UNIVERSITY OF Southampton

POINT OF CARE TESTING TO REDUCE UNNECESSARY ANTIBIOTIC USE FOR LOWER RESPIRATORY TRACT INFECTIONS IN OLDER ADULTS IN PRIMARY CARE: A RANDOMISED FEASIBILITY TRIAL.

IRAS - 341760

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1. Full Title of Project;

Point of Care Testing to Reduce Unnecessary Antibiotic Use for Lower Respiratory Tract Infections in Older Adults in Primary Care: A Randomised Feasibility Trial.

2. Summary of Research (Abstract)

Aim

To explore the feasibility of a trial investigating using, and evaluating the use of, pathogen-detection point-of-care tests to help guide the management of LRTIs in older adults in a primary care setting.

Objectives

1. To assess the feasibility of conducting a trial investigating the use of lateral flow type point-of-care testing to improve the management of older adults with LRTIs in primary care, including recruitment, randomisation, and data collection.

2. To understand the acceptability of, and barriers and facilitators to using COVID-19 and Influenza A/B lateral flow type tests, with and without biomarker point-of-care tests, to help guide the management of lower respiratory tract infections (LRTI) in older adults in primary care.

3. To estimate the effects of using these tests on use of antimicrobials, in order to inform a future sample size calculation.

4. To understand the experiences of people with RTIs and primary care clinicians on point-of-care testing for respiratory viruses and biomarkers, and its effect on prescribing.

Design
4-arm randomised feasibility trial with nested qualitative study.

Participants and Setting
Adults aged 65 years and over with symptoms of an LRTI consulting primary care.

Interventions
- A] SureScreen COVID-19/Influenza A/B lateral flow alone
- B] SureScreen COVID-19/Influenza A/B lateral flow in combination with FebriDx
- C] SureScreen COVID-19/Influenza A/B lateral flow in combination with SureScreen CRP

Control
Usual care.

Feasibility Outcome Measures

- Recruitment rate – number of participants per month
    - The number of randomised participants recruited per month.
    - Follow-up rate: Proportion of follow up diaries returned at end of study

    - Withdrawals
    - Proportion eligible for study
- Compliance to study procedures –
    - The proportion of participants who have valid test results.
    - The proportion of participants who had the correct number of tests done in their assigned group
- Acceptability of intervention -
    - Clinicians' acceptability of using the intervention(s) (1-10 scale)
    - Participants acceptability of the intervention (1-10 scale)
    - Participant refusal

Exploratory Outcome Measures

- Percentage of participants prescribed antibiotics on day of recruitment and within 28 days from consultation.
- Percentage of participants prescribed antivirals on day of recruitment and within 28 days from consultation.
- Percentage of cases in which testing changed clinician's prescribing decision
- Average time taken to return to usual activities
- Percentage of re-consultations within 28 days from consultation.
- Percentage of hospitalisations within 28 days from consultation.

End Point

The study will end when 180 participants have been recruited, 30 total for each site, and 4 weeks had elapsed since the last recruitment for the final diary to have been sent. Alternatively, 10 months have elapsed without full recruitment.

Impact and Dissemination

This trial will help inform investigators whether the study design is feasible on a larger scale by looking at recruitment rates, compliance, and other feasibility outcomes. Furthermore, it will allow exploratory analysis of any obvious trends on whether point of care testing influences antibiotic prescribing in older adults.

3. Background and Rationale

Antibiotic Use for LRTIs in Primary Care

LRTIs often result in an antibiotic prescription in a primary care setting[1], with 60% of all antibiotics in general practice being prescribed for RTIs[2], and prescribing for LRTIs ranging from 33% of cases to 80% for adults depending on the practice[3]. However, around 70% of all respiratory infections are caused by viruses[4]. Viruses are not affected by antibiotics, and therefore any antibiotic prescription given for them is unlikely to cause any improvement[5]. In the UK around 50% of primary care consultations for RTIs result in an antibiotic prescription[4]. However, this can range from 20%-80%[4]. NICE guidelines state that antibiotics have a limited efficacy in treating a large proportion of RTIs in adult and children, as shown by evidence in numerous randomised placebo-controlled trials[6]. This is because RTIs are very often self-limiting and complications from withholding antibiotics are rare[6]. One of the reasons for the high number of prescriptions in primary care is the fact it is very difficult to distinguish viral and bacterial respiratory infections using clinical manifestations[7].

Furthermore, some patients coming to their GP with a respiratory illness are in an at-risk group who may be more seriously affected by any sort of illness. These are those that are immunocompromised or adults over the age of 65[8]. In these groups, viral infections are more likely to lead to a bacterial co-infection or other complications[9]. For example community acquired LRTIs and pneumonia (CAP) are common causes of mortality and morbidity in older adults (>65 years)[10]. Because of this, clinicians prescribe antibiotics just in case as it is hard to determine the causative agent(s) of infection[11, 12, 13].

Antiviral Use for LRTIs in Primary Care

Despite NICE guidelines stating that both oseltamivir and zanamivir are recommended for treatment of influenza in adults if they are in an at-risk group[14], antivirals are rarely used in primary care for LRTIs. This is likely due to the difficulty in distinguishing bacterial and viral infections[15]. Testing for pathogens and host response may also lead to more confidence in prescribing antivirals, like oseltamivir.

