is recognised by the NIHR Engagement and Dissemination Centre as a case study in how an Integrated Care Board (ICB) can support evidence use. Dissemination and Knowledge Mobilisation will be supported by a specialist Communications Officer. We will also work with the University of Bristol's Policy Bristol unit, which specialises in enhancing the influence and impact of research on policy and practice. We will collaborate with them to produce and disseminate a policy briefing to summarise the policy implications of our research.

## DATA HANDLING

Data will be collected and retained in accordance with the UK Data Protection Act 2018 and General Data Protection Regulation (GDPR).

### MAIN TRIAL DATA

Only fully anonymised data sets will be sent from the GP practices, local laboratories and ICBs. Data will be entered into a purpose designed REDCap database and data validation and cleaning will be carried out throughout the study. Standard operating procedures (SOPs) for database use, data validation and data cleaning will be available and regularly maintained.

Access to the database will be via a secure password-protected login with access restricted to university personel qualified by experience and training.

### EMBEDDED QUALITATIVE STUDY

Participants' names and contact details, along with the pseudonyms used for the interview, will be stored on a secure password protected University network filestore space where access will be limited to the members of the research team involved in the interviews. A file that links pseudonyms/study IDs to the interview data ID will be stored in a separate password protected location to avoid someone without authorisation being able to link names to anonymised data files.

Interviews will be digitally audio recorded using University of Bristol approved encrypted digital recorders. Encrypted recordings will be uploaded to the University network filestore space and from there they will be transferred to the University approved transcription company via the secure file uploading feature of their website.

## Access to Data

### SOURCE DATA

For monitoring purposes, the CI will allow monitors from the sponsor (or delegate), persons responsible for the audit, representatives of the REC and of the Regulatory Authorities to have direct access to source data/documents.

### ANONYMISED STUDY DATA

The Senior IT Manager (in collaboration with the Chief Investigators) will manage access rights to the data set. Prospective new users must demonstrate compliance with legal, data protection and ethical guidelines before any data are released. We anticipate that fully anonymised study data will be shared with other researchers to enable international prospective meta-analyses.

## Archiving

This study will be sponsored by the University of Bristol, the data custodian will be the CIs. All anonymised research data will be kept indefinitely in line with NIHR policy on data sharing. Non-essential study documentation will be deleted at the end of the study. All essential study documentation will be retained in a secure location during the conduct of the study and for 5 years after the end of the study in line with University archiving policy, after which these essential documents will be destroyed.

## Data sharing

Data will not be made available for sharing until after publication of the main results of the study. Thereafter, anonymised individual patient data will be made available for secondary research, conditional on assurance from the secondary researcher that the proposed use of the data is compliant with the NIHR position on the sharing of research data.[20] A minimum requirement with

respect to scientific quality will be a publicly available pre-specified protocol describing the purpose, methods and analysis of the secondary research, e.g. a protocol for a systematic review.

### Auditing

All quantitative data collection variables will be subjected to a 10% audit check.

## 10. TRIAL MANAGEMENT

The trial protocol has been developed in discussion with senior staff at Bristol Trials Centre (BTC) unit. The BTC is a UK Clinical Research Collaboration registered Clinical Trials Unit. Professor Pete Blair, Professor of Epidemiology and Statistics, with BTC is a co-applicant and lead statistician for this trial. Professor Sandra Eldridge, Professor of Statistics at BTC, has provided support and informal advice. The trial will conform to the BTC standard operating procedures. The central research team will prepare all the trial documentation and data collection forms, specify the randomisation scheme, develop and maintain the study database, check data quality as the trial progresses, monitor recruitment and carry out trial analyses in collaboration with the clinical investigators.

### Day-to-day management

The study will be managed by the Trial Management Group (TMG), which will meet face-to-face or via MS Teams. This group has been in place for WP1 to 4 and will continue to lead WP5. The TMG will be chaired by the Chief Investigators and will include all available members of the named research team.

