Understanding acute functional decline and its relationship to urinary tract infection in older people living in care homes



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For my grandparents:
Ron, Diana, Jim and Daphne.

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Abstract

Background: Acute functional decline in care home residents is often assumed to be caused by urinary tract infection (UTI), although other causes are possible. UTI is itself challenging to diagnose in care home residents due to lack of classic symptoms and signs, cognitive impairment limiting a history, and urine incontinence complicating sample collection. Additionally, many are likely to have asymptomatic bacteriuria (ASB), which means the urine dipstick test is not recommended as a diagnostic aid in United Kingdom (UK) guidelines in this population. Missing a UTI risks possible bloodstream infection, unplanned hospital admissions, and death. However, inappropriate use of antibiotics in the absence of infection adds to the burden of antimicrobial resistance. All these factors contribute to GP diagnostic uncertainty.

Aim: To explore the relationship between acute functional decline, ASB and UTI in care home residents, as well as consider novel diagnostic approaches, to improve the diagnostic pathway for acute functional decline/care home UTI in the future.

Methods: Three studies were undertaken with diverse methodological approaches. 1) A qualitative study with UK care home staff explored experiences of recognising and managing acute functional decline and views on point-of-care tests (POCTs) in care homes. Data were collected via telephone in semi-structured interviews and analysed thematically. 2) A systematic review and meta-analysis of studies describing ASB prevalence and risk factors in populations relevant to UK primary care. 3) A prospective cohort study of care home residents in England. This aimed to assess feasibility and acceptability of delivering the study in

a UK care home setting, capturing episodes suspected to be UTI by care home staff, as well as exploring new approaches that may improve UTI diagnosis in the future.

Results: Care home staff described that their initial assessment of someone with an acute functional decline involved checking a urine dipstick, with most considering that UTI was the most likely cause of acute functional decline. They had a limited awareness of ASB and the impact of pre-test probability on test performance. They were willing to consider diagnostic innovation in the care home setting but warned against over-medicalising and highlighted their need for training and support.

64 studies measuring the prevalence of ASB in settings relevant to a UK community context were identified and included in the systematic review. Whilst there was considerable heterogeneity amongst these studies, results of the meta-analysis confirmed that prevalence of ASB increases with age and is most prevalent in care homes.

A cohort of 81 care home residents were recruited from 8 care homes in England, with 24 episodes suspected to be UTI by care home staff captured over follow up. Whilst the study was broadly feasible and acceptable, the qualitative evaluation found that sample collection was extremely challenging and that a fully powered study would require a significant increase in dedicated research staff time. Just over a third of the possible UTI episodes presented with an acute functional decline. There were some adverse outcomes including one death, but numbers were too small to be able to explore associations. Serial urine samples collected from asymptomatic care home residents showed weekly variation, including change between ASB states. Three novel POCTs for UTI were evaluated, but on a small number of samples limiting interpretation of the diagnostic accuracy data. Research staff highlighted difficulties in reading results in some of the tests that risked misinterpretation. Care home staff felt these tests were acceptable but

emphasised the need for simplicity and speed in any future UTI POCT to be used in the care home setting.

Conclusion: A lack of recommended rapid diagnostic tests currently contributes to clinical uncertainty in those assessing care home residents with acute functional decline/suspected UTI. ASB prevalence in care home residents is lower than previously estimated, but still high enough on a population level to preclude use of the urine dipstick as a diagnostic aid. However, the urine microbiome of care home residents is potentially more complex than anticipated, which complicates the interpretation of isolated urine cultures and may also impact the performance of novel UTI POCTs. More work is needed to understand the pathogenesis of care home UTI so that we can better predict outcomes, target treatments and clinical support and inform the development of further POCTs to help with assessments in the future. However, this sort of research is challenging to deliver in a care home setting, and to be successful will require a significant investment in time, resource and a change in care home research culture.

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List of Abbreviations

AMR antimicrobial resistance.

AMS antimicrobial stewardship.

ASB asymptomatic bacteriuria.

AST Antimicrobial Susceptibility Testing.

CE Conformité Européene.

CFS Clinical Frailty Scale.

CFU/ml colony forming units per millilitre.

CI confidence interval.

CINAHL Cumulative Index to Nursing and Allied Health Literature.

CPRD Clinical Practice Research Datalink.

CQC Care Quality Commission.

DISCO UTI DIagnoSing Care hOme UTI Study.

DMARDs Disease-Modifying Anti-Rheumatic Drugs.

E. coli Escherichia coli.

EAU European Association of Urology.

eCRF electronic case report form.

ENRICH Enabling Research in Care Homes.

EUCAST European Committee on Antimicrobial Susceptibility Testing.

GCP Good Clinical Practice.

GP General Practitioner.

ICF Informed Consent Form.

IDSA Infectious Diseases Society of America.

INR International Normalised Ratio.

IQR interquartile range.

JBI Joanna Briggs Institute.

LTCF long term care facilities.

MeSH Medical Subject Headings.

mPCR multiplex polymerase chain reaction.

NEWS2 National Early Warning Score 2.

NHS National Health Service.

NICE National Institute for Health and Care Excellence.

NIHR National Institute for Health and Care Research.

OECD Organization for Economic Co-operation and Development.

PIS Participant Information Sheet.

POCT point-of-care test.

PPI Patient and Public Involvement.

PRISMA Preferred Reporting Items for Systematic reviews and Meta-Analyses.

RCT randomised controlled trial.

RDN Research Delivery Network.

RESTORE2™ Recognise Early Soft Signs, Take Observations, Respond Escalate.

SACU Specialist Antimicrobial Chemotherapy Unit.

SBARD Situation, Background, Assessment, Recommendation, Decision.

SCI Science Citation Index.

SDEC Same Day Emergency Care.

SGLT2 Sodium-Glucose Transport 2.

SIGN Scottish Intercollegiate Guidelines Network.

SMI Standards for Microbiological Investigation.

UK United Kingdom.

UKHSA UK Health Security Agency.

UTI urinary tract infection.

µl microlitres.

Chapter 1

Background and aims

1.1 Overview of chapter

In this chapter, I introduce concepts that are central to this thesis; acute functional decline, urinary tract infection (UTI) and asymptomatic bacteriuria (ASB). I also describe the landscape of United Kingdom (UK) care homes for older people. I contextualise my own clinical and academic interest in care home medicine and reflect on how my personal experience has resulted in my focus on this thesis topic. I outline my overall aims and objectives for the thesis and give an overview of its structure. Finally, I describe how patient and public involvement has shaped my research and impacted its delivery and outcomes.

1.2 Introduction

As a practising General Practitioner (GP), I commonly encounter clinical scenarios like the one described in Box 1; concerns raised about a care home resident experiencing an 'acute functional decline'. I practice evidence-based medicine and want to know how best to care for these patients. However, there is limited empirical evidence available to support me in deciding the best course of action and the problem is complex, so I often experience clinical uncertainty.

Box 1. Clinical scenario *A GP is working for a busy practice triaging urgent phone calls. The next call is to a nurse working at the local care home for older people, which specialises in dementia. The nurse explains that she is worried about a 92 year old resident who has been more confused than usual today, less mobile and not eaten her breakfast or lunch. The nurse is concerned that the resident might have a UTI and has done a urine dipstick test, which is positive. The nurse is asking for antibiotics. The GP can see in the patient's records that she has had multiple previous courses of antibiotics for similar presentations presumed to be UTI. But how can the GP know what is causing her symptoms today, and should they give her antibiotics? If so, which ones? Is the patient at risk of deteriorating, or will she get better on her own?*

What contributes to this uncertainty? Firstly, acute functional decline is a non-specific clinical presentation of unwell older adults with many possible causes, including UTI. (Section 1.4) Acute functional decline can include physical symptoms such as fatigue, loss of appetite, changes in mobility or activities of daily living, and/or changes in cognition.[1] It's incidence, natural history, and outcomes are currently unknown in the care home setting.

Secondly, UTI can be defined in several ways; symptoms attributable to an infection in the urinary tract (syndromic definition), bacteria found in the urine that meet a certain threshold (laboratory definition), or a combination of a set of symptoms with microbiological evidence that they could be associated with an infection. In the care home population, symptoms of UTI are not necessarily present or able to be communicated. (Section 1.6) In addition, care home residents commonly have bacterial colonisation of the urinary tract even when well, known as ASB. (Section 1.5) This complicates the interpretation of the currently available diagnostic tests for UTI. (Section 1.6.5)

In the scenario described in Box 1, the care home resident who is experiencing acute functional decline has a diagnostic test result (in this case, from the urine dipstick) that suggests there are bacteria in the urine. However, as the triaging GP, I cannot be sure if the acute functional decline is caused by a bacterial UTI, or if the patient has ASB and there is an

alternative cause for her presentation. (Figure 1.1) This is important in this vulnerable population because missing a UTI risks serious adverse outcomes including bloodstream infections, hospital admissions, or death. In contrast, prescribing antibiotics unnecessarily in the absence of a bacterial UTI risks side-effects and antibiotic-resistance, both of which are also more likely in care home residents. There is also the opportunity cost of missing or delaying the diagnosis of the true cause of the acute functional decline. (Section 1.4)

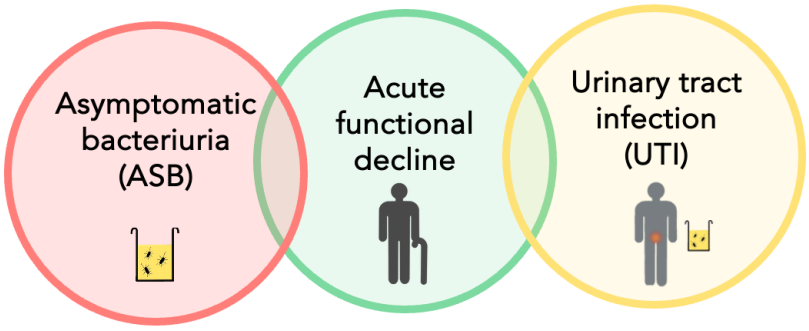


Figure 1.1: Diagram illustrating the potential cross-over between acute functional decline, ASB and UTI

In this thesis, my objective is to explore in care home residents the relationship between acute functional decline, urinary tract infection, and asymptomatic bacteriuria, and to consider novel diagnostic approaches. (Section 1.8) My hope is that this work will contribute to the improvement of the diagnostic pathway for acute functional decline/care home UTI, leading to less clinical uncertainty experienced by clinicians like me in these scenarios in the future. This chapter is a narrative overview of the relevant background and will provide further insights into the scale, complexity and importance of the problem being addressed.

1.3 Care homes for older people in the UK

1.3.1 Scale, diversity and workforce

There are around 380,000 older people currently living in care homes in the UK, which is 2.5% of the total population over 65 years of age.[2, 3] Care homes are long term care facilities (LTCF) defined in law as providing accommodation together with personal or nursing care.[4] There are approximately 16,500 different care homes providing care for older adults across

the UK.[5] Around half of the UK care home population live in care homes without nursing (residential) and half in care homes with nursing.[2, 3] The UK care home workforce is approximately 750,000 people.[5] Care homes are run by a number of different entities: 81% of the care home population live in homes run by companies for profit, 13% in homes run by not-for-profit organisations and 6% in homes run by the local authority. Several independent care home groups run large numbers of homes, with the top four providers having 800 care homes between them[6] and 11% of the market share.[2] The average capacity of care homes is 52,[7] but they can range from under 10 to more than 100 beds.[8] Care homes must be registered and meet a set of minimum standards; they are inspected and regulated by different independent bodies across the four nations.[9] In England, 51.1% of older care home residents have their placement funded by the local authority.[10] However, there is also an increasing trend for 'luxury' care homes, where a larger proportion of residents are self-funded.[11] It is anticipated that the number of care homes and care home beds in the UK will continue to rise with the ageing population.[5]

1.3.2 Resident demographics

According to the 2021 Census of England and Wales, the median age of the care home population is 86 years and 70% are female. 56.4% are aged over 85 years old (the 'oldest old'). 97.5% identify as "White" (vs 93.6% in all over 65s) and 98.6% report their main language as English (or Welsh in Wales). Many live with multiple long-term conditions and frailty.[12, 13] Around 70% identify as disabled with severe limitation of day-to-day activities, and 31.8% report to be in bad or very bad health.[3] The Alzheimer's Society estimate that 70% of those living in care homes live with severe cognitive impairment or dementia.[14] Average life expectancy is 12 months for those in care homes with nursing, and 24 months for those in homes without nursing.[15]

1.3.3 Healthcare provision for UK care homes

Most of the healthcare for UK care home residents is provided by primary care and this population contribute significantly to GP workload.[16–18] They are vulnerable to clinical deterioration and have a higher hospital admission rate compared to older people living in

their own homes.[19] Unfortunately, hospitalisation can result in adverse outcomes for older people such as physical deconditioning, delirium, and hospital acquired infection.[20] For many care home residents, therefore, unscheduled hospital admissions can and should be avoided.[21]

The Enhanced Health for Care Homes framework was introduced in England in 2016 as part of a government-led drive to improve support for people living and working in care homes. This framework financially incentivises GP practices to provide regular visits to care homes and establish a collaborative, multi-disciplinary approach, in part to avoid unnecessary hospital admissions.[22] Similar schemes are established in Scotland and Wales. For the majority of practices who have taken up this scheme, care homes under their care receive a weekly visit from a regular GP and urgent problems are dealt with by their triage system. In the latest iteration of the NHS 10-year plan, there is a further commitment to provide hospital-level care to care home residents in the community, supported by monitoring technology including wearables.[23]

The model for healthcare provision for care homes in the UK differs from other high income countries in continental Europe and the United States. There, care homes are more likely to have easy access to a specialist doctor, including having a doctor continuously on site.

1.3.4 Research in UK care homes

UK care homes and care home residents have historically been under-represented in health and social care research. However, care home residents should be considered a special population and researched as a distinct entity from older adults who live in their own homes. As described in Section 1.3.2, they have amongst the most complex health needs with most living with advanced frailty, multiple long-term conditions and cognitive impairment. In addition, interaction with the healthcare system differs with their own tailored services,[24] a different model of GP support (Section 1.3.3), and the unique role of care home staff in initiating contact with healthcare professionals. Expectations of care and/or ceilings of care may differ. Finally, living in close proximity to others and the use of shared communal spaces

increases the risk of outbreaks of infectious diseases,[25] as evidenced by the devastating impact of the COVID-19 pandemic.[26]

The Enabling Research in Care Homes (ENRICH) Network from the National Institute for Health and Care Research (NIHR) was established in 2012 to support care home engagement and participation in research, but despite this many care homes remain research naive.[27] The variation in size, management, staffing, and population (Section 1.3.1) means that care homes are heterogeneous, and this contributes to the challenge of conducting research in this setting. In England, the work of ENRICH has recently been taken on by the Research Delivery Network (RDN) in a nationwide restructuring of support for research delivery.[28]

1.4 Acute functional decline

1.4.1 Definition and causes

Older people living with frailty, including those residing in care homes, can experience a functional decline when experiencing acute illness.[29] This can include physical symptoms like fatigue, loss of appetite, changes in mobility or activities of daily living and/or changes in cognition.[1] However, there is no consensus definition of acute functional decline.

Acute functional decline is a non-specific presentation,[29] and, in older people presenting to hospital, it can be the result of a broad range of differential diagnoses.[30–32]

Causes of acute functional decline
Infection
Dehydration/acute kidney injury
Electrolyte abnormalities
Stroke/transient ischaemic attack
Endocrine disorders
Medication side effects
Constipation
Anaemia

Table 1.1: Potential causes of acute functional decline in frail older adults presenting to hospital.

1.4.2 Prognosis and management

In older adults living in their own homes, acute functional decline is associated with transitions of care, including admission to a care home and hospitalisation.[33] In qualitative work I published prior to my doctoral fellowship GPs described experiencing diagnostic uncertainty when encountering acute functional decline in older adults.[34] Although infection is just one of many possible causes (Table 1.1), they described their use of broad-spectrum antibiotics as a strategy for managing older people with this presentation, either as a trial of treatment or as a best attempt to reverse the deterioration when hospital admission was inappropriate.[35]

A gradual functional decline is expected for care home residents.[36] and physical functional decline over time is a predictor of mortality.[37] Importantly, however, there are no observational data on acute functional decline in care homes related to final diagnosis, prognosis, or management.

1.4.3 Studying acute functional decline

Acute functional decline is inconsistently described in medical records and in the research literature. Trivialising or ageist labels like 'off legs', 'acopia' or 'social admission' have previously been used to describe these patients.[29, 38] As a subjective presentation, it is challenging to monitor and/or research. More recently some 'soft signs' of possible deterioration have been incorporated into the Recognise Early Soft Signs, Take Observations, Respond Escalate (RESTORE2™) monitoring and escalation tool for care homes.[39] These include lethargy, agitation, changes in mobility and reduced food or fluid intake. However, presence of 'soft signs' trigger a set of clinical observations, rather than contribute themselves to an early warning score.

Guideline	Definition of significant bacteriuria
UK Health Security Agency (UKHSA) *England*	Not defined
Scottish Intercollegiate Guidelines Network (SIGN) *Scotland*	Not defined
National Institute for Health and Care Excellence (NICE) *England and Wales*	$>10^5$ colony forming units/millilitre (CFU/ml)
European Association of Urology (EAU) *Europe*	$>10^5$ CFU/ml in two consecutive samples in women, and in one sample for men
Infection Diseases Society of America (IDSA) *USA*	$>10^5$ CFU/ml in two consecutive samples in women (preferably within two weeks), and in one sample for men

Table 1.2: Comparison of definitions of significant bacteriuria in different guidelines.

1.5 Asymptomatic bacteriuria

1.5.1 Definition

Asymptomatic bacteriuria (ASB) is the detection of a significant level of bacteria in a person's urine in the absence of symptoms or signs of UTI (see Table 1.3). The definitions/measurement of 'significant bacteriuria' vary between different national and international guidelines. (Table 1.2)

1.5.2 Prevalence and risk factors

Prevalence of ASB has been shown to increase with age and to be higher in women than in men.[40, 41] Other known risk factors for ASB include chronic indwelling urinary catheters, spinal cord injury and diabetes.[42]

Care home residents are thought to be at particularly high risk of having ASB. The UKHSA primary care diagnostic decision tool for UTI states that about half of older adults living in care homes by age 80 have ASB,[41] and the Scottish Intercollegiate Guidelines Network (SIGN) UTI guideline gives a range of 23-70%.[40] However, both of these guidelines base their recommendations on non-systematic reviews[40, 43–45] which include some primary

studies that were published 40-70 years ago.

Longitudinal studies have suggested that ASB status may fluctuate over time in adult community dwelling and care home populations.[46–54]

1.5.3 Screening, treatment and outcomes

Most guidelines do not recommend screening or treating ASB, except in people who are pregnant.[40–42, 55] In younger women there is some evidence that ASB may be protective against subsequent UTI.[56] However, for those living in care homes it remains unclear as to the long term outcomes of those with ASB, with some evidence suggesting worse survival.[53, 57] Treatment of ASB with antibiotics in female care home residents has been shown to result in increasingly resistant bacteria causing subsequent UTI.[58]

1.6 Urinary tract infection in care homes

1.6.1 Clinical presentation and diagnostic challenges

A UTI is an infection affecting the urethra, bladder, ureters and/or kidneys caused by bacteria. UTI can be categorised as localised or systemic depending on symptoms and signs (Table 1.3).[55]

However, in older people these symptoms and signs traditionally associated with a UTI syndrome have limited diagnostic value.[59] UTI can present non-specifically, including with an acute functional decline. Patient history can also be limited if there is cognitive impairment. Finally, incontinence can also complicate the capture of a clean urine sample. All these factors are more likely to be present for those living with advanced frailty or dementia. UTI is therefore particularly challenging to diagnose in care home residents, where 70% are living with severe cognitive impairment or dementia,[14] and over 50% experience urinary incontinence.[60]

The UKHSA primary care diagnostic decision tool for suspected UTI lists specific symptoms and signs to look for in older adults. (See Section 1.6.5.3 and Figure 1.2)

Localising symptoms and signs
Dysuria
Urinary frequency
Urinary urgency
Nocturia
Haematuria
Cloudy urine
Foul smelling urine
Incontinence
Suprapubic pain/tenderness
Systemic symptoms and signs
Fever
Rigors
Hypotension
Tachycardia
Nausea and vomiting
Flank pain/tenderness
Delirium
Non-specific symptoms and signs
Acute functional decline
Reduced mobility/falls
Changes in behaviour
Reduced appetite
Fatigue/drowsiness

Table 1.3: Symptoms and signs of UTI

1.6.2 Treatment of UTI

Antibiotics are currently the first-line treatment for UTI. UK prescribing guidelines currently state three days of antibiotics for women and seven days for men, regardless of age, for acute localised UTI. The only adaptation for care home residents is that trimethoprim is not recommended due to the high risk of resistance associated with institutionalised older adults.[61]

Recurrent UTI is defined as at least two episodes of UTI within 6 months, or at least three within a year.[55] Prophylactic daily antibiotics is one strategy for recurrent UTI, though these should be reviewed at least 6 monthly according to NICE guidelines. Other recommendations include topical vaginal oestrogen for women who are peri/post-menopausal

and methenamine hippurate as an alternative to antibiotic prophylaxis.[62]

1.6.3 Incidence and outcomes of UTI in care homes

UTI is commonly diagnosed and treated in care home residents. A 2017 point prevalence survey of antibiotic prescribing of nearly 18,000 residents in UK care homes showed that 6.3-9.6% residents were taking antibiotics, with UTI being the most common indication. Of those taking antibiotics, 38.7% were for UTI (52.5% for acute infection, 47.1% as prophylaxis). The European Association of Urology (EAU) identify functional status deterioration in older institutionalised women as a risk factor for recurrent UTI.[55]

UTI is a common cause of avoidable admissions to hospital from care homes (8%), and 8% of these result in mortality.[21] Deferring antibiotics or not treating UTI in older people significantly increases the risk of bloodstream infection and death.[63]

1.6.4 Microbiology of care home UTI

Most of our knowledge on the mechanisms of UTI pathogenesis comes from basic science and animal models. UTIs are established when uropathogens colonise the urethra and migrate to the bladder, facilitated by cellular adhesion. In the bladder they can release toxins and trigger an inflammatory response.[64] Some chronic or recurrent infections are thought to be caused by biofilm formation, or intracellular invasion.[65] Host factors in older adults that can increase risk of UTI include immunosenescence, mucosal senescence, prostate enlargement in men, and vaginal atrophy and pH changes in post-menopausal women.[66]

In samples collected from consecutive suspected UTI episodes from five care homes in the USA, *Escherichia coli (E. coli)* was the most commonly isolated uropathogen (53.6%), followed by other Enterobacteriaceae including *Proteus mirabilis* (14.6%), and *Klebsiella* species (13.9%). Although the gut is known to be a reservoir for uropathogens, no association has been shown between the gut microbiome and the incidence of UTI in care home residents [67].

The use of urine culture to explore the urine microbiome is limited as not all bacterial

species can be routinely cultured.(Section 1.6.5.2) Serial samples from a small number of asymptomatic care home residents using quantitative PCR of 16S rRNA genes in urine samples showed that length of stay in the care home and clinical frailty were correlated with significant changes in microbiome composition.[68] This included an increase in *Aerococcus urinae*, which is a potential uropathogen not easily identifiable using conventional culture methods. Increasing use of sequencing technologies are likely to evolve our understanding of changes to the urine microbiome in care home residents when experiencing a UTI.

Caution is often taken in the interpretation of culture results from care home residents due to perceived risk of contamination due to challenges with urine sampling secondary to mobility, bladder control and incontinence. However, paired culture results from urine samples were comparable when obtained from incontinence pads and in-out catheter samples in 52 older women experiencing incontinence in an inpatient setting in France,[69] and clean-catch samples and in-out catheter samples in 101 female care home residents with incontinence in the USA.[70]

1.6.5 Diagnostic tests

1.6.5.1 Urine dipsticks

A urine dipstick is a test strip of pads that change colour in the presence of different targets within a urine sample. It is an example of a point-of-care test (POCT) and results are readable within minutes. Dipsticks include tests that, if positive, indicate possible bacteriuria; leukocyte esterase (an enzyme in white blood cells, suggesting there is inflammation), nitrite (produced by the breakdown of nitrates by some bacteria) and blood (inflammation in the urinary tract can lead to bleeding). Dipsticks are widely used as diagnostic tests in patients with suspected UTI. However, their use in people with ASB can lead to false positives, misdiagnosis of UTI and unnecessary antibiotic prescribing. The current UKHSA guidelines address this by advising avoiding routine urine dipstick use in people for which the clinical diagnosis of UTI may be less certain and who are at higher risk of ASB; specifically those with an indwelling urinary catheter and older people over the age of 65.[41] The SIGN guideline cautions about interpretation of positive urine dipsticks in women aged over

65 who are at higher risk of ASB. However, the EAU and the Infectious Diseases Society of America (IDSA) guidelines do not specify an age cut-off for use of urine dipsticks. The IDSA instead only cautions about use of dipstick in spinal cord injury patients due to their increased risk of ASB.

In a recent systematic review of the diagnostic accuracy of the urine dipstick (positive leukocyte esterase or nitrate) in symptomatic older adults the pooled sensitivity was 92% (95% confidence interval (CI): 76–97%) with a specificity of 39% (95% CI: 19–62%), a positive predictive value of 52% (95% CI, 39–64%) and an NPV of 86% (95% CI: 70–94%).[71] This review included four studies, three of which were in the care home setting. Three studies were of UTIs with localising symptoms only. The reference standard was a culture showing bacteriuria showing at least 10^5 colony forming units per millilitre (CFU/ml). The diagnostic utility of the urine dipstick therefore remains unclear in care home residents presenting with non-specific symptoms and signs like an acute functional decline. However, the 'To dip or not to dip' quality improvement initiative in UK care homes showed that training for staff on UTIs and advice against routinely using urine dipsticks could successfully reduce antibiotic prescribing for UTI.[72]

1.6.5.2 Urine microscopy and culture

Laboratory tests on urine samples usually involves measuring cellular components with microscopy and quantifying bacteria that can be grown from the urine using culture. The UK Standards for Microbiological Investigation (SMI) on urine outline best practice and provide guidance on interpretation of results.[73] This takes into account the specimen type, total growth, any clinical details and additional information from microscopy (e.g. presence of white cells). Diagnoses are categorised as probable UTI, possible UTI, no UTI, probable contamination and colonisation.

Standard Urine Culture (SUC) has acted as the 'gold standard' for UTI diagnosis since the 1950s. However, this has been challenged in recent years with advances in culture techniques like Expanded Quantitative Urine Culture (EQUC) and next generation sequencing, and a

greater understanding of the urine microbiome.[74]

Importantly, results from a urine microscopy and culture can take several days to be returned to the ordering clinician. This is too slow to influence acute prescribing in primary care.

1.6.5.3 Relevant UTI diagnostic guidelines for UK primary care

The UKHSA primary care diagnostic decision tool for suspected UTI in adults over 65 years (reproduced in Figure 1.2) advises not to perform urine dipsticks. (Section 1.6.5) If there are no symptoms/signs of sepsis or systemic UTI, it advises checking for new symptoms or signs of localised UTI. This includes new onset dysuria alone or two of more of: fever, new frequency/urgency, new incontinence, new or worsening delirium/functional decline, suprapubic pain or visible haematuria. These are based on the Loeb criteria, which were developed in 2001 in a consensus exercise to determine the minimum criteria for the initiation of antibiotics for care home residents.[75] If sufficient symptoms and signs are present, the UKHSA tool recommends obtaining a urine specimen before starting immediate antibiotics (for all men, those with severe localised symptoms or high risk of complications), or delayed antibiotics (for women with mild symptoms and low risk of complications). Care home residents are likely to fall into the category of 'high risk of complications'. The justification for urine culture is to check the resistance profile of cultured bacteria and to review the choice of antibiotics if appropriate, rather than as a diagnostic aid.[41]

The SIGN guideline 160 on the management of suspected bacterial lower urinary tract infection in adult women includes a section on those aged over 65 years.[40] It is not applicable to men. It advises that use of dipsticks is not recommended for women living in care homes, and suggests sending a urine culture to confirm the identity of the pathogen and antibiotic sensitivity, but not for diagnosis.[40]

The National Institute for Health and Care Excellence (NICE) quality standard on UTI in adults only applies to women under 65 years of age and those with urinary catheters.[61] There is no NICE guideline applicable to older adults.

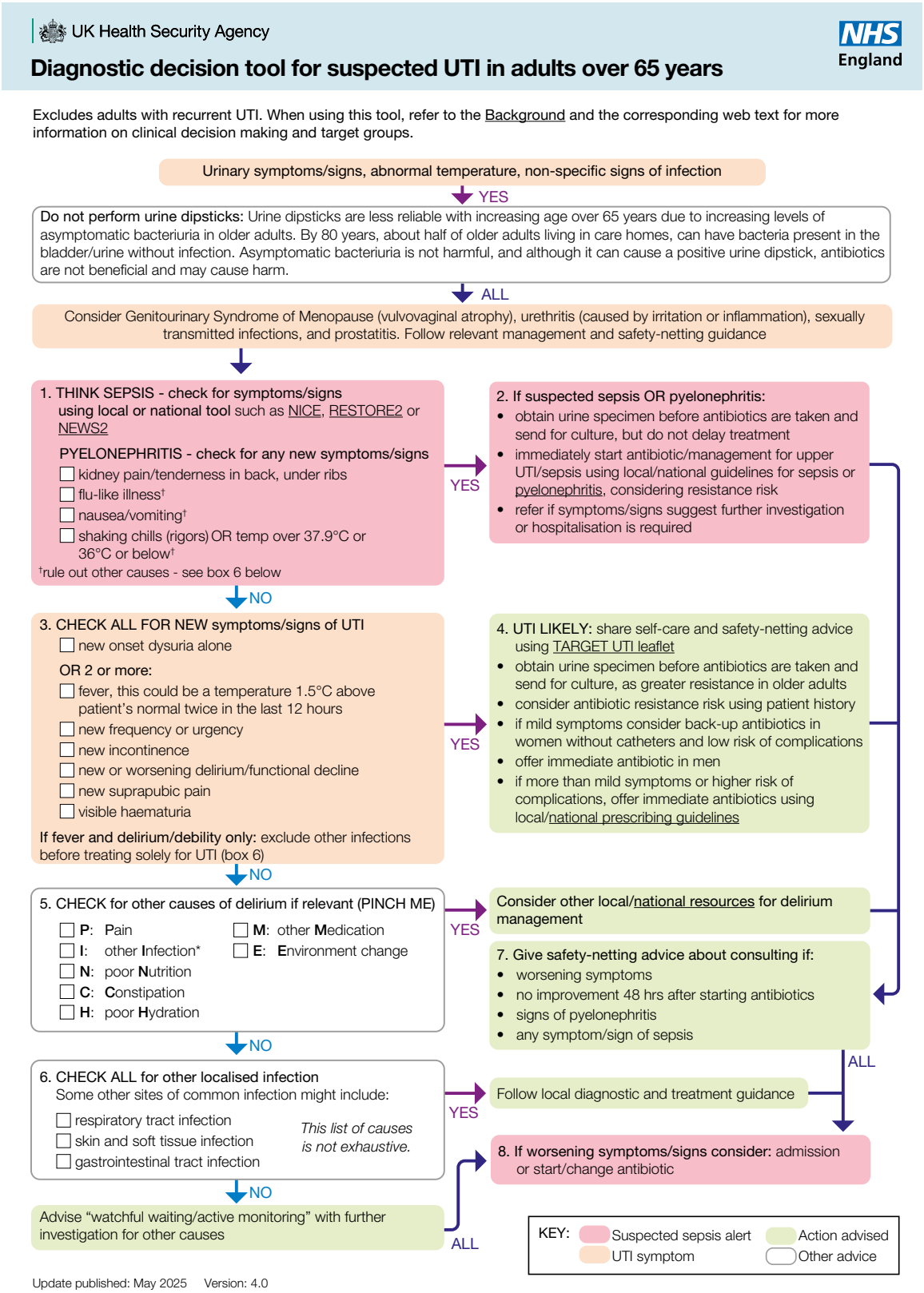


Figure 1.2: UKHSA diagnostic decision tool for suspected UTI in adults over 65 years

1.6.5.4 Novel diagnostic tests for UTI

There are several novel UTI diagnostics available or in development that have the potential to improve diagnostic accuracy of UTI at point-of-care.[76] Tests include those that can detect urinary biomarkers indicating a host response to infection, the presence of specific bacteria and/or that can provide a rapid antibiotic sensitivity test result. The diagnostic accuracy of some of these are currently being evaluated in women presenting to primary care with uncomplicated UTI.[77] However, they have never previously been evaluated in a care home setting.