The highest fatality rate from influenza is in those over the age of 65 (>80% of deaths)[16]. In the UK during the 2022/2023 flu season, 454 influenza outbreaks occurred, with 413 of these occurring in care homes[17]. Additionally, during the same season 14,623 deaths were associated with influenza, with 12,546 (85.8%) of these deaths being adults over the age of 65[17]. This shows that older adults are at a higher risk of infection and fatality from influenza. There is some evidence to suggest that the use of antivirals can have a positive effect on reducing the number of symptomatic days and reduce the time to return to usual activities[18]. Specifically, it was found that those over the age of 65, with a high illness severity, comorbid conditions, and had been ill for more than 48 hours, benefitted the most[18]. Those who fit into this subgroup reduced their symptomatic days by 3.2 days from taking the antiviral oseltamivir[18]. This benefit was less so for those with less severe illness, shorter illness duration, and those without comorbidities, but it does show there is some benefit to giving antivirals to specific patient groups[18]. However, this trial did not implement a placebo group for comparison[18]. This makes it hard to decipher whether the change was from oseltamivir itself, or simply because of the placebo effect. Additionally, treatment with oseltamivir caused side effects such as nausea and vomiting[18], which arguably is not worth the beneficial effects. Furthermore, older adults were underrepresented in the study, with only 6% of the total population in the intervention group being over 65[18]. Because of this, it is hard to know whether antivirals had a significant effect on illness days. Currently, antivirals are seldom used in European primary care as not only it is hard to distinguish the causative agent of RTIs[16] but antivirals are normally seen as ineffective due to lack of substantial evidence[18].

There is potential that if clinicians are more confident in their diagnosis of viral infections, they may be able to begin prescribing antivirals to help reduce symptom length and reduce return to usual activity time. However, it is important to only prescribe antivirals when necessary to prevent the emergence of resistance, as is the case with antibiotics. The same care should be taken when prescribing antivirals as with antibiotics to ensure similar mistakes are not made.

Point-of-Care Testing for LRTIs in Primary Care

Point-of-care testing (POCT) provides a way in which clinicians can quickly and easily test patients to help inform antibiotic prescribing decisions[19]. By being able to identify particular pathogens and/or estimate host response, clinicians can be more confident in their decision to prescribe antibiotics[20]. POCTs have also been shown to reassure patients who may have otherwise been unwilling to not receive antibiotic treatment[21]. Additionally, it has been

shown, using a direct cost-of-illness calculation, that using POCTs in primary care in Germany for those presenting with influenza-like illness reduced the costs of illness in older adults by 26% than costs without diagnostic support, as it allowed the correct treatment to be given immediately[22]. There are many different POC tests and most of them fit into two categories – biomarker-based testing and pathogen-based testing.

The Use of POCTs to Reduce Antibiotic Prescribing

Several systematic reviews have shown the benefit of CRP point-of-care testing in reducing the number of antibiotics being prescribed in primary care for respiratory tract infections[11, 23, 24, 25, 26].

POCTs are already used more widely in mainland Europe. In one study, they found that the use of CRP POCTs in nine general practices in the Netherlands resulted in a change of prescribing decision in 27% of patients that were tested, with 57% of these changing from antibiotic prescribing pre-test to no antibiotic prescribing post-test[27]. However, 40% of these changes were not according to the guideline recommendations, suggesting testing may not affect prescribing in a systematic way[27]. This shows that despite increasing confidence somewhat, a single POCT is still used in conjunction with clinical manifestations to ensure the appropriate treatment is given. This also suggests that clinicians do not have full confidence in CRP POC testing and still rely on their own clinical judgement. Additionally, in another study, it was found that GPs used different CRP cut off points depending on the patient[28]. If a patient had more severe clinical manifestations, a lower CRP cut off was used, and vice versa[28]. This demonstrates that clear guidelines need to be implemented alongside POCTs to ensure they are being used correctly.

There are still barriers to the implementation of point-of-care testing in primary care. In one study, stakeholders were interviewed about their opinions on barriers and facilitators to the implementation of POCTs in the UK[21]. Several stakeholders believed that some POCTs have been developed without or before an exact clinical need or pathway benefit has been established[20]. Additionally, even if there was a clinical need, the volume and accuracy provided by laboratory testing could still put need for POC testing into questions[21]. Others were worried about overuse of POCTs and clinicians becoming too reliant on the results rather than their own judgement[20, 21, 29]. Some GPs have also stated that they'd rather rely on their own clinical assessment than the results of a POCT[30]. There have also been issues with clinicians worrying that POCTs will add to a clinician's already busy workload[20, 31]. Further concerns were raised about the specificity, sensitivity, and reliability of POCTs[20]. This could lead to serious diagnoses being missed, and potentially severe consequences[20]. Evidence needs to be provided that can convince GPs that a POCT will be a great enough benefit to be worth using.