### Trial Oversight

The existing Programme Steering Committee (PSC) for the Optimal Testing Grant will take on the role of Trial Steering Committee (TSC). The TSC has an independent Chair, Rafael Perrera (Professor of Medical Statistics at the University of Oxford). The committee includes Professor Danielle van der Windt (Professor of Primary Care Epidemiology), who has experience of Cluster Randomised Trials in Primary Care, and two experienced PPI representatives (John Walsh and Liz Clark). Additional TSC members have been recruited to provide additional expertise in trial methodology and primary care research: Brian Nicholson (associate professor at the University of Oxford and an academic GP) and Sandra Eldridge (Professor of Statistics, Bristol Medical School). Meetings have been pencilled in every 6 months, but the frequency will be decided at the first meeting. At the first TSC meeting, the committee will agree on its terms of reference. As this is a small, low risk trial, the TSC will also take on the role of data monitoring committee (DMC).

### Chief Investigators

The co-chief investigators (Penny Whiting and Jessica Watson) will be responsible for:

- Arranging clinical oversight of the safety of patients participating in the trial, including an ongoing review of the risk/benefit with the clinicians available in the team.

- Arranging for medical judgement in assigning seriousness, causality and expectedness of SAEs where it has not been possible to obtain local medical assessment with clinicians in the team.
- Arranging with clinicians in the team medical judgement in assigning expectedness.
- Immediate review of all reportable SAEs.
- Ensuring safety reports are prepared in collaboration with appropriate members of the TMG group for the main REC and TSC.
- Reporting safety information to the independent oversight committee identified for the trial (TSC).
- Expedited reporting of SAEs to the REC within required timelines.
- Central data collection of SAEs.

## Sponsor

The Sponsor, University of Bristol, will be responsible for overall oversight of the study.

# 11. SAFETY

Definitions of terms relating to adverse events are shown in Table 3. This study is a low-risk study, the intervention is indirect, and within the existing standard of care, so the participation risks are minimal. Therefore, only SARs will be reported to the TSC.

**Reporting SARs**

All SARs will be reported directly to the trial sponsor within 24 hours of occurrence. Reporting to the sponsor will be done directly and in accordance with the University Hospitals Bristol and Weston NHS Foundation Trust (UHBW) safety reporting standard operating procedure (SOP), using the UHBW reporting form. Specifically, the following documentation will be provided to the trial sites for the recording of SARs; WI_002 Instructions for completion of SAEs UHBW_v11.2 22.MAR.2023, TMPL_025 SAE SUSAR Initial Report v11 13.JUN.2024 TMPL_ 026 SAE SUSAR Follow Up Report v11 24.AUG.2023

The potential SAR will also be recorded in the trial log by the research team in accordance with GCP. The practising clinician and a clinician within the central research team will assess the causality of the SAR. In instances where the assessment of causality differs, the practice clinicians' decision will take precedence.

**TABLE 3. DEFINITIONS OF TERMS**

| Term | Definition |
|---|---|
| Adverse Event (AE) | Any untoward medical occurrence |

| | |
|---|---|
| Serious Adverse Event (SAE) | A serious adverse event is any untoward medical occurrence that meets one or more of the following criteria:<br>• results in death<br>• is life-threatening<br>• requires inpatient hospitalisation or prolongation of existing hospitalisation*<br>• results in persistent or significant disability/incapacity<br>• consists of a congenital anomaly or birth defect<br>• 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.<br>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) | SAE that is possibly, probably or definitely related to intervention. Note that SARs are only possible at Intervention Practices. |
| Suspected Unexpected Serious Adverse Reaction | An SAR the nature and severity of which is not consistent with the information about the intervention. Note that, as no SARs have been identified and none are expected, any SAR would be a SUSAR.) |
| *Definition of hospitalisation is an unplanned overnight stay. Note however that the patient must be formally admitted – waiting in outpatients or ED would not count as hospitalisation (even though this can sometimes be overnight). Prolongation of an existing hospitalisation qualifies as a SAE. Planned hospital stays would not be counted as SAEs, nor would stays in hospital for "social reasons" (e.g. respite care, the fact that there is no-one at home to care for the patient). Also, if patients had a day-case operation, this would not qualify as hospitalisation. However, if a planned operation was brought forward because of worsening symptoms, this would be considered as an SAE. | |

# 12. MONITORING, AUDIT AND INSPECTION

The study will be monitored and audited in accordance with the Sponsor's policy, which is consistent with the UK Policy Framework for Health and Social Care Research. All study related documents will be made available on request for monitoring and audit by the sponsor, the relevant REC and for inspection by other licensing bodies.