1.6.6 Antimicrobial stewardship in relation to UK care homes

Care home residents are frequently prescribed antibiotics, [78–80] and, compared to their community dwelling counterparts, are colonised with a higher proportion of antibiotic-resistant bacteria.[81–83] They are also at increased risk of *Clostridioides difficile* infection due to age and exposure to antibiotics, and experience worse outcomes from this.[84] There is a commitment in the most recent UK National Antimicrobial Resistance Action Plan to support health and social care teams with clinical decision support, and a focus on care homes as a setting which has previously been overlooked.[85] There is insufficient evidence to date to show that interventions designed to reduce inappropriate antibiotic use in care home settings (mainly education and/or clinical guidelines) are effective.[86]

1.6.7 Summary of care home specific challenges for UTI diagnosis and management

Many of the difficulties associated with diagnosing and managing UTI in the care home setting are also true for some community dwelling older adults. However, there are additional challenges for care home residents, making this a particularly important topic for research. These are summarised in Table 1.4.

Challenges of UTI diagnosis and management for older adults	Additional challenges for care home residents
Localising symptoms and signs may not be present	70% live with cognitive impairment, and may not be able to describe symptoms
Changes in urination patterns may not be possible to detect in those who experience continence issues and samples harder to collect	Over 50% experience urinary incontinence
ASB prevalence increases with age, which impacts currently available diagnostic tests	Prevalence of ASB is thought to be particularly high in care home residents
No POCT recommended to aid in diagnosis – the urine dipstick is to be avoided	Care home staff may use urine dipsticks despite guideline recommendations
Higher risk of antibiotic side effects including *Clostridioides difficile* infection	Increased risk of *Clostridioides difficile* and experience worse outcomes
UTIs can result in bloodstream infections, hospital admissions and mortality	Colonised with a higher proportion of antibiotic-resistant bacteria, risking failure to respond to antibiotics and adverse outcomes

Table 1.4: Summary of additional challenges associated with diagnosing and managing UTI in care home residents.

1.7 My interest in the care of older people and care homes

I am a GP with a clinical interest in the care of older people. This began when, as a trainee, I took responsibility for the care of residents in a local nursing home. I enjoyed the opportunity to get to know a group of patients well when it otherwise felt increasingly difficult to provide good continuity of care. I subsequently worked as an Interface GP in a community based Same Day Emergency Care (SDEC) unit. This involved the assessment of acutely unwell adults, most of whom were older and living with frailty. The unit aimed to provide care closer to home and avoid the need to transfer patients to hospital. In this role I also took on clinical responsibility for patients under the care of Hospital at Home, which often involved care home residents. In my current clinical role as a care home GP I look after patients residing in a medium-sized nursing home with specialist dementia care.

On a personal level, over the last decade my family and I have also been involved in the care of ageing grandparents. We supported my grandfather who became increasingly unwell in his nineties, and died in a care home. My grandmother developed dementia in her eighties and we helped her to continue to live at home until her death. She was survived by my

grandfather, who now lives with severe frailty and is supported by a live in carer and by my parents.

My personal experience with care home medicine and with my own relatives is an important context, which I took into account reflexively in my qualitative work (Chapters 2 and 3).

1.8 Aims, objectives and structure of thesis

The overall aim of this thesis is to explore in care home residents the relationship between acute functional decline, urinary tract infection, and asymptomatic bacteriuria, and consider novel diagnostic approaches for acute functional decline/care home UTI in the future.

To achieve this aim, I will answer the following research questions:

1. What is the experience of UK care home staff in recognising and managing episodes of acute functional decline?

2. How are UK care home staff using existing POCTs in their assessment of acute functional decline?

3. What is the willingness of UK care home staff to use additional POCTs in their assessment of acute functional decline in the future?

4. What is known about the proportion of care home residents who have ASB and how does this compare to community dwelling adults?

5. What are the risk factors for ASB?

6. Is it feasible and acceptable to deliver a prospective cohort study in UK care homes that captures information about incidence, symptoms and outcomes of episodes of possible UTI?

7. What proportion of suspected UTI in care homes is associated with acute functional decline?

8. How are episodes of suspected UTI in UK care home residents managed clinically?

9. Are there any predictors of adverse outcomes in episodes of suspected UTI in UK care homes?

10. What are the risk factors for ASB in UK care home residents, and how stable is asymptomatic carriage of bacteria over time?

11. What is the diagnostic performance/acceptability/usability of novel POCTs for UTI in a UK care home setting?

The objectives related to these questions, and how these map to the structure of this thesis are summarised in Table 1.5. In the final chapter I will draw together the findings of all the studies, reflect how I have made progress towards the overall aim of the thesis and outline the next steps for research in this area.

1.9 Patient and Public Involvement

Patient and Public Involvement (PPI) informed the design, execution and dissemination of the feasibility observational cohort study described in Chapters 5 and 6. It was important to me, the wider study team and the funding body that the research should be with and for care home residents and those who support them. I recruited two public co-applicants to help work up the grant application and protocol; one relative of a care home resident and one professional (Senior Care Home Assistant) to ensure that both the interests and views of the residents and the care home were represented. One co-applicant continued to be involved with the study and attended steering group meetings throughout.

I recruited additional contributors to form a PPI group; three men and seven women from diverse ethnic backgrounds. Seven have lived experience of supporting a loved one in a care home, several act as carers, one is a former care home employee. Several also have lived experience of UTI. The PPI group informed discussion around the early design and management of the feasibility study and had input on the participant facing materials. They

Objective	Study design	Chapter
To describe the beliefs and experiences of care home staff in recognising and managing care home residents with acute functional decline.	Qualitative interview study with UK care home staff	Chapter 2
To explore the current use and interpretation of POCTs by care home staff in episodes of acute functional decline.		Chapter 3
To explore care home staff views on the potential for diagnostic innovation in care homes.		Chapter 3
To describe the prevalence and risk factors for asymptomatic bacteriuria in adults in different age/population groups including care homes.	Systematic review and meta-analysis	Chapter 4
To determine the feasibility and acceptability of delivering a prospective cohort study of UK care home residents capturing episodes suspected to be UTI by care home staff.	Feasibility cohort study of UK care home residents with embedded exploratory diagnostic accuracy study	Chapter 5
To describe clinical characteristics, management and outcomes of episodes suspected to be UTI by UK care home staff, including those presenting with an acute functional decline.		Chapter 6
To explore risk factors for ASB in UK care home residents and describe the microbiology results of repeat urine samples taken from asymptomatic participants.		
To explore the usability and diagnostic accuracy of three novel POCTs for UTI in care home residents with suspected UTI.		Chapter 7

Table 1.5: Objectives for the thesis, mapped to study design and relevant chapter(s).

were updated every 3 months via email, with an online meeting every 6 months.

I have been fortunate to have worked with very engaged PPI contributors who thought carefully about the research, asked challenging questions and have been able provide solutions to issues faced. They have actively participated in meetings and responded to interim questions via email. Their help in participant facing materials has been particularly valuable. For example, the early dissemination fact sheet was completely redesigned based on feedback on readability (font size), language and overall message.

One contributor commented: *"I think this is a study where it's all about lived experience - think we've all had UTIs or have cared for someone who has. So my input has been rather more technical than usual. I am used to speaking a lot about the research e.g. methodology - but that has been less so re this study. There's been so much to say from a patient perspective."*

1.10 Summary of chapter

In this chapter I described the common clinical challenge of a care home resident presenting with acute functional decline and why GPs like me experience so much diagnostic uncertainty in these cases.

Acute functional decline in care home residents is often assumed to be caused by UTI, although other causes are possible. UTI is itself challenging to diagnose in care home residents due to the lack of classic symptoms and signs and the fact that many live with dementia, which means that a clinical history may not be possible. Changes in urination patterns are difficult to detect in people who experience continence issues, which is common in care homes. This also makes urine samples difficult to collect. Finally, many care home residents are likely to have ASB, which affects current diagnostic tests. As a result, the readily available urine dipstick test is not recommended in care home residents with suspected UTI in UK guidelines, and no other POCT is currently recommended to help in our assessment.

Current guidelines simply advise using symptoms and signs to determine who of those with suspected UTI receives antibiotics, although these have a poor diagnostic value for UTI in

older people, and many of these may be difficult to determine in those living with dementia and/or incontinence. Urine microscopy and culture is the current gold standard for laboratory diagnosis of UTI, but is an outdated technique, equally at risk of being affected by ASB, and takes several days for a result to be returned, which means that it cannot help with acute prescribing decisions.

Missing a UTI in care home residents, many of whom live with multiple long-term conditions and frailty, risks possible bloodstream infection, unplanned hospital admissions, and death. However, inappropriate use of antibiotics in the absence of infection adds to the burden of antimicrobial resistance (AMR), already high in this group.

It is the overlap between acute functional decline, ASB and UTI and lack of diagnostic tests that gives rise to the considerable diagnostic uncertainty that I and other GPs experience, and which I have described in the research I conducted prior to my doctorate. Currently, GPs tend to prescribe antibiotics for presumed UTI for care home residents with acute functional decline, and this may represent over-diagnosis and overuse of antibiotics, driving AMR. The aim of this thesis is to further explore the relationship between acute functional decline, ASB and UTI in care home residents, as well as consider novel diagnostic approaches, to improve the diagnostic pathway for acute functional decline/care home UTI in the future.

In the next chapter I begin by exploring acute functional decline from the perspective of care home staff.

Chapter 2

How do care home staff recognise and manage acute functional decline in care homes? A qualitative exploration of UK care home staff experience.

2.1 Overview of chapter

In this chapter I present the first of two sets of findings from a qualitative interview study I carried out with UK care home staff. The aim of this chapter is to explore the beliefs, practices and experiences of UK care home staff who are typically the first to recognise and respond to acute functional decline in residents. I describe and explore the key themes: recognition of acute functional decline, early response to residents, and monitoring. The findings highlight the uncertainty that care home staff experience during these episodes and their perception that such episodes are caused by UTI.

2.2 Background and rationale

Older people living with frailty, including those residing in care homes, may experience a functional decline during acute illness.[29] This can include physical symptoms like fatigue,

loss of appetite, changes in mobility or activities of daily living and/or changes in cognition.[1] In Chapter 1 I highlighted qualitative work undertaken prior to this doctorate in which GPs described diagnostic uncertainty when assessing an older patient presenting with an acute functional decline.[34] This can lead to GPs prescribing antibiotics [35] although infection is just one of many possible causes of this presentation.[30–32] Antibiotics are likely overused in care home settings, resulting in higher levels of antimicrobial resistance among care home residents.[81, 83]. Care homes have been identified as a priority setting for antimicrobial stewardship (AMS) interventions in the latest iteration of the UK National Antimicrobial Resistance Action Plan.[85]

For older people living in care homes, it is the care home staff who typically first recognise and respond to residents experiencing an acute functional decline and who potentially set in motion the chain of events that result in an antibiotic prescription. If we are going to develop interventions suitable for care home residents and staff that improve antimicrobial stewardship in this setting it is essential to explore what usually happens in these early stages prior to any healthcare professional involvement. However, currently little is known about the experience and understanding of care home staff of these episodes.

This chapter is based on a published version of these findings.[87]

2.3 Aims and objectives

2.3.1 Aim

To explore the recognition and management of acute functional decline by care home staff.

2.3.2 Objectives

To understand from care home staff:

- What they consider to be an 'acute functional decline' in residents they care for, and its natural history

- What, if any, parameters they monitor in residents, and how, if at all, any changes are monitored
- The severity or duration of an episode that would prompt them to seek help
- Whether they have any training or protocols in place for these episodes
- If or how the COVID-19 pandemic changed their approach to acute functional decline

2.4 Methods

2.4.1 Study design and justification

A qualitative methodology was chosen as this is an area where little is known and a directly pertinent literature is lacking. Qualitative research is appropriate for capturing and exploring people's experiences and perceptions of phenomena – in this case the approaches adopted by care home staff to acute functional decline among older residents. Semi-structured interviews were used because this method of data collection is appropriate for capturing people's experiences and perceptions and has considerable power to explain actions, decisions and processes.

We used principles of grounded theory to guide data collection and analysis.[88] In practice, this meant analysis of early interviews were used to inform the approach to sampling. We targeted subsequent sets of interviews to get the viewpoints that seemed important and to capture as wide a range of experiences among care home staff as possible (theoretical sampling). Data were analysed thematically using the approach of constant comparison, whereby data collected inform ongoing data collection so that themes and findings were grounded in the data.

2.4.2 Recruitment and sampling strategy

We recruited care home staff aged 18 or over, who were currently working in a care home for older adults in England, Scotland, or Wales. Advertisements were circulated via a mixture

of social media, research mailing lists, direct contact with care homes and snowballing.

Sampling was purposive. We wanted to understand how the role of the individual and the care home they worked in potentially affected their views and experiences. We therefore targeted care home staff with a range of roles, experience, and location to achieve maximum variation in the following:

- Participant
  - Job role
  - Experience (years, types of homes)
- Employing care home
  - Type of home (residential, nursing, mixed)
  - Size (number of beds)
  - Management of the home (private company, voluntary/charity organisation, local council)
  - Setting (rural, town, inner city)
  - Location

Recruitment continued until the study team agreed that there was sufficient information power.[89] This was when no amendments to the topic guide were considered necessary, when no new codes or significant themes were emerging and the team felt that there was sufficient detail to explain the themes.

2.4.3 Eligibility

Inclusion Criteria

- Willing and able to give informed consent for participation in the study
- Aged 18 years or above
- Currently working in a care home in England, Scotland or Wales with at least one year of experience

Exclusion Criteria

- Unable to participate in an interview in English
- Unable to complete an interview within 6 weeks of recruitment
- Previously interviewed as part of the study

2.4.4 Informed consent

Potential participants responding to the advertisement received an email explaining the purpose of the interview study, including the options for timing and format of the interview, along with a copy of the latest approved version Participant Information Sheet (PIS) and Informed Consent Form (ICF). The PIS clearly stated that the participant was free to withdraw from the study at any time for any reason without a penalty, and with no obligation to give the reason for withdrawal. Potential participants were given the the opportunity to ask any further questions via email or telephone, or they could choose to decline any further contact at this stage. An interview was arranged if participants were happy to proceed. There was a further opportunity to review the PIS and ICF before the interview started, and for any questions to be addressed. Verbal informed consent was recorded using the standardised wording from the ICF before the interview started.

2.4.5 Data collection

Telephone interviews were conducted by AM between January 2021 and April 2022. None of the participants were known to AM beforehand. Participants were offered an interview at a time convenient to them and were reimbursed with a £20 gift card for their participation.

Interviews were semi-structured, following a flexible topic guide developed and pilot tested by the research team. (See Appendix A.1) Interviews lasted between 60-80 minutes, were audio-recorded, and were transcribed verbatim by a professional transcriber.

2.4.6 Data analysis

Coding and thematic analyses of the data was completed by AM using NVivo for Mac software to support data management. The interview transcripts were open coded; related codes were combined to create categories. Material within the categories was subsequently reviewed for explanation, before looking at how the categories combined to support emerging narratives. Earlier interviews were re-coded in the light of ongoing analysis and early analysis brought out topics which were added to the topic guide.[90]

AM established an audit trail from the raw data of the interview transcripts through coding to development of themes to ensure dependability. The research team discussed the initial coding framework, as well as ideas for categories emerging from the data, and subsequently, the final themes to ensure their credibility and confirmability. Group discussions with AM allowed reflexive practice throughout the process. These processes enhanced the trustworthiness of the approach and, consequently, the credibility of the findings.[91]

2.5 Findings

2.5.1 Participant characteristics

47 care home staff responded to the advertisements circulated over the 15 months of recruitment. Of these, 3 did not meet the inclusion criteria for the study (did not work in a care home for older adults) and 19 did not respond after being provided further information. As described in Section 2.4.2, recruitment stopped once the team agreed there was sufficient information power to explain and elaborate on the themes that emerged in the analysis.[89]

Purposive sampling resulted in recruitment of participants with a mix of roles and experience in care homes ranging from 1 to over 25 years. Most participants were women, reflecting

Gender	Female		23
	Male		2
Job role	Without nursing qualification	Carer	3
		Senior carer	3
		Deputy manager	2
		Manager	7
		Other	1
	With nursing qualification	Nurse	2
		Advanced nurse practitioner	1
		Manager	6
Years' experience in care homes	1-5		5
	6-10		5
	11-15		3
	16-20		5
	21-25		1
	>25		5
Type of care home	Residential		8
	Nursing		9
	Combined residential and nursing		7

Table 2.1: Characteristics of included participants and their employing care homes.

the demographic of the care sector. Approximately half of the participants had a nursing qualification, so we were able to explore the impact of clinical training on their perceptions and responses to acute functional decline.

2.5.2 Overview of themes and subthemes

The themes and subthemes that emerged during analysis are summarised in Table 2.2 and are explored in more detail below.

Recognising residents with acute functional decline within the care home	Noticing changes from normal
	Describing and communicating about the episode
	Feeling anxious about the resident
Early response to residents with acute functional decline within the care home	Sharing or shifting responsibility
	Assessing the resident
Monitoring residents with acute functional decline within the care home	Observing residents
	Triggers for seeking additional clinical support
	Contacting GPs or other sources of clinical support

Table 2.2: Themes and subthemes.

2.5.3 Theme 1: Recognising acute functional decline within the care home

2.5.3.1 Noticing changes from normal

All interviews opened with an opportunity for participants to describe what they understood by 'acute functional decline'. In response, participants tended to list a series of changes in both behaviour and activities of daily living. Some participants also mixed in specific symptoms or clinical signs of acute illness, mainly those associated with infection.

> *'Mobility going down, off their food, nausea, pallor, breathlessness, if they complain of pain or discomfort, going to the toilet. If they are actually hot to touch. . . '*
>
> P10, female manager, nursing qualification, combined nursing/residential home, >25 years' experience

Participants said that sometimes the changes they noticed were subtle and required knowing the resident well. Several highlighted that some residents exhibited symptoms unique to them; examples included a flushed face or a painful neck. Most participants felt confident that they could detect an acute functional decline, with some attributing this to their years of experience of working in care homes, and some to their clinical training. However, many participants said it was the carers with no clinical training that were best placed to notice a change because they interacted the most with residents.

'Because you're there a lot with those people, you get to know their likes, their dislikes, their routines and if they veer from any of that you know there's something wrong.'

P1 (Manager – nursing qualification, residential home, >25 years' experience)

One challenge identified by some participants was recognising a change in residents who normally fluctuated day to day, such as those living with severe dementia. In these residents it was difficult to differentiate an acute functional decline from a *'bad day'*. Several participants characterised *'bad days'* or *'off-days'* as short-lived and less severe episodes, with residents returning to baseline quickly.

2.5.3.2 Describing and communicating about the episode

All participants were asked about the terms that they would use to describe or communicate to each other about residents who were experiencing an acute functional decline. Many participants gave examples of phrases that indicated that a resident was different to normal like *'not themselves', 'a bit off'* or *'they're just not right'*. Others used words that indicated ill health like *'poorly'* or *'generally unwell'*. Some participants just talked about having and sharing *'concerns'*.

Several participants reflected how the language used within the care home differed to that used when communicating with healthcare professionals.

'So the carer would report it as, as that, 'oh I'm a bit concerned about the resident today,' and then obviously describe their concerns. When we are talking to the doctors, to medical professionals we probably would then say 'there's been an acute decline."

P8, female manager, no nursing qualification, residential home, 20-25 years' experience

A few participants explored the potential mismatch between the language used within the care home and the potential severity of the decline or the illness the resident was experiencing. This could be a barrier when communicating to healthcare professionals.

'It can be a bit frustrating because it's like 'well they're just saying they don't feel

right' they said but and then you're thinking well I can't kind of present this to a GP as if they don't feel right when there's nothing clinically telling me that there isn't anything wrong.'

P15, female deputy manager, nursing qualification, combined nursing/residential home, >25 years' experience

As a result of this mismatch one participant had introduced training to improve inter-professional communication. In contrast, another participant felt that it was important to retain the use of simple language within the care home because most of the staff did not have a background of clinical training.

'We don't like to use too much medical jargon and work just work around them. It can, it can instil a bit of fear sometimes, I think. I think it's important that they understand as much as you because I am the only medical trained person in the home. . . '

P24, female advanced nurse practitioner, combined residential/nursing home, 11-15 years' experience

2.5.3.3 Feeling anxious about the resident

Several participants talked about their anxiety for residents when they were experiencing an acute functional decline. For some this was because episodes did not all follow the same trajectory or have a predictable outcome. Participants talked about how sometimes an acute functional decline turned out to be just an *'off day'*, in others it was an early sign of an acute but potentially reversible illness, whilst in others still it could mean that the resident was approaching end-of-life.

For some participants the anxiety was also driven by a close relationship with the affected resident. Others talked about the ongoing emotional impact from their experience in the early stages of the COVID-19 pandemic. The uncertainty and fear for residents appeared to impact some participants' responses to episodes, including having a low threshold to escalate.

'We get quite worried when our residents get like UTIs and stuff because obviously

if they're left untreated, if any infection is left untreated it could turn sepsis and, obviously, we don't want that. . . '

P4 (female senior carer, residential home, 6-10 years' experience)

2.5.4 Theme 2: Early response to residents with an acute functional decline within the care home

2.5.4.1 Sharing or shifting responsibility

Many participants talked about quickly sharing what they had observed about a resident amongst their team. This could either be to validate what they had noticed or to escalate to someone more senior who could support them. Some described not wanting to hold any responsibility for a potentially unwell resident in case something went wrong, whilst some described a culture of automatically escalating everything to someone with clinical training.

'So, if it was noticed by a carer for example it'd go to the senior. If the senior was unsure which 90 per cent of the time, they know how to handle it, they'd come up to management, but it then be discussed, and it would go to our advanced nurse practitioner.'

P18 (female manager, no nursing qualification, residential home, 6-10 years' experience)

Escalation appeared to alleviate anxiety for participants and removed the sense of having personal responsibility. However, one participant highlighted how a low threshold for escalation within the care home had the potential to over-burden the limited nursing staff available.

'The care staff certainly know when to escalate. In fact, to some extent, it probably is the opposite way that care staff will escalate too much; somebody clears their throat, they're running down to the clinic to tell the nurse.'

P13 (female manager, nursing qualification, nursing home, 21-25 years' experience)

2.5.4.2 Assessing the resident

Most participants described how a resident who had been identified as experiencing an acute functional decline would be assessed at an early stage. During this assessment, most

participants said a set of clinical observations would be taken. Some participants went on to use these to calculate a score, using National Early Warning Score 2 (NEWS2)[92] or RESTORE2™.[39] Participants said that observations helped them to get an initial sense of the severity of any illness and were reassured if they and/or the early warning score were normal. There were several examples of upskilling of non-clinical staff to take observations as a result of the COVID-19 pandemic.

Many participants also said that they would collect a urine sample from the resident and do a urine dipstick as part of their initial assessment. This was because a UTI was perceived by them to be a common or usual cause for an acute functional decline. Some participants said they would do a urine dipstick for everyone, whilst others qualified that they would only collect a urine sample if there were urinary symptoms reported. Others felt that GPs expected a urine dipstick to be done. However, there were also participants who said that they were unclear whether a urine dipstick was recommended in current guidelines.

> *'If their urine is a bit iffy, I would also probably do a urine dip, but I mean we've been given so much conflicting advice on whether that's helpful or not in people over the age of 65.'*
>
> P7 (Female senior carer, residential home, 1-5 years' experience)

Some participants with a nursing qualification talked about doing a more thorough clinical assessment. This might involve a physical examination, as well as ruling in or out what they thought were other possible causes for an acute functional decline. Participants mentioned constipation, dehydration, medications, pain, or psychological triggers. Several participants talked of the increased responsibility the care home took for looking after the resident before escalating to the GP because of the limitations on home visits during the COVID-19 pandemic.

Doing a lateral flow test for COVID-19 had become routine in the assessment of unwell residents for many participants at the time the interviews were conducted. Several participants described how during the pandemic they had worried all the time that their residents could have COVID-19, and one participant felt that their clinical judgement had been compro-

mised by this fear. In contrast, several participants felt that the pandemic had not changed the way in which they responded to residents with an acute functional decline.

2.5.5 Theme 3: Monitoring residents with an acute functional decline within the care home

2.5.5.1 Observing residents

Some participants said they would adopt a *'watch and wait'* approach, especially if presentation was perceived to be less severe (eg. reduced food intake), if the clinical observations were normal and if there were no particularly concerning features on their assessment. This generally meant a period of closer monitoring with repeated checks of clinical observations, often coupled with encouraging oral fluids. Some nursing staff described initiating other interventions during this time including giving analgesia, antipyretics and, if constipated, laxatives.

> *'In the meantime, we would keep an eye on them. The odd just basic things like start a fluid and food chart to make sure they were hydrated and check their output and we would, we would start that as well to monitor.'*
> P10 (female manager, nursing qualification, combined nursing/residential home, >25 years' experience)

The purpose of this approach was, for some of these participants, to help them differentiate a potential *'off day'* from something more serious. Allowing a short period of time to pass gave those who were going to get better anyway the opportunity to do so, and/or any simple interventions a chance to work. Some participants felt it was positive that this could prevent unnecessary GP contacts.

Some participants described when they would seek advice for those who were not getting better on the *'watch and wait'* approach. The length of time participants allowed before seeking additional clinical support in these cases ranged from a few hours, to the next shift, and in one home there was a *'rule of thumb'* of three days.

2.5.5.2 Triggers for seeking additional clinical support

All participants described potential triggers for wanting to seek additional clinical support for the resident. Participants had different tolerance levels to exposing themselves to risk. Those without clinical training tended to want to escalate sooner.

> *'We've been told by our manager that if we're not sure with something, we should report it straight away because then if something does happen, we're, we're covered in the fact in that we have reported it but it was their, the professional's decision not to do anything else about it.'*
>
> P4 (female senior carer, residential home, 6-10 years' experience)

Some participants said that it was the perceived severity of the illness or their own anxiety that prompted escalation. For some, severity was indicated by the speed or degree of the change from normal. For others, it was red flag symptoms like total loss of mobility or extreme confusion. Participants with a nursing qualification described sometimes having a *'gut feeling'* to escalate. They said that this feeling was driven by their experience of similar episodes, and/or knowing the resident well.

> *I do believe that nurses have a sixth sense where they do pick up on things and I don't think it's always possible to put it into words why you think something's not right.*
>
> P12 (Manager – nursing qualification, nursing home >25 years' experience)

In homes that had adopted early warning score tools like NEWS2, the overall score or changing score would determine what they did next, including escalation to a GP or ambulance service.

2.5.5.3 Contacting GPs or other sources of clinical support

Participants had varying experiences of contacting GPs about unwell residents. Some had a good relationship with their usual GP, whilst others described challenges in communication. Several participants felt the need to be forceful in getting their point across. Others talked about the need to be succinct, and how they had learned to deliver information GPs would

expect.

> *'They usually would expect us when we ring, we are prepared when we ring the doctor, so we, we have a list of who needs a GP and next to them is observations and, obviously, if we need to dip urine, we dip urine prior to ringing the doctor so we have all that information, we have the facts. It just makes the whole process a lot easier.'*
>
> P19 (female manager, no nursing qualification, 16-20 years' experience)

Several participants talked about how the early warning score tools had improved communication with GPs and given them greater confidence in explaining the potential severity of illness, as well as being a way of avoiding lay terminology.

> *'So being able to say, "Their NEWS is at 6," that's like such a shorthand of saying, they're not quite right and I also semi know what I'm doing so please listen. It's just been brilliant, it's been a brilliant tool.*
>
> P7 (female senior carer, residential home, 1-5 years' experience)

As these interviews were carried out towards the end of the pandemic, many assessments with GPs were carried out over the phone with care home staff or as a video call. Some participants explained that GPs appeared to rely on their judgement when making a clinical diagnosis – for example, accepting their assessment that a person might have a UTI. Others talked about the usual response of the GP to prescribe antibiotics for residents with an acute functional decline. Several participants described frustration at the lack of face-to-face input or investigation by GPs during this period.

There were several examples of alternative care models using remote specialist nurses who were able to advise on next steps. Advice could include trying the watch and wait approach, simple interventions or escalation to a GP. Participants with access to these services valued the specialist support and the quicker response compared to contacting their GP directly. Some care homes had directly employed advanced nurse practitioners who were able to provide rapid in-house assessments, and, in one case, prescribe medication. In these care homes GPs were rarely involved in the assessment and management of residents experiencing

an acute functional decline.

2.6 Discussion

2.6.1 Summary of findings

Care home staff described acute functional decline as having a diverse illness course. Some described difficulties distinguishing transient fluctuations in functional ability, which may be normal for some residents, from a more significant deviation. The uncertainty around the illness trajectory caused anxiety for care home staff during these episodes, which could result in careful monitoring and/or early escalation. Clinical observations were often measured as part of an initial assessment, sometimes to calculate an early warning score. Participants described commonly checking a urine dipstick, driven both by a belief that acute functional decline is often caused by UTI as well as anticipating a request from the GP when escalated. There were some participants with a nursing qualification who considered a broader range of differentials for acute functional decline, and several examples of more advanced assessments being done by care home staff including simple interventions. There were also cases where advanced nurse practitioners were involved in the clinical management of these residents within the care home, without necessarily involving a GP.

2.6.2 Comparison with existing evidence

Some of the themes in this analysis align with those identified by a recent scoping review on care home staff recognition of acute deterioration (a sudden decompensation of physiological and/or mental status which could necessitate hospital admission).[93] This review also highlighted the importance of the knowledge of a resident's baseline, the transfer of responsibility up the hierarchy within the care home, the recording of clinical observations and use of early warning scores as communication tools.

The variation in practice around using tools for recognition and communication of acute deterioration in care homes in the UK has also been previously described.[94, 95] Critically high NEWS2 scores measured in care home residents on admission can predict poor out-

comes,[96] but it is unclear how well the score performs when measured in care homes, or how it can be practically adopted. For example, a recent Norwegian qualitative study with care home staff and GPs described the limitations of using early warning scores for acute functional decline in care homes, including how some of the recommendations, like repeat observation checks, were not feasible for the setting.[97]

In our study the participants described how the language used by staff in care homes to describe an unwell resident could result in challenges when communicating with healthcare professionals. This is something that communication tools like Situation, Background, Assessment, Recommendation, Decision (SBARD) – which is embedded in RESTORE2™ – are meant to solve. However, a systematic review concluded that there is limited high quality evidence to show that it is effective at improving patient safety[98] and, in a recent study, was shown not to improve communication between care home staff and clinicians in the USA.[99]

This analysis adds further insights into the care of UK care home residents in the post-pandemic era and explores more of care home staff beliefs about underlying causes of acute functional decline, particularly around association with UTI. From the participants' descriptions, acute functional decline is a continuum of clinical presentations ranging from subtle changes from baseline to a severe acute deterioration. Interpretation of these changes is complex and must take into account a knowledge of the resident and their usual pattern of functional changes.