Currently, there is some evidence towards using CRP testing for LRTIs to reduce the use of antibiotics in primary care. CRP testing is recommended to be considered for adults presenting with LRTI in primary care[32]. The results of CRP should be taken into consideration in terms of antibiotic prescribing with guidelines stating antibiotics should only be prescribed immediately when CRP is over 100mg/L[32]. Despite this being stated in NICE guidance, there is still uncertainties about the use of CRP POCTs, and further RCTs should be conducted to ensure its benefit[32].

At present, there is little to no evidence about using pathogen based POCTs or using POCTs for older adults to reduce antibiotic prescriptions. Without this knowledge, it would be hard to justify the implementation of pathogen-based POCTs. Therefore, more evidence is

needed to understand the benefits of pathogen-based testing or pathogen-based testing in combination with host response testing for LRTIs in older adults in primary care.

POCTs and Antivirals

In one study, implementation of influenza POCTs in primary care workflows was investigated[33]. This study was nested into the English national sentinel surveillance network, with approximately 78,500 patients taking part[33]. Nasal swabs were taken from patients presenting with acute influenza-like illness and acute respiratory illness and tested using the Abbott ID NOW analyser[33]. Several outcomes were recorded, the main one being the number of valid influenza swabs taken and tested, but also antibiotic and antiviral prescribing rates[33]. It was shown that patients who received a positive POCT result for influenza were significantly more likely to receive antivirals on the day of the results[33]. Conversely, those who were positive for influenza were less likely to receive an antibiotic prescription[33]. However, as the main aim of the study was to investigate influenza POC testing, and not antivirals, no data was collected regarding the effects of antiviral prescription.

Another similar study was then conducted the following year[34]. This study recruited 184,813 patients over the age of 6 months presenting with influenza-like illness[34]. Similarly to the previous study[33], the Abbott ID NOW was used to test the samples[34]. Their main outcome was the number of POCT virologically confirmed influenzas in the study population, but a secondary outcome was influenza antiviral prescribing[34]. They found that the odds of receiving an antiviral after a positive influenza POCT result was 21.1[34]. However, only six patients, out of 648 total participants (128 of which had positive influenza POCTs), were given antivirals, with five having a positive result for influenza[34]. This shows that despite POC testing, antiviral prescribing is still rarely used. Conversely, they found that the odds of receiving an antibiotic after receiving a positive influenza result was 0.6[34]. Of the 205 patients receiving antibiotics, 30 (14.6%) had a positive result for influenza[34]. This suggests that POC testing for influenza could increase the likelihood of being able to be treated with antivirals, and also reduces the odds of an unnecessary antibiotic prescription. However, due to the very small number of those receiving an antiviral prescription, it would be very hard to know if POCTs had any effect on prescribing. It is important to understand the thoughts of prescribers on the use of antivirals, as that plays as important a role as influenza confirmation in prescribing decisions.

However, another study found differing results. Patients over the age of 18 in hospitals presenting with acute respiratory illness who had been unwell for 10 days or less were recruited[35]. Patients were randomised to a control group or the intervention group, which involved nose and throat swabbing to be tested for a panel of respiratory pathogens using the BioFire FilmArray Respiratory Panel 2[35]. 307 participants were randomised to the testing group, with 100 having influenza[35]. The use of molecular POCTs for influenza did increase the use of neuraminidase inhibitors and nearly all patients with influenza were given appropriate antiviral treatment[35]. However, it was also found that most patients with influenza in both the mPOCT group and the control group were given antibiotics regardless[35]. This is thought to be because that the identification of a virus by PCR does not rule out the presence of a concomitant bacterial infection[35]. This leads to clinicians continuing to prescribe antibiotics when patients are admitted to hospital[35]. However, this study was done in secondary care, where prescribing habits likely differ from primary care due to the risk of hospital-acquired infections, and different resources being available. Despite this, there remains uncertainty of the effects of POC testing on antiviral prescribing.

Because of the differing results on the effectiveness of POCTs to aid antimicrobial prescribing, it is important for future studies to determine the best way to use POCTs to influence prescribing. Further research is needed to determine how to use POCT testing effectively in primary care to guide appropriate antibiotic and antiviral prescribing in selected populations who will benefit most.

Why is this Research Needed Now?

While there are several studies investigating the use of biomarker tests for RTI in primary care, there is a lack of evidence on the use of lateral-flow type pathogen-based point-of-care testing, specifically in older adults. Additionally, there is a further lack of evidence for the use of a combination of biomarker and pathogen based POCTs for LRTIs in primary care. As primary care manages the majority of respiratory tract related illnesses, it is vital to understand the impact POC testing would have on antimicrobial prescribing in this setting. As a feasibility trial, we will aim to investigate recruitment, follow up rate, randomisation, and will use qualitative interviews to understand the thoughts of those involved in the study. Additionally, these interviews will also aim to understand why clinicians are may still prescribe antibiotics when the infection is more likely to be confirmed to be a viral infection. By doing this, we will be able to understand the clinician's thought process behind prescribing and how POC testing can help assist them. As exploratory outcomes, this study will look at whether the use of the SureScreen SARS-CoV-2/Influenza A&B lateral flow test will help to reduce the number of unnecessary antibiotic prescriptions for older adults in a primary care setting. Furthermore, this study will compare, using descriptive statistics, the effectiveness of the standalone lateral flow test to a combination of the SureScreen lateral flow and FebriDx biomarker POCT at reducing unnecessary antibiotic prescriptions. This could potentially combat the limitations of both tests and give clinicians more confidence in their prescribing decisions. Finally, data about the use of antivirals for respiratory tract infections in primary care will be collected, as well as investigating whether the use of POCTs would increase antiviral prescribing.