# 13. ETHICAL AND REGULATORY CONSIDERATIONS

## Research Ethics Committee (REC) review and reports

Research Ethics Committee and Health Research Authority (HRA) approval will be sought through the HRA for the trial. We believe the proposed research poses minimal risks to individual participants and does not raise any untoward ethical issues. Research ethics review of the protocol for the study and other study related essential documents will be carried out by a UK Research Ethics Committee (REC). Any amendments to these documents, after a favourable opinion from the REC/HRA has been given, will be submitted to the REC/HRA for approval prior to implementation.

The CI will notify the REC of the end of the study and if the study is ended prematurely (including the reasons for the premature termination). Within one year after the end of the study, the CI will submit a final report with the results, including any publications/abstracts, to the REC.

Study specific training activities will be carried out to ensure that the rights, safety nd wellbeing of research participants are protected, and that research data are reliable. Members of the research team will be qualified by education, training or experience.

## Ethical Issues

We will follow the recommendations of the Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials.[21] We consider our proposed CRTC a "pragmatic trial" as defined by the HRA as it does not involve "extra interventions beyond those required as part of the patient's routine care".[22]

We believe that the proposed research poses minimal risk to individual patients. The primary ethical concern is the potential risk that a patient may not receive a specific test that they would have received under current testing practices, potentially leading to a very rare event going undetected. However, the testing panels implemented in the study have been developed through extensive research and independent evaluation. Only tests identified as clinically useful for managing the specified long-term conditions have been included, thereby minimizing any clinical risk. While the possibility of an adverse event cannot be entirely eliminated, this risk is considered negligible. This very small risk needs to be balanced with the potential harms of over testing to a much larger group of patients. If a clinician decides that an individual patient requires additional tests over and above those recommended in the Evidence Based Testing Strategies (EBTS) then these can be added based on clinical need.

As this is a cluster RCT the intervention will be implemented at a practice level and we will not be gaining individual informed consent from all patients with long-term conditions to receive the intervention. Our primary outcome, testing volume, is based on aggregate data (number of tests per month) and so cannot be linked back to individual patients. We therefore do not consider it proportionate to gain individual informed consent from all patients with long-term conditions. This is not the case for patient reported outcomes (patient activation, satisfaction and test result understanding), where a subset of patients will be recruited and consented to provide patient reported outcome data.

We will ensure that all staff at recruited practices are aware of the study and are able to provide patients with verbal information if requested. As well as this, a study poster advertising the GP practices participation in the study will be displayed in patient waiting rooms in intervention practices. The poster will display the study web address and contact details of the research team so that patients can find out more about the study or ask any questions.

## Regulatory Compliance and Research Governance

This study will be conducted in accordance with the UK Policy Framework for Health and Social Care Research. Any amendments to the study documents must be approved by the sponsor prior to submission to the REC. Before any site can enrol patients into the study, the CIs or designee will obtain confirmation of capacity and capability for each site in-line with HRA processes and wait for updated sponsorship from the Sponsor before commencing research at these sites. For all amendments the CIs or designee will confirm with the Sponsor, the HRA (+/- REC) and sites' R&D departments that permissions are ongoing.

## Data protection and patient confidentiality

The University of Bristol will be the data custodian. All data held in Bristol will conform to University of Bristol's Data Security Policy and in Compliance with the Data Protection Act 1998. Data obtained by paper will be entered onto and maintained on an SQL Server database system maintained by University of Bristol Information Services. All electronic data files will be saved in a secured computer and to a password protected University of Bristol network space, in accordance with the University of Bristol's data security policies.