2.6.3 Strengths and limitations

This analysis provides new insights from UK care home staff exploring their understanding of a salient topic in their own terms. We were successful in recruiting participants with a range of roles and experience from care homes across the UK, However, a limitation of the study design is that we did not interview the GPs linked to the participants to understand both sides of the negotiation of care for residents. For example, it is unclear whether the expectation of GPs and/or their usual response in prescribing antibiotics contributed to the

participants' belief that UTI was usually the cause of an acute functional decline.

It is important that the context of the COVID-19 pandemic is considered when assessing the transferability of the results. Early interviews took place during the third national lockdown in the UK, and the final interviews were carried out when the last remaining government-enforced restrictions on social distancing were being relaxed. However, as described in the findings, the impact of the pandemic was explored during the interviews; some participants felt that little had changed in their recognition and assessment processes.

2.6.4 Implications for practice and future research

It is useful for GPs and other healthcare professionals to understand the expertise that care home staff have in their own residents, and to recognise that significant work may have been done in monitoring and managing the resident before they seek outside advice. These results also show there is variety in care home responses to acute functional decline which, in some cases, can be risk averse. This is perhaps unsurprising given many care home staff have no formal clinical training. It may be helpful to consider strategies to support the care home workforce to be able to retain knowledge and good practice and to improve consistency across care homes. It may be also useful to explore whether there are measures that could reduce uncertainty and resultant anxiety in these cases. This could involve earlier access to allied health care professionals and/or more point-of-care diagnostic testing. Care home staff views on point-of-care testing are described in Chapter 3.

The findings of this analysis indicate that care home residents with acute functional decline vary considerably in presentation, illness trajectory and outcome which means that it is challenging to explore from a research perspective. Further work is needed to better describe and potentially phenotype these presentations. Knowing that care home staff associate acute functional decline with UTI is an important first step towards improving differential diagnosis of these presentations and reducing unnecessary antibiotic use by healthcare professionals in any onward contacts. However, given the lack of observational data on these episodes from care homes, we cannot be sure how much of the acute functional decline seen

there is truly caused by UTI.

2.7 Conclusions

These results highlight the complexities around the identification and management of care home residents experiencing an acute functional decline from the perspective of care home staff. More work is needed to better understand the physiology of these episodes in the care home setting, how to delineate the potential different subtypes and risk profiles (eg. subtle functional changes vs physiological deterioration) and its relationship to UTI. Understanding more about the different causes and outcomes of these episodes could empower care home staff, reduce anxiety, and may help direct diagnostic testing and/or interventions that could result in better outcomes for care home residents.

2.8 Chapter summary

In this chapter I have explored the experiences of UK care home staff of acute functional decline through the analysis of qualitative interview data. Care home staff described that whilst knowing a resident well can help with recognition, it not always straightforward, particularly in those living with dementia. They, like GPs, experience anxiety and uncertainty about what can be an unpredictable and varied illness trajectory, which sometimes results in a low threshold to escalate to outside clinical support. Many care home staff assume that an episode of an acute functional decline is caused by UTI, but from this study it is not clear how much of this is driven by GP prescribing behaviour. Symptoms and signs of UTI episodes as suspected by care home staff including any associated functional decline are described in the results of the observational cohort study in Chapter 5. Additional point-of-care diagnostic testing in care homes may be one solution to reducing clinical uncertainty in episodes of acute functional decline. The views of care home staff on this are explored further in the next chapter.

Chapter 3

How do care home staff currently use and view point of care tests in their assessment of acute functional decline? A qualitative exploration of UK care home staff experience.

3.1 Overview of chapter

In this chapter I present the second set of findings of the qualitative interview study with UK care home staff. In Chapter 2 I described how the care home staff interviewed often attributed acute functional decline to UTI, and used a urine dipstick in their assessment of unwell residents. The aim of this chapter is to explore more deeply the experience of care home staff of using POCTs when managing acute functional decline/suspected UTI and their understanding and interpretation of results. I also explore their views on the potential introduction of more POCTs to the care home setting in the future, including ideal test characteristics.

3.2 Background and rationale

Acute functional decline without a clear cause in older care home residents represents a diagnostic challenge to healthcare professionals and may lead to unnecessary empirical antibiotic prescriptions or avoidable hospital admissions. Acute functional decline may have a number of different underlying causes including UTI,[30–32] although observational data is lacking in care homes. However, there is a lack of evidence and/or guidance on how to investigate these episodes in primary care, other than to avoid the use of the urine dipstick as a diagnostic test.[41]

As discussed in Chapter 1, urine dipsticks remain the only commonly available POCT for UTI but are not recommended in older adults due to risk of false positives associated with ASB.[40, 41] Despite this and additional evidence that reducing their use can be an effective antibiotic stewardship measure,[100] urine dipsticks continue to be widely used in care homes. This includes during episodes of acute functional decline, as described in Chapter 2. However, there are now novel UTI diagnostics that have the potential to improve diagnostic accuracy of UTI and could be introduced into care homes in the future.[76]

The beliefs of the care home staff about the diagnosis of UTI have been described in previous qualitative interview studies but with limited interrogation of their interpretation of dipsticks [72, 101] and no studies have previously explored wider attitudes towards point-of-care testing. This is critical to understand prior to the introduction of any novel POCTs in the future. Therefore, this study aimed to explore the perspective of care home staff on current POCT use in care homes in the context of acute functional decline and their views on the potential for diagnostic innovation in this setting.

3.3 Aims and objectives

3.3.1 Aim

Explore the current use and interpretation of POCTs by care home staff and their views on additional point-of-care testing in the future.

3.3.2 Objectives

To understand from care home staff:

- What their experience is of using different POCTs in the care home
- How (if at all) point-of-care testing is used in the management of acute functional decline
- How they interpret and use existing POCT results
- In what situations would (further) point-of-care testing be most useful?
- What characteristics should a POCT have to be used in a care home?

3.4 Methods

The methods for this study are described in Section 2.4. The topic guide can be found at Appendix A.1.

3.5 Findings

3.5.1 Participant characteristics

Twenty five care home staff took part in interviews, as outlined in Chapter 2.5.1. Demographics are summarised in Table 2.1.

3.5.2 Overview of themes and subthemes

Participants were asked how POCTs were currently being used as part of usual care in the homes they worked in. All participants described regularly using or being familiar with urine dipstick tests, and these were used in their assessments of someone with acute functional decline. At the time of interviews, several participants were still regularly using lateral flow tests for COVID-19. There was also one example of a care home that had introduced a fingerprick blood test for an inflammatory marker. A few participants said they were able

to use blood glucose meters but this was only in supporting diabetes management, rather than in acute assessments.

The majority of the discussion in the interviews was around the commonly used urine dipstick, and we used this example to develop and refine the subthemes on current POCT use. Table 3.1 summarises all the themes and subthemes that emerged from interviews.

Current use of POCTs in care homes: the urine dipstick	Deciding to test
	Reasoning for test
	Reading vs interpreting a test result
	Test result impact on suspected diagnosis
	Gateway to further tests or treatments
	Limitations of test
Potential impact of expanding use of POCTs in care homes	Earlier diagnosis and treatment
	Communication and decision tool
	Risk of over-medicalisation
	Need for additional infrastructure

Table 3.1: Themes and subthemes.

3.5.3 Theme 1: Current use of POCTs in care homes: the urine dipstick

3.5.3.1 Deciding to test

Urine dipsticks were used by many participants as part of their assessment of a resident experiencing an acute functional decline, when a dipstick was one of only a few *'tools'* they had to investigate. Participants used information from the dipstick and their other assessments both to make sense of the situation and justify getting outside clinical support or treatments.

> *'Personally I would use the tools that I have that that maybe help tell the story of what's going on for that person and that's a quick and easy one you can do.'*
> P20 (Manager – nursing background, mixed nursing and residential home, over 25 years' experience)

In most cases it was a decision made within the care home to carry out the dipstick. In some homes this was by instruction from a senior member of staff or nurse, but some said junior carers would carry them out independently if they came across a resident they were concerned about. However, there was also one example of a remote nurse-led clinical support service directing investigations, and a few participants described checklists being used to help with decision making.

> *'We can relate to this little checklist and go through it and make aware that that we're following the right steps because they always ask for a urine sample and they always ask what their, the, the little stick was saying...'*
> P4 (Female senior carer, residential home, 6-10 years' experience)

Some participants indicated that their GP would expect the result of a dipstick to always be available prior to the care home contacting them with their concerns. Conversely, others had been told specifically not to carry out dipsticks by healthcare professionals. Some described having received inconsistent messaging on the value of urine dipsticks. There were several examples of the test being done by care home staff despite explicit instructions not to. These participants said they had done it *'just in case'* or because they personally found the information helpful, even if a healthcare professional did not.

> *'It came from a care home liaison nurse that they weren't to dip. Everything was to go through the labs instead. That's not to say that we don't buy dipsticks and we don't use dipsticks because it does give us a good indication.'*
> P13 (female manager, nursing background, nursing home, 21-25 years' experience)

The biggest barrier to carrying out a dipstick was difficulty getting a urine sample due to incontinence or mobility issues. Participants said that residents could not necessarily pass urine on demand, and it was not always easy to predict when someone might need to use the toilet. Collecting a urine sample from some residents could therefore be extremely time consuming, and in some cases may not be possible at all. Participants described using bed pans, commodes and, more rarely, in-out catheters.

> *'We've tried to and people for example on commodes and having a receptacle*

underneath to catch any urine that's passed and I've got people who could sit there for three hours and do nothing but the moment you turn your back, they'll do it.'

P13 (female manager, nursing background, nursing home, 21-25 years' experience)

3.5.3.2 Reasoning for test

Participants mostly thought dipsticks were a good way to rule in and/or rule out a UTI as a cause of illness. However, participants described using the test for residents with varying indices of suspicion for UTI. For example, some said they only did a dipstick if they strongly suspected UTI to be the cause of a resident's symptoms – this included those with urinary symptoms and/or a history of UTI, as well as those experiencing non-specific symptoms like acute functional decline.

'To do a dipstick I would be looking for if somebody's got a high temperature, if they're complaining of pain on micturition, whether they're passing blood in their urine, if it's smelly, concentrated, different colour from the normal, if they're more confused than usual, those are things that could prompt me to do a dipstick.'

P14 (female nurse, nursing home, 21-25 years' experience)

However, dipsticks were also described as being used in situations when staff weren't sure what was going on and couldn't find another plausible explanation for illness.

'I'd say even if someone is slightly unwell, we always just check everything straight away and if there's no indication there, we would then dip the urine. It's normally literally straight away as soon as possible really, just in case. It's rather to be safe than sorry.'

P3 (Female carer, mixed residential and nursing home, 6-10 years' experience)

Others described doing dipsticks automatically in response to a resident they were worried about – it was part of their routine, and they didn't consciously consider whether they suspected a UTI as a cause.

3.5.3.3 Reading vs interpreting a test result

Participants described different approaches to interpreting a dipstick result, with some participants looking for any colour change on the stick and others looking for changes in specific sub-tests on a multi-test dipstick. Leukocytes, nitrites, blood and protein were considered to be strongly associated with UTI. A dipstick with any changes in colour in these sub-tests was described as *'positive'*. Some participants thought that the more intense the colour change, the more likely or more serious the UTI.

> *'Well of the two I'm talking about that we look for is leukocytes, bloods, I mean blood or protein, if any two of these are positive, I'm automatically thinking this person could have a UTI and also if there's more pluses than one that is a stronger indication for me.'*
> P14 (female nurse, nursing home, 21-25 years' experience)

However, some participants without clinical training said that whilst they had the skills needed to carry out a urine dipstick, they did not feel confident that they could interpret the result. Several participants highlighted this as a specific training need, and one gave an example of how an online resource had helped them overcome this knowledge gap.

> *'We could technically dip it, but we wouldn't be able to diagnose a patient, that would be the nurse.'*
> P3 (Female carer, mixed residential and nursing home, 6-10 years' experience)

> *'We've got a guideline where again it's just one that I found off the internet and printed off and said, "Look, you know, this and this could possibly mean this," but we generally just pass that information onto the doctor.'*
> P8 (Female manager, non-nursing background, residential home, 20-25 years' experience)

3.5.3.4 Test result impact on suspected diagnosis

In cases where UTI was strongly suspected by participants, a positive dipstick result helped to consolidate this opinion.

'If it's obvious that it is a urine infection, you know, it's there in black and white for you to see with the numbers that are there I will generally treat that.'
P24 (female advanced nurse practitioner, combined residential/nursing home, 11-15 years' experience)

However, a negative result when UTI was strongly suspected did little to persuade them otherwise and could still result in care home staff sending the urine sample to a laboratory for culture.

'If the urine's showing it's clear it might just be it's not being picked up on the urine urinalysis, it might just need a proper, so they usually make a decision to take a proper tests and then maybe have a chat with the GP just to say, "We're going to take the urine specimen because they're not right."'
P20 (Manager – nursing background, mixed nursing and residential home, over 25 years experience)

In cases where UTI was not strongly suspected, one person described how a negative result would prompt them to consider alternative causes for illness. However, a positive result, in someone who was well and in whom UTI was not strongly suspected, could still be seen as UTI requiring treatment.

'It could be that they're starting with a urine infection that hasn't got a hold of them yet. So, it could be the start of something that needs treating quite quickly before they become more unwell.'
P19 (female manager, non-nursing background, 16-20 years' experience)

3.5.3.5 Gateway to further tests or treatment

In care homes without nursing staff, the result of a urine dipstick was usually immediately relayed to a clinician to help them decide the next steps. However, if the dipstick was positive some participants said they sent away the urine for culture without necessarily involving the GP.

'The girls know that if there's protein or blood in the urine that that needs to be

passed on. So they know, they don't probably understand why it's there. They know it shouldn't be there and so they pass it on.'

P1 (female manager – nursing background, residential home, >25 years' experience)

'The GP would know because we'd always let them know we'd done a urine sample. We get consent but sometimes we do pre-empt and say, "I really think it is and I've sent it," and they trust our judgment.'

P10 (female manager, nursing background, combined nursing/residential home, >25 years' experience)

Several participants said they expected that a GP would prescribe antibiotics in response to a positive test, particularly when combined with care home suspicion of UTI. Some therefore perceived doing a dipstick as a good and/or necessary gateway step to get treatment to residents quickly.

'Normally I would get the sample, send it and inform the GP because of what I've told them, they don't even hesitate, they just prescribe antibiotics for that person.'

P14 (female nurse, nursing home, 21-25 years' experience)

However, others felt that antibiotics wasn't always the right course of action and were given out unnecessarily. One participant recognised the role of the dipstick in this outcome.

'I think it's because...the minute you say that it's positive you're almost hoping you're going to get antibiotics and I think they were given out when they weren't needed...'

P05 (Female manager, nursing background, mixed residential and nursing home, 16-20 years' experience)

3.5.3.6 Limitations of test

Only a few participants questioned the diagnostic performance of dipsticks. Several identified the risk of false positives and how this might contribute to inappropriate antibiotic use. Some still described using them despite this understanding.

'We did dipstick it which obviously I know you're not supposed to do but, you know, because it's gonna show bacteria anyway isn't it and, you know, antibiotics is not always the be all and end all...'

P08 (Female manager, non-nursing background, residential home, 20-25 years' experience)

Other concerns were the effects of urine concentration and contamination on dipstick results. Several also worried about tests expiring. One participant also mentioned how user technique may impact a result.

'Sometimes the carers dip the urine for us if we are busy so depending on the technique, they've used they could contaminate the lab stick itself.'

P14 (female nurse, nursing home, 21-25 years' experience)

Another downside identified by some participants was that a positive result could not predict which antibiotics would work, in contrast to a urine culture with antibiotic sensitivities done in a laboratory. Some felt that prescribing just based off the dipstick could therefore cause a delay in the correct antibiotic being given.

'If you can instantly get a sample sent off and get the right antibiotic that then, you know, well it saves the cost of antibiotics of somebody that's not going to work but it's more so for the resident that gets it quicker.'

P6 (Female manager, non-nursing background, mixed nursing and residential home, 0-4 years' experience)

3.5.4 Theme 2: Potential impact of expanding use of POCTs in care homes

All participants were asked to consider the theoretical increased POCT use in care homes in the future. Most participants felt that more POCTs would be beneficial to residents and in particular wanted tests that could help in assessing those who were unwell – much like the way in which they already used the urine dipstick. Tests for infection, anaemia and monitoring International Normalised Ratio (INR) were thought to be most useful. In

contrast, there were also several participants who felt that they already did enough testing within their care home, or that more testing would be outside the scope of their practice.

> *'It is quite hard to say what we really improve in the aspect of the testing side of things. I do think we're quite good at diagnosing or, you know, getting that person the support and help they need when it's necessary.'*
> P3 (Female carer, mixed residential and nursing home, 6-10 years' experience)

When asked about which biological samples would be preferable for collection and use in POCTs, most participants said that fingerprick blood tests would be the easiest to obtain from care home residents. However, one participant highlighted that they would not be allowed to take blood tests because they were a residential home without registered nurses. Many also felt that both urine and swab samples were possible with practice and experience.

> *'The majority are fine with but again it's just the behaviours we do sometimes have to wait and we can't always get it on that day. Urine, as I say, we've got different ways that we, we manage to get it. . . .[Finger prick samples], that's far easier than actually getting a full sample of blood yeah.'*
> P6 (Female manager, non-nursing background, mixed nursing and residential home, 0-4 years' experience)

Participants felt that residents were likely to feel more comfortable or confident about having tests done by someone they knew in a setting that was familiar to them.

> *'I think when they're unwell, actually they really look for you to, 'I don't feel well, can you help me?' Rather than, 'get a doctor,' you know, they're looking at you to just make them better and I think anything you can do in that role is, is just beneficial for them.'*
> P5 (Female manager, nursing background, mixed residential and nursing home, 16-20 years' experience)

3.5.4.1 Earlier diagnosis and treatment

Participants felt that increased use of POCTs could help unwell residents get an earlier diagnosis and treatment and therefore could increase the probability of a recovery. Some also identified that doing tests in house could prevent unnecessary trips to the GP practice, or even a hospital admission. They identified that POCTs removed the opportunity cost in waiting for assessments in other settings.

> *'Because they wouldn't be waiting for an appointment to the hospital or, you know, for us to take them. Sometimes they can be in A+E for twelve hours, you know, before anything's done ... and in the meantime, they're not getting the treatment that they require so it's about getting the opportunity for that treatment in the right place in the right time by the right person, isn't it?'*
> P11 (female manager, nursing background, nursing home, 6-10 years' experience)

Several participants spoke about the specific advantage of early diagnosis and treatment to care home residents in mitigating or avoiding the systemic effects of a serious illness and the potential long recovery time.

> *'I think the thing that maybe is not considered as much is that acute decline once resolved creates a whole cascade of other issues in that person. Weight loss, exhaustion, fatigue, probably sometimes it's extended confusion, you know, change to their normal patterns of behaviour because they simply haven't been able to keep up their daily routines for a couple of weeks and even just that causes like muscle wastage and all sorts of things. So, from our perspective it will keep people well for longer if we were able to carry out diagnostic tests that would mean that their acute symptoms were resolved quickly.'*
> P7 (Female senior carer, residential home, 1-5 years' experience)

3.5.4.2 Communication and decision tool

Several participants discussed how being equipped with a test result would add value to their interactions with other healthcare professionals. Some said that an abnormal test result could help justify their contact with GPs when they felt someone was unwell, and

that it might mean their concerns would be taken more seriously. Several participants also felt that GPs would see value in them providing POCT results that would help them with their assessment and potentially reduce GP workload.

> *'Because we could give them so much more than just saying, "Oh well we think they've got an infection. They're showing some signs of an infection." And even then, I just say, "Oh their infection markers are raised so there's obviously something going on."'*
>
> P4 (Female senior carer, residential home, 6-10 years' experience)

Several participants considered how a normal POCT result could also be used for their own reassurance when someone was unwell. A normal result had the potential to reduce care home staff uncertainty and resultant anxiety, which may also mean they could decide not to use other healthcare resources.

> *'Because it gives you an answer as well or it gives you the fact that there isn't anything there. It it's the case of ruling things out isn't it when somebody's unwell and if you've got more equipment that you can use there and then, then you can rule that out and rule that out and, and, you know, it's, yeah so much better.'*
>
> P6 (Female manager, non-nursing background, mixed nursing and residential home, 0-4 years' experience)

3.5.4.3 Risk of over-medicalisation

There were some participants who felt that a downside to doing more POCTs was over-medicalising the care home. One participant felt that doing a blood test, in particular, crossed a line between a home and a clinical environment.

> *'I don't know, I'd be, I'd be very careful I think where we're going. We are a care home, we're not a hospital.'*
>
> P9 (Female deputy manager, nursing background, mixed nursing and residential home, over 25 years' experience)

> *'I guess what we are constantly having to do is walk that line between this being a resident's home and a clinical environment.'*

P22 (Manager, nursing background, 6-10 years' experience)

Several participants felt that doing additional testing was unlikely to add anything further to their existing pathways and/or would be inappropriate because residents sick enough to need them would be better off in a hospital environment.

Some participants also raised how it may not always be appropriate or possible to respond to results due to an agreed ceiling of care. They did not want to risk subjecting residents to unnecessary tests that could then not be acted on and felt it was important that residents views were taken into account when considering doing any test.

> *'You could do all that but actually at the end of it, if the lady doesn't, "No I don't want anything doing, I've told you, don't mess about with me, leave me alone." I think you've got to respect their wishes.'*
> P9 (Female deputy manager, nursing background, mixed nursing and residential home, over 25 years' experience)

3.5.4.4 Need for additional infrastructure

Many participants emphasised that if more POCTs were going to be introduced into a care home and expected to be done by the staff there were several additional considerations. It would be important to train staff properly and to develop clear protocols. Several participants discussed how there would need to be acceptance on the part of key stakeholders including the residents, family members and local GP practice who would be supporting them, in particular around result interpretation.

> *'It is about training the staff, it's about staff and taking our responsibility and accountability to make sure they actually carry out that test. Because I find you find with the equipment it's just left in cupboards if they're not using it daily, you know, it's not routinely used or sometimes you find that staff, they shouldn't do, I'm not saying it's acceptable, but things do get neglected as well.'*
> P11 (female manager, nursing background, nursing home, 6-10 years' experience)

> *'I think the main thing is be prepared for the outcome because there's no point in*

doing all those tests and just going, "Oh what do we do now?", "Oh nothing we'll wait until tomorrow or something." I think whatever you do has got to have the outcome there as well.'

P9 (Female deputy manager, nursing background, mixed nursing and residential home, over 25 years' experience)

Participants also felt it was important to consider funding additional staffing and or an enhanced reimbursement for the upskilling and time required to do the tests.

'I think the more, the more information and the more training you give carers to do these things, the more they're gonna be seen to be the skilled workers that they are. And I think, you know, it needs to be reflected in the pay bracket. I would just say as an aside if you're giving extra diagnostic tests for carers to do. Equally, in an ideal world you'd have more staff so that you're not expected to do, you know, so many more tasks in a day where you already have no time.'

P7 (Female senior carer, residential home, 1-5 years' experience)

Taking this on would require additional responsibility, and staff would not want to be accountable if something went wrong. Other practical considerations included ascertaining who would be funding the test and finding space for storage.

'I think they would be worried about the implication of getting it wrong, I think because they understand they don't know what they don't know. But I think if they were coached, you know, for a period of time and competency assessed regularly, I think that would be great, I think it would be fabulous.'

P1 (Female manager, non-nursing background, residential home, over 25 years' experience)

3.6 Discussion

3.6.1 Summary

All participants had experience of using POCTs — commonly the urine dipstick — in their work in care homes. They described routinely using urine dipsticks to help them understand

why a resident may be unwell, including when experiencing an acute functional decline. Most thought dipsticks were a reasonable test for ruling in or ruling out UTI. Test result interpretation varied with clinical suspicion of UTI. Positive test results regardless of clinical suspicion were leveraged to get additional support for presumed UTI, like further help from a healthcare professional, confirmatory urine culture and/or antibiotic treatment. A negative result with a high index of suspicion resulted in a similar approach, often with the rationale that negative tests were possible in the early phase of a true UTI. A negative test with a low index of suspicion for UTI might prompt consideration of other diagnoses. Whilst some participants discussed the potential for false positive tests, few described how the high prevalence of ASB contributed to this. Several participants described continuing to use dipsticks despite clear advice not to.

Participants were generally positive about the prospect of doing additional POCTs in the care home, provided there was a clear benefit to the resident and they would be well supported in training, interpretation and next steps. They felt results from further POCTs could be similarly leveraged to help them get support for unwell residents. However, some participants cautioned against over-testing and over-medicalising the care home environment.

3.6.2 Comparison with existing evidence

There are limited studies to date involving point-of-care testing in care home settings; one Dutch study has shown that a POCT serum CRP could safely reduce antibiotic prescribing for lower respiratory tract infection,[102] whilst another showed that POCT serum CRP/procalcitonin were not able to help distinguish between ASB and UTI. [103] In qualitative work linked to the latter study doctors called for a test with a high negative predictive value to help rule out UTI when only non-specific symptoms predominated.[104]

Dipstick use in care homes has been discussed in several previous qualitative studies conducted alongside the development or test of an intervention to improve UTI diagnosis. Care home nurses in Australia also described how they would rule in a UTI with a positive

dipstick in those with non-specific clinical presentations, before being exposed to an intervention designed to reduce dipstick use.[72] Interviews with UK stakeholders, including care home staff, for the development of an educational leaflet and diagnostic UTI flowchart in older adults similarly revealed there was limited knowledge on ASB, and staff also described feeling pressured to do a dipstick test by GPs.[101]

3.6.3 Strengths and limitations

This is to our knowledge this is the first exploration of care home staff views on the requirements of POCTs that would be fit for purpose in the care home setting. This study also provides new insights from UK care home staff on how dipsticks are used and interpreted as a diagnostic test in different clinical contexts. We were successful in recruiting participants with a range of roles and experience from care homes across the UK. However, we did not interview the GPs linked to our participants to understand the role of the tests from their perspective.

3.6.4 Implications for future research and/or practice

Novel POCTs for UTI have the potential to transform management for unwell care home residents given the lack of tools and investigations that are currently possible in the care home setting. However, it is important to consider where these would fit in the pathway for staff seeking help for unwell residents, including those experiencing acute functional decline. Our participants described how they use dipstick results to access healthcare advice, tests and treatments for UTI and would potentially use additional POCTs in a similar way. As per our participants, new tests would need to be introduced as part of an agreed interaction with GPs or other healthcare providers and ideally should be able to be independently interpreted by care home staff if they are to reduce demand on other services. If new tests for UTI are not clearly targeted to specific clinical contexts, cannot differentiate between ASB and UTI, or risk being misinterpreted they may still contribute to antibiotic overuse.

Our participants have further highlighted the challenges around time taken to get urine samples, and how it may be impossible to get a sample from those who are incontinent.

Fingerprick blood samples were felt to be the easiest to acquire from this patient population. Future tests and diagnostic strategies will need to take this into account – for example, tests that can be used on urine collected in incontinence pads, or tests which use blood biomarkers taken from a fingerprick sample rather than urine. The views of residents, their families and other healthcare professionals supporting the home will be paramount in ensuring successful implementation.

In the meantime healthcare professionals supporting care homes need to be mindful of the fact that dipsticks may continue to be used even after recommendations or incentives to reduce use. The drivers of this behaviour appears to be uncertainty, a lack of other options to investigate an unwell resident, a misunderstanding of the relative importance of different subtests within a dipstick, and a limited insight into the impact of asymptomatic bacteriuria on test results. It is important to continue to educate care home staff around the rationale for avoiding dipsticks, how to correctly interpret them if they are used, and to provide additional clinical support where there is diagnostic uncertainty.

3.6.5 Conclusions

Care home staff lack tools to investigate when someone is unwell and use urine dipsticks to fill an information void, despite conflicting advice and poor evidence base. Additional point of care tests and/or alternative care pathways may help to investigate and manage care home residents with an acute functional decline or suspected UTI, but these need to consider the specific needs of care home settings and would need buy in from all stakeholders in the care delivery pathway. Training and ongoing support for new tests will be critical to ensure they remain used and interpreted correctly.

3.7 Chapter summary

In this chapter I have explored how care home staff currently use and interpret the urine dipstick as the main POCT they have available to investigate residents who are experiencing an acute functional decline. They have described how they leverage positive results to obtain

clinical support, and they discussed how they would hope that additional POCTs introduced into the care home setting in the future could be used in a similar way. I have highlighted that how urine dipstick results are interpreted differently depending on the clinical suspicion for UTI as the cause of illness, and have cautioned how future POCTs will have to have clear guidelines for use and interpretation. Care home staff views on three novel POCTs for UTI will be explored as part of Chapter 6. Few participants in my study mentioned the impact of ASB on urine dipstick interpretation. In the next chapter I will describe the prevalence of ASB in the care home setting through a systematic review and meta-analysis of the literature.

Chapter 4

What is the prevalence of asymptomatic bacteriuria in care home residents and community dwelling adults?

4.1 Overview of chapter

In Chapter 1 I described how current UK guidelines do not recommend using urine dipsticks as a diagnostic test for UTI in older adults over 65 years because ASB prevalence increases with age and this can result in false positives. ASB prevalence has been shown to be particularly high amongst care home residents in individual studies. However, no attempt has been made to bring together the evidence and appraise it collectively. In Chapters 2 and 3 I described how, despite guidelines, care home staff continue to use urine dipsticks to assess residents experiencing acute functional decline/suspected UTI and can use the results to justify consulting a GP. Up to date information about the likelihood of ASB in the urine of care home residents and older adults could result in a more nuanced interpretation of dipstick results by GPs assessing these patients. In this chapter I therefore present a systematic review and meta-analysis of studies of ASB prevalence and risk factors for ASB in different settings, including care homes. I describe the study design including inclusion criteria and search strategy, outline the results, and discuss how the findings may impact

the current community UTI diagnostic guidelines. Finally, I identify evidence gaps where future research is needed.

4.2 Background and rationale

The urine dipstick is the only POCT routinely available in the National Health Service (NHS) for use in UTI diagnosis, but current UK guidelines for primary care advise against its use in older adults aged over 65.[40, 41] This is because the prevalence of ASB rises with age, and detecting ASB rather than a UTI can give a false positive dipstick result. This is particularly important in patients for whom the diagnosis is less certain, like those with dementia unable to describe their symptoms and/or those presenting with non-specific symptoms like an acute functional decline. False positive dipstick results can lead to inappropriate antibiotic prescriptions, and this is a driver for AMR.

Prevalence of ASB has been shown to be particularly high in the care home population in individual studies but no attempt has been made to bring together the evidence and appraise it collectively. The UKHSA primary care diagnostic decision tool for UTI (Figure 1.2) states that about half of older adults living in care homes by age 80 have ASB,[41] and the SIGN UTI guideline gives a range of 23-70% for female care home residents.[40] However, these and other international guidelines are based on a limited number of narrative reviews,[40, 44, 45] which include some primary studies that were published 40-70 years ago. In that time there have been significant changes in population health that may have impacted the prevalence of ASB; life expectancy has increased by approximately a decade [105] and many people now live much longer with chronic diseases. It may not remain appropriate for age 65 to remain as a threshold for urine dipstick testing, and there could be other risk factors for ASB to consider when deciding to test, like co-morbidities or frailty.

As described in Chapters 2 and 3, many care home staff continue to perform urine dipsticks despite advice not to, and GPs may receive an unsolicited urine dipstick result when assessing residents with non-specific symptoms. An up-to-date and improved estimate of the prevalence of ASB in care homes and other adult communities, as well as knowledge of

other risk factors, could support a more nuanced interpretation of dipsticks results, as well as further development of UTI diagnostic guidelines.