4. Aims and Objectives

Aim

To explore the feasibility of a trial looking at using, and evaluating the use of, pathogen-detection point-of-care tests to help guide the management of LRTIs in older adults in a primary care setting.

Objectives

1. To assess the feasibility of conducting a trial investigating the use of lateral flow type point-of-care testing to improve the management of older adults with LRTIs in primary care, including recruitment, randomisation, and data collection.

2. To understand the acceptability of, and barriers and facilitators to using COVID-19 and Influenza A/B lateral flow type tests, with and without biomarker point-of-care tests, to help guide the management of lower respiratory tract infections (LRTI) in older adults in primary care.

3. To estimate the effects of using these tests on use of antimicrobials, in order to inform a future sample size calculation.

4. To understand the experiences of people with RTIs and primary care clinicians on point-of-care testing for respiratory viruses and biomarkers, and its effect on prescribing.

5. Research Plan/ Methods

This study will explore the use of several point-of-care tests in general practice settings. These sites will be asked to recruit older adults presenting with LRTIs and use licensed POCTs to help guide their managements. Each site will use all POCTs and the order in which they use them will be randomly assigned. This study aims to be conducted during the 2024/2025 winter flu season, as recruitment is likely to be higher during this period.

5.1. Target Population

Adults over the age of 65 with a suspected lower respiratory tract infection.

5.2. Inclusion Criteria

1) Age 65 or over
2) Presenting to primary care with symptoms of a lower respiratory tract infection beginning less than seven days prior to appointment.
    a) Symptoms must include an acute cough and one other symptom:
        i) Shortness of breath
        ii) Sputum
        iii) Chest pain
3) The ability to provide written informed consent.

5.3. Exclusion Criteria

1) Clinical diagnosis of pneumonia
2) Patient is already receiving antibiotics and/or antivirals or has used antibiotics/antivirals in the past 30 days.
3) Patient declines URT swabbing or finger prick blood testing.
4) Patient has cystic fibrosis
5) Patient has bronchiectasis
6) Patient is terminally ill
7) Patient is unable to comply with trial procedures
8) Patient has dementia, and/or is not able to consent themselves to trial procedures.

5.4. Setting

This study will take place in NHS primary care settings in England (e.g. general practices).

5.5. Participant Screening and Recruitment

Participants will be screened and recruited by primary care sites. Before the study, training will be provided to the reception and triage staff of participating sites. Patients who potentially meet the inclusion criteria will be directed towards clinicians who have been trained in screening and consenting. Research active general practices use a variety of approaches to manage longer research appointments. Some sites will book potential participants into special ‘research slots’, which are longer than usual slots, some will book them in to the end of a surgery session so it doesn’t matter if they over-run, others will do the initial consultation and then ask the patient to see a research nurse or other member of the

research team at the site, and others will just accept that they over-run on these consultations

When the appointment occurs, the clinicians will explain that they meet the criteria to take part in a study. The study will take place over the winter flu season 2024/2025. It will begin September/October 2024 and will end early June 2025. This ensures the study covers the period where the highest rate of consultation occurs in primary care for flu like illness. Additionally, it will continue until June of the following year to ensure the recruitment numbers match the target. Furthermore, regional influenza/COVID-19 statistics will be collected throughout the study, to know when the highest rates of infections occurred during the study period.

Recruitment will be done opportunistically due to the nature of LRTIs. This means, when a participant calls a participating site to make an appointment, a trained receptionist, if the site is agreeable to this method, will be able to triage them to a participating clinician, if they are eligible for the study. The receptionists will be given a list of the inclusion criteria. They will be asked to ascertain if the participant fits the list of inclusion criteria on the list. Receptionists usually ask patients their birth date and symptoms when making appointment so it would not be out of the norm for them to obtain these details for screening purposes. If possible, the receptionist will also ask the participant if they would be interested in taking part in a study. If they say yes, they will be directed to a study clinician who will be able to ascertain if the participant is eligible for the study. This method will be proposed to sites, but it is up to the site and how it feels the process would work best as to how they manage recruitment. This will be discussed at site set up meeting to ensure sites are happy with the recruitment process. Study procedures will continue as shown in the flow diagram (figure 1).