For practice level data, no personal data (e.g. name and address, or any data from which a participant might be identified) will be collected in this study. Limited pseudonymised data, such as patient postcodes, will be collected at baseline to enable the derivation of Index of Multiple Deprivation (IMD) deciles. Postcodes will be retained only for the duration required to perform this conversion and will be deleted immediately thereafter, ensuring that no postcode information is held within the analysis dataset. The data collected from GP electronic health records will be anonymised. Data relating to the characteristics of the individual practices (E.g. How many patients registered? Number and types of clinician etc.) will be collected on electronic forms directly into the REDCap database at baseline.

For participants completing patient level questionnaires, each participant will be assigned a unique study ID at the point of data collection (completion of baseline questionnaires). In the first questionnaire patients will be asked to share their email address. This will be used to send out the invitation of follow-up questionnaires and to link baseline and follow-up questionnaires. This will be stored securely within the RedCAP database for the duration of the follow-up (6 months). Once the patient has filled out all three questionnaires, the email addresses will be removed from the RedCAP database and stored separately from the questionnaire data in a dedicated study folder with restricted access (only to the study team). The questionnaire 4, which will only be asked at the last time point (at 6 month follow-up), includes a question on unplanned hospital admission. Name and address will be requested for patients who consent to providing paper questionnaires, and name and date of birth will be requested for patients who report unplanned hospital admission This information will be stored separately from the questionnaire responses in a dedicated study folder with restricted access. We will only use this information to ask their GP to check their medical records to see whether this admission was linked to the monitoring of their long-term condition. Once this has been checked, the date of birth and name of the participant will be deleted.

Interviews will be recorded on an encrypted digital recorder which will be locked in a secured cabinet at the Department of Population Health Sciences. Recordings will be transferred onto a computer as soon as possible after each interview and stored only in a password protected drive maintained by the University of Bristol. Only the qualitative researchers working on this study will have access to this drive. Recordings of consultations or interviews about healthcare hold confidential and sensitive personal information and full anonymisation e.g. of health condition / history may damage the research potential of the data. Transcripts will be anonymised before storage by replacing any references to names or places. An anonymisation log of all replacements made will be retained.

Recordings and transcriptions will be named with a study-assigned participant number, centre initials, and the date of recording. There will be no participant identifiers in files, databases, or transcripts, which will only be labelled with study assigned participant numbers. All recordings will be securely transferred to a University of Bristol approved transcription company or transcriber that has signed the required confidentiality agreements. All transcripts will be anonymised upon receipt.

As in line with NIHR policy all anonymised research data will be kept indefinitely for open access. All nonessential data will be wiped upon completion of the study. Essential study documents will be kept for up to 5 years, after which they will be deleted and all copies destroyed in accordance with the University of Bristol's secure erasure of data policy.

## Safeguarding and reports of poor practice

The research team will ensure that all GCP guidelines are complied with throughout the trial. Any reports of safeguarding failures or poor practices will be recorded in the trial log and escalated directly to the trial PI and sponsor. All credible allegations will be reported directly to the NIHR and appropriate professional bodies. The NIHR "Fraud, safeguarding or security concern or incident reporting form" will be provided to the trial sites and stored in the study site documentation so reports may be made anonymously to NIHR for investigation.

## Financial and other competing interests

The research team must disclose any ownership interests that may be related to products, services, or interventions considered for use in the trial or that may be significantly affected by the trial. Competing interests will be reported in all publications and in the final report.

## Indemnity

Indemnity for patient clinical care is subject to GP practices usual arrangements. The University of Bristol has arranged Public Liability and Professional Negligence insurance in respect of its responsibilities.