4.3 Aim and objectives

4.3.1 Aim

To describe the UK community epidemiology of ASB, in order to support development of UTI diagnostic guidance for older adults, including those living in care homes.

4.3.2 Objectives

To systemically search for and synthesise the available evidence relating to the following questions:

- What is the prevalence of ASB in adults in different age/population groups in a context relevant to UK primary care?
- What are the risk factors for ASB in a context relevant to UK primary care?

4.4 Methods

4.4.1 Design and search strategy

The review protocol was based on the principles outlined in the Cochrane handbook on Systematic Reviews of Interventions.[106]. There is no guidance from the Cochrane Collaboration for systematic reviews of prevalence. The protocol was registered in the PROSPERO database in January 2023 (reference CRD42023394152).

The development of the search strategy and the search itself was supported by an information specialist (NR). The search strategy used Medical Subject Headings (MeSH) and free text words adapted for each database including terms for bacteriuria and asymptomatic disease. Searches were carried out in Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCOHost, 1982-present)], Embase (OvidSP, 1974-2016 June 02),

Medline and Medline In-Process (OvidSP, 1946-present) and Science Citation Index (SCI) Expanded/CPCI-S(Web of Science Core Collection, 1945-present) from 1990 to May 2025. The initial search was carried out in February 2023 and last updated in May 2025. The full search strategy is available in Appendix B.1.

4.4.2 Inclusion and exclusion criteria

Inclusion criteria were:

- Adult study participants (aged ≥18 years) that were not suspected to have a UTI. Studies were included if they recruited above and below age 18 provided either the number of participants below 18 was very small and/or there was enough information to exclude this group. Studies were included if they recruited participants with and without suspected UTI, provided there was enough information to exclude those with symptoms.

- Cross-sectional studies, prospective cohort studies, case-control studies and trials recruiting from a primary care relevant population.

- Studies that measured the prevalence of ASB with or without risk factors for ASB. We allowed any definition of ASB.

- Studies from Organization for Economic Co-operation and Development (OECD) member countries to enhance applicability to the UK, a high income country.

- No language restrictions. This was a change from the registered protocol to reduce bias.

Exclusion criteria were:

- Studies from inpatient hospital settings (including the emergency department). People in these settings are unwell (with or without suspected UTI) and may have a different prior probability for ASB.

- Studies exclusively including people who are pregnant, as ASB is a risk factor for miscarriage and is considered differently in pregnancy. The study was considered if pregnant people were a subgroup that could be excluded from the review.

- Studies exclusively including people who have known risk factors for ASB (use of urinary catheters, pre-/post- urological or gynaecological surgery, neurogenic lower urinary tract dysfunction, post renal transplant, structural urological abnormalities). The study was considered if these people were in a subgroup that could be excluded from the review.

- Studies published before 1990, so that the included population would be more similar to present day.

- Animal studies

- Laboratory studies

4.4.3 Screening and assessment of studies

The Covidence platform was used for the management of screening and assessment of studies.[107] Two authors (AM, AS, PCW, MK, CC, or UU) independently screened the titles and abstracts of all references in our search and checked the full texts of those potentially relevant for eligibility. Disagreements were resolved by discussion with a third author. We hand searched reference lists in relevant systematic reviews for additional studies.

4.4.4 Data extraction

Data were extracted using a standardised and piloted data extraction form, and a second author independently checked this for accuracy (AM, AS, UU). We extracted study characteristics (including design, recruitment setting, dates of data collection, inclusion/exclusion criteria), participant characteristics (including sex and age), urine sampling technique, ASB definition and measurement, and results (including total population, number with ASB, and totals with ASB in any subgroups). If studies included subgroups that did not meet our

inclusion criteria (eg. symptomatic individuals, participants recruited from inpatient settings) these were removed at the time of data extraction. For each study we recorded any risk factors that were found to be statistically significantly associated with ASB.

4.4.5 Quality assessment

The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for studies reporting prevalence data was used to assess the quality of each included study.[108] Two authors (AM and either PCW, MK, or UU) independently assessed the study in nine domains. For each domain a question is posed (Eg. Domain 1: Was the sample frame appropriate to address the target population?) to which an answer of Yes/No/Unclear/Not applicable can be given. For Domain 8: Was there appropriate statistical analysis? we decided to score all studies as 'Not applicable', because even if confidence intervals (CIs) were not reported for the prevalence, we were able to calculate these from the data. We resolved any disagreements by discussion with a third author. A table detailing how decisions were made for each domain is included in Appendix B.2.

4.4.6 Statistical analysis

Stata software was used to generate forest plots showing prevalence and 95% CIs for each study. The pooled prevalence from cross-sectional, cohort studies, and trials was calculated using a random effects meta-analysis. Case-control studies were excluded from the meta-analysis because they cannot be used to estimate the true prevalence. If multiple thresholds for bacteriuria had been recorded, we included prevalence using the threshold of 10^5 CFU/ml as defined by NICE, IDSA and EUA.[42, 55, 109] Otherwise, we included prevalence at the threshold used by the study. Subgroup analysis was carried out by the setting from which participants were recruited (primary care/community, outpatient clinic, pre-operative clinic, care homes or mixed settings).

To assess the robustness of the pooled prevalence estimate, we conducted the following post-hoc sensitivity analyses:

- Study quality; all studies in which at least one domain was answered as 'No' on the JBI Checklist were excluded

- Colony-forming unit (CFU) threshold for bacteriuria; studies using any threshold other than 10^5 CFU/ml were excluded

- Number of samples needed for ASB diagnosis; studies in which ASB was confirmed on just one sample (as opposed to two consecutive samples) were excluded

If sufficient information was provided in the paper, the proportion of females in each study was calculated on a scale of 0 (all male) to 1 (all female), and a mean or median age of included participants was calculated. Meta-regression using a random-effects model was then carried out to determine effect of age and sex on ASB prevalence. Bubble plots were used to display the results of meta-regression analyses graphically.

Calculating the overall proportion of female participants in each study may mask the effect of sex on ASB prevalence. To further explore this, a meta-analysis was carried out comparing the paired difference in risk of ASB between male and female participants in those studies that included both sexes and where prevalence by sex was reported separately.

AM carried out the statistical analysis with support from TF.

4.5 Results

Figure 4.1 shows the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram of study selection. We screened 4519 studies based on title and abstract, excluding 3804 and leaving 715 for a full text review. 650 full text articles were excluded after eligibility assessment, with the most common reasons related to clinical setting, study design or not having collected the data to be able to calculate prevalence of ASB. We contacted the authors of three studies to request additional unpublished data. Data were made available for one study, and we were able to include this in the analysis. Overall, 64 studies were included in the descriptive analysis, including 35,888 participants in total.

References for these studies can be found in Appendix B.3.

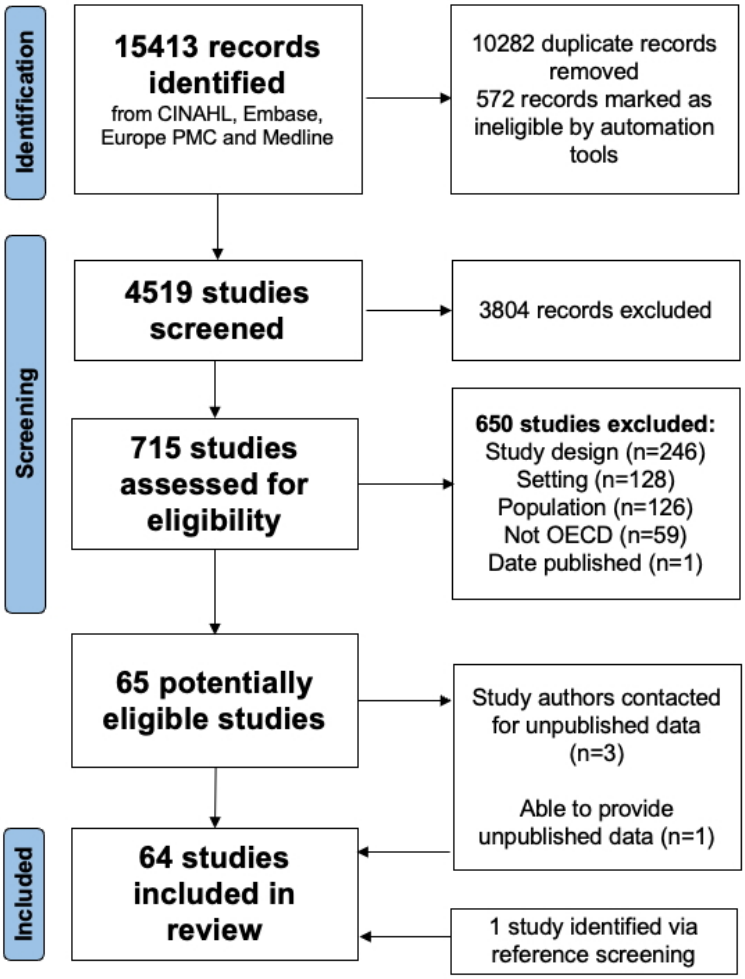


Figure 4.1: PRISMA flow diagram

4.5.1 Characteristics of included studies

Table 4.1 summarises some of the important characteristics of the included studies. For a complete list of studies and their characteristics please refer to the table in Appendix B.4. Studies ranged in size from 30 to 8508 participants. 39 studies specifically aimed to explore ASB prevalence and/or risk factors, with the remainder reporting a prevalence of ASB as part of a wider study. There were 13 case control studies. Most of these studies aimed to compare the prevalence of ASB in a group with a particular condition (eg. diabetes, autoimmune rheumatoid diseases) with healthy controls. 13 of the included studies recruited from care homes.

27 studies included females only, with one study including males only. Of the 36 studies including a mix of sexes, only 18 reported prevalence in females and males separately. 36 studies included people with an age range that crossed age 65, but only two reported prevalence separately by age category.[110, 111]. Two other studies that only included people aged over 65 years also reported prevalence in different age categories.[46, 112] The age range of included participants was not reported in 15 studies.

4.5.2 Quality assessment of included studies

Included studies varied in quality. No study had a low risk of bias in all relevant domains. 25 studies had at least one domain with a high risk of bias. The most common areas for studies to be at higher risk of bias were in sampling approaches (Domain 2) and in the description of the study subjects and setting (Domain 4). Results are summarised in Figure 4.2.

4.5.3 ASB definition

The definition and measurement of ASB varied considerably between the different studies. Only 9 studies outlined the specific symptoms that had to be absent for participants to be considered asymptomatic. 25 studies required bacteriuria to be detected on two consecutive samples, while the others required just one sample. Most studies used urine culture to quantify bacteriuria. 51 studies included a cut-off of greater than 10^5 CFU/ml for bacteriuria to be considered significant. Two studies carried out urine cultures for participants only if a urine dipstick was positive. One study used flow cytometry to measure bacteriuria. One study used multiplex polymerase chain reaction (mPCR) as well as culture, finding a much higher ASB prevalence using mPCR when compared to culture in the same participants (0.29 compared to 0.02).[113]

4.5.4 Prevalence and risk factors for ASB

Prevalence of ASB in the total participants included in each study ranged from 0.01 to 0.48. 31 studies assessed risk factors for ASB, although which factors were assessed varied considerably between studies. 7 studies found a statistically significant association between increasing age and ASB, but 16 studies did not. The most common risk factors with a

statistically significant association with ASB were female sex (10 studies), incontinence (5 studies), diabetes (5 studies) and duration of diabetes (5 studies).

4.5.5 Meta-analysis

51 studies were included in the random-effects meta-analysis. Overall pooled prevalence of ASB was 0.17 (95% CI: 0.14 to 0.20) (Figure 4.3). There was high heterogeneity between studies (I^2 = 99.12%).

In a sensitivity analysis exploring the effect of removing studies in which at least one domain was answered as 'No' on the JBI Checklist the estimate remained similar in the remaining 20 studies at 0.17 (95% CI 0.11 – 0.22). I^2 remained high at 99.06%. The remaining sensitivity analyses (excluding studies using any threshold other than 10^5 CFU/ml as the threshold for bacteriuria, and excluding studies in which ASB was confirmed on just one sample) also had similar pooled prevalences and are presented in Table 4.2.

4.5.5.1 Recruitment setting

Studies were categorised according to the setting from which they recruited. Subgroup analysis by setting is shown in Figure 4.4. Care homes had a significantly higher pooled prevalence of 0.31 (95% CI: 0.25 to 0.36) compared to primary care/community settings (prevalence 0.07, 95% CI: 0.04 to 0.10) and outpatient settings (prevalence 0.14, 95% CI 0.09 to 0.19).

4.5.5.2 Sex

Information on proportion of each sex included was available for 45 studies. Meta-regression showed that there was no relationship between the proportion of females in each study and ASB prevalence (co-efficient 0.020, 95% CI: -0.14 to 0.18, p =0.80).

However, 17 studies separately reported the prevalence for men and females. Amongst these studies, the risk of ASB was consistently higher in females than in men, with an overall pooled risk difference of 0.11 (95% CI 0.09 to 0.13). (Figure 4.5).

4.5.5.3 Age

A mean or median age was available or could be calculated for 36 studies. Increasing age was associated with an increase in the prevalence of ASB in a random-effects meta-regression (co-efficient 0.005, 95% CI: 0.003 to 0.007, p<0.001). This relationship is shown in the bubble plot in Figure 4.6, Plot A. The co-efficient for age when accounting for the proportion of females in each study was 0.006 (95% CI: 0.003 to 0.007, p <0.05), similar to age alone.

12 of the 36 studies included in this meta-regression were care home studies, making up 12 of the top 15 studies with the oldest mean/median age. Excluding them from the meta-regression reduced the co-efficient to 0.002 (95% CI: 0.0003 - 0.005, p=0.02). (Figure 4.6, Plot B) We therefore carried out a further meta-regression post-hoc with both age and care home setting as predictors. The co-efficient for age when controlling for care home setting was 0.003 (0.0006 - 0.005, p=0.015), and co-efficient for care home setting when controlling for age was 0.115 (0.04-0.20, p=0.005).

4.6 Discussion

4.6.1 Summary of findings

This systematic review identified 64 studies published since 1990 estimating ASB prevalence in populations that may be applicable to UK primary care, including 35,888 participants in total. Prevalence in individual studies ranged from 0.01 to 0.48. In the meta-analysis, pooled prevalence from 51 studies was 0.17 (95% CI: 0.14 to 0.20) with high heterogeneity (I^2 = 99.12%). Sub-group analysis showed that ASB prevalence was highest in care homes 0.31 (95% CI: 0.25 to 0.36), including in comparison to primary care/community settings (prevalence 0.07, 95% CI: 0.04 to 0.10), despite the fact that many of the individual studies from primary care/community settings also included older people (mean ages, where reported, were 52-84.7). Amongst the 17 studies that reported ASB prevalence separately by sex, the risk of ASB was consistently higher in females than in males, with an overall pooled risk difference of 0.11 (95% CI 0.09 to 0.13). Meta-regression demonstrated a significant association between increasing age and increasing prevalence of ASB. However, most studies with

the oldest mean/median age of participants recruited from care homes, and removing these from the meta-regression reduced the slope of the predicted linear association. A post-hoc meta-regression including age and care home setting as predictors showed that both had a significant effect on ASB prevalence.

4.6.2 Strengths and limitations

To our knowledge this is the first systematic review on this topic, generating for the first time pooled estimates of ASB prevalence in different settings including care homes. However, confidence in the findings is limited by the significant heterogeneity between studies, in particular the lack of a consistent definition for 'asymptomatic' and different thresholds for bacteriuria. Major differences between studies (including setting, age and sex) mean that an overall pooled prevalence figure does not add clinical value.

The subgroup analysis by setting showed important differences between care homes and other settings. Although we have been able to show the association between increased age and the increased prevalence of ASB, our analysis is limited in being able to fully establish the effect of other risk factors for ASB including sex and age categories due to the lack of reporting by subgroup in many included studies. Excluding papers from non-OECD countries means that the results may not be applicable to low- or middle-income countries, but does improve their applicability to the UK context.

4.6.3 Comparison with existing evidence

Our pooled prevalence estimates for ASB in care homes and community settings are lower and more precise than the prevalence ranges given in the UK, US and European guidelines for UTI.[40, 42, 55] This is likely due to the limitations of the literature reviews informing these guidelines including over-reliance on secondary sources without direct appraisal of the primary studies, and the age of some of the studies they cited. There has been no previous meta-analysis.

For example, in our review the pooled prevalence of ASB in care home settings is 0.31 (95%

CI: 0.25 to 0.36) from 13 studies. In comparison, the SIGN guideline gives a range of 23-70%.[40] This guideline cites seven papers that assess ASB prevalence for post-menopausal women in care homes. Of these, two are narrative reviews (one from 1980),[45, 114] and two are primary studies from the 1980s.[115, 116] Three citations are related to two primary studies included in our review.[51, 117] It is possible that our pooled prevalence for care homes is affected by including studies with both males and females; in the 4 studies from care homes where prevalence was reported separately by sex, three showed a higher prevalence in females. However, at least 2908 of the 3703 participants (78.5%) from the 13 included care home studies were female.

4.6.4 Implications for research and/or practice

Our analysis suggests that living in a care home is an independent predictor of increased prevalence of ASB, and is not just a function of advanced age. However, it remains unclear whether there are unmeasured confounding factors contributing to this 'care home' risk. For example, incontinence, experienced by up to 50% of care home residents,[60] was shown to be a risk factor for ASB in 5 individual studies included in our review. Care home residents are also more likely to be living with frailty,[13] which, if a risk factor, may also explain or contribute to the 'care home' risk. However, frailty was not assessed as a risk factor by any included study.

It is unclear how much of the assumed age related increase in ASB prevalence in the community has historically been affected by data from care homes. Removing the care home studies from our meta-regression for age reduced the slope of the predicted linear association between age and ASB. In community settings, therefore, age may be a less important risk factor than previously thought. Although risk of ASB between sexes was not compared in the majority of included studies, female sex was a significant risk factor for ASB in those that did. Taken together, this indicates that, in community settings, it is possible that urine dipsticks may have more clinical value than previously assumed for some adults over 65 years, particularly men.

In the care home setting, it is helpful to know that just under one third of residents are likely to have ASB. This is still significant enough to avoid dipstick use due to the risk of false positives and therefore there remains a need for improved diagnostic approaches to UTI in this setting. A POCT that could differentiate between ASB and UTI and remove the risk of false positives would be revolutionary to the clinical assessment of care home residents with suspected UTI. An evaluation of novel UTI POCTs in a care home setting is presented in Chapter 6.

Overall, there is a lack of recent, rigorous and relevant evidence on ASB prevalence to UK primary care. Currently we do not know enough about risk factors/combinations of risk factors to be able to understand the risk of individual patients. This will be critical in helping guide the use of dipsticks and/or other UTI POCTs, in the future. There is an urgent need for a definitive prevalence study in the UK (or similar setting) to inform guidelines and resources on UTI diagnosis in both care home and community-based older adults.

4.6.5 Conclusion

This systematic review confirms that prevalence of ASB increases with age and is most prevalent in care homes. However, it demonstrates that ASB prevalence may be lower than previously thought – both in community and care home settings. The 'over 65' cut-off for dipstick use may be restricting opportunities for a widely available and low cost test to aid UTI diagnosis in some people for whom the risk of ASB may be negligible, for example, community dwelling older men without co-morbidities. Further research is needed in both community and care home settings to confirm these findings, to highlight groups that may benefit from access to the dipstick test, and to guide recommendations for policy.

4.7 Summary of chapter

In this chapter I have estimated prevalence of ASB in care homes, but have highlighted the lack of good quality evidence of risk factors for ASB in this and community settings. Only

one included study was of a UK care home population, and this was published in 2001. In the next chapter I present the results of a small observational cohort study of residents living in care homes in England, including the prevalence of ASB in this cohort at baseline.

Study design		Prospective cohort	17
		Cross-sectional	25
		Case-control	13
		Trial	9
Setting		Care homes	13
		Community/primary care	14
		Outpatient clinic	26
		Pre-operative	5
		Mixed	5
		Not stated	1
Aim		ASB prevalence/risk factors	38
		Other	26
Included ages		All <65 years	3
		All >65 years	10
		Range crosses 65 years	36
		Missing	15
Included sexes		All female	28
		All male	1
		Mixed	35
Included only participants with specific conditions		Diabetes	14
		Rheumatoid conditions	3
		Liver disease	2
		HIV	1
ASB definition	**Samples**	1	39
		2	25
	CFU threshold	10^2 CFU/ml	1
		10^3 CFU/ml	1
		10^4 CFU/ml	4
		10^5 CFU/ml	52
		10^8 CFU/ml	1
		Any growth	1
		Not defined	3
		NA - flow cytometry	1

Table 4.1: Summary of characteristics of included studies (n=64)

Study	JBI Appraisal tool for Prevalence Studies									At least one domain 'No'
	1. Sample frame	2. Sampling	3. Sample size	4. Subjects/ setting	5. Coverage	6. Identifying condition	7. Condition measured	8. Appropriate analysis	9. Response rate	
Abrutyn 1991	Yes	No	Unclear	No	Unclear	Yes	Yes	NA	NA	Y
Aguirre-Avalose 1999	Yes	Unclear	Unclear	No	NA	Yes	Yes	NA	Yes	Y
Akkus, 2024	Yes	Unclear	NA	Yes	NA	Yes	Yes	NA	NA	N
Aviles, 2009	Yes	Unclear	Unclear	No	Unclear	Yes	Yes	NA	Unclear	Y
Balasoiu 1997	Yes	Unclear	NA	Yes	Unclear	Unclear	Yes	NA	NA	N
Beerepoot, 2012	Yes	Unclear	NA	Yes	Unclear	Unclear	Yes	NA	Unclear	N
Bengtsson, 1998	Yes	Unclear	Unclear	No	Unclear	Yes	Yes	NA	Unclear	Y
Biggel, 2019	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	NA	Yes	N
Bilsen 2023	Yes	No	NA	Yes	Unclear	Yes	Yes	NA	Unclear	Y
Bonadio, 2004	Yes	No	NA	No	Unclear	Unclear	Yes	NA	Unclear	Y
Bouvet, 2014	Yes	Yes	NA	No	Unclear	Unclear	Yes	NA	Unclear	Y
Boyko, 2005	Yes	No	NA	Yes	Unclear	Unclear	Yes	NA	Unclear	Y
Brostrom, 2002	Yes	No	NA	No	Unclear	Unclear	Yes	NA	Unclear	Y
Butler, 1995	Unclear	Yes	NA	No	NA	Unclear	Yes	NA	Unclear	Y
Coorevits, 2017	Yes	No	NA	No	NA	Yes	Yes	NA	Unclear	Y
Cordero-Ampuero, 2013	Yes	Unclear	NA	No	Unclear	Unclear	Yes	NA	Unclear	Y
del Rio, 1992	Yes	Yes	Unclear	No	NA	Unclear	Yes	NA	NA	Y
Efe, 2010	Unclear	No	Unclear	No	Unclear	Yes	Yes	NA	Unclear	Y
Frazee, 2015	Yes	No	NA	No	Unclear	Yes	Yes	NA	Unclear	Y
Gazzani, 2001	Yes	Yes	Unclear	No	Yes	Unclear	Yes	NA	Yes	Y
Georgiadou, 2015	Yes	No	NA	Yes	Unclear	Unclear	Yes	NA	Unclear	Y
Giamarellou, 1998	Yes	Unclear	NA	No	Unclear	Yes	Yes	NA	Unclear	Y
Gugino, 1998	Yes	No	Unclear	No	Unclear	Unclear	Unclear	NA	Unclear	Y
Harding, 2002	Yes	No	NA	No	Unclear	Unclear	No	NA	Unclear	Y
Hawn, 2009	Yes	No	NA	Yes	Unclear	Yes	Yes	NA	Unclear	Y
Hedin, 2002	Yes	No	Unclear	No	Unclear	Yes	Yes	NA	Unclear	Y
Hunold, 2025	Yes	Yes	NA	No	Unclear	Unclear	Yes	NA	NA	Y
Ishay, 2006	Yes	No	Unclear	Yes	Unclear	Yes	Yes	NA	Unclear	Y
Jackson, 2004	Yes	Yes	NA	Yes	Yes	Unclear	Yes	NA	Yes	N
Karunajeewa, 2005	Yes	Yes	Unclear	Yes	Unclear	Unclear	Yes	NA	Unclear	N
Kjölvmark, 2016	Yes	Yes	NA	Yes	Unclear	Unclear	Yes	NA	Unclear	N
Ko, 2024	Yes	Yes	Unclear	Yes	Unclear	Unclear	Yes	NA	Unclear	N
Kocoglu, 2007	Yes	Unclear	Unclear	No	Unclear	Yes	Yes	NA	Unclear	Y
Koseda-Dragan, 1998	Yes	Unclear	Unclear	No	Unclear	Unclear	Yes	NA	Unclear	Y
Kunin, 1993	Yes	Yes	NA	Unclear	Unclear	Yes	Yes	NA	Yes	N
Leihof, 2021	Yes	Unclear	NA	No	Unclear	Yes	No	NA	Unclear	Y
Martín Álvarez, 2000	Yes	No	NA	No	Unclear	Unclear	Yes	NA	Unclear	Y
Martínez-Vélez, 2016	Yes	Unclear	Unclear	No	NA	Unclear	No	NA	Unclear	Y
Matteucci, 2007	Yes	No	Unclear	Yes	Unclear	Unclear	Yes	NA	Unclear	Y
Matthiopoulou, 2023	Yes	No	Unclear	Yes	Unclear	Yes	Yes	NA	Unclear	Y
Meiland, 2006	Yes	Yes	NA	Yes	Unclear	Yes	Yes	NA	Unclear	N
Mendoza, 2002	Yes	No	Unclear	Unclear	Unclear	Yes	Yes	NA	Unclear	Y
Mims, 1990	Yes	Unclear	Unclear	No	Unclear	Yes	Yes	NA	Unclear	Y
Nastos, 2011	Yes	Unclear	Unclear	No	Unclear	Yes	Yes	NA	Unclear	Y
Nicolle, 2012	Unclear	Unclear	NA	Unclear	Unclear	Unclear	Yes	NA	Unclear	N
Ouslander, 1996	Yes	Unclear	Unclear	No	NA	Yes	Yes	NA	Yes	Y
Papazafiropoulou, 2010	Yes	No	Unclear	Yes	Unclear	Yes	Yes	NA	Unclear	Y
Raz, 2001	Yes	Unclear	Unclear	Yes	Unclear	Unclear	Yes	NA	NA	N
Ribera, 2006	Yes	Unclear	NA	Yes	Unclear	Unclear	Yes	NA	Unclear	N
Rodhe 2006	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	NA	NA	N
Rodríguez-Pardo, 2021	Unclear	Yes	NA	Yes	Unclear	Unclear	Yes	NA	NA	N
Samuels, 2024	Yes	Unclear	Unclear	No	Unclear	Unclear	Yes	NA	Unclear	Y
Savvala, 1998	Yes	Unclear	Unclear	No	Unclear	Unclear	Yes	NA	Unclear	Y
Semetkowska-Jurkiewicz, 1996	Yes	Unclear	NA	No	Unclear	Yes	Yes	NA	Unclear	Y
Şener, 2013	Yes	Yes	Unclear	No	Unclear	Yes	Unclear	NA	Unclear	Y
Senior, 1999	Yes	No	NA	No	Unclear	Yes	Yes	NA	Unclear	Y
Sotiropoulos, 2005	Yes	No	Unclear	Unclear	Unclear	Unclear	Yes	NA	Unclear	Y
Sousa, 2014	Yes	Unclear	NA	Unclear	Unclear	Unclear	Yes	NA	Unclear	N
Sundvall, 2014	Yes	Yes	NA	No	Unclear	Yes	Yes	NA	Yes	Y
Turan, 2008	Yes	Unclear	Unclear	Yes	Unclear	Yes	Yes	NA	Unclear	N
Varli, 2009	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	NA	Unclear	N
Ye, 2014	Unclear	Yes	Unclear	Yes	Unclear	Unclear	Yes	NA	Unclear	N
Yoo, 2009	Yes	No	Unclear	No	Unclear	Unclear	No	NA	Unclear	Y
Zhanel, 1995	Yes	Unclear	Unclear	Yes	Unclear	Yes	Yes	NA	Unclear	N

Figure 4.2: Assessment of each included study against the JBI Critical Appraisal Checklist for studies reporting prevalence data.

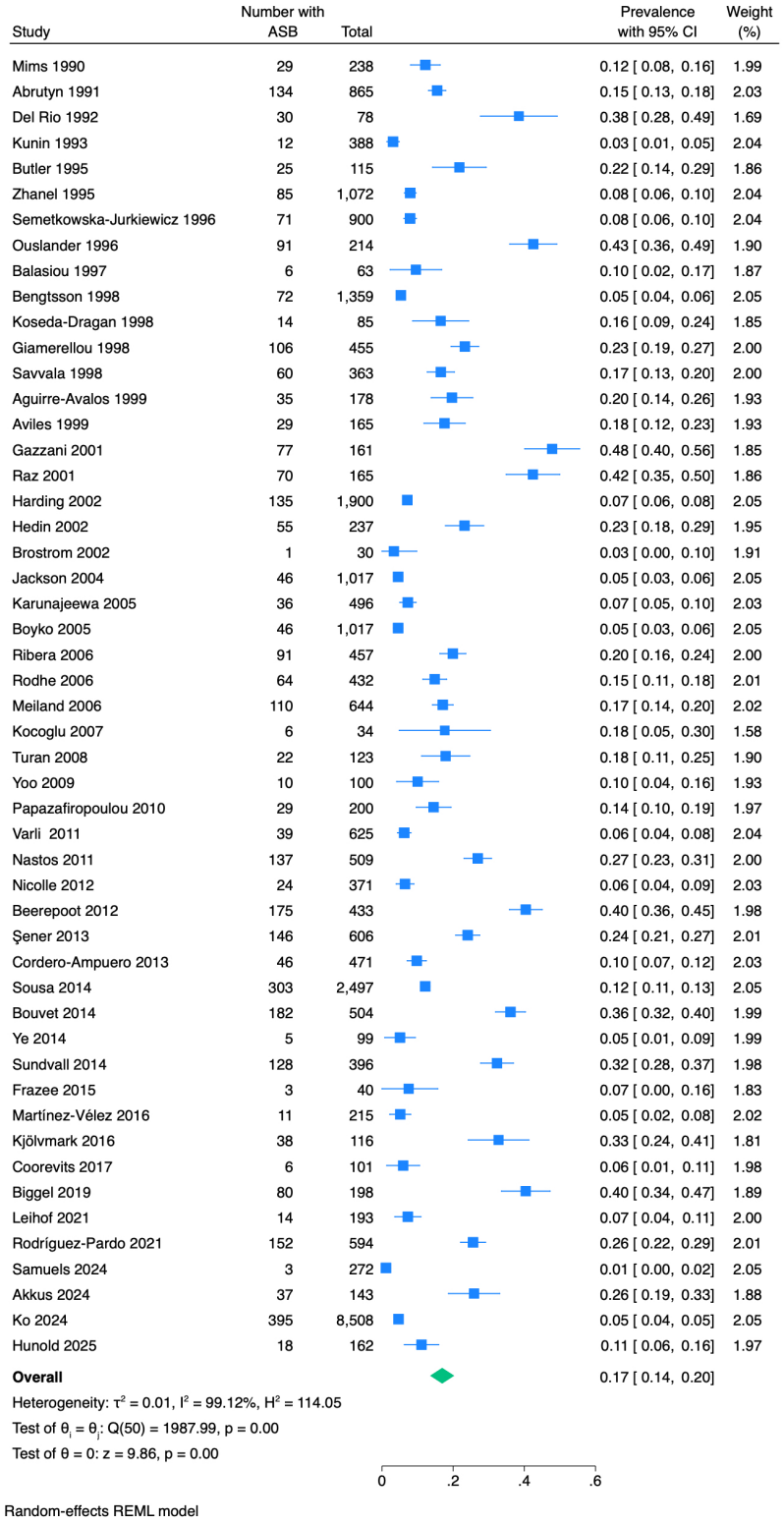


Figure 4.3: Forest plot of prevalence estimates of ASB across 51 included studies, ordered by date published. Squares represent individual study weights; horizontal lines show 95% CIs; the diamond shows the pooled estimate.