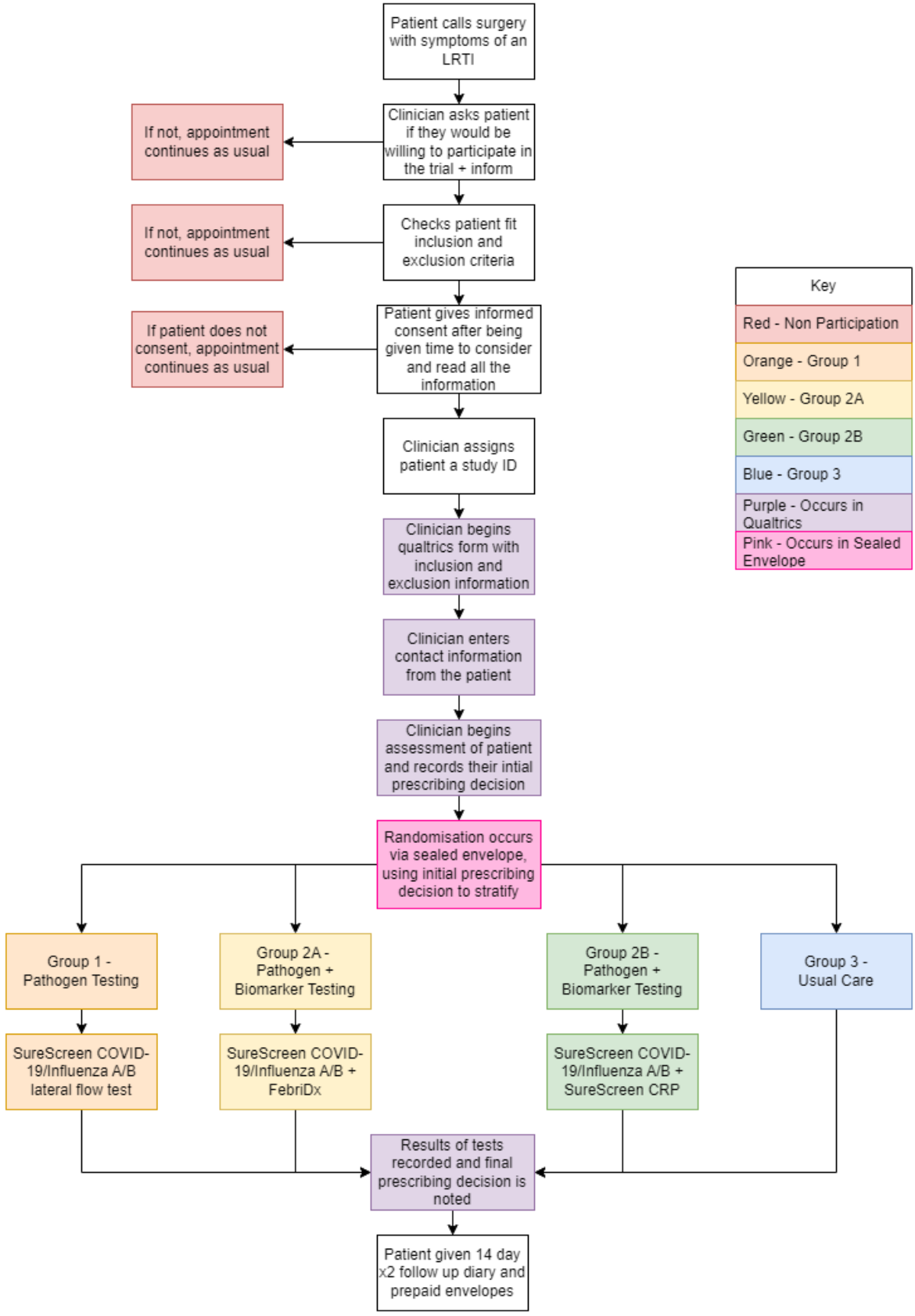

Figure 1 – A flow diagram detailing the study procedures. Recruitment methods may be tweaked depending on the opinions of the sites involved

5.6. Recruitment Process, Consent, and Registration

A study clinician will explain what the study involves and will provide the patient with an information sheet if they are interested. They will also conduct a formal assessment of eligibility. The patient will be given an opportunity to ask questions and take time to consider participation. If the patient is eligible and wants to take part in the study, they will be invited to sign a consent form. This will include an optional consent item to be contacted by the research team about taking part in a qualitative interview about their experiences of being in the study. Participants will need to provide consent during their consultation for their LRTI symptoms.

Once consent has been given, the clinician will collect information about the participant such as age, gender, and ethnicity, alongside information about their symptoms and presenting LRTI illness. Once the test(s) have been conducted, if in group 1 or 2, results from those tests will also be recorded, alongside information about treatment given to the patient, if any. This will be done on an online form.

5.7. Ensuring Equality, Diversity, and Inclusion for Study Participants

Following the NIHR INCLUDE framework, we will seek to ensure that under-served groups are included by recruiting general practices in areas of socio-economic and ethnic diversity and encouraging and facilitating recruitment of patients who are diverse in terms of ethnicity, gender, and socio-economic deprivation. Monitoring will be done of socioeconomic status, ethnicity, and gender during the recruitment phase, and under-represented groups will be subsequently targeted.