## Amendments

The Sponsor will determine whether an amendment is substantial or non-substantial. All amendments will be processed through the HRA and where appropriate the REC. If applicable, other specialist review bodies (e.g. CAG) will be notified about substantial amendments in case the amendment affects their opinion of the study. Amendments will also be notified to NHS R&D departments of participating sites to confirm ongoing capacity and capability to deliver the study.

## Access to the final trial dataset

Anonymous research data will be stored securely and kept for future analysis. Members of the TMG will develop a data sharing policy consistent with University of Bristol policy. Data will be kept anonymous on secure access computers, and access will be via written confidentiality and data sharing agreements (DSA) with the CI (or his appointed nominee), supervised by the CIs with the involvement of other members of the research team. Post-trial this may involve the Bristol Data Service who will allow access according to our pre-specified criteria. Any request approved will be covered by a written DSA, detailing limitations of use, transfer to 3rd parties, data storage and acknowledgements. The person applying for use of the data will be scrutinized for appropriate eligibility by members of the research team. All requests will require their own separate REC approval prior to data being released. Data will not be released prior to analyses for purposes that might detrimentally affect the study integrity.

# 14. DISSEMINATION POLICY

A comprehensive dissemination plan will be developed by the project team. It is anticipated that the Protocol will be submitted to BMJ Open. The results of the trial will be published in the academic press and all participating GP practices will be offered a lay summary of the main findings of the study. We will disseminate the findings both at a primary care level via ICBs and national conferences as well as international conferences. We will work with the specialist communications team, our public contributors, and our Plain English Panel to ensure that summaries and findings are accessible to patients. Public contributors will work with the academic team members to produce accessible summaries of the different components of the research project.

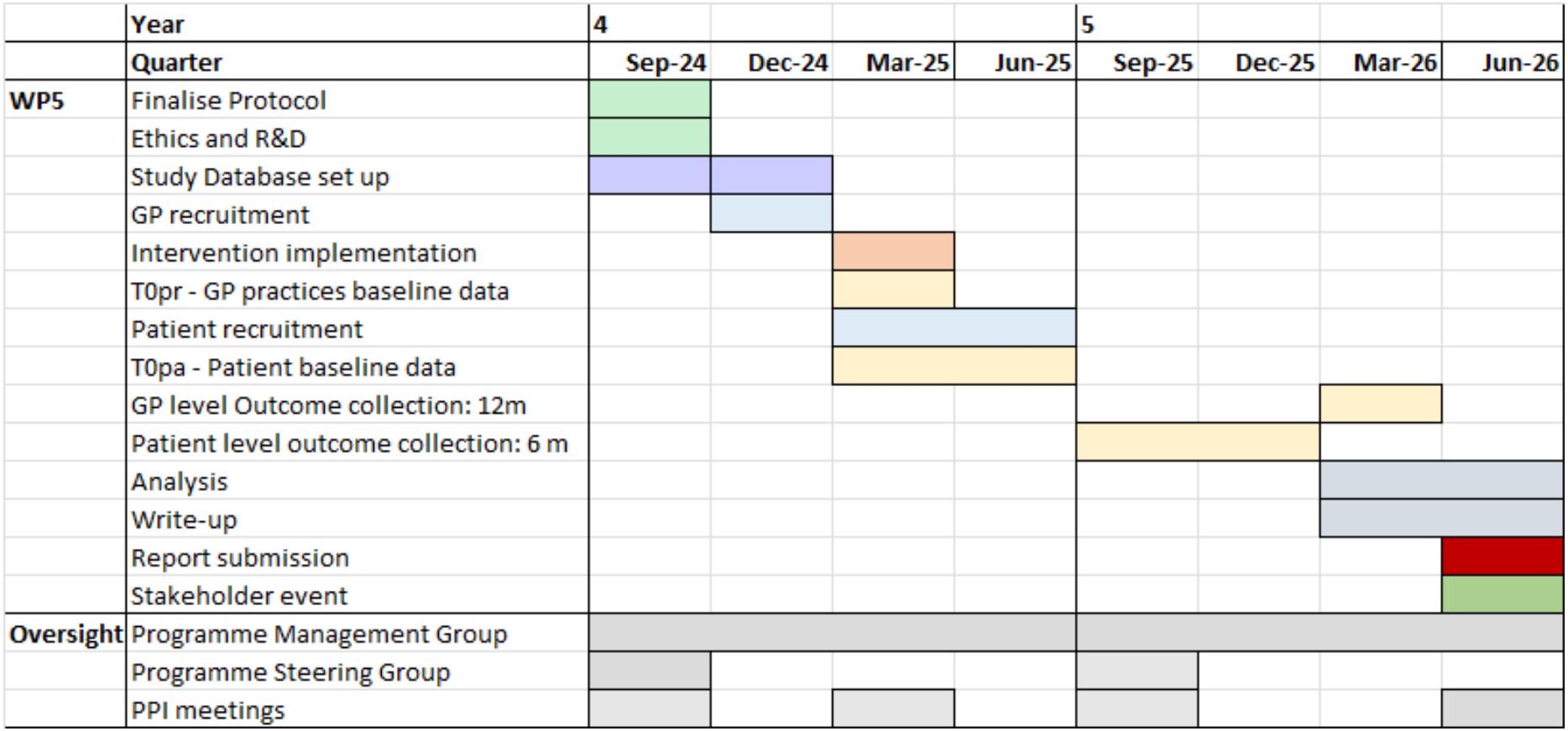
On completion of the implementation study a final report will be prepared for the NIHR and once approved made publicly available on their website.