Scenario	Number of included studies	Pooled prevalence (%)	95% CI	I^2 (%)
Primary analysis	51	17	14 - 20	99.12
Studies in which at least one domain was answered as 'No' on the JBI Checklist were excluded	20	17	11 - 22	99.06
Studies using any threshold other than 10^5 CFU/ml as the threshold for bacteriuria were excluded	41	16	13 - 20	98.56
Studies in which ASB was confirmed on just one sample (as opposed to two consecutive samples) were excluded	19	19	14 – 23	97.27

Table 4.2: Results of sensitivity analyses.

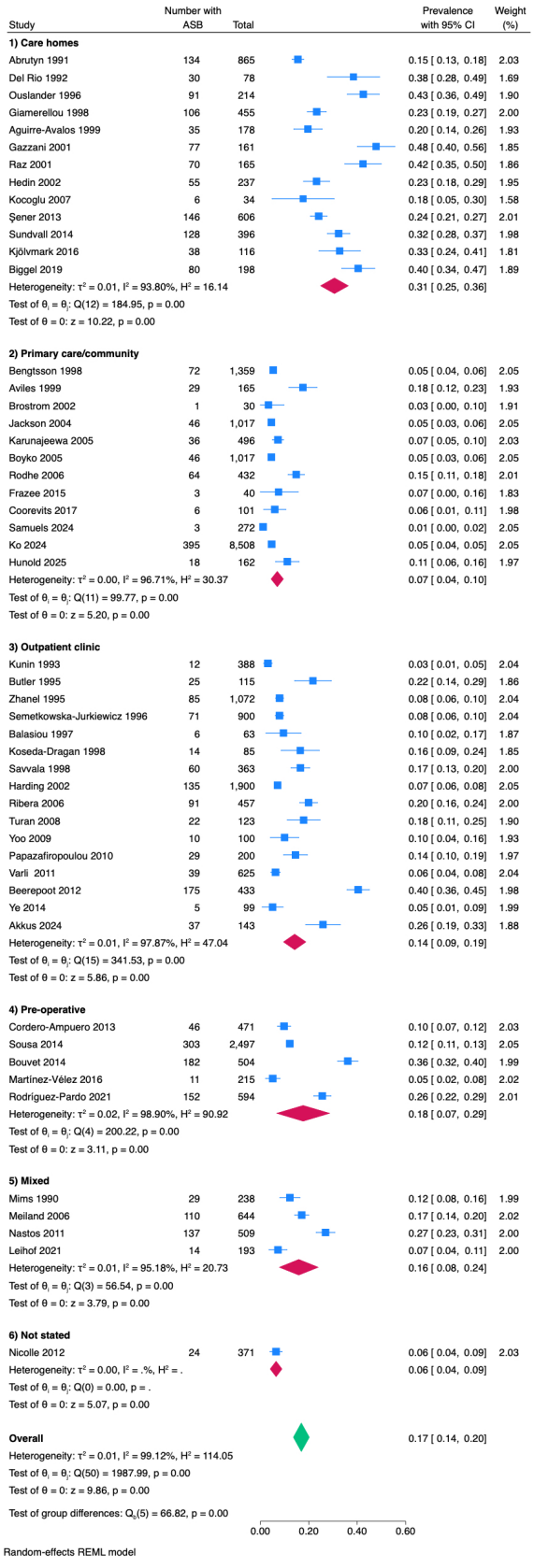


Figure 4.4: Forest plot of ASB prevalence, grouped by study setting. Random-effects models were used to estimate pooled prevalence within each subgroup.

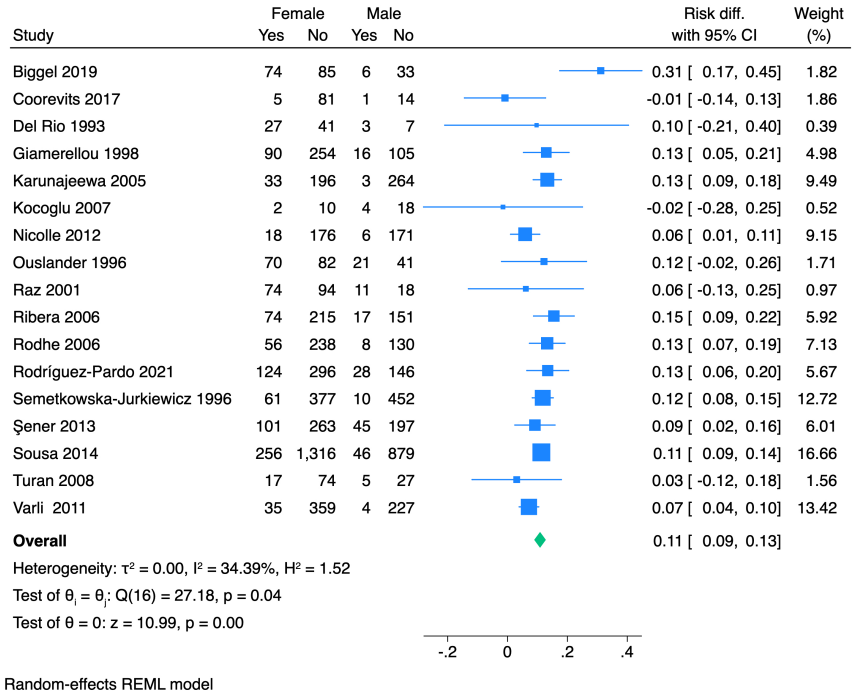


Figure 4.5: Forest plot showing the risk difference of ASB between female and male participants in the 17 studies that reported prevalence by sex. A positive value indicates increased risk towards females.

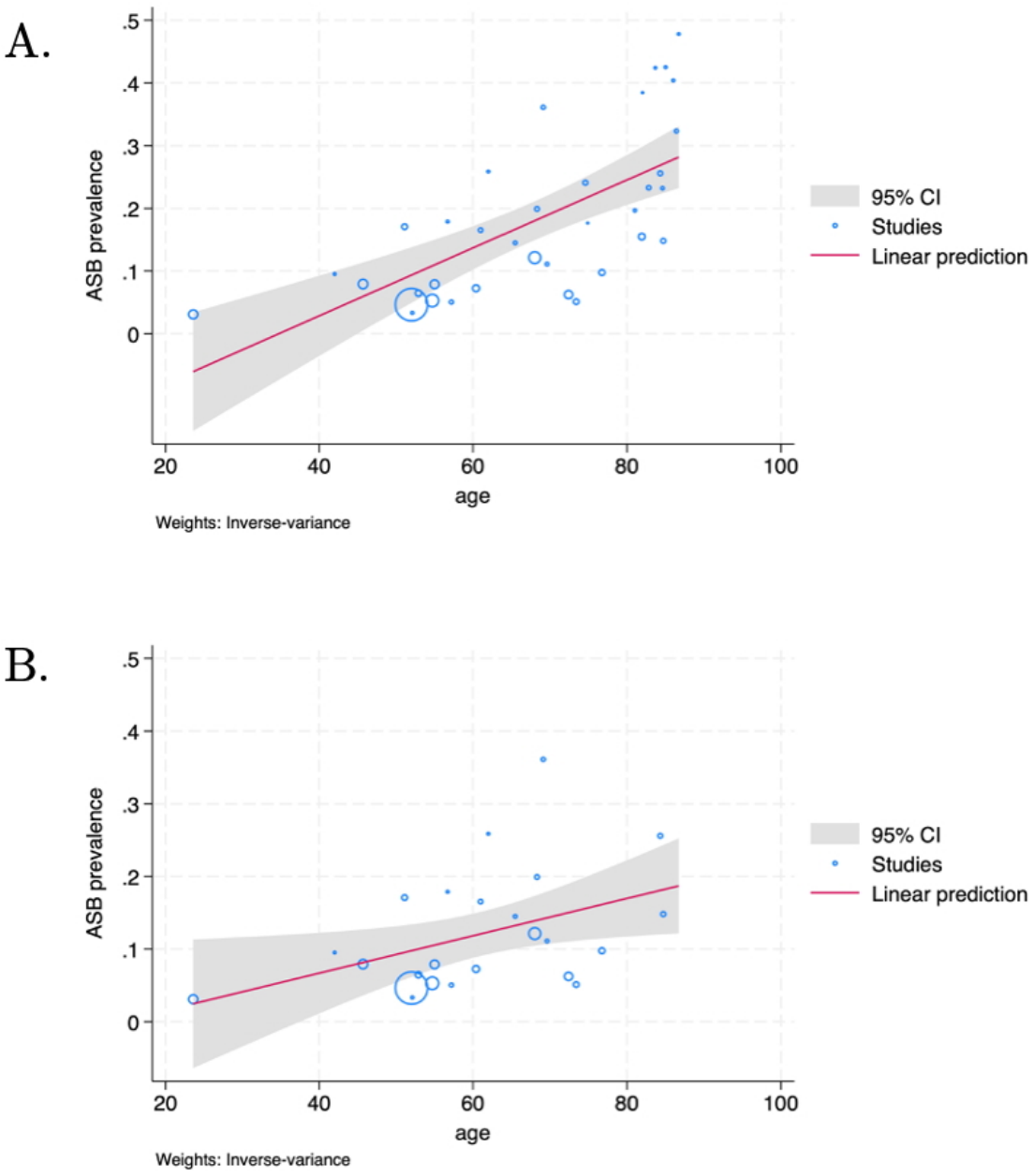


Figure 4.6: Bubbleplots showing the predicted linear relationship between age and ASB prevalence. In Plot A, all 36 studies with a mean/median age were included. In Plot B, 12 studies from care homes were excluded, leaving 24 studies.

Chapter 5

How feasible and acceptable is a prospective cohort study of UK care home residents with capture of information about possible UTI episodes?

5.1 Overview of chapter

Over the following three chapters I present the methods and results of the DIagnoSing Care hOme UTI Study (DISCO UTI), a cohort study of care home residents in England. This primarily aimed to assess feasibility and acceptability of delivering a prospective cohort in a UK care home setting capturing episodes suspected to be UTI by care home staff — including those presenting with an acute functional decline — and the timely collection and testing of urine samples. In this chapter, I describe the methods of the cohort recruitment and follow up, and of the qualitative evaluation. I present the feasibility and acceptability quantitative and qualitative findings, and the descriptive statistics of the recruited cohort. I also reflect on the implications for future UK care home research on this topic. Chapters 6 and 7 describe the exploratory methods and results of this study.

5.2 Background and rationale

Diagnosis of UTI in older people living in care homes is challenging because signs and symptoms can be non-specific, patient history can be limited due to cognitive impairment, urine samples can be hard to obtain due to continence issues, and our existing diagnostic tests may give false positives due to the prevalence of ASB. It is likely that UTI is over-diagnosed and over-treated, particularly in those presenting with an acute functional decline, exposing care home residents unnecessarily to antibiotic side effects and driving AMR. However, improving accurate and early detection of true UTI as well as reliably ruling it out could prevent complications such as bloodstream infections and hospital admissions. New approaches are urgently needed to combat the diagnostic uncertainty experienced by clinicians and care home staff, and to help better target antibiotics. Possible approaches include the identification of symptom clusters and/or resident characteristics associated with the highest risk of severe illness or poor outcomes from acute functional decline/possible UTI (Chapter 6), developing a greater understanding of the relationship between ASB and subsequent UTI (Chapter 6) and, finally, the introduction of novel UTI POCTs (Chapter 7).

Exploring these approaches will ultimately involve a large prospective observational study of care home residents. Much of the longitudinal care home research on UTI to date has been conducted in the USA and European countries, often in a single long term care facility, where there is no challenge of heterogeneity between care homes (Section 1.3.1) and where there may be better clinical oversight.[46, 51, 53, 54, 112, 118] Before an adequately powered study can be conducted in the UK, evidence is needed on the feasibility and acceptability of research procedures in UK care homes, many of which are naive to research. (Section 1.3.4) Understanding feasibility and acceptability of recruitment, data collection, repeated urine sampling and follow-up of residents across a number of different care homes will be essential before funding is sought for the definitive study. Estimates are also needed to inform sample size calculations, recruitment rates, and potential POCTs for assessment of diagnostic accuracy. The purpose of DISCO UTI was to provide this data needed to inform a further adequately powered prospective observational study on UTI in UK care homes.

5.2.1 My role in this study

DISCO UTI was a collaboration between the University of Southampton (Sponsor), the University of Oxford, the University of Bristol and Public Health Wales. I was a Co-Chief Investigator along with my DPhil supervisor Professor Nick Francis. I led on the grant application, protocol development, development of study materials, ethics application, ordering and storing supplies and PPI recruitment and meetings. I also took on the trial management for the study, with supervisory support from senior trial managers at both the University of Southampton and University of Oxford. This included the design and maintenance of the electronic case report form (eCRF) hosted on the RedCAP platform. I was the principal investigator for the Thames Valley sites and I coordinated the research nurses at the University of Oxford and Solent NHS Trust who carried out the research activities at the care homes. I did some of the recruitment and follow up visits at the Thames Valley care homes and I collected all of the qualitative data. I have also carried out all of the data analysis for this thesis.

5.3 Aims and objectives

5.3.1 Aim

The overall aim of the study was to assess the feasibility and acceptability of delivering a prospective cohort study of UK care home residents that included the capture of data and samples related to episodes suspected to be UTI by care home staff.

5.3.2 Objectives

- Feasibility objectives
  - To describe the rate of recruitment of care homes and participants
  - To describe the baseline characteristics of a recruited cohort (including demographics, medical diagnoses, medications, frailty and functional ability)

  - To describe incidence and timing of possible UTI episodes over follow up
  - To describe completeness of data and urine sample collection
  - To determine feasibility of collecting urine samples from participants, including serial samples in asymptomatic participants and samples collected during possible UTI episodes
  - To identify barriers and facilitators to implementing the study from the perspective of care home and research staff
- Acceptability objectives
  - To describe the views of participants, consultees and care home staff on taking part in the study
  - To describe the views of participants, consultees and care home staff on providing/collecting urine samples for the study

Exploratory aims and objectives related to predictors of poor outcomes, asymptomatic bacteriuria and novel UTI POCTs can be found in Chapters 6 and 7.

5.4 Methods

5.4.1 Overview

DISCO UTI was a prospective observational study. A cohort of care home residents was recruited from care homes in England and followed up for up to a year. Eligible participants did not have acute symptoms attributable to possible UTI at the time of inclusion. Samples were collected from participants at baseline and repeated weekly for 4 weeks from a subset of participants who remained asymptomatic. Further data and urine samples were collected if participants developed possible UTI during follow up. Participants, consultees, care home staff and research staff were interviewed about study feasibility and acceptability.

5.4.2 Sample size

As a feasibility study, the sample size was based around the feasibility outcomes. Previous studies had suggested that between 25%[78] and 40%[119] of residents would develop a possible UTI during a 12 month follow-up period. With 100 participants this would equate to 25-40 participants with possible UTI, which would be a reasonable number to calculate data capture and follow-up rates for the possible UTI cohort.

5.4.3 Recruitment

The study was based in two NIHR RDNs: Thames Valley and Wessex. Strategies to recruit care homes were different in each region.

In Wessex Solent NHS Trust was set up as a single site. They already had established relationships with care homes and used their pool of contacts to sign homes up to the study. Some of these had participated in research previously, whilst others were research naive.

In the Thames Valley we circulated information about the study via the NIHR ENRICH network, contacted care homes via a charity with many homes in the area and contacted homes directly if details were publicly available.

Once a care home had agreed to take part in the study, we asked them to circulate posters and written information to all potentially eligible residents and/or their family members.

5.4.4 Screening and eligibility assessment

Members of the research team spoke to interested residents and/or family members as highlighted by the care home to discuss the study further and to screen for eligibility.

5.4.4.1 Inclusion criteria

- Willing and able to give informed consent for the study, or if lacking capacity, a consultee willing to complete a consultee declaration form.

- Permanently living in a care home (nursing, residential or mixed).

- Aged 65 or over.

5.4.4.2 Exclusion criteria

- Current suspected UTI. *We wanted all participants to be asymptomatic at baseline. Someone could be reassessed for eligibility once they had completed any treatment and they were asymptomatic again.*

- Temporary/respite resident. *More likely to move out of the home during the course of the study, and therefore would not be able to complete follow up.*

- Terminal illness limiting life expectancy such that inclusion would be inappropriate (as judged by care home staff).

- Medical condition or treatment likely to result in severe impairment of the immune system. *More prone to infections more generally and may not experience typical illness course.*

- Experiencing faecal incontinence to the extent that it would be impossible to obtain an uncontaminated urine sample (as determined by care home staff). *We wanted there to be reasonable chance of collected an uncontaminated urine sample during the course of the study.*

- Indwelling urinary catheter or regular use of intermittent catheterisation. *This would change risk of ASB, and catheter-associated UTI is considered a distinct condition.*

- Structural urological abnormalities. *Risk factor for ASB and complicated UTI.*

- Current renal tract malignancy. However, those with prostate cancer were eligible if they did not require catheterisation and were not considered terminally ill. *Changes to urinary tract may change pathophysiology of UTI.*

5.4.5 Consent/Consultee declaration

Mental capacity was assessed according to the Mental Capacity Act 2005, which provides a legal framework within which health and care professionals must act. Eligible care home residents who had capacity were informed about the study and provided with a Participant Information Sheet (PIS) supplemented by a simplified PIS and verbal explanations. Written informed consent or witnessed verbal informed consent was obtained once the resident had weighed up the information and decided they wanted to take part.

It was also important that this study included those who lacked capacity to consent for themselves given the high prevalence of cognitive impairment amongst those living in care homes (70%).[120] If an eligible care home resident lacked capacity to provide consent, a legal representative/guardian was consulted to act as their 'consultee'. They were provided with information about the study and given a Consultee Information Sheet (CIS). If they felt that that the person would have wanted to be included in the research then they were asked to sign a written Consultee Declaration Form, or the research team completed a witnessed verbal consultee declaration.

5.4.6 Baseline visit

Following consent baseline data was collected from the participant, care home staff and/or the care home record including:

- Demographics
  - Age
  - Sex
  - Ethnicity
- Medical diagnoses from the following list: dementia, Type 1 or Type 2 diabetes, chronic kidney disease, benign prostatic hyperplasia, overactive bladder, recurrent UTI, prostate cancer, other cancer.

- Current medications
  - Number of oral medications *(measure of polypharmacy)*
  - Whether their medications included any of the following drugs/classes that were either a potential risk factor for UTI, or a potential treatment for urinary symptoms: Sodium-Glucose Transport 2 (SGLT2) inhibitors, prophylactic antibiotics, methenamine hippurate, Disease-Modifying Anti-Rheumatic Drugs (DMARDs), topical oestrogen, finasteride or tamsulosin, anticholinergic medications to treat overactive bladder.
- Antibiotic courses prescribed within last 6 months and the indication for each course (if recorded)
- Clinical frailty score. *Taken from care home record if recorded, or calculated following discussion with the participant/consultee/care home staff.*
- Baseline functional ability (mobility, any support needed for activities of daily living, including using the toilet)
- Any chronic urinary symptoms
- Awareness of needing to pass urine

A copy of the baseline visit eCRF data capture form can be found in Appendix C.1.

A baseline urine sample was collected from all (see Section 5.4.8).

5.4.7 Follow up

Participants initially consented to a six month follow up. Recruitment was significantly slower and more challenging than anticipated (see Section 5.7.2). Given that we were not going to hit our planned target of 100 participants, we instead decided to follow up participants we had already recruited for longer in order to capture additional UTI episodes. The

follow up was therefore extended to up to 12 months via an amendment to the protocol. Participants who had been recruited prior to the protocol change still had the option of completing follow up at six months.

5.4.7.1 Repeat urine sampling from asymptomatic participants

We selected 25 participants to provide repeat weekly samples for the first 4 weeks of follow up, provided they remained asymptomatic. For this group we aimed to achieve diversity in sex, capacity, clinical frailty scale and baseline culture results.

5.4.7.2 Possible UTI episodes

Care home staff were asked to alert the research team if a participant in the cohort developed a 'possible UTI' whilst in follow up. 'Possible UTI' was defined as any situation when staff had decided to consult with a healthcare professional because they had detected a change in the resident or their urine and believed that a UTI was a likely cause. This was regardless of whether a subsequent clinician thought that UTI was a likely/the most likely diagnosis. However, it did not include participants who became unwell from an alternative source that was clearly not a UTI at onset (e.g. respiratory/skin infection or cerebrovascular event).

At the time of identifying a participant as having a possible UTI care home staff were asked to first follow their usual procedures for contacting healthcare for advice/support and in parallel notify the research team who arranged three additional study visits: symptom onset(as soon as possible), day 14 and day 28. At each visit, the following were recorded:

- Participant reported symptoms (if able)
- Care home staff reported symptoms/signs
- Objective findings recorded in the care home record including clinical observations
- Current functional status of participant (including details of change from baseline)
- Urine dipstick result (if done by the care home staff as part of usual care)

- Diagnosis/treatments/management provided by usual clinical team

Urine samples were collected at each visit. Care home staff were encouraged to collect a sample prior to any treatments being started, and to save this in a clinical fridge for the research team to process at their visit.

5.4.8 Withdrawal

Each participant/their consultee had the right to withdraw the participant from the study at any time. In addition, the research team could withdraw a participant from the study if necessary for reasons including:

- Ineligibility (either arising during the study or retrospectively having been overlooked at screening)
- Withdrawal of consent
- Participant requiring palliative care

5.4.9 Urine samples

5.4.9.1 Sample collection

Urine samples were collected with support from the care home staff and/or the research team. The method of sample collection was recorded. Although clean catch mid-stream urine samples were encouraged, we recognised that this was not possible for all participants.

Urine samples collected were divided, with priority given to a sample for usual clinical care. The order of priority for the research samples was 1) clinical sample (if requested), 2) research microbiology analysis (boric acid tube), and 3) research POCT(s) (see Chapter 6). Research samples were posted to the Specialist Antimicrobial Chemotherapy Unit (SACU), Public Health Wales using the Royal Mail Tracked 24 service.

5.4.9.2 Microbiology analysis

Analysis was carried out by staff at SACU. Methods are described in Chapter 6.

5.4.9.3 Statistical analysis

StataNow/BE 18.5 for Mac was used for statistical analysis. Recruitment, attrition, and data completeness were described using rates and proportions. The overall cohort and repeat sampling cohort were described using proportions.

5.4.10 Qualitative evaluation

Study participants, consultees, care home and research staff were interviewed to gain insights about the experience of taking part in, supporting and delivering the study. The aims of the evaluation were to understand the acceptability of the study and its procedures to participants and consultees, and to understand how feasible the study was to deliver in a care home setting.

5.4.10.1 Methods

Individual semi-structured interviews were carried out with participants, consultees and care home staff. The research staff were interviewed in a focus group, to gather multiple perspectives and allow exploration of points of consensus and disagreement. Two topic guides (one for residents/consultees/care home staff and one research staff) were developed from the existing literature on study evaluation and the experiences of the research team in overseeing the research. The interview topic guides were piloted with an initial small set of interviews and amended accordingly. Further adaptation occurred in light of ongoing analysis to fully explore emerging ideas and themes. (For topic guides, see Appendix C.2, C.3)

5.4.10.2 Recruitment

When residents with capacity consented to take part in the study, they gave optional consent to be contacted to also participate in an interview. Some consultees who had acted on

behalf of participants were also invited to interview. Managers of participating care homes circulated an invitation to participate in interviews to their staff. Research staff who had supported the study were asked to participate in an online focus group. Care home staff, research staff and consultees who were not already a study participant gave informed consent prior to their interview/focus group. Care home staff were reimbursed with a £20 voucher for their time, to enhance recruitment.

5.4.10.3 Data collection

Data were collected from participants, consultees and care home staff in semi-structured interviews, in person (participants) or remotely (consultees and care home staff). Data were collected from research staff in an online focus group, as an efficient way to gather multiple perspectives. The interviews/ focus group followed a flexible topic guide and were digitally audio recorded. Recordings were transcribed verbatim by an approved professional transcription service.

5.4.10.4 Data analysis

A pragmatic approach to thematic analysis was used involving the stages of familiarisation, generating initial codes, combining codes to create categories, reviewing the material in the categories for explanation and then exploring how the categories combine to support emerging narratives. An iterative approach was taken; re-coding earlier interviews in the light of ongoing analysis and early analysis bringing out topics to be added to the topic guide for the individual interviews. NVivo software was used to support data management and analysis.

5.5 Feasibility and acceptability quantitative results

5.5.1 Care home and participant recruitment

In the Thames Valley 83 care homes on the ENRICH mailing list were invited to hear more about the study. Four responded, and two of these took part. We asked a charity that runs many homes in the area to send out information. Three of their homes expressed interest,

Care home	Residential/nursing	Owned by	Location	Number of residents	Number of participants
1	Residential	Private	Rural	28	8
2	Residential	Private	Suburban	42	10
3	Nursing	Not for profit	Urban	80	15
4	Residential	Not for profit	Urban	23	8
5	Nursing	Not for profit	Suburban	66	15
6	Residential	Private	Suburban	35	7
7	Residential	Private	Suburban	34	8
8	Residential	Private	Urban	25	10

Table 5.1: Characteristics of participating care homes

and one took part.

In Wessex, 19 homes were approached. Six homes were unable to participate because they were already participating in another research project, three homes felt they did not have enough eligible residents, one did not have capacity due to staffing levels, four were not interested, and one did not respond. Five homes took part.

Overall, eight care homes took part in the study. The characteristics of the care homes recruited are listed in Table 5.1.

At least seven people were recruited from each home. In total, 81 care home residents were recruited to the cohort over nine months of recruitment. A graph of recruitment over time is shown in Figure 5.1.

5.5.2 Description of cohort at baseline

Of the 81 participants, 54.3% had capacity to consent and the remainder had a consultee. 71.6% were female and mean age was 85.5 (sd 8.4, range 65 - 100 years). 68 (84.0%) were living with moderate or severe frailty - scoring 6 or 7 on the Clinical Frailty Scale (CFS). 66 (75.3%) were living with polypharmacy (taking five or more medications). 20 (24.6%) had had a least one UTI treated with antibiotics in the six months prior to entering the cohort. One participant was taking prophylactic antibiotics, and one was taking methanamine hippurate. Characteristics of the cohort at baseline are summarised in Table 5.1.

Characteristic		
Sex, n (%)	Male	23 (28.4%)
	Female	58 (71.6%)
Age, mean (sd)		85.5 (± 8.4)
Ethnicity	White	80 (99.8%)
	Black British, Carribean or African	1 (1.2%)
BMI, mean (sd)		25.6 (± 5.1)
Clinical Frailty Scale, n (%)	2 (Well)	2 (2.5%)
	3 (Managing well)	1 (1.2%)
	4 (Vulnerable)	2 (2.5%)
	5 (Mildly frail)	8 (9.9%)
	6 (Moderately frail)	43 (53.1%)
	7 (Severely frail)	25 (30.9%)
Capacity to consent, n (%)	Yes	44 (54.3%)
	No	37 (45.7%)
Comorbidities, n (%)	Dementia	39 (48.1%)
	Diabetes	12 (14.8%)
	Chronic kidney disease	17 (21.0%)
	Overactive bladder	1 (1.2%)
	Benign prostatic hypertrophy	0 (0%)
	Recurrent UTI	4 (4.9%)
	Prostate cancer	2 (2.5%)
	Other cancer	13 (16%)
	None of the above	23 (28.4%)
Total oral medications, n (%)	0-4	23 (28.4%)
	5-9	42 (42.0%)
	10 or more	24 (29.6%)
Antibiotics within last 6 months, n (%)	Yes	38 (47%)
	No	37 (45.7%)
	Unknown	6 (7%)
UTI within last 6 months, n (%)	Yes	20 (24.7%)
	No	61 (75.3%)

Table 5.2: Characteristics of cohort at baseline

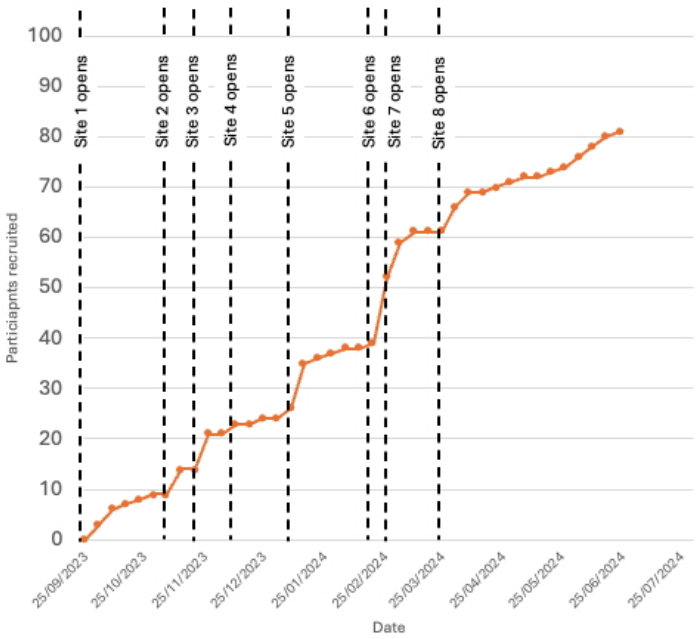


Figure 5.1: Recruitment of participants over time. Vertical dashed lines indicate when sites were opened over the recruitment period.

5.5.3 Follow up and withdrawals

Median follow up was 255 days (interquartile range (IQR) 271 - 309, range 30 - 368 days).

There were 13 withdrawals: eight deaths, three withdrew consent for ongoing follow up, and two moved out of the participating care home.

5.5.4 Possible UTI events during follow up

There were 24 possible UTI episodes from 19 (23%) participants (4 men, 15 women) during follow up with an overall incidence of 0.1 per 100 resident days. One participant had three possible UTI episodes, and two participants had two episodes. 19 of these episodes occurred within the first 6 months of follow up and 5 episodes occurred from 6 to 12 months of follow up. (Figure 5.2) One participating care home had no possible UTI episodes during follow up (all participants in this home completed follow up at 6 months).