5.8. Randomisation

This study will be a randomised controlled trial, and will randomise patients on the individual level. Patients will be randomised to one of four groups by the study clinician. These groups are:

- Group 1 - Pathogen-Based POCT (SureScreen COVID-19/Influenza A/B lateral flow test)
- Group 2a - Pathogen-Based POCT and Biomarker-Based POCT (SureScreen COVID-19/Influenza A/B lateral flow test and FebriDx)
- Group 2b - Pathogen-Based POCT and Biomarker-Based POCT (SureScreen COVID-19/Influenza A/B lateral flow test and SureScreen CRP)
- Group 3 – Usual care

Randomisation will be done using software called Sealed Envelope. This will easily allow the clinician to randomise the patient after accessing their eligibility for the trial, and gaining their informed consent. Randomisation will be done 2:1:1:2 as groups 2a and 2b are both looking at biomarker-based POCTs in combination with pathogen-based POCTs and therefore do not need a full 60 participants for each, but in combination.

Randomisation will be stratified. This is so that one testing group does not have drastically different characteristics to another group. For example, if all the participants who are initially going to be prescribed antibiotics are assigned to group 1 and all participants who are not initially going to be prescribed antibiotics are assigned to group 3, this would skew the results. To combat this, stratified randomisation can be used to ensure an even spread of antibiotic prescribing intentions among the different testing groups. As per the example, stratification in this study would be done based on initial decision to prescribe antibiotics.

This will be done on the three levels indicated on the data collection form used by the clinicians: immediate antibiotics, delayed antibiotics, and no antibiotics.

5.9. Intervention and Control

All tests in this study are licensed for use in the UK. Participants will be randomised between groups 1, 2a, 2b, and, 3 -

Group 1 - SureScreen COVID-19/Influenza A/B Lateral Flow Testing Group (Pathogen Detection)

Group 1 will use the SureScreen COVID-19/Influenza A/B lateral flow POCT to test participants in the trial. This is an antigen detection test and will only test for influenza, and COVID-19. This is to understand the effect of a pathogen-based test on antibiotic prescribing and other outcomes.

Group 2A - FebriDx Testing + Pathogen Detection

Group 2A will test participants with two tests. These will be the SureScreen COVID-19/Influenza A/B lateral flow POCT and FebriDx. This group will look at the effect of using both a pathogen-based test and a biomarker test on antibiotic prescribing and other outcomes.

Group 2B - SureScreen CRP Testing + Pathogen Detection

Group 2B will also use two tests. These will be the SureScreen COVID-19/Influenza A/B lateral flow POCT and the SureScreen CRP test. This group will also look at the effect of using both a pathogen detection POCT and a biomarker POCT on prescribing antibiotics and other outcomes.

Group 3 - Usual Care

Group 3 will be the usual care group. This group will not use any form of point-of-care test. This group will be used as a comparator to the testing groups to see if there has been any change on the outcome factors, such as antibiotic prescribing rate.

Follow Up

Participants will receive a 28 day follow up diary, split into two-week sections. This will allow them to continue to monitor their symptoms until they are better, as well as any follow up consultations, hospitalisations, or antibiotic prescriptions. This is to investigate the consequences of using POCTs in primary care. This is to ensure the testing has not prevented anyone receiving the care they need. For example, if a test was negative for a bacterial infection when the participant did have a bacterial infection, they may not receive antibiotics. The diary allows us to see whether the participant had to reconsult to receive the antibiotics they needed but did not receive the first time due to a negative result. This is unlikely but important to collect data on to ensure it is not a regular occurrence. During the follow up period for each participant, they will be contacted by the study team, either by phone call or email, to remind them to fill in the study diary and/or return it. Participants will be contacted once a week between the hours 9am to 3pm. Participants will be encouraged to reach out to their GP if they are experiencing poor physical or mental health. This is signposted in their participant information sheet, and participating practices will be encouraged to inform all participants to contact their GP if they are struggling physically or mentally.

5.10. Outcome Measures

Feasibility Outcome Measures

- Participant Recruitment and Follow up –
    - The number of participants recruited per month.
    - The amount of missing data (with reasons where possible)
    - The number of withdrawals
- Compliance to study procedures –
    - Test results:
        - The proportion of participants with full test results
        - The proportion of test attempts with a successful result (for each test)
    - The number of times each test is attempted.
    - Result from lateral flow test with control line (positive or negative).
    - Result from CRP test with control line (positive or negative).
    - Result from FebriDx with control line (positive or negative).
    - Test failure rate.
        - Why has test failed?
- Acceptability of intervention -
    - Clinicians' and Participants' acceptability of using the intervention(s):
        - 1-10 scale on data sheets indicating clinician's satisfaction on one and/or both intervention(s).
        - 1-10 scale on data sheets indicating participant's satisfaction one and/or both intervention(s).

Exploratory Outcome Measures

- Participants prescribed antibiotics on day of recruitment.
- Participants prescribed antibiotics within 28 days from consultation.
- Participants prescribed antivirals on day of recruitment.
- Participants prescribed antivirals within 28 days from consultation.
- Follow up information regarding the participants' recovery regarding their LRTI within 28 days from consultation:
    - Return to usual activity
    - Re-consultation
    - Hospitalisation

5.11. Data Collection

Participant data will be collected by the clinicians and participants. Clinicians will fill in an online form for each participant which will include information about the testing method, if assigned one, symptoms, and whether antibiotics or antivirals are prescribed. The participant will be able to withdraw their consent and this form will be destroyed if this is the case. Data collected before withdrawal unless participant requests otherwise. Follow up data will be collected by the participants of the trial for 28 days. This will include information about repeat consultations, hospitalisations, and any further tests regarding their LRTI. This will be done through a diary or electronic data collection system depending on the participant's preference and ability. All data will be collected and stored following the data protection act (2018) guidelines.