## 15. REFERENCES


1. The King's Fund. Long-term conditions and multi-morbidity. 2013
2. Barnett K, Mercer SW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380(9836):37-43. doi: 10.1016/S0140-6736(12)60240-2 [published Online First: 2012/05/15]
3. NHS Digital. Quality and Outcomes Framework (QOF) - 2015-16. 2016. https://digital.nhs.uk/data-and-information/publications/statistical/quality-and-outcomes-framework-achievement-prevalence-and-exceptions-data/quality-and-outcomes-framework-qof-2015-16.
4. Elwenspoek MMC, Patel R, Watson JC, et al. Are guidelines for monitoring chronic disease in primary care evidence based? *BMJ* 2019;365:l2319. doi: 10.1136/bmj.l2319 [published Online First: 2019/06/15]
5. National Institute for Health and Care Excellence (NICE). Clinical Guideline 182. Chronic kidney disease (partial update). *National Clinical Guideline Centre* 2014
6. National Institute for Health and Care Excellence (NICE). Clinical Guideline Update (NG28). Type 2 diabetes in adults. *Internal Clinical Guidelines Team* 2015
7. National Institute for Health and Clinical Excellence (NICE). Clinical Guideline 127. Hypertension. *National Clinical Guideline Centre* 2011
8. Legido-Quigley H, Panteli D, Car J, et al. Clinical guidelines for chronic conditions in the European Union. Observatory Studies Series
9. O'Sullivan JW, Stevens S, Hobbs FDR, et al. Temporal trends in use of tests in UK primary care, 2000-15: retrospective analysis of 250 million tests. *BMJ* 2018;363:k4666. doi: 10.1136/bmj.k4666 [published Online First: 2018/11/30]
10. NHS England. The 2nd Atlas of Variation in NHS Diagnostic Services in England, 2017.
11. Busby J, Schroeder K, Woltersdorf W, et al. Temporal growth and geographic variation in the use of laboratory tests by NHS general practices: using routine data to identify research priorities. *Br J Gen Pract* 2013;63(609):e256-66. doi: 10.3399/bjgp13X665224 [published Online First: 2013/04/02]
12. Whiting D, Croker R, Watson J, et al. Optimising laboratory monitoring of chronic conditions in primary care: a quality improvement framework. *BMJ Open Qual* 2019;8(1):e000349. doi: 10.1136/bmjoq-2018-000349 [published Online First: 2019/04/19]
13. Glasziou PP, Irwig L, Heritier S, et al. Monitoring cholesterol levels: measurement error or true change? *Ann Intern Med* 2008;148(9):656-61. doi: 10.7326/0003-4819-148-9-200805060-00005 [published Online First: 2008/05/07]
14. Blakemore A, Hann M, Howells K, et al. Patient activation in older people with long-term conditions and multimorbidity: correlates and change in a cohort study in the United Kingdom. *BMC Health Services Research* 2016;16:1-11.
15. Hibbard JH, Stockard J, Mahoney ER, et al. Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. *Health Serv Res* 2004;39(4 Pt 1):1005-26. doi: 10.1111/j.1475-6773.2004.00269.x [published Online First: 2004/07/03]
16. NHS. Friends and Family Test (FFT) 2023 [Available from: https://www.nhs.uk/using-the-nhs/about-the-nhs/friends-and-family-test-fft/ accessed 19/1/2024 2024.
17. Lilford RJ, Bentham L, Girling A, et al. Birmingham and Lambeth Liver Evaluation Testing Strategies (BALLETS): a prospective cohort study. *Health Technol Assess* 2013;17(28):i-xiv, 1-307. doi: 10.3310/hta17280 [published Online First: 2013/07/10]
18. Kok M. Guidance Document: Evaluating public involvement in research: UWE Bristol, 2018.