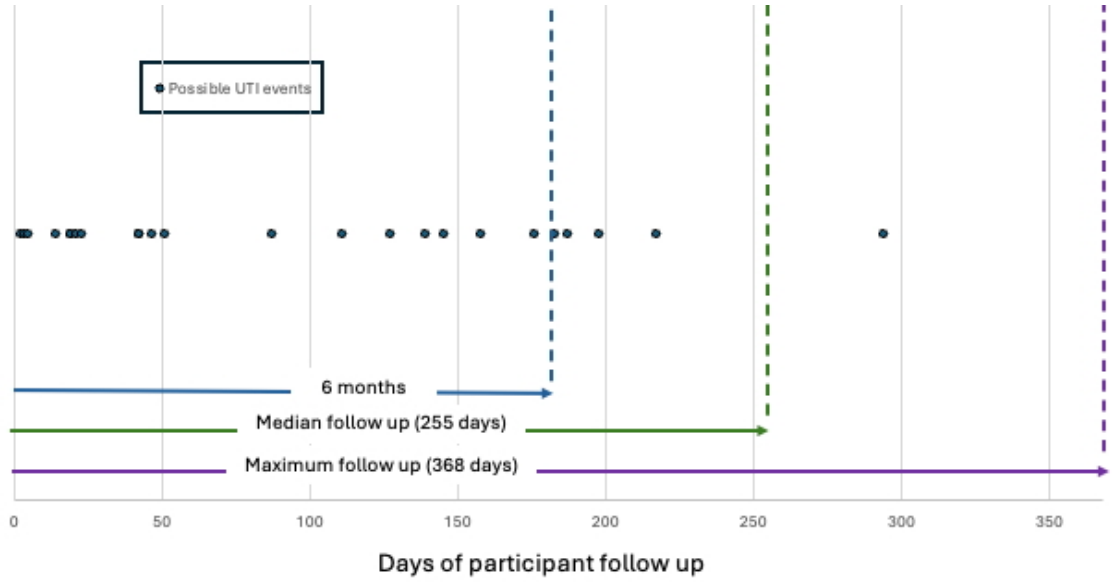


Figure 5.2: Timing of possible UTI events over days of participant follow up

5.5.5 Completeness of data collection

Of the scheduled research visits, the visits that were actually carried out are summarised in Table 5.3. If the visit was carried out, data collection was complete for that visit.

5.5.5.1 Visits for repeat urine sampling

Two participants were removed from the weekly sampling group after one week; one because they developed symptoms (switched to possible UTI visits instead), and one was finding repeated samples distressing.

Of the 90 visits, 88 (98%) were carried out. Two visits were not done, with no reason documented in the eCRF.

5.5.5.2 Visits for possible UTI episodes

Median days from symptom onset to the episode being reported to the research team was two days (IQR 1 - 3.25, range 0 - 12 days). 9/24 episodes (35%) were reported within one day. 17/24 episodes (71%) had their symptom onset research visit on the same day (IQR 0 - 1, range 0 - 4 days).

Visit		Visits carried out
Baseline		81/81 (100%)
Repeat sampling	Week 1	24/24 (100%)
	Week 2	22/22 (100%)
	Week 3	21/22 (95.4%)
	Week 4	21/22 (95.4%)
Possible UTI	Onset	24/24 (100%)
	Day 14	20/23 (95.7%)
	Day 28	20/22 (90.9%)
Total		233/240 (97%)

Table 5.3: Proportion of each type of study visit carried out

Four follow up visits were not done, with no reason documented in the eCRF.

5.5.6 Completeness of urine sample collection

215 of the 243 (88.4%) total possible urine samples were collected during the study. Reasons for the 28 missing samples are summarised in Table 5.4.

5.5.6.1 Baseline

Baseline urine samples were collected from 80/81 (98.8%) participants. One participant developed a possible UTI episode shortly after being recruited, before their baseline sample had been collected.

5.5.6.2 Repeat urine sampling

Of the 24 participants in the weekly sampling group, 17 (68%) had urine samples collected every week for each of the four weeks. Two participants were removed from the repeat sampling group as above. In total 84/90 (93.3%) of the possible repeat samples were collected.

5.5.6.3 Possible UTI: onset

19/24 (79%) had a urine sample sent from their symptom onset visit. 5/19 (26%) of these were collected prior to antibiotics being initiated.

Visit		Reason for sample not being collected			
		Modifiable for future study		Not modifiable for a future study	
Baseline		Developed possible UTI before baseline sample collected	1		
Repeat sampling		Visits not done, no reason given	2	Challenges getting sample during study visit (including participant refusal)	4
Possible UTI	**Onset**			Participant admitted to hospital, not present	1
				Participant died	1
				Multiple attempts/visits but sample unable to be obtained due to incontinence and/or illness severity	3
	Follow up	Visits not done, no reason given	4	Multiple attempts/visits but sample unable to be obtained due to incontinence and/or illness severity	1
		Episode reported late by the care home so just had a day 28 visit (no day 14)	1	Participant withdrawn	5
				Participant admitted to hospital, not present	1
				Participant symptomatic from a further possible UTI, so onset visit done instead	1

Table 5.4: Reasons for study visits not carried out. Reasons are divided into those modifiable and not modifiable for any future study.

5.5.6.4 Possible UTI: day 14 and 28

16/24 episodes (67%) had samples collected at both follow up visits. There were 16 missing samples.

5.6 Feasibility and acceptability qualitative findings

5.6.1 Recruitment

Characteristics of the cohort participants (11), consultees (3) and care home staff (4) who took part in individual interviews, and research staff (8) who participated in the focus group are summarised in Table 5.5.

5.6.2 Overview of themes and subthemes

The themes and subthemes that emerged during analysis are summarised in Table 5.6 and are explored in more detail below.

5.6.3 Study feasibility

5.6.3.1 Work required in recruitment

In the focus group, the research team said that many residents and family members were interested in the study after hearing about it and were happy to participate. However, in some care homes, they felt that care home staff were not proactive in identifying possible participants, were slow to suggest residents to approach, and/or did not contact potential consultees in advance.

> *'With DISCO, what all the care homes seem to be doing is giving us names, you know just a few names here and there. So the actual planning the recruitment is a little bit more difficult really.'*
> Female research nurse

They also said that it took a lot of work/coordination to contact consultees and consent residents, and this sometimes took multiple visits and/or multiple research staff. The process

Group	Characteristic		Number
Cohort participant (n=11)	Sex	Male	4
		Female	7
	Clinical frailty scale	4 (Vulnerable)	2
		5 (Mildly frail)	1
		6 (Moderately frail)	6
		7 (Severely frail)	2
	Samples given	Baseline only	1
		Repeat sampling	7
		UTI episode(s)	4
Consultee (n=3)	Sex	Men	1
		Woman	2
	Relationship to participant	Spouse	2
		Child	1
	Also a cohort participant		2
Care home staff (n=4)	Sex	Male	1
		Female	3
	Job role	Manager	1
		Deputy manager	1
		Carer	2
Research staff (n=8)	Sex	Male	0
		Female	8
	Job role	Research nurse	4
		Research clinical assistant	4
	Region	Thames Valley	2
		Wessex	6

Table 5.5: Characteristics of participants in the qualitative evaluation

Theme	Subtheme
Study feasibility	Work required in recruitment
	Challenges with urine sample collection
	Communication issues
	Suggestions to improve feasibility in future studies
Study acceptability	Importance of topic
	Acceptability of study processes
	Acceptability of providing urine samples
	Suggestions for future research in care homes

Table 5.6: Themes and subthemes

was easier when there were more research staff available to do the recruitment and baseline visits.

> *'I think the difference in the two areas [Thames Valley vs Wessex] was that obviously there was more of us [Wessex], so we were going in and we could literally – there was at least three of us going in wasn't there? Sometimes there was four of us that went in at the beginning. So we could literally just go off and do a few each.'*
>
> Female research nurse

It was possible to collect data from the care home record, but this required care home staff to help find the information needed and went more smoothly when staff had the time to support them.

5.6.3.2 Challenges with urine sample collection

The process of collecting urine samples was considered challenging, though possible, by both care home staff and the research team. They explained that it could take a long time, sometimes multiple visits, to obtain a urine sample. This was often related to resident factors such as unpredictability and incontinence.

> *'Sometimes you just can't get a sample because they're so incontinent that they*

can't – the staff did try to put them on the toilet but they're just so incontinent that they just, you know, pee'd all the time. So there isn't ever a time. So as far as minimum goes, the ones with capacity you can go and ask them and they'll do it for you that day. But for the other home sometimes I've gone three or four times to try and get one and they haven't been able to.'

Female research nurse

'You know they take the bowl out to hand it to you and drop it on the bathroom floor. We've had them drop it on the floor. We've had they flushed the toilet. We've had bowlfuls of toilet water. I mean the list goes on. It's – we could write a book, but it's – yeah, on paper it looks really easy but the reality is, yeah, it's not.'

Female research nurse

Some care home staff felt that collecting urine samples felt like just part of their *'usual work'*. However, others felt that sometimes timing of research visits was suboptimal and the need to collect extra samples could add to their workload.

'Because any other time you're either getting up, getting lunch ready or getting them ready for tea, you know, so it's just that morning bit is just so empty but once it gets to like 11.45 onwards you're full on with lunch service and that's sometimes when you need to be like "Really? The time you turn up at this time and it's really busy."'

Female carer

5.6.3.3 Communication issues

Communication within the care home was highlighted as an issue by the research team. For example, in some homes they felt the message that a urine sample was needed from a participant was not passed on at handover. In contrast, one home was described at being extremely proactive at collecting samples requested in advance.

'I'd email them who I wanted, I'd go in. Literally I've had someone waiting in the car for me outside before because it's here, it's in the fridge, they'd taken it the first one of the day. I'm in and out and done.'

Female clinical research assistant

Variation in the reliability of communication from the care home was also described by the research team in the context of possible UTI episodes. Reasons for a delayed notification of an episode provided by the care home staff to the research team included staff forgetting, not being able to find the research team's phone number or not knowing that a resident was taking part in the study. The research team felt that over time the homes were less good at letting them know if a participant had a possible UTI.

> *'In the beginning when that enthusiasm was still there, the first home that we opened that called me a couple of times, but then after that – and then the other home I didn't get any calls. I just had to happen upon it when I went for the visit.'*
>
> Female research nurse

This contrasted with the views of care home staff who felt that they were trying their best in the context of their workload and staff turnover. Several mentioned that they relied on contact from the research team to remind them about notifying about UTI episodes, rather than feeling that they should be proactive. Some felt communication had not been an issue.

> *'It was straightforward 'cause we had varied contact, we could contact with them, there was no other problem at all, no other problem. If at all they were always calling to remind us anyway if there are any samples about getting contact with them, the conversation was good, there was no problem.'*
>
> Male carer

5.6.3.4 Suggestions to improve feasibility in future studies

Both the research team and care home staff suggested that increasing the staff time available to participate in the research would improve the study if done again in the future. This could be either upskilling and paying a member of the care home staff or having more dedicated research staff.

> *'Most care homes have got that person in anyway so you could say if I give that*

person an extra hour's wages do you reckon they can do samples for this person, these people, then you'd probably get, "Yeah, that'd be fine", they're willing to do that and then that's their job of collecting x amount of urine samples for you.'

Female care home manager

Research staff described how care home staff acting as the gatekeeper to contacting consultees meant delays/difficulties in obtaining a consultee declaration. They suggested that family members in future should be able to opt in to being contacted about research when their relative moved into the care home.

'I know that we've been doing another study and we've had similar issues and we've been trying to think of ways that the care homes can get that consent from relatives as a generic for research, so that we don't have this issue again 'cause it's just gonna continue. Even if it's in the protocol, I think the care home will still – they wouldn't be happy with us just contacting relatives without that, somewhere, documented that they have agreed to be contacted for any research purposes. So I think that is something, a broader issue for any research in care homes going forward.'

Female research nurse

Finally, the research team described how smaller care homes, particularly those not purpose built, did not necessarily have suitable areas for some of the study tasks, which made their presence less convenient. This felt this should be considered when selecting which care homes to participate in future research.

'Some of the homes which are really quite small and have lots of people and feel very, very chaotic and they don't have meeting spaces or extra rooms that we can go and work in, we were probably more of an inconvenience in. But some of the homes where they are purpose built so they've got lovely bits that we can kind of hide away and not really get in the way too much and find the participants easily and we were much less of a nuisance probably.'

Female research nurse

5.6.4 Study acceptability

5.6.4.1 Importance of study topic

In general, the study topic was considered important to participants. This was either due to personal lived experience or knowledge of the potential morbidity of UTI in people like themselves. Some participants had not personally experienced UTI but were motivated to participate because of the desire to help others.

> *'I just thought it was a very good idea because I know if it's not diagnosed, it can be very serious. Well I know if it hasn't been diagnosed, you can actually die, I do know that, yes.'*
>
> Female participant, repeat sampling group, one possible UTI

> *'I thought if it helps other people, you know who come in on behind us, I was quite willing to help.'*
>
> Male participant, one possible UTI

Similarly, care home staff thought the study was important and relevant to care home residents and felt that UTI diagnosis was an area where improvement was needed. They, too, were keen to help others in the future.

> *'But then it's also the concern of, you know, prescribing without you know a full culture growth, you know, broad spectrum antibiotic use as we know is not good, especially in the elderly, you know, affecting their resistance to other infections at all so you know, the earlier, the more specific you can diagnose a UTI surely that's gonna have a positive impact on the residents.'*
>
> Male deputy manager

5.6.4.2 Acceptability of study processes

Participants found the process of recruitment, data collection and visit frequency acceptable. They commented that they liked the written information provided. Some said they liked the fact that they could revisit the written information if they wanted to. Most said that they would not have preferred an alternative format (eg. audio, video).

'Because I don't have a fancy phone or anything to gather information. I do like things written down so that I can refer back to them.'

Female participant, repeat sampling group, three possible UTIs

Consultees had no issues with the process of acting on behalf of their loved one. One commented that he would not have allowed his wife to participate if he had felt the study would cause any distress, and another described making decisions on her mother's behalf as *'normal'*.

'I've done all my mums stuff for god knows how many years. So it's just normal to me because I've always looked after mum's...gone to all the hospital appointments with her, done everything with her. So for me it was just normal, just another thing that I do for mum.'

Consultee

Care home staff perceived that participating in research had been an overall positive experience for the residents.

'I think it was a change from maybe their daily routine and felt that they were able to contribute, you know, to future development; I think they were quite proud and quite, you know, felt quite... I'm trying to think of the right term... I think it just made them feel special that they were part of a project in some ways.'

Male deputy manager

5.6.4.3 Acceptability of providing urine samples

Most participants did not mind giving urine samples for the study. Many were used to giving samples, or felt that as the urine was going to be produced by them anyway it was not a problem for it to be used for research. Most participants would have been happier giving more samples if needed, including blood samples, though several said that a once weekly urine sample would be the most that they could tolerate.

'Yes, not a problem. I don't think it would be for most women; I mean it's something you've over the years have done, either for the doctors, or when you were

younger when you were pregnant, it's a fairly simple straightforward process.'
Female participant, repeat sampling group, three possible UTIs

One participant, however, described experiencing stress as a result of giving urine samples as it was physically challenging for her to urinate into a container. This participant was withdrawn from the weekly sampling cohort after the first week.

'I cannot do it into the pot, you know. It's just very, very stressful for me and I miss and then I get it all over my clothes and the floor.'
Female participant, repeat sampling group

5.6.4.4 Suggestions for future research in care homes

Most participants did not feel that there were any aspects of the study that needed to be improved and almost all participants interviewed said that they would take part in a similar study again. However, several commented that they wished the results of the research tests had been available to participants during the study. Some participants and care home staff said they wanted more regular feedback to residents and families during the study and earlier dissemination of overall results.

'I think you like to know what has been done, and how you've done, right or wrong...'
Female participant

When asked about other aspects of care home UTI that could be important to research in the future, participants and care home staff mentioned UTI prevention, risk factors for recurrent UTI, the impact of hydration and hygiene, rapid diagnosis and antibiotic avoidance.

'I mean it causes a lot of – 'cause they have hallucinations and all sorts don't they, so I do think the diagnosis and the treatment should be quick because she was getting quite poorly, where it would take us so long to just get a doctors appointment and get a sample done or whatever. Then they just sort of talked to me over the phone in the end and then said, "Oh yeah, we'll just give her antibiotics." But yeah, where they don't do the water samples and everything

now, it does need to be diagnosed a lot quicker.'

Consultee

'If there's an alternative to putting 'em straight on medication. I know that's probably a 'no' but it's just they're very quick to blind prescribe and... or a way we could... the prevention of them. I know we're supposed to make 'em drink more but yeah, I think sometimes people automatically in care homes put behaviour down to a UTI when it's not always.'

Female manager

5.7 Discussion

5.7.1 Summary of findings

Eight care homes from England participated in the DISCO UTI study. From these, 81 care home residents were recruited to the cohort. Recruitment was lower than anticipated and, as a result, follow up was extended from six months to a year, with the aim of capturing more possible UTI episodes. The cohort were followed up for a median of 255 days. Of the 81 participants, 71.6% were female, mean age was 85.5 and 54.3% had capacity to consent. There were 24 possible UTI episodes from 19 (23%) participants during the study. 233 of 240 (97%) of total scheduled study visits took place with complete data collection. 215 of 243 (88.4%) of the total possible urine samples were collected successfully. 19 of the 24 possible UTI episodes (79%) had a urine sample collected in the onset visit but only 5 of these were prior to antibiotics being administered.

In the qualitative evaluation, the research team identified several barriers to recruitment, including care home staff acting as gatekeepers. They described the considerable work required to recruit participants, which sometimes took several visits. Similarly, multiple visits were sometimes required to collect urine samples from participants. There were challenges with urine sample collection associated with incontinence and unpredictable behaviour from participants. The research team described issues in communication with the care homes including delayed notification of possible UTI episodes. They also perceived that there had

been waning of enthusiasm for the study from the care homes over time. Both care home and research staff suggested that a future study could be improved with additional dedicated staff time. The study topic was considered important to almost all who took part or who supported the study, and participating was generally considered acceptable by care home residents and consultees. Most care home residents had not minded providing urine samples for the study, and would have been willing to give additional urine samples and blood samples if necessary.

5.7.2 Personal reflections on study feasibility

I can reflect further on additional factors affecting feasibility that were not captured in the interviews from my perspective as Co-Chief Investigator. Care homes were not given any financial reimbursement for taking part in the research; indeed, I was advised not to cost this by ENRICH who said there was no precedent for doing so. This may have contributed to the challenge of recruitment. Recruiting care homes, particularly in the Thames Valley region which I led, proved to be extremely difficult. The ENRICH mail-out reached a large number of care homes but few responded despite multiple invitations and a webinar organised to advertise the study. Some care homes that did get in touch stopped responding to emails. I had an expression of interest from one care home manager, but the decision maker was higher up in the organisation and I was unable to get the site agreement signed. Recruitment of care homes by Solent NHS Trust was much more successful, in part because they maintain relationships with care homes even when they are not actively participating in research.

Secondly, as a small feasibility study, we did not have the funds to cover staff time to contact or visit the homes as regularly as needed - ideally, someone would have visited each of the care homes daily and checked if any of the participants were experiencing possible UTI episodes. In the Thames Valley region, nurses could only visit once weekly and could not necessarily respond quickly to episodes if they were notified. The study was also low priority; there were three nurses initially assigned to DISCO UTI who either left their post or were moved to other projects during the study. In the Wessex region there were more research staff available via Solent NHS Trust and they used a slightly different model to

recruit. Care homes provided a list of consultees who were happy to hear from the team and they were contacted in advance of a site visit. Up to four research team members would then attend over one to two days and do all the consenting for participants with capacity, and the baseline data collection and sample collections for all. This is reflected in the sharp upticks in recruitment in Figure 5.1.

5.7.3 Comparison with existing evidence

Many of the challenges identified in delivering the DISCO UTI study have been experienced by other groups carrying out research in a UK care home setting. During a recent randomised controlled trial (RCT) conducted in 91 care homes in England, the authors identified similar issues with gatekeeping where paternalistic attitudes towards residents resulted in restricted access to potentially eligible residents.[121] In this study, a lack of understanding of research principles also meant that care home staff were keen to select those who were 'easiest' to consent, rather a random or representative sample.

The increased length of time required for site visits was highlighted by a second group who carried out two RCTs in England.[122] They described often needing to wait for appropriate times for research procedures around usual care. However, the authors reflected that the increased time spent in the home was a positive because of the resultant close relationship that developed between participants, care home staff and research staff. This group also noted that some care homes did not have appropriate or quiet spaces to speak to residents or carry out research activities, like some of the homes participating in DISCO UTI.

A recent review proposed potential solutions to some of the challenges with care home research.[123] To address the difficulty in recruitment of care homes, it was recommended to establish interdisciplinary collaborations between universities, general practice and care homes, where research projects are co-created, citing as an example the Living Lab in Ageing and Long-Term Care in Maastricht (Netherlands).[124] Like the suggestion from our focus group with research staff, the review also recommended that it should be documented whether residents and family members are happy to be approached about research at the

point of admission to a care home, to remove the potential for care home staff (or GPs) to act as gatekeepers for research.

5.7.4 Strengths and limitations

This is the first prospective study capturing information about possible UTI episodes in UK care homes, providing vital information on feasibility and acceptability of such a study. The qualitative evaluation has helped to explain aspects like the delayed visits at the onset of possible UTI, caused in part by a lack of proactive communication from the care home, and some of the missing urine samples, caused by worse incontinence or behaviour changes during illness. We have also been able to identify potential improvements to a future study design including increased research staff time and/or upskilling care home staff to support with study delivery.

We did not reach our initial sample size target of 100 participants. Despite this, the cohort was sufficient to assess feasibility and acceptability. We made the decision to extend follow up for the participants we had recruited, thinking this would allow us to capture more possible UTI episodes. However, as shown in Figure 5.2, most of the possible UTI episodes were in the first 6 months of the study. Research staff described the potential waning of enthusiasm for the study by care home staff over time which is likely to have resulted in missed possible UTI episodes. A full study would need to consider ways to combat research fatigue in sites, or increase the number of recruiting sites.

5.7.5 Implications for future research and/or practice

Research in care homes is vital if we are to generate evidence that will support the healthcare of this vulnerable population. However, this study, like others before it, has shown that in practice it can be extremely challenging to deliver research in UK care homes. Some of the issues we experienced were related to the small scale of our funded study, like the amount of research nurse time costed. However, some were due to the lack of research knowledge and experience of care home staff and the busy environment of care homes, where there were often issues with staff shortages/turnover and many other competing tasks.

In order for a adequately powered study to be successful in the future there would need to be a significant increase in dedicated staff time to the study. This would allow regular visits and better support of research tasks like urine sampling, thus reducing the impact on care home staff time and the reliance on them to communicate about possible UTI episodes. We would need to consider how to best access all eligible residents within a care home site; this may involve selecting care homes who are part of a research network or 'living lab', whose staff may act less like gatekeepers. We would also need to consider whether urine samples could be collected from incontinence pads as a last resort; this could potentially reduce the amount of missing samples and is also likely to reduce the time burden of sample collection. I have contributed to the development of several funding applications for a further study with these design modifications, but unfortunately these have been unsuccessful to date.

Going forward, research must be considered a priority by the organisations that own and run care homes. Given the vast number of these in the UK, widespread change is unlikely to happen unless driven by government policy. Alternatively, as the care home sector is a largely private market, the change could be driven by public eduction of the benefits; with people preferentially choosing research active care homes for themselves or loved ones. However, there also needs to be a move towards appropriately reimbursing care homes for their participation in research. If care homes were paid for research activities and participated in enough studies, it may become profitable for larger care homes/chains to employ research-focused staff, in a model similar to some research active GP practices.

Finally, care home researchers must share experience and expertise to avoid repeated exposure to the same challenges. The establishment of a care home researcher network to sit within ENRICH/RDN may facilitate more collaborative work in the future.

5.8 Conclusions

An adequately powered cohort study of care home residents capturing information and samples related to possible UTI episodes may be feasible in UK care homes. However, it would require a significant increase in research staff time and amendments to the protocol

to improve completeness of episode and sample capture. Working with existing networks of care homes and researchers may be one approach to deliver this study in the future.

5.9 Chapter summary

In this chapter I have described the feasibility and acceptability outcomes of a cohort study of 81 care home residents in England in which we captured information on possible UTI episodes suspected by care home staff that occurred during follow up. In the next chapter I describe some of the exploratory outcomes of this study, including clinical characteristics and outcomes of the possible UTI episodes, ASB prevalence and risk factors, and the results of the microbiology analyses of urine samples collected from both asymptomatic participants, and those experiencing possible UTI.

Chapter 6

Exploring new approaches that may improve diagnosis of UTI in care homes.

6.1 Overview of chapter

In Chapter 5 I gave an overview of the methods of the DISCO UTI cohort study, and presented the feasibility and acceptability results. In this chapter I present some of the exploratory results from this study. I describe the possible UTI episodes, as suspected by care home staff, that occurred during follow up, and how the pattern of microbial presence from samples taken during these episodes relates to earlier samples taken when the participant was asymptomatic. Following on from the systematic review in Chapter 4, I describe the prevalence of ASB in this cohort at baseline and its risk factors. I also explore the pattern of microbial presence in the repeat samples taken weekly from a subsection of the cohort who remained asymptomatic. Finally, I use the findings to generate new hypotheses to be tested in future studies.

6.2 Background and rationale

New approaches to diagnosing UTI are urgently needed for care home residents to reduce diagnostic uncertainty, particuarly for those with non-specific symptoms like acute functional

decline. DISCO UTI was a cohort study of care home residents in England. It primarily aimed to assess feasibility and acceptability of delivering a prospective cohort in a UK care home setting including capturing episodes suspected to be UTI by care home staff. The results of DISCO UTI were to inform a further adequately powered prospective observational study on UTI in UK care homes to assess potential new approaches. These approaches include:

1) To identify symptom clusters and/or resident characteristics associated with the highest risk of severe illness or poor outcomes from acute functional decline/possible UTI. This may better target antibiotic prescribing and/or enhanced monitoring by primary care. As described in Chapter 2, care home staff experience anxiety about the potential deterioration of residents and this in part drives help-seeking behaviour. However, currently, there is limited evidence on predictors of poor outcomes. The UKHSA UTI diagnosis quick reference tool for adults over 65 in primary care (Figure 1.2) highlights symptoms associated with possible systemic UTI, likely localising UTI, and unlikely UTI, but these are not specifically tailored to the care home population and focus on diagnosis rather than the outcome.[41] A retrospective US study has identified predictors of hospitalisation with UTI in care home residents, but these were resident demographic characteristics and potential risk factors rather than features of illness presentation.[125]

2) To better understand the relationship between ASB and subsequent UTI. As described in Chapter 4, the pooled prevalence of ASB in care home residents from studies published since 1990 was calculated to be 0.31 (95% CI: 0.25 to 0.36). Longitudinal studies have suggested that ASB status fluctuates over time in adult community dwelling and care home populations.[46–54, 112] However, the frequency of changes in ASB states (absent, transient, or persistent) and their relationship with subsequent symptomatic UTI is not well described. Prior/changing ASB status could help interpret subsequent culture results in the context of possible UTI. To date, the care home study with the most frequent urine sampling regime collected samples every two weeks from 195 residents over an 18 month period in the USA during the 1980s.[54] There have been no previous attempts at research involving

serial urine sampling in UK care homes.

3) To consider the potential role for novel UTI POCTs. This is covered in Chapter 7.

In this chapter I will describe the exploratory objectives and results from DISCO UTI, and will discuss the hypotheses generated for future research.

6.3 Exploratory objectives

- To describe clinical characteristics of the possible UTI episodes as suspected by care home staff, and its outcomes
- To describe any predictors of poor outcome from possible UTI (deterioration, hospitalisation, mortality)
- To describe the microbiology results of urine samples collected during possible UTI episodes
- To describe any association between different participant characteristics and baseline ASB status
- To describe any association between baseline ASB status and subsequent possible UTI
- To describe the microbiology results of repeat urine samples taken from asymptomatic participants

6.4 Methods

The methods of the DISCO UTI cohort study, including recruitment, data and urine collection and postage are described in Chapter 5 (Section 5.4).

6.4.1 Microbiology analysis

Analysis was carried out by staff at SACU.

6.4.1.1 Urine microscopy

Urine microscopy was performed using Sysmex UF 5000 for Urine (version 3.0). The following results were recorded in the eCRF when available in the Laboratory Information Management System:

- Red blood cell (RBC)
- White blood cell (WBC)
- Squamous epithelial cell (SEC)
- Bacteria
- Casts
- Yeast

6.4.1.2 Urine culture

Urine samples were diluted before spiral plating on a chromogenic UTI plate. After 18-24 hours aerobic incubation at 35±2°C colony counts were performed taking dilution factor into account. A total colony count and species specific colony count was recorded, with the most predominant organism first. Purity of growth was categorised as pure, one predominant, mix of two species, or a mix of greater than two species.

6.4.1.3 Grading results

The results were recorded as 'positive' if the result indicated a probable or possible UTI based on the SMI on urine investigation.[73] They were graded according to the criteria listed in Table 6.1.

	Grade	Definition
Probable UTI	**1**	Culture at $\geq 10^5$ CFU/ml of pure culture, irrespective of WBC levels.
Possible UTI	**2**	Culture at $\geq 10^5$ CFU/ml with predominant growth (where the 2nd or 3rd organisms are at least 3xlog2 CFU/ml below the predominant organism) irrespective of WBC.
	3	Growth of 2 organisms (dual culture: where both are $\geq 10^5$ CFU/ml or one is $\geq 10^5$ CFU/ml and the other $\geq 10^4$ CFU/ml) accompanied by WBC
	4	Pure or predominant culture at $10^4 - 10^5$ CFU/ml accompanied WBC
	5	Predominant culture at $10^4 - 10^5$ CFU/ml of a UTI pathogen species accompanied by WBC
	6	Pure or dual culture (where both present are known urinary pathogens at $10^3 - 10^4$ CFU/ml accompanied by WBC.

Table 6.1: Grading criteria for 'positive' urine culture results

6.4.1.4 AST

AST was performed by European Committee on Antimicrobial Susceptibility Testing (EUCAST) standardised disc diffusion on all pure or predominant organisms from positive urines.

6.4.2 Data analysis

6.4.2.1 Definitions

Asymptomatic bacteriuria

In asymptomatic participants, any culture result that was interpreted as probable or possible UTI (see Table 6.1) was considered 'significant bacteriuria' and therefore classed as ASB.

Urinary tract infection

In samples from participants experiencing a possible UTI, any culture result that would be interpreted as probable or possible UTI was considered 'positive' for UTI.

Acute functional decline

In possible UTI episodes, this was defined as acute changes including physical symptoms like fatigue, loss of appetite, changes in mobility or activities of daily living and/or changes

in cognition.

6.4.2.2 Statistical analysis

StataNow/BE 18.5 for Mac was used for statistical analysis. Recruitment, attrition, and data completeness were described using rates and proportions. The overall cohort and repeat sampling cohort were described using proportions. Individual t test (continuous variables) and Chi square (categorical variables) were used to compare characteristics between participants with and without ASB at baseline.

6.5 Results

6.5.1 Possible UTI episodes

There were 24 possible UTI episodes from 19 (23%) participants (4 men, 15 women) during follow up with an overall incidence of 0.1 per 100 resident days.

6.5.1.1 Clinical presentation

During analysis each of the episodes was categorised based on the UKHSA diagnostic decision tool for suspected UTI in over 65s,[41] based on the symptoms and signs that had been recorded in the eCRF.(Table 6.2) Based on the diagnostic decision tool, only 12 (50%) episodes would be considered UTI 'likely', with either systemic or localising symptoms and signs.

6.5.1.2 Acute functional decline

Three episodes (13%) were associated with a decline in function in eating, dressing or toileting, and one was associated with a fall. Two of these episodes were also associated with confusion and one with symptoms/signs of UTI (according to the UKHSA diagnostic tool). There were also seven episodes with confusion alone. Combining these, 9/24 (37.5%) of all possible UTI episodes experienced by this cohort could be considered as presenting with an 'acute functional decline'. However, 3/24 (12.5%) episodes had a 'Don't know' response to the prompt about changes in activities in daily living.