Table 1 – Summary of data collection

Data Collection	Day of Consultation	Follow up – Until Symptoms End	Follow up – Weekly for 28 days
Eligibility Criteria	**X**		
Demographics	**X**		
Symptoms	**X**	**X**	
Suspected Clinical Diagnosis	**X**		
Nasal Swab Sample	**X**		
Finger Prick Blood Sample - FebriDx	**X**		
Finger Prick Blood Sample – SureScreen CRP	**X**		
SureScreen COVID-19/Influenza A/B Result	**X**		
FebriDx Result	**X**		
SureScreen CRP Result	**X**		
Management Plan (Treatment)	**X**		
Test Satisfaction (Clinician and Participant)	**X**		
EQ-5D-5L			**X**
Use of Additional Antibiotics			**X**
Additional Healthcare Consultations			**X**

Study data will be collected through Qualtrics. A screening form will begin the process, to ensure the participant meets the inclusion criteria. The next form is the contact form which contains the participants contact details. This form will only be linked to the main data collection form through the participant's unique identifier. This is to ensure that any personal data is kept separate from the study results. This data must be linked to be able to contact the participant and to remove their personal information if the participant requests it.

The third is the clinician data form and will collect the trial data. This will consist of a Qualtrics form. This clinician data form will collect information about participants demographics, severity of their illness, and what treatment the clinician initially believes to be suitable. If in a testing group, the form will contain information about the tests they are conducting. This will include time taken to perform the test, testing problems, tests results, and satisfaction with the test. Furthermore, it will also ask if the clinician's initial treatment plan has changed since performing the test. Clinicians will be asked if they are intending to prescribe antibiotics or antivirals. By prompting them to think about prescribing antivirals, this may lead to an increase in antiviral prescriptions due to the suggestion. This has been acknowledged and will be taken into account during the result analysis by plotting the

number of antiviral prescriptions over the course of the study, to see if there is an increase. Qualitative data will also be collected to understand if this has been the case. This will involve asking clinicians if they usually prescribe antivirals and if they felt more inclined to prescribe them during this study.

Follow up data will be collected in the form of a paper-based participant diary. The follow up period will last 28 days and will be in the form of two 14 day diaries. This is to reduce costs, as a 7 day diary would required 4 paid envelopes to send back rather than 2. It is also to ensure that some data is collected, as it is more likely for someone to fill in the diary in the first two weeks than the last two weeks. If the diary spanned the whole 28 days, it is more likely no diary will be sent back and no data will be collected. 14 days is a compromised between costs and data collection.

Qualitative data will be collected from semi-structured interviews with clinicians and participants. This will be done in the form of audio or video recording. This will then be transcribed verbatim.

5.12. Data Analysis

Descriptive statistics will be produced based on the feasibility outcomes. This will involve percentages for binary outcomes and mean (SD) for those that are continuous. Additionally, those with a skewed distribution will have the median calculated (IQR). Further descriptive statistics will also be produced for the exploratory outcome measures. This will inform as to whether a full-scale trial is viable and useful. Figures will be used to illustrate the descriptive results. No analytical statistics of exploratory outcomes will be done as due to the size of the feasibility study, the results would be underpowered and could give false negatives.

5.13. Sample Size Calculation

Sample size will be based on follow up rate of participants in the study, as this is a feasibility study. The results from follow up rate from this study combined with reliable estimates from other similar studies will be used to inform the sample size of a future, larger study if it is deemed feasible.

With a sample size of 180 we can estimate a follow up rate of 70% to within a 95% confidence interval of +/- 7%.

be 95% +-6.69%.

5.14. Nested Qualitative Research

A nested qualitative process evaluation will be conducted to explore health professional and participant experiences of the intervention and being in the trial. Semi-structured interviews will be carried out with:

1. 10-20 practice staff who were actively involved in the study
2. 10-15 patients who took part in the study and expressed interest in taking part in a follow-up qualitative interview.

Primary Care Staff Recruitment and Consent

Primary care staff actively involved in stage one will be directly invited to participate in a qualitative interview. Participants will be purposively sampled on gender, clinical role, years' experience, and site to ensure a diverse range of views are included. Potential participants will be emailed written information in the form of a patient information sheet (PIS). Interested

participants will be invited to contact the study team by email or phone call to arrange an interview. Participant consent will be provided verbally and by audio-recorded at the start of the interview (with audio-recorded agreement to each statement on the consent form), and after the participant has been given the opportunity to have any questions answered.