19. Lewis T, Wood M, Myers M. Pathology: GIRFT Programme National Specialty Report. 2021. https://www.gettingitrightfirsttime.co.uk/wp-content/uploads/2022/05/Pathology-4May22j.pdf.
20. NIHR. NIHR position on the sharing of research data 2024 [Available from: https://www.nihr.ac.uk/documents/nihr-position-on-the-sharing-of-research-data/12253 accessed 19/01/2024 2024.
21. Weijer C, Taljaard M, Grimshaw JM, Edwards SJ, Eccles MP, Ottawa Ethics of Cluster Randomised Trials Consensus Group. The Ottawa statement on the ethical design and conduct of cluster randomized trials: A short report. Research Ethics. 2015 Mar;11(1):52-60.
22. Health Research Authority. [Available from: http://www.hra-decisiontools.org.uk/consent/]
23. Davey HM, Barratt AL, Butow PN, et al. A one-item question with a Likert or Visual Analog Scale adequately measured current anxiety. *J Clin Epidemiol* 2007;60(4):356-60. doi: 10.1016/j.jclinepi.2006.07.015 [published Online First: 2007/03/10]

## Appendix 1: Study Gantt Chart



## Appendix 2: Overview of how each outcome maps to the study objectives, data to be collected on each outcome and details on how data will be analysed

| Objective | Outcome | Data collection and analysis |
|---|---|---|
| 1. Does the *Test Smart* intervention reduce rates of testing for monitoring of LTC in primary care? | Monthly practice level blood testing rates in the 12 months prior to implementation and 12 months post implementation | Data to be collected via automated searches of the primary care electronic health records |
| 2. Does the Test Smart intervention improve patient activation? | Patient Activation (PAM) | Patient completed Patient Activation Measure (PAM) questionnaire (Appendix 3) |
| 3. Is there any evidence that the *Test Smart* intervention may cause harm through reduced testing? | Monthly practice level unplanned hospitalisation rates amongst patients with LTC in the 12 months prior to implementation and 12 months post implementation<br>Monthly practice level A&E visits amongst patients with LTC in the 12 months prior to implementation and 12 months post implementation<br>Estimated false positive and false negative test results | Data to be collected via automated searches of the primary care electronic health records<br><br>We will use model parameters from WP2 to estimate false positive and false negative test results. |
| 4. Does the *Test Smart* intervention improve patients' satisfaction with their monitoring appointments? | Patient satisfaction | Patient completed NHS Friends and Family test (Appendix 3) |
| 5. Does the *Test Smart* intervention improve patient understanding of their test results? | Patient understanding of blood tests | Patient completed questionnaire adapted from the BALLETS study (Appendix 3) |