Category	Symptoms/signs	Number of episodes (%)
Symptoms/signs of systemic UTI	Back pain, flu-like illness, nausea/vomiting, rigors or measured fever	2 (8%)
Symptoms/signs of localising UTI	New onset dysuria alone or two or more of fever, new frequency or urgency, new incontinence, new or worsening delirium, new suprapubic pain, visible haematuria	10 (42%)
Confusion/behaviour change alone	Confusion/change in behaviour in the absence of one of the UTI symptoms/signs	9 (38%)
Other symptoms (urinary)	Any urinary symptoms that are not in UTI symptoms/signs category, without confusion	2 (8)
Other symptoms (non-urinary)	Any other symptoms that do not fit into other categories, without confusion	1(4%)

Table 6.2: Possible UTI episodes (n=24) categorised by symptoms and signs. Systemic and localising UTI defined as per UKHSA diagnostic decision tool for suspected UTI in over 65s.[41]

6.5.1.3 Clinical management and outcomes

Clinical management for the possible UTI episodes provided by the care home/healthcare team is summarised in Table 6.3. 13 (54.2%) had a urine dipstick result recorded in the card home record - all of these were recorded as positive. 23 (95.8%) episodes had at least one course of antibiotics prescribed during the 28 day follow up; 18 of these were for nitrofurantoin. Two episodes had 2 courses of antibiotics prescribed. 15 of the antibiotic courses were prescribed for 6 or 7 days, including for 11 female participants.

In 11 (45.8%) episodes participants still had symptoms at the day 14 visit, and 6 (25%) had ongoing symptoms at day 28. There were 4 (16.5%) episodes with adverse outcomes; two resulting in hospital admission (one then going on to end-of-life care), a second episode resulting in end-of-life care, and one death. It was not possible to explore clinical predictors of adverse outcomes due to the small number of events.

Care home management	Vital signs recorded in care home record		14 (58.3%)
	Urine dipstick result recorded in care home record		13 (54.2%)
	Clinical support from GP		13 (54.2%)
	Clinical support from care home support service		11 (45.8%)
GP management	Urine culture requested		12 (50%)
	Diagnosis of UTI made		17 (70.8%)
	Antibiotic prescribed at onset		18 (75%)
	Antibiotics prescribed at any time point		23 (95.8%)
	First course of antibiotic prescribed	Amoxicillin	1
		Co-amoxiclav	1
		Fosfomycin	1
		Nitrofurantoin	18
		Trimethoprim	1
		Unknown	1
	Duration of first course of antibiotic prescribed	1 day	1
		3 days	7
		6 days	2
		7 days	13
Outcomes	Symptoms resolved by day 14 visit		8 (33.3%)
	Ongoing symptoms at day 28 visit		6 (25%)
	Hospital admission		2 (8.3%)
	Death		1 (4.2%)
	End of life care		2 (8.3%)

Table 6.3: Management and outcomes of the 24 possible UTI episodes.

6.5.1.4 Microbiology results for samples collected during possible UTI

The proportion of UTI positive samples at each of the visits during the possible UTI episodes is summarised in Figure 6.1. It is likely that there are fewer positive samples associated with the onset visit due to the prior administration of antibiotics.

13 (54.1%) of the episodes had at least one positive culture result from urine collected at one of the three study visits. For ten of these episodes, *E coli* was one of the predominant organisms, with *Enterococcus faecalis* in two episodes, and *Klebsiella pneumoniae* and *Kleb-*

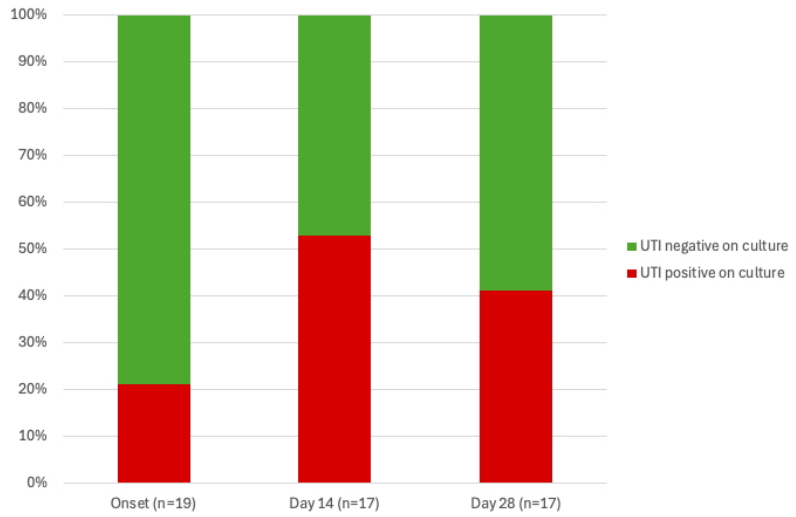


Figure 6.1: Proportion of culture positive results in samples collected at different visits during possible UTI episodes. Only 5 samples collected at onset were prior to antibiotic administration.

siella oxytoca in one each. AST results for the isolates from samples associated with possible UTI episodes are summarised in Appendix D.1.

6.5.1.5 Overall summary of episodes

Figure 6.3 shows each participant who experienced at least one possible UTI over time, including information on symptom category (see Table 6.2) and duration, antibiotic timing, and urine culture results.

It shows that some participants (eg. 6, 11) continued to have symptoms despite a negative urine culture. For others (eg. 9, 10, 13, 18, 19) symptoms resolved but they continued to have a positive urine culture. Several participants had an initial negative urine culture (eg. 10, 13) after antibiotics before their cultures became positive by the day 14 visit.

6.5.2 Baseline samples from asymptomatic participants

There were 80 baseline urine samples collected at recruitment into the cohort when the participants were asymptomatic. 26 (32.5%) met our definition for ASB. ASB was more common in women (43.6%) than men (8.7%) (Chi-square, p = 0.004). Participants with ASB were older than those without ASB, but this was not significant (individual t test,

			POSSIBLE UTI EPISODE									
PARTICIPANT	SEX	BASELINE SAMPLE	EPISODE NO.	SYMPTOM CATEGORY	Abx	ONSET VISIT	Abx	ONGOING SYMPTOMS	DAY 14 VISIT	Abx	ONGOING SYMPTOMS	DAY 28 VISIT
1	Female		1	Confusion					Visit not done			Visit not done
2	Female		1	Symptoms/signs of systemic UTI				Ongoing			Resolved	
3	Female	Sample sent same time as onset	1	Other (not urinary)				Ongoing			Ongoing	
			2	Other (urinary)				Resolved			Resolved	
4	Female		1	Confusion		No growth			Visit not done			Visit not done
5	Male		1	Confusion				Resolved			Resolved	No growth
6	Female		1	Other (urinary)		No growth		Ongoing			Resolved	Multiple attempts - contaminated
7	Female		1	Confusion		Passed away						
8	Female		1	Symptoms/signs of UTI				Ongoing			Ongoing	
9	Female		1	Symptoms/signs of UTI				Ongoing			Resolved	
10	Female		1	Confusion		No growth		Resolved			Resolved	
			2	Confusion				Ongoing			Ongoing	
11	Male		1	Symptoms/signs of systemic UTI		In hospital		Ongoing			Resolved	
12	Male		1	Symptoms/signs of UTI				Resolved			Resolved	
13	Female		1	Symptoms/signs of UTI				Ongoing				New symptoms so onset sample
			2	Confusion		No growth		Resolved			Resolved	
			3	Symptoms/signs of UTI				Resolved			Resolved	
14	Male	No growth	1	Confusion		No growth		Unknown	In hospital			
15	Female		1	Symptoms/signs of UTI		Multiple attemps - incontinence		Resolved	No growth		Resolved	
16	Female		1	Confusion				NA	Not done due to late reporting		Ongoing	
17	Female		1	Symptoms/signs of UTI		Multiple attempts - not able to produce		Ongoing	Multiple attempts - incontience		Ongoing	
			2	Symptoms/signs of UTI		Mutiple attempts - not available		Ongoing	Deterioration		EoL	Deterioration - EoL
18	Female		1	Symptoms/signs of UTI				Resolved			Resolved	
19	Female		1	Symptoms/signs of UTI				Ongoing			Resolved	

KEY:

Positive urine culture
Negative urine culture
No sample collected
No visit
Withdrawn
Antibiotics prescribed

Figure 6.2: Schematic summarising each of the 24 possible UTI episodes

p=0.16). No other characteristic or co-morbidity had a significant association with ASB. (Table 6.4)

Characteristic		**ASB (n= 26)**	**No ASB (n = 54)**	**p value**
Age		87.3 (± 8.5)	84.5 (±8.3)	0.16
Sex	Male	2 (8%)	21 (39%)	**0.004**
	Female	24 (92%)	33 (61%)	
Capacity	Yes	13 (50%)	31 (57%)	0.53
	No	13 (50%)	23 (43%)	
Clinical frailty scale	2 (Well)	0 (0%)	2 (4%)	0.75
	3 (Managing well)	0 (0%)	1 (2%)	
	4 (Vulnerable)	0 (0%)	2 (4%)	
	5 (Mildly frail)	3 (12%)	5 (9%)	
	6 (Moderately frail)	14 (54%)	28 (52%)	
	7 (Severely frail)	9 (35%)	16 (30%)	
Moderately/severely frail	Yes	3 (12%)	10 (19%)	0.43
	No	23 (88%)	44 (81%)	
Comorbidities	Dementia	11 (42%)	28 (52%)	0.42
	Chronic kidney disease	5 (19%)	12 (22%)	0.76
	Diabetes	2 (8%)	10 (19%)	0.2
	Recurrent UTI	1 (4%)	3 (6%)	0.74
Antibiotics within last 6 months		15 (58%)	23 (43%)	0.39

Table 6.4: Comparison of participants (n=80) with and without ASB in their baseline urine sample.

6.5.2.1 Microbiology results for baseline samples

Purity of growth of the 80 baseline urine samples is summarised in Figure 6.1.

Of those with ASB, the predominant organism was *E.coli* for 15 participants and *Klebsiella pneumoniae* for 7 participants. 30 isolates from 25 participants underwent AST. Of these, 10 (33.3%) were resistant to trimethoprim and 4 (13.3%) were resistant to co-amoxiclav. Full AST results are summarised in Appendix D.2.

6.5.3 Repeat samples from asymptomatic participants

24 participants selected to provide weekly samples whilst asymptomatic. Characteristics of these participants, including the culture result of their baseline urine samples are summarised in Table 6.5.

Characteristic		**n (%)**
Sex	Male	9 (37.5%)
	Female	15 (62.5%)
Clinical Frailty Scale	2 (Well)	1 (4.2%)
	3 (Managing well)	1 (4.2%)
	4 (Vulnerable)	2 (8.3%)
	5 (Mildly frail)	3 (12.5%)
	6 (Moderately frail)	11 (45.8%)
	7 (Severely frail)	6 (25%)
Capacity to consent	Yes	15 (62.5%)
	No	9 (37.5%)
ASB status	ASB	8 (33.3%)
	No ASB	16 (66.7%)
Purity of growth on culture	No growth	4 (16.7%)
	Pure	10 (41.7%)
	1 predominant	4 (16.7%)
	Mixed 2	2 (8.3%)
	$>$ 2 mixed	4 (16.7%)

Table 6.5: Characteristics of the participants (n=24) selected to provide weekly samples whilst asymptomatic.

8 of the 24 (33.3%) participants (all female) in the repeat sampling group met our ASB definition with their baseline culture, but 11 overall (45.8%) had ASB at at least one time point (10 female, 1 male). Two participants had ASB in all five repeat samples. Seven participants had at least one change in ASB status over the five week sampling period. One male participant had no growth in all samples collected.

Repeat sampling participant	Sex	Baseline	Week 1	Week 2	Week 3	Week 4
1	Female	ASB	ASB	ASB	ASB	ASB
2	Female	ASB	ASB	ASB	ASB	ASB
3	Female	ASB	ASB		ASB	ASB
4	Female	ASB	ASB			
5	Female	ASB	ASB			
6	Female	ASB				
7	Female	ASB				
8	Female	ASB				
9	Female				ASB	
10	Male				ASB	
11	Female				ASB	
12	Female					
13	Female					
14	Male					
15	Female					
16	Male					
17	Male					
18	Male					
19	Male					
20	Male					
21	Male					
22	Female					
23	Male					
24	Female					

Key

ASB	ASB
	Bacterial growth, not meeting ASB definition
	No growth
	No sample
	Not processed

Figure 6.3: Heat map showing purity of growth on culture for the 5 weeks of asymptomatic sampling. (See Section 6.4.2.1 for ASB definition)

6.5.3.1 Microbiology results for repeat samples

Of the 11 participants with ASB at at least one time point, 7 had predominant or pure growth of *E. coli*, 3 had *Klebsiella pneumoniae* and one had *Streptococcus agalactiae*. All participants with ASB at more than one time point had the same predominant bacteria in all samples meeting the ASB definition. Of the those with no samples that met the ASB defintion, there was variation seen in the nature of organisms grown from week to week across participants. One participant had no growth in all samples collected and one participant had a mix of two species in all. For the remainder, there was at least one change in purity of growth over the five weeks of sampling. 13 participants had *E. coli* growth, and 7 had *Klebsiella* growth at some level in one or more samples.

6.5.4 Association between baseline ASB and subsequent possible UTI

7 of the 26 (26.9%) with ASB at baseline went on to have a possible UTI episode. Serial culture results in these seven participants are shown in Figure 6.4. Three of those with ASB had at least one of the same bacteria grown at baseline growing in subsequent cultures

collected during possible UTI episodes (participants 8, 9 and 13 in Figure 6.4). Participant 8 had pure growth of the same organism (*Klebsiella pneumoniae*) when asymptomatic, and in urine taken at all three visits associated with the subsequent possible UTI. In contrast, participant 10 had *Klebsiella pneumoniae* growing in the urine when asymptomatic at baseline, but a different organism (*Enterococci*) growing during their first possible UTI episode, and predominantly *Klebsiella oxytoca* in the second episode.

6.6 Discussion

6.6.1 Summary of findings

Nearly a quarter of participants experienced at least one possible UTI (as suspected by care home staff) during follow up. 50% of these episodes were associated with symptoms and signs typically associated with UTI, and 37.5% were associated with an acute functional decline. All but one episode resulted in at least one antibiotic prescription. There were two episodes resulting in hospital admissions, two in end-of-life care and one in death.

21% of the urine samples collected during the onset visit of a possible UTI episode were positive, according to the laboratory definition, but most of the samples were collected after antibiotics had started. A higher proportion were positive at the day 14 and 28 follow up visits. For some participants symptoms persisted despite a negative urine culture, whilst in others there was a return to a positive culture after an antibiotic course, despite a resolution of symptoms.

34% of the cohort met our ASB definition in their baseline urine sample, and sex was the only statistically significant risk factor. 24 participants were selected to provide weekly samples for the first five weeks of follow up whilst asymptomatic. Two of these participants met the ASB definition in all of their repeat samples and seven participants had at least one change in ASB status over the five week period.

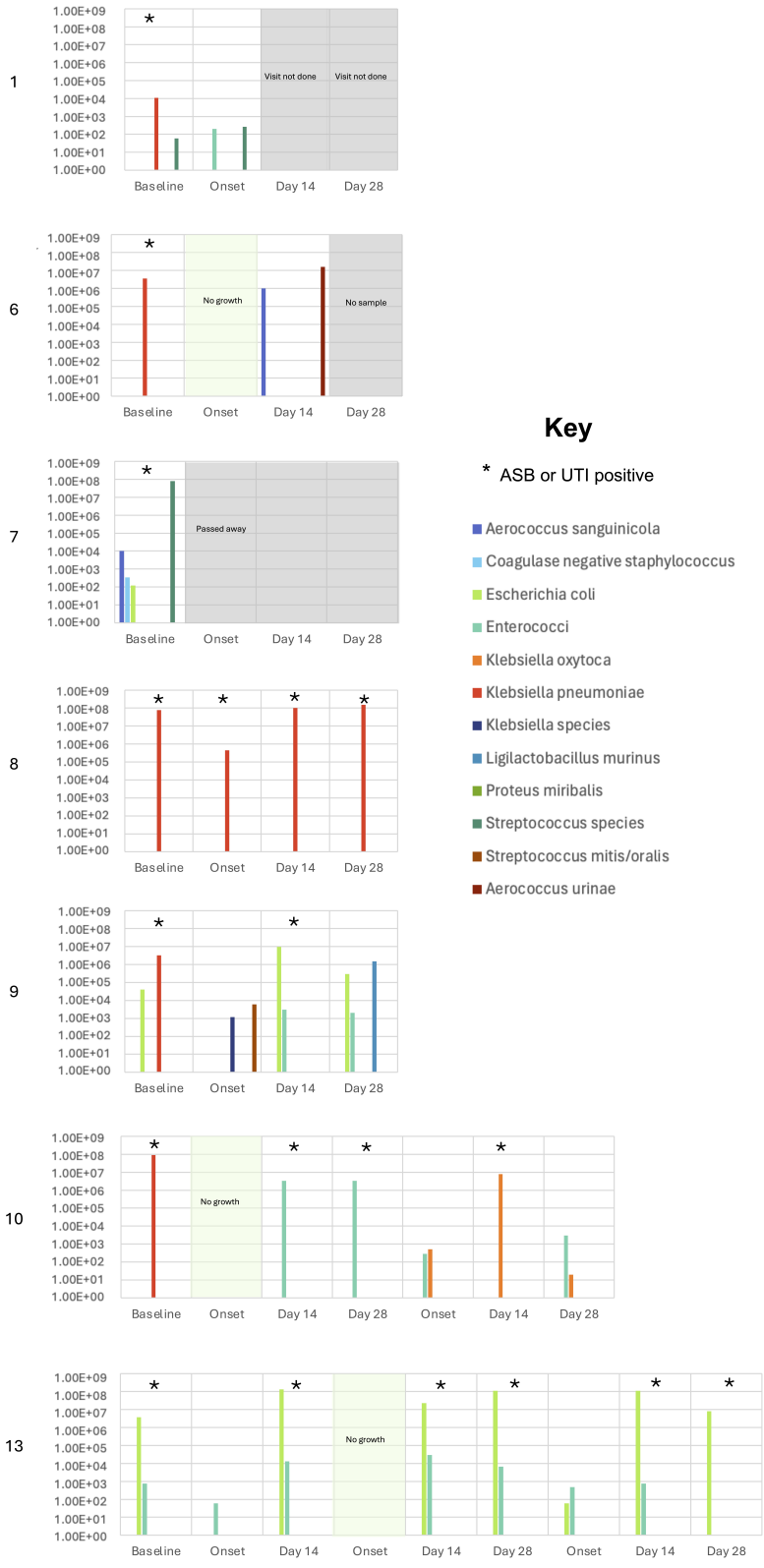


Figure 6.4: Culture results for the 7 participants who experienced at least one possible UTI during follow up, and had ASB at baseline. Y axis scale is logarithmic. * indicates culture is 'positive' for ASB or UTI. (See Section 6.4.2.1 for definitions)

6.6.2 Comparison with existing evidence

A prospective study of 1263 care home residents from 11 care homes in Belgium captured information about care home suspected UTI over 3 months of follow up.[126] During this time there were 137 episodes, but only 16 of these met the authors strict definition for 'true UTI'; a minimum number of signs/symptoms and a positive urine culture. Although strong smelling urine was the most common symptom for care homes to suspect UTI, the only symptoms that predicted a 'true UTI' were acute dysuria and acute suprapubic pain. Participants had typical UTI symptoms in 46.7% of suspected episodes, similar to the proportion in our study. The study was limited in their small number of 'true UTI' episodes and the fact that some of the symptoms they explored were also in their reference definition. Their definition may also not be applicable to those living with dementia who cannot express symptoms.

Regarding ASB, a study of a single large care home in Turkey collected samples at two monthly intervals and followed the cohort of 197 residents for a year.[53] There were no differences in the number of people experiencing urosepsis from those who had or did not have ASB at the beginning of the study, although mortality at one year was higher in those with ASB. A similar difference in mortality was demonstrated in a study of a single large care home in the USA where urine samples were collected every two weeks from all residents for up to 18 months; mean samples collected per participant was 23.[54] In both studies, it was postulated that differences in mortality were likely due to ASB being associated with other risk factors, and is therefore a marker of overall vulnerability. In the US study the authors broadly describe the natural history of ASB over time; 13% of their cohort had persistent ASB in all samples, 35% had no positive culture result for any sample, and the remainder had transient ASB. However, they did not describe how cultures when asymptomatic relate to the UTI episodes experienced by the cohort. Authors of a further US study describe these three ASB states similarly in a cohort of male veterans residing in a single large care home where samples were taken every three months from 1 to 4.5 years. Our study is the first with evidence that urine culture results can vary as often as weekly, and that gives detailed comparisons between asymptomatic and subsequent symptomatic samples.

6.6.3 Strengths and limitations

This is the first study of care home residents to compare culture results taken at different time points from the same participants when both asymptomatic and experiencing a possible UTI. However, our cohort was too small to be able to calculate associations, for example, between symptom patterns and outcomes. Our repeat sampling group was selected to capture a range of participant and sample characteristics. Although we are able to describe patterns with changes in ASB status, as a selected sample, it is not generalisable. The impact of sample contamination also remains unclear and therefore how much of the ASB identified is actually bacteria from the perineum, rather than colonising the urinary tract.

6.6.4 Implications for future research and practice

The clinical management of the 24 possible UTI episodes indicates that current practice does not conform to existing guidelines. 13 of the episodes had a urine dipstick result recorded in the care home record, despite this not being recommended in adults over 65 years.[40, 41] All dipsticks recorded had a positive result, which may represent the confirmation bias of the care home staff. A urine culture had not been requested by the clinical team for half of the episodes, despite the UKHSA guidance that this should be done for all suspected UTI in this age group.[41] This included 3 of the 4 participants who had recurrent UTI episodes during the course of the study. Finally, antibiotic duration was six or seven days for 11 female participants treated for possible UTI. This goes against the NICE guideline, which recommends just three days for all women over 16 years of age [61]. However, the UK is one of the few places in Europe where such a short duration is recommended, without modification for those at risk of serious illness.[127] A UTI diagnosis and management guideline tailored to the care home population may help support decision making in the future.

In samples collected from possible episodes of UTI for some participants, the urine showed a return to 'positivity' within a few weeks of antibiotic treatment. It is unclear whether this represents re-establishment of their usual asymptomatic carriage (ie. the urine findings are incidental, and UTI was not the cause of their symptoms) or incomplete treatment/recurrence of a UTI. In addition, some of the participants with a positive culture

taken at baseline when asymptomatic had the same organisms growing in subsequent possible UTI episodes. Does this mean that bacteria that colonise without causing symptoms subsequently develop pathogenicity? Or does a person's 'usual' *E. coli*, for example, get outcompeted by a different pathogenic strain? Or, is it that the person has ASB and the symptoms have been misattributed to UTI? Finally, could some people have UTI all along, but their symptoms are missed or not expressed? Metagenomic analysis of bacteria taken at different time points could help us understand this more; this is planned as a further exploratory analysis of our samples.

Our exploratory results also indicate that some care home residents have weekly changes in bacterial growth from urine culture. Changes were seen between ASB states as quickly as one week to the next. This challenges the concept of ASB as a stable, binary condition in care home residents, and calls into question the relevance of the various ASB definitions described in Chapter 1 (Figure 1.2). These findings also indicate that an isolated urine culture in an asymptomatic care home resident is very unlikely to be helpful. However, it remains unclear how much of the microbiological variation over time may be predictable within an individual, and/or how much is related to sample contamination in this population. Frequent serial sampling in a large number of care home residents would be required to definitively answer these questions.

6.7 Conclusions

This study provides early insights into possible rapid changes in the urine microbiome over time in both symptomatic and asymptomatic care home residents, potentially further complicating the challenge of UTI diagnosis. An isolated urine sample in an asymptomatic care home resident is unlikely to be helpful and the concept of ASB as a static, binary condition may not be applicable to this population. Further research is needed to advance our understanding of the urine microbiome in care home residents and the microbiological and physiological processes underpinning their possible UTI episodes.

6.8 Summary of chapter

This exploratory work has provided new insights into the potential complexity of the urine microbiome of care home residents and has generated new research questions to explore in future studies. In the next chapter I describe how a final approach that may improve UTI diagnosis in care home residents, novel POCTs for UTI, was also explored as part of the DISCO UTI study.

Chapter 7

Exploring the use of novel point-of-care tests for diagnosing UTI in care homes.

7.1 Overview of chapter

In Chapter 1 I noted that while several novel POCTs have been developed for the diagnosis of UTI, none have yet been evaluated in a care home setting. In Chapter 3 I described how care home staff currently lack accurate tools to investigate when someone is unwell and use urine dipsticks to fill an information void. I also described care home staff willingness to do additional point-of-care testing to facilitate earlier diagnosis of unwell residents. In this chapter I describe the evaluation of three novel POCTs in the DISCO UTI cohort study using urine samples collected during possible UTI episodes. I describe the feasibility of introducing the tests into a care home study, explore the views of research and care home staff on the usability and acceptability of these specific tests in care homes, and compare the POCT results with urine microscopy and culture performed in the laboratory.

7.2 Background and rationale

UK guidelines recommend the use of the urine dipstick to increase diagnostic accuracy when assessing people under 65 years of age in those where the diagnosis of UTI is less clear.[40,

41] Part of the challenge of diagnosing UTI in older people in the care home setting, where dipsticks are not recommended, is the lack of alternative rapid tests. The use of the urine dipstick in this population, where the prevalence of ASB is high, increases the risk of false positives and the use of unnecessary antibiotics, which drives AMR. Novel approaches to rapid diagnostic testing for UTI are one strategy that may improve antimicrobial stewardship in care homes.

Initiatives like the Longitude Prize have encouraged innovation to tackle AMR; its winner in 2024 was the Sysmex Astrego PA-100 analyser, which detects bacteriuria and provides antibiotic sensitivities in 45 minutes. Several additional emerging UTI POCTs have shown promise in younger people.[128] Whilst some, including the Sysmex Astrego PA-100, are currently being evaluated in primary care in the UK,[77] none have yet been evaluated in the care home population, where challenges associated with sample acquisition and contamination could affect the precision/clinical use of results. Carrying out a fully powered diagnostic accuracy study in care homes would help determine which test(s) are able to improve diagnostic accuracy in this setting. However, there may be unknown barriers to doing this form of study in care homes.

An early indication of the performance of promising novel POCTs in care home residents, particularly those that seem to be able to differentiate between ASB and infection, could help estimate parameters for a future study as well as focus further POCT development. Understanding POCT acceptability and usability by care home staff is critical to ensure that new tests will be fit for this setting. An evaluation of three novel POCTs for UTI was therefore embedded in the DISCO UTI feasibility cohort study.

7.3 Aims and objectives

7.3.1 Aim

Establish the feasibility of carrying out a diagnostic accuracy study of novel POCTs for UTI in older adults living in UK care homes, and the acceptability of these diagnostics to care

home staff.

7.3.2 Objectives

- To describe the process of introducing POCTs for diagnostic evaluation into a cohort study of care home residents.
- To describe the proportion of eligible participants who had the POCT evaluation, and, if available tests were not used, the reasons why.
- To explore care home staff views on potential acceptability and usability of the POCTs.
- To explore research staff views on study processes and usability of the POCTs.
- To identify modifications needed to improve study design for a future definitive study.
- To describe the sensitivity and specificity of each included POCT.

7.4 Methods

The POCT evaluation was embedded in the DISCO UTI study. The methods of the DISCO UTI study including participant recruitment, timing of research visits, data collection and sample collection are fully described in Chapter 5 (Section 5.4).

7.4.1 Overview

Urine samples collected from participants with possible UTI (onset and day 28 visits) were tested by the research staff using up to three POCTs. Results were for research purposes only, and were not shared with care home staff who had no access to, and did not use the POCTs. The views of care home and research staff on the usability and acceptability of the tests were explored in focus groups.

7.4.2 Feasibility methods

Dates of key milestones for each included POCT were recorded including date of supply agreement, date of supply and date tests were introduced into the study.

For each participant visit eligible for a POCT evaluation, the index test(s) and results were recorded in the eCRF. The explanation as to why a POCT was not used if it was available was also recorded.

7.4.3 Qualitative methods: feasibility, acceptability and usability

We used focus groups with care home staff and research staff as this is an efficient way to gather multiple perspectives and allowed exploration of points of consensus and disagreement. Topic guides were developed from the existing literature on POCTs, study evaluation and the experiences of the research team in overseeing the research. (See Appendix E.1 for the topic guide for care home staff and Appendix C.3 for the topic guide for research staff). Data were analysed thematically.

7.4.3.1 Recruitment and data collection

We asked one care home site to advertise the focus group amongst its staff with written information. Recruiting from one site was a pragmatic decision, as it was necessary for the group interview to be in person (so that participants could try out the tests) and the different sites were not geographically close. Care home staff were reimbursed with a £20 voucher for their time, to enhance recruitment. During the focus group, participants were given an explanation of how the tests worked, a demonstration of their use, a printed reference sheet (see Appendix E.2), and were also able to handle/try out the devices on dummy samples.

We also invited research staff who had supported the study to participate in an online focus group. They were not reimbursed for their time.

Both focus groups followed a flexible topic guide and were digitally audio recorded. Recordings were transcribed verbatim by an approved professional transcription service.

7.4.3.2 Data analysis

A pragmatic approach to thematic analysis was used involving the stages of familiarisation, generating initial codes, combining codes to create categories, reviewing the material in the categories for explanation and then exploring how the categories combine to support emerging narratives. An iterative approach was taken; re-coding earlier interviews in the light of ongoing analysis and early analysis bringing out topics to be added to the topic guide. NVivo software was used to support data management and analysis.

7.4.4 Exploratory: diagnostic accuracy methods

7.4.4.1 Population

The exploratory prospective diagnostic accuracy study was embedded in the DISCO UTI cohort study in which 81 care home residents were recruited from 8 care homes in England and followed up for up to a year. The eligibility criteria and the recruitment strategy for participants in the cohort are detailed in Chapter 5. To be eligible for the diagnostic accuracy study, participants had to be experiencing a 'possible UTI', defined as any situation in which staff had decided to consult a healthcare professional because they had detected a change in the resident or their urine and believed that a UTI was a likely cause. (See Chapter 5.4.7.2) All participants consented to the diagnostic accuracy study when they were recruited to the cohort. Urine samples collected in the onset and day 28 visits associated with the possible UTI were tested.

7.4.4.2 Index tests

There were three novel POCTs for UTI evaluated (for images, see Appendix E.2). Devices were loaned and consumables were provided free of charge to use in the study by POCT manufacturers. Training was approved or delivered by the POCT manufacturers. All POCTs were used by research staff according to the manufacturers' instructions. POCTs were neither used nor accessible to care home staff. Index test results were not shared with participants, care home staff or the usual healthcare team. No specific instructions were given to research staff about the order in which tests were run, if more than one POCT was available.

Utriplex lateral flow test kits (prototype)

This is a qualitative, single use (disposable) lateral flow test manufactured by Mologic Ltd, trading as Global Access Diagnostics. It is not yet certified in the UK or on the market. It detects a combination of urinary biomarkers: matrix metalloproteinase-8 (MMP8) and human neutrophil elastase (HNE). Each test is individually packaged. During testing, the test wick is held in the urine sample for 15 seconds. A binary result (positive/negative) appears as a combination of lines in the results window, similar to a pregnancy test. Results are read by eye after five minutes.

Tests were delivered in batches to the two regions that hosted the study (Thames Valley and Wessex). Batches were checked with positive and negative external quality control materials before being used. The test was carried out by research staff in the care home during the study visit, with the result recorded in the eCRF. Expiration date and colour of the silica control beads was recorded on opening. If the device failed (no lines or no control line) research staff were asked to record this and then repeat the test. Utriplex tests were available at all participating sites because the visiting research team carried supplies to visits.

Lodestar DX

This is a molecular test using loop-mediated isothermal amplification (LAMP) technology, manufactured by Llusern Scientific. It is not yet certified in the UK or on the market. It consists of a UTI test panel for six of the most common uropathogens (*Escherichia coli, Klebsiella, Proteus mirabilis, Staphylococcus saprophyticus, Enterococcus, Pseudomonas aeruginosa*) and an electronic reader device which runs and reads the reactions and converts to a positive or negative result for each pathogen. 10 microlitres (µl) of urine is mixed with a diluent and pipetted into tubes before being inserted into the device. Results are displayed via lights on a display (red – detected, green – not detected) after 35 minutes. The test can be used with urine samples collected on the same calendar day, regardless of the time elapsed since collection.