Participant Recruitment

Participants recruited to the study will be asked to express interest in taking part in a follow-up interview during recruitment. Contact details for those interested will be collected by the primary care clinicians. Participants will be purposively sampled for interview to ensure a range of gender, ethnicity, illness severity, randomisation group and POCT result. A separate PIS for the interviews will be shared, and consent taken, via the same process as above for primary care staff.

Data collection

Interviews will be semi-structured using pre-developed interview topic guides to explore participants' views on use of POCTs. Interview guides will be drafted; however, these may be further developed iteratively depending on the responses to previous interviews. Questions will focus on the perceived ease-of-use of the POCTs and their views on the feasibility for POCTs to be integrated into UK primary care, including the barriers and facilitators. Finally, we will also ask for their views on using POCTs to inform antimicrobial prescribing for older adults with LRTIs. We believe that semi-structured interviews are preferable over questionnaires due to the richer qualitative data they provide, opportunity to explore additional themes as indicated, and the relatively small number of primary care staff members involved in the study. The interviews themselves may be in-person or remote (Microsoft Teams), depending on preferences and feasibility.

Data analysis

Qualitative interviews will be audio-recorded and downloaded onto the University of Southampton secure server immediately after the interview and transcribed verbatim. Transcripts will also be stored on a secure server. Video and audio recordings will be deleted once they have been transcribed. Transcribing will be undertaken by a University-approved professional transcription service, with appropriate confidentiality agreements in place.

Analysis will take place using thematic analysis, and will include reading and familiarisation with the transcripts, noting and recording initial themes and then conducting systematic and detailed open coding using NVivo software. The coding of the first set of interviews will generate an initial coding framework, which will be discussed with the members of the research team (including PPI members). This will be further developed and refined as analysis proceeds. The research team will also critically discuss the categories and themes developed from the data, to ensure trustworthiness and increase rigour.

6. Disseminations, Outputs, and Anticipated Impact

6.1. Scientific Research Outputs

There will be several outputs of this study. The first is a protocol paper which will outline the protocol to be used in the feasibility study. Secondly, there will be two results papers; one will present the quantitative results, while the other will present the qualitative results. Finally,

a plain English summary of the results will be done to distribute to participants at the end of the study.

Both quantitative results and qualitative results will be presented at a conference.

6.2. Anticipated Impact

This study will help to ascertain how feasible it would be to create a similar study on a larger scale. If the study finds that point-of-care testing for LRTIs does reduce antibiotics on this small scale, a larger study can then be done to find out the true impact. Furthermore, if this study shows that it is feasible to conduct a study in this way, then it will also lend to the evidence that a future, larger study is needed.

In a larger study, better and more significant evidence will be found as to whether point-of-care testing reduces the use of antibiotics in primary care. Additionally, it will allow investigators to see whether antiviral prescription rates change through the use of point-of-care testing, and whether these prescriptions also improve patient outcomes. By doing this smaller feasibility study, it will help design a larger trial to determine if POCTs can be used to better guide treatment, reduce necessary antibiotics, and deduce cost effectiveness.

If a larger study was to find a significant reduction in antibiotic use in primary care, then policy could be informed to implement point-of-care testing into routine general practice.

6.3. Sharing the Progress and Findings of our Research with Study Participants

Participants will be provided with an ideal timeline of the study. This will be included in the participant information sheets which will be given to them to read before giving their informed consent to join the trial. Participants will be emailed the results of the study once it has ended. Once the study has completed and the findings have been analysed, a summary of results will be given to the participants. This will be assisted by the public contributors to help create a plain language summary of the findings so all participants can fully understand them. Participants communication will be done through their preferred method of email, SMS, or physical.

7. Ethics and Safety Monitoring

All aspects of the study will be in accordance with the UK Policy Framework for Health and Social Care Research and Good Clinical Practice (GCP). The study does not pose any particularly unusual or challenging ethical issues. The main ethical issues will be around obtaining appropriate informed consent, ensuring the safety and rights of research participants and ensuring confidentiality. We will obtain approval from the MHRA, HRA and an HRA Research Ethics Committee prior to commencing the research.

Currently, the POCTs being used for this study do not have strong evidence for clinical effects. However, the risks will be explained to the participants, and they will provide informed consent.

We do not anticipate any significant adverse events and so will not have specific SAE processes but will monitor all adverse events.

8. Patient and Public Involvement

This study has involved public involvement throughout the design and implementation process. This is to ensure the public interest is kept throughout all elements of the study and

that they are involved in its creation. Two public contributors have consulted on all patient facing documents to ensure they are accessible in language and contain all the information required to inform the participant of the study's aims and methods. These public contributors are over 65 due to the age of the recruitment population, as well as having experience with chest infections and receiving antibiotics from their GP. This is so they are as similar to the target population as possible, and can give advice based on their own experiences. The public contributors helped to maintain a consistent reading level across all documents to ensure that all the information can be easily understood by all participants. They also read over the protocol to make sure all study procedures would be acceptable to patients.The public contributors will also consult throughout the study period, to ensure that the direction of the study is maintained and remains within the public interest. Once the study has finished, the contributors will help consult on plain English result reports, which will be sent to the participants of the study to inform them of the results. This will ensure the entire study is within the public's best interests and everything presented to participants is accessible.

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