| | | |
|---|---|---|
| 6. What is the acceptability and fidelity of the *Test Smart* intervention? | Adherence to the testing panels | • Proportion of patients with LTC who receive all the tests listed in the testing panels in the 12 month period post implementation.<br>• Proportion of patients with LTC who receive additional tests not listed in the testing panels in the 12 month period post implementation. |
| | Access to web-based communication tools (HCPs and patients) | • Number of times ~~Accurx text~~automated messages with links to website sent to patients<br>• Number of downloads of HCP training videos<br>• Number of patient animation downloads<br>• Number of website visits |
| | Barriers and facilitators to delivering the components of the intervention | • Process evaluation |
| 7. What is the cost-effectiveness of the *Test Smart* intervention? | NHS costs/savings of implementing the *test smart* intervention. Comparison of costs and consequences for decision makers to judge cost-effectiveness of further implementation | Data to be collected from study records (for intervention development and delivery); GP and hospital records (for NHS costs of monitoring and hospitalisations). Analysis will be finalised in a Health Economics Analysis Plan (HEAP) |
| 8. What are the barriers and facilitators to the widespread adoption, integration and sustainability of the *Test Smart* intervention | • Clinician and patient views on the intervention experience<br>• Stakeholder engagement activities | • Process evaluation |

# Appendix 3 : Patient level questionnaires

## Questionnaire 1: Patient Activation Measure (PAM)[15]

Below are some statements people sometimes make when they talk about their health. Please indicate how much you agree or disagree with each statement as it applies to you personally by circling your answer. Your answers should be what is true for you and not just what you think others want you to say. If the statement does not apply to you, tick N/A.

| | Strongly disagree | Disagree | Agree | Strongly agree | N/A |
|---|---|---|---|---|---|
| When all's said and done, I am the person who is responsible for taking care of my health | | | | | |
| Taking an active role in my own health care is the most important thing that affects my health | | | | | |
| I know what each of my prescribed medications do | | | | | |
| I am confident that I can tell whether I need to go to the doctor or whether I can take care of a health problem myself | | | | | |
| I am confident that I can tell a doctor concerns I have even when he or she does not ask | | | | | |
| I am confident that I can follow through on medical treatments I may need to do at home | | | | | |
| I have been able to maintain (keep up with) lifestyle changes, like eating right or exercising | | | | | |
| I know how to prevent problems with my health | | | | | |
| I am confident I can figure out solutions when new problems arise with my health | | | | | |
| I am confident that I can maintain lifestyle changes, like eating right and exercising, even during times of stress | | | | | |

## Questionnaire 2: Patient experience (NHS family and friends test[16])

Thinking about your recent blood testing for monitoring long term conditions:

| | Very good | Good | Neither good nor poor | Poor | Very poor | Don't know |
|---|---|---|---|---|---|---|
| A. Overall, how was your experience of our service? | | | | | | |
| B. Please can you tell us why you gave your answer? | | | | | | |

## Questionnaire 3: Your blood test results (adapted from Ballets study[17])

| | | | | | | |
|---|---|---|---|---|---|---|
| C. | How well do you feel you understand what your blood tests tell you about your health? | Completely understand | Understand a little | Unsure | A bit confused | Do not understand at all |
| D. | How satisfied were you with the amount of information you were given about your blood test results? | Very satisfied | Satisfied | Neither satisfied not dissatisfied | Dissatisfied | Very dissatisfied |
| E. | How clear was the information you were given about your blood test results? | Very clear | Clear | Neither clear nor unclear | Unclear | Very unclear |
| F. | How worried were you when waiting for your test results?[23] | Not at all worried | A little worried | Moderately worried | Very worried | Extremely worried |

## Questionnaire 4: Unplanned hospital admissions (6 month follow up only)

| | Yes | No | Unsure |
|---|---|---|---|
| G. Have you had any unplanned hospital admissions in the past 6 months? | | | |
| H. If yes, please provide your details. Your GP will be asked to check your medical records to see whether this admission was linked to the monitoring of your long term condition. | [Name]<br>[DOB] | | |