Four Lodestar DX devices were loaned to the study. Control materials, test strips and

diluent were stored refrigerated at 4 degrees C. Each device was checked with positive and negative external quality control materials before being used. In the Thames Valley region research nurses took the devices by car to research visits, and the sites stored the test strips and diluent in their clinical fridges at 4 degrees. The tests were carried out in the care home and results recorded in the eCRF. In the Wessex region, the devices, test strips, and diluent were stored in central clinical research offices; the test strips and diluent were stored at 4 degrees. Urine samples collected at site visits were brought to the offices to be tested, and results recorded in the eCRF. If the device failed or the results were invalid, research staff were asked to repeat the test. Lodestar DX tests were possible for participants in all sites.

Astrego PA-100 analyser with the PA AST panel U0501 (Sysmex Astrego)
Astrego PA-100, manufactured by Sysmex, uses a nanofluidic chip to trap single bacteria from a urine sample in nanochannels, then rapidly tests their growth against different antibiotics. It has a Conformité Européene (CE) mark and is on the market in the UK and Europe. 400 µl of urine is pipetted into a single use cartridge that is inserted into the analyser. The analyser detects bacteriuria at concentrations greater than 5 x 10^4 CFU/ml within 15 minutes. If positive for bacteriuria, it then assesses the susceptibility of the bacteria to five antibiotics (co-amoxiclav, ciprofloxacin, fosfomycin, nitrofurantoin, trimethoprim). Full results take 45 minutes and are shown on a digital display. It requires fresh urine (<30 minutes old) and cannot be used if the patient is taking antibiotics.

Two Astrego PA-100 devices were loaned to the study. These are large and not easily portable. In the Thames Valley region, one was set up in the site with the most participants, and was therefore only available to participants in this care home if they experienced a possible UTI. Cartridges were stored at the site. In Wessex the device was set up and cartridges stored in one central research office and samples were brought to the office for testing. All care homes were within a 20 minute drive of the office and therefore Astrego PA-100 was available to participants in all Wessex sites. Devices in

both locations underwent monthly quality control testing by research staff. Results were recorded in the eCRF by research staff.

7.4.4.3 Reference test

The reference test was enhanced urine microscopy and culture carried out at SACU, as described in Chapter 6.4.1. The reference test was usually carried out several days after the index test due to time spent in transit. The results were recorded as 'positive' if the result indicated a probable or possible UTI based on the SMI on urine investigation.[73] Staff at SACU were blinded to any information about the participant, clinical symptoms or signs relating to the possible UTI episode, and the results of the index tests. Results were recorded in the eCRF. Results of the reference test were not shared with the rest of the research staff, the participant, the care home or the usual clinical team.

7.4.4.4 Sample collection and processing

As described in Chapter 5.4.9.1, urine samples were collected from participants with support from the care home staff and/or the research team. Urine samples were divided, with priority given to a sample for usual clinical care. The order of priority for the research samples was 1) clinical sample (if requested), 2) research microbiology analysis (boric acid tube), and 3) research POCTs.

7.4.4.5 Sample size calculation

There was no sample size calculation as this was an exploratory analysis.

7.4.4.6 Statistical analysis

Sensitivity, specificity and predictive values with 95% CIs were calculated for each POCT at each time point, if possible, in Stata BE for Mac.

7.5 Results

7.5.1 Feasibility

Although discussions with the POCT companies had started prior to the study opening (September 2023), it took longer than expected to get the supply agreements in place. There were additional delays due to time taken for devices/consumables to be received and the research team to be trained. Delays are summarised in Table 7.1.

Test	Study open	Agreement	Delay since study opening (days)	In use	Delay since agreement (days)	Total delay (days)
Utriplex	22/09/2023	08/01/2024	108	22/02/2024	45	153
Lodestar DX	23/09/2023	19/01/2024	118	18/04/2024	90	208
Astrego PA-100	24/09/2023	05/03/2024	164	13/05/2024	69	233

Table 7.1: Time taken for each POCT to be used in the study.

The timeline in Figure 7.1 indicates when each POCT became available for use in the study compared to when the possible UTI events occurred during follow up. Of the 24 possible UTI episodes, Utriplex was available for 19, Lodestar DX for 14, and Astrego PA-100 for 10.

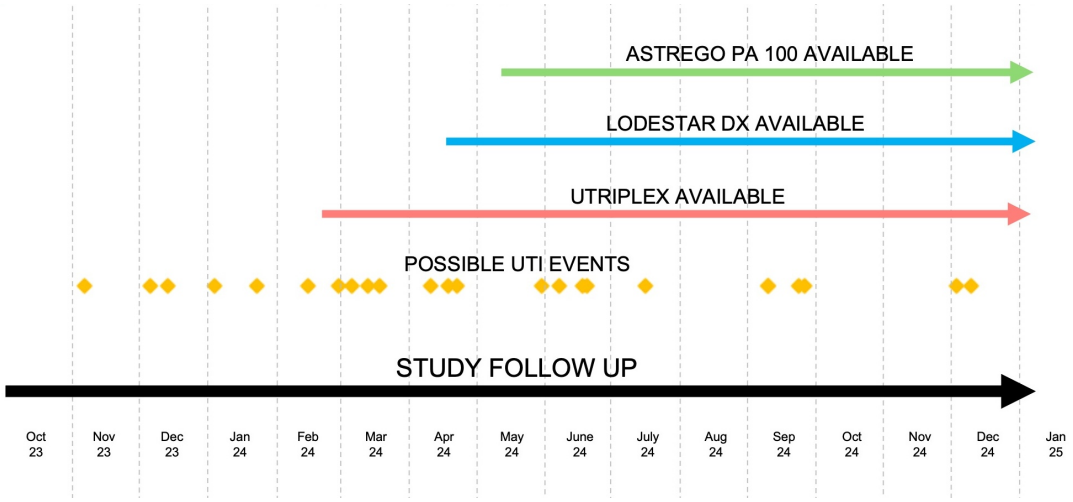


Figure 7.1: Timeline of DISCO UTI participant follow up, indicating when possible UTI events occured (yellow diamonds) and when each of the include POCTs became available for use by the research team.

For each possible UTI episode, the POCTs could have been used at two time points (onset and day 28). Reasons for tests not being done, if available, are summarised in Table 7.2.

	Utriplex		**Lodestar DX**		**Astrego PA-100**		**Total**
	Onset	D28	Onset	D28	Onset	D28	
Total tests possible	18	19	14	14	10	10	85
Test not done	7	8	8	5	9	2	39
Withdrawn	1	3	1	1	1	1	8
Unable to get sample	3	2	3	1	3	1	13
Unable to get to device (in central office)	0	0	1	0	1	0	2
On antibiotics	0	0	0	0	1	0	1
No consumables	0	0	0	1	0	0	1
Sample too small	2	0	2	0	2	0	6
Visit not done	0	3	0	2	1	0	6
No reason	1	0	1	0	0	0	2
Proportion tests done of possible (%)	**61**	**58**	**43**	**64**	**10**	**80**	**54**

Table 7.2: Reasons for POCTs not being done at eligible visits.

7.6 Qualitative findings

Characteristics of the care home staff (6) and research staff (8) who participated in the focus group are summarised in Table 7.3.

7.6.1 Theme 1: Potential usability of individual tests within a care home setting

7.6.1.1 Utriplex

Care home staff liked the simplicity of the Utriplex test, feeling that it would be easy to use and to read as it was a binary result. They felt it was less prone to user/interpretation error than the urine dipstick they were familiar with. From a practical perspective they

Group	Characteristic		Number
Care home staff (n=6)	Sex	Male	2
		Female	4
	Job role	Deputy manager	1
		Senior carer	1
		Carer	4
Research staff (n=8)	Sex	Male	0
		Female	8
	Job role	Research nurse	4
		Research clinical assistant	4
	Region	Thames Valley	2
		Wessex	6

Table 7.3: Characteristics of the participants in the two focus groups.

liked how comfortable it was to hold and how the risk of getting urine on themselves was lower compared with a dipstick. They also commented that the training burden would be minimal and that less skilled staff would therefore be able to use it.

> *'Because the dipstick, if you don't look it clearly, you won't know which of them fall on each of the colour to know the results. So you need to look at it critically to get the results, but with this it's simple, straight and forward.'*
>
> Female care home carer

Research staff also valued ease of use but said in practice it was hard to read the result with some of the 'positive' lines appearing very faintly.

> *'We've had one like that with a big clear red line but we've also had two or three where you're like, "Well there's a slight shadow, can you see that? Is that my eyes? Is it tricking me?"...[Name] and I were debating for hours. I was like, "I can see it." She was like, "I can't see it." And I was like, "I can definitely see something."'*
>
> Female clinical research assistant

Both care home and research staff thought that the speed of the test was a positive feature. Care home staff commented that speed to result meant that if something went wrong with the test (ie. invalid result) they would be able to repeat it quickly.

7.6.1.2 Lodestar DX

Care home staff perceived this test to be more complex than Utriplex or a dipstick because of the steps required in the diluting stage. They were concerned about the number of steps and how each of these added a point at which something could go wrong. They said the skills required (ie. pipetting) were more technical than they were used to - but that they would be happy to learn how to do this with more training. They felt any training would need to be in depth, and also that staff would have to be continually using the test or else there was a risk of forgetting the steps. One of the biggest concerns from care home staff was the time that would be required to do the test and potentially repeating it if it went wrong. This would divert staff away from other critical jobs.

Care home staff liked the concept of being able to detect different bacteria in the urine, but thought that this result would be more interesting to a GP than themselves. However, they were not sure whether knowing which bacteria were present would help them get a prescription for the correct antibiotic from the GP more quickly. They wanted the device to be able to print or send electronically the result for their records.

Research staff felt the test, whilst more complex to use, was something they were able to pick up relatively easily as experienced clinical researchers. They were less convinced that care home staff would be able to use it easily. The research team similarly felt there was a risk of deskilling quickly unless you were using the test all the time.

> *'So yes, if you did it once or twice and you remember how to do it, but then if you've got 30 members of staff who may well be the ones doing it, they probably wouldn't all do it often enough to know it. So unless you really had some kind of champions that knew how to do it, but if they weren't in that day, it's quite a difficult one to just sort of pick up and do if you hadn't done it before'.*
>
> Female research nurse

They also felt that reading the test was confusing and that it was not intuitive to understand the meaning of the green and red lights.

> *'It would be nice to know that the control and positive being green was right. Not the green and red, I think that is confusing.'*
> Female clinical research assistant

Research staff also highlighted the relatively short shelf life on the consumables, which also had to be kept at a precise temperature in the fridge. They felt this may impact its ability to be easily adopted by care homes.

> *'The only thing is the shelf life of the tests is only three months, so you'd have to remember wouldn't you to be ordering more...Reordering them every couple of months really and you're ordering a lot.'*
> Female research nurse

7.6.1.3 Astrego PA-100

Care home staff felt that this device appeared simple to use and to read. Like Utriplex, they felt that this would require less training, and could mean that it was accessible to less skilled staff. However, similar to Lodestar DX, they were worried about the length of time to a final result, and in particular how this would impact them if the test needed to be repeated. They wanted the result to either be able to be printed or sent to them electronically for their records. Overall, they perceived the biggest benefit of this test was that it could reduce the time taken for a GP to prescribe the correct antibiotic for an unwell resident, but only if there was buy in/support from the GP for them to be using the test.

> *'Just because of the delay, to avoid delay treatment and not having a try, let's try this one [antibiotic] or let's try that one, so it's more accurate in terms of what happens.'*
> Female care home deputy manager

Research staff felt the PA-100 was simple to use and could easily be adopted by care home staff. However, they commented that the error codes and symbols that appeared on the

screen were not straightforward to interpret.

> *'I haven't really interpreted them hugely 'cause we've just filled it in on REDCap. So what 'one book' or 'two book' means, I don't know but then I haven't needed to know, if you know what I mean. I think if you had a prompt next to you telling you what all those things meant. They haven't developed – from what I can see there isn't like a thing that says, 'This means this, this means this.' So I haven't hugely digested that information but obviously if you had a tool that told you that. Pretty straightforward.'*
>
> Female clinical research assistant

Research staff also commented that the size of the device would limit its usability in some care homes.

> *'I just think it's the space. It's a big machine isn't it and some of these – you think when you look at some of the little clinical spaces they have, they've tiny little cupboard rooms haven't they really...'*
>
> Female research nurse

7.6.2 Theme 2: Future integration of UTI POCTs in a care home setting

7.6.2.1 Considerations for routine clinical use

Care home staff described how a new POCT would be used by them to provide additional information in their contacts with healthcare professionals if they were worried about a resident. Their goal was to get help and any treatment needed by the resident quickly. Care home staff described their time as pressured and having to manage lots of competing tasks. For this reason, speed of use of any new POCT was critical. They felt that five minutes was ideal and that ten minutes would be the maximum they would want to spend testing one person's urine.

Staff also expressed a strong preference for pad urine samples to be able to be processed by POCTs in the future - this would mean that they were possible to be used on all residents, including those with incontinence issues. This would also free up care home staff time due

to the work and time burden of trying to collect urine samples.

> *'Because even if you have some sort of mobility, to give a proper sample is difficult and time consuming because you need to clean them, not always they are able to cope with all the process. It is a lot.'*
>
> Female deputy care home manager

Care home staff were clear that training and support for any new POCT would be critical to their adoption and use. The extra information provided by some of the example POCTs (eg. ID of bacteria, antibiotic sensitivities) was not something they could personally derive value from, and was only useful if acted on by a clinician/prescriber. They said that there would need to be buy in from multiple parties for novel POCTs to be used effectively in the future.

> *'They need to have an agreement reached with, let's say, the pharmacy, the GP has already agreed with the pharmacy and the care home that since you're having this and you're sure you can do it, you have to do the test, send to the pharmacy, get the prescription. If that cannot be reached, then I think it's pointless. The main reason for this one [Astrego PA-100] is so that you can get your prescription first and improve the quality of life of the resident. So the agreement has to be there between all parties involved.'*
>
> Male care home senior carer

Finally, staff noted that all of the example POCTs used single use plastic consumables. They felt that POCT developers should consider the environmental impact of the waste generated by their tests. The cost of the test and disposing of the waste was also considered important by a deputy care home manager who took part in the focus group.

7.6.2.2 Considerations for future research

The focus group with research staff highlighted important considerations for a potential future diagnostic accuracy study on UTI POCTs in care homes. They described how the addition of the POCTs to the DISCO UTI study had resulted in complexity and increased time per research visit. This had had a significant impact on staffing requirements.

'Getting back to site and doing all three tests concurrently . . . the Llusern needed to warm up for a while. . . we usually had two or all of us actually there if we happened to be in because then we could all be doing one each. Like on Monday we had two samples to process across – well we did five tests because one could do three and one could do two of them. So that was the three of us sort of going round in circles. So that certainly added, if you think that's three people's worth of time, probably took us an hour and a half. So that's an extra four and a half hours of work.'

Female research nurse

In addition, they had to consider the volume of the sample with more urine needed, particularly once all three POCTs were in use. They explained how they had realised during the study not to throw away any excess sample in case of test failures.

'So then we just had to repeat it, but thankfully we kept the sample until – we always keep the samples until three tests have been done and then the next one was fine.'

Female clinical research assistant

From the study perspective, Astrego PA-100 had been the hardest POCT to include due to the time constraints of the sample (the requirement to be tested within 30 minutes of being produced) and the size/lack of portability of the machine. One device was based in a central clinical research office which involved samples being driven quickly back to be processed in time. However, the team needed to be on site when the sample was actually produced for this to work.

'We had that this week where we had one on day one and one on day 28, so trying to synchronise them to do the wee samples, almost at the same time so that we could then rush back. It was just impossible.'

Female research nurse

They suggested that in future studies it would be sensible to just use one device per home in a clustered design. This would reduce some of the complexity and the total sample volume

required.

> *'I would say if you were gonna trial the point of care tests in care homes, I'd do them one at a time or one in some care homes, one in another, one in another, rather than trying to get them to do multiple ones 'cause that is quite complex and time consuming. But yeah there's definitely a question that's worth answering.'*
> Female research nurse

7.6.3 Individual test performance

Test performance for each index test is summarised in Table 7.4.

7.6.3.1 Utriplex

Utriplex tests were evaluated in 11 possible UTI episodes at onset and 12 at day 28. At onset, two of the tested samples were positive on microscopy and culture in the laboratory, and at day 28 six samples were positive. One Utriplex test failed (no control line), following this, a second test was successfully used on the same sample.

For onset visit urine samples sensitivity was 100% (95% CI: 15.8 - 100%) and specificity was 33.3% (95% CI: 7.5 - 70.1%). PPV was 25% (95% CI: 3.2 - 65.1%) and NPV 100% (95% CI: 29.2 - 100%).

For day 28 urine samples sensitivity was 66.5% (95% CI: 22.3 - 95.7%) and specificity was 83.33% (95% CI: 35.9% - 99.6%). PPV was 80.0% (95% CI: 28.4 - 99.5%) and NPV was 71.4% (95% CI: 29.0 - 96.3%).

7.6.3.2 Lodestar DX

Lodestar DX tests were evaluated in five possible UTI episodes at onset and nine at day 28. For onset samples there were two test failures, but no repeat tests were carried out. There are therefore only three valid results.

- One test was positive for *E. coli*, which matched the culture result.

- One test was positive for *Enterococcus*, *Klebsiella* and *E. coli*. The culture showed mixed growth, which included *Enterococcus* and *Pseudomonas* but not *E coli* or *Klebsiella*.

- One test was negative, and the culture result was no growth.

For day 28 samples there was one test failure, which was not repeated. There are therefore 8 valid results. All Lodestar DX tests were positive for at least one bacteria.

Sensitivity of the Lodestar DX test at day 28 was 100% (95% CI: 47.8 - 100%) and specificity was 0% (95% CI: 0% - 70.8%). PPV was 65.5% (95% CI: 24.5 - 91.5%).

7.6.3.3 Astrego PA-100

Astrego PA-100 was evaluated in only one sample at onset, and eight at day 28. At onset both the index and reference tests were positive. Astrego PA-100 reported this as fully sensitive to the panel of antibiotics. The laboratory reported that the *E. coli* cultured was resistant to ciprofloxacin.

There were two test failures on day 28 samples - in both the test was repeated but only one got a subsequent valid result. There are therefore seven valid results in total. Of these, three were positive. Comparing AST results between Astrego PA-100 and the laboratory:

- One Astrego test reported the bacteria were resistant to nitrofurantoin only, though it was close to the clinical breakpoint for ciprofloxacin. The laboratory reported the *E. coli* cultured was fully sensitive.

- One Astrego test reported the bacteria were resistant to ciprofloxacin, trimethoprim and fosfomycin. The laboratory reported that the *E. coli* cultured was resistant to ciprofloxacin, trimethoprim, pivmecillinam, and cefalexin, but sensitive to fosfomycin.

- One Astrego test reported the bacteria were resistant to trimethoprim. Co-amoxiclav, fosfomycin and nitrofurantoin were not applicable (though low growth rate meant AST

results were not accurate for these). It reported it was sensitive to ciprofloxacin at increased exposure (though there was an interpretation difficulties warning with this result). The laboratory reported the *of Klebsiella pneumoniae* cultured was resistant to trimethoprim, and nitrofurantoin and fosfomycin were unsuitable. It reported that it was sensitive to co-amoxiclav and ciprofloxacin.

Sensitivity of the Astrego test at day 28 was 75% (95% CI: 19.4 - 99.4%) and specificity was 100% (95% CI: 29.2% - 100%). PPV was 100% (95% CI: 29.2 - 100%) and NPV was 75.0% (95% CI: 19.4 - 99.4%).

Index test (POCT)		**Onset**				**Day 28**			
		Reference test (Culture)				**Reference test (Culture)**			
		UTI positive	Pure or one predominant, not meeting UTI criteria	Mixed growth	No growth	UTI positive	Pure or one predominant, not meeting UTI criteria	Mixed growth	No growth
Utriplex	Positive	2	1	3	2	4	0	1	0
	Negative	0	0	1	2	2	0	4	1
Lodestar DX	Positive	1	0	1	0	5	0	3	0
	Negative	0	0	0	1	0	0	0	0
Astrego PA-100	Positive	1	0	0	0	3	0	0	0
	Negative	0	0	0	0	1	0	3	0

Table 7.4: Comparison of each index test with the reference standard at the two time points in the possible UTI episode (onset and day 28).

7.6.3.4 Comparison across POCTs

There were five participants who had their urine tested on all three POCTs at the same visit (all day 28). A table showing how all these results compared to each other and the reference test is shown in Table 7.5. There were two participants for which all tests were in agreement. Utriplex and Astrego PA-100 results matched for all five participants.

		Index tests			Reference test
Visit	**Symptoms**	Utriplex	Lodestar DX	Astrego PA-100	Culture
Day 28	Ongoing	Positive	Positive	Positive	Positive
Day 28	Ongoing	Negative	Positive	Negative	Negative
Day 28	Ongoing	Negative	Positive	Negative	Negative
Day 28	Resolved	Positive	Positive	Positive	Positive
Day 28	Resolved	Negative	Positive	Negative	Positive

Table 7.5: Results of the three POCTs compared to urine culture in the five participants who had their urine tested on all at the same visit.

7.7 Discussion

7.7.1 Summary of findings

Three novel POCTs for UTI were evaluated as part of the DISCO UTI feasibility cohort study in care homes. For all there was a significant delay in their use due to the time taken for supply agreements to be agreed (108 - 168 days after the study opened). Further delays were incurred due to time taken for tests and consumables to be delivered and to train the research staff. Even once available, only 54% of POCTs were done at the eligible 'possible UTI' episode visits. The most common reasons for this were the urine sample not being successfully collected, the participant having been withdrawn or the collected sample being too small.

Research staff described added complexity to research visits once POCTs were added to the study and a considerable increase in staff time per visit. They highlighted difficulties in reading results in some of the included tests that risked misinterpretation. They suggested that for future research on POCTs in care homes it may be wise to limit each home to one POCT to reduce the time and volume of sample needed.

Care home staff said that would be willing to use any of the three novel POCTs if they reduced the time it takes for an unwell resident to receive the necessary treatment. They particularly liked some aspects of the Utriplex test including its simplicity (minimising

training burden) and speed to a result. This would fit in with their broader desire to not divert too much time to testing and could be used by a larger number of staff including those less skilled. For a new test to have the most impact, they said that it ideally would be possible for use on urine collected in incontinence pads. Care home staff were less interested in being able to identify specific bacteria in the urine or knowing antibiotic sensitivities. In the future, they wanted POCT developers to consider the environmental impact of single use plastic consumables.

The small number of tests performed within the study using each POCT limit the way in which the performance data can be interpreted. There were six test failures overall; three of these were not repeated.

7.7.2 Comparison with existing evidence

There is only one other study evaluating the addition of a POCT for improving UTI diagnosis in care homes. This Dutch study found that POCTs for serum C-reactive protein and procalcitonin were not able to distinguish between ASB and UTI in 247 episodes of suspected UTI in care home residents.[103] The model of care for care home residents in the Netherlands differs to those in the UK as there is a resident geriatric physician who takes overall responsibility for tests and treatments. The residents recruited to the study were clinically suspected by a doctor or nurse to have a UTI, which differs to our inclusion criteria of UTI as suspected by care home staff (who may not have a clinical background). The authors used a stringent definition for 'true UTI' taking into account symptoms, signs and urine culture results. Whilst there is an accompanying qualitative paper,[104] this interviewed doctors and nurses about the theoretical value of the serum inflammatory biomarker POCTs before the diagnostic accuracy study took place. There are no data on the views of care home staff on the tests or what would make a good test from their perspective.

7.7.3 Strengths and limitations

This is the first time these novel UTI POCTs have been evaluated in a care home setting. Understanding the feasibility of the tests being used in a care home during possible UTI

episodes as part of a diagnostic accuracy study is a critical first step before considering a fully powered study. Unfortunately, there were considerable delays in deploying the POCTs within the cohort study which contributed to the low numbers of each test being used. A longer lead in could be built into a future study design. However, 35% of the tests possible were not done because either the sample was too small, or no sample could be collected. The urine samples had to be divided to be sent for the reference test (the priority), and up to three POCTs. Reducing the number of POCTs used per site could have improved this, and clustered design was also suggested by the research staff in their focus group as a way of reducing time and complexity per research visit.

Qualitative data give the first views of care home staff on novel UTI POCTs that have the potential to be introduced into care home settings in the near future. There are important messages for manufacturers, researchers and clinical teams about how POCTs should potentially be adapted to make them more suitable for the care home setting, including their use on incontinence pad urine samples. Limitations of the care home staff focus group included that participants all worked in one care home, albeit in different roles, and whilst they were able to interact with the tests in the session, they had not actually used them in real life. The decision to include staff from one site was pragmatic, but findings could have been corroborated if time had allowed a second focus group with staff from another care home. That said, the views of the research team were able to provide some insights on the real world usability of the tests.

The delay in introducing the tests to the study, the low numbers of possible UTI episodes and the low proportion of tests that were possible that were done has resulted in very limited useful data on diagnostic performance. Where sensitivity and specificity could be calculated the confidence intervals are very wide. A larger, fully powered study is needed. In addition, prior to introduction to care homes, it would be important to ascertain the performance of any promising tests run and interpreted by care home staff, rather than trained researchers.

7.7.4 Implications for research and clinical practice

The inability to get a sample in eligible research visits was often due to the participant becoming incontinent, less physically able, or less able to follow instructions during a possible UTI episode. Modifications to the study design that could account for this could be to introduce in-out catheter sampling, which is very unlikely to be acceptable, or to inflate the sample size to allow for missing data. It may be that for POCTs for UTI to be truly viable in the care home setting they either need to be able to work on incontinence pad samples, or use serum biomarkers. If such a test were developed it would be useable for more care home residents, confer advantages in usual care (limiting time taken obtaining urine samples) as well as increasingly the likelihood that tests would actually be done in a future diagnostic accuracy study. The qualitative results have also identified other key priorities from care home staff that POCT developers can use when designing novel products or refining existing technology for use in the care home sector. Their desire for simplicity and speed is an important insight.

Two of the three POCTs included in DISCO UTI are designed to detect bacteriuria. This is important as ASB could impact test utility, similar to a dipstick. However, there may be an advantage in testing urine quickly at point-of-care. For example, it is possible that a POCT for bacteruria may outperform the culture because urine does not spend time in transit, reducing the risk that bacteria from contamination continue to multiply, resulting in fewer false positives. Alternatively, causative bacteria may die in transit to the laboratory resulting in more false negatives compared to rapid testing. POCTs that also test for evidence of host inflammation may be more successful in differentiating between ASB and UTI. Tests that include targets for urinary biomarkers, like Utriplex, may therefore have an advantage in the care home setting. There are several biomarkers with evidence that they may be able to differentiate between ASB and UTI in older adults, but currently only from case-control studies and not real-world settings.[129, 130] We plan to do a further exploratory analysis of urinary biomarkers in samples collected from participants in DISCO UTI.

As outlined in Chapter 1, urine microscopy and culture is an outdated diagnostic method

and is widely considered an imperfect reference standard for UTI. Future research assessing diagnostic accuracy of these tests will need to consider how this can be taken into account either with the statistical analysis or an adapted reference standard. There has been a recent attempt to develop a research reference standard for UTI research, derived through a Delphi exercise.[131] However, this is intended to be applicable to all adults, in all settings and has not yet been validated in a real world population. There are some aspects of this research reference standard that may be challenging to collect from a primary care population, particularly care home residents - like blood cultures and serum blood tests. Further work could be considered to adapt this reference standard for use in care home research.

7.7.5 Conclusions

Care home staff are willing to try novel UTI tests, valuing simplicity and speed. However, we have demonstrated that there are a number of challenges to POCT testing for possible UTI in a diagnostic accuracy study in a care home setting. There are research processes and logistics to improve and the challenges of obtaining urine samples will need to be addressed in any future study.

7.8 Chapter summary

In this chapter I have described the evaluation of three novel POCTs for UTI in the DISCO UTI study. I identified a number of challenges that make the conduct of diagnostic accuracy studies in this setting challenging, and these will need to be taken into account when planning future research. I take forward these findings along with those from preceding chapters to the next and final chapter of this thesis. There I integrate my findings and draw final conclusions from my work.

Chapter 8

Discussion and conclusions

8.1 Overview of chapter

In this final chapter I summarise and synthesise the findings of this thesis, and link these back to the overall aim for the research. I discuss the strengths and limitations of the approach taken. I reflect on some of the challenges encountered with care home research and make some practical suggestions for future research in this setting. Finally, in view of my results, I will explore potential implications for clinical practice, policy and future research.

8.2 Summary of the problem and research aims

The questions at the centre of this thesis arose from the uncertainty that I (and other primary care clinicians) experience when assessing a care home resident presenting with acute functional decline. This is because this non-specific presentation in care home residents is often assumed to be caused by UTI, although other causes are possible. UTI is itself challenging to diagnose in care home residents due to the lack of classic symptoms and signs, and that many live with dementia, which means that a clinical history may not be possible. Changes in urination patterns are difficult to detect in people who experience continence issues and make urine samples difficult to collect. Finally, many care home residents are likely to have ASB, which affects the analysis and interpretation of current

diagnostic tests. As a result, the widely available urine dipstick test is not recommended in care home residents with suspected UTI in UK guidelines. Missing a UTI in care home residents risks possible bloodstream infection, unplanned hospital admissions, and death. However, inappropriate use of antibiotics in the absence of infection adds to the burden of antimicrobial resistance, already high in this group.

It is the overlap between acute functional decline, ASB and UTI and lack of diagnostic tests that gives rise to the diagnostic uncertainty that I and others experience. As it stands, therefore, when a care home resident experiences acute functional decline and a GP is contacted, they are often prescribed antibiotics for a presumed UTI. However, we do not know how many of these patients actually have a UTI and benefit from antibiotics, and for how many the true cause for the decline is missed. It is important to conduct research into this presentation to develop an evidence base that improves the care and outcomes for care home residents, as well as to explore the role for antimicrobial stewardship interventions in this setting.

The overall aim of the thesis was therefore to further explore the relationship between acute functional decline, ASB and UTI in care home residents, as well as consider novel diagnostic approaches, to improve the diagnostic pathway for acute functional decline/care home UTI in the future.

8.3 Summary of key findings by chapter

8.3.1 Chapter 2

I explored the recognition and management of acute functional decline from the perspective of care home staff in a qualitative interview study. Many care home staff described that their initial assessment of someone with an acute functional decline involved checking a urine dipstick, with most considering that UTI was the most likely cause of acute functional decline. They also discussed how the natural history and prognosis of acute functional decline episodes could vary considerably, and how at onset it could be challenging for them

to differentiate a transient fluctuation in functional ability from a more serious illness. Their anxiety about the potential for deterioration and poor outcomes drove some of their help-seeking behaviour. **These results suggested that the association between acute functional decline and UTI likely starts with the initial communication from the care home when they seek help from primary care.**

8.3.2 Chapter 3

Expanding the use of POCTs may be one way of improving the assessment and diagnostic certainty in care home residents presenting with an acute functional decline and/or suspected UTI. I therefore explored the views of care home staff on their use of existing POCTs, and on potentially expanding their use. The urine dipstick was the most widely used POCT, particularly in assessing acute functional decline. Care home staff described wanting to gather information to help understand what was going on but having limited tools to do so, and using positive results as a justification to contact the GP. Some knew that dipsticks were not recommended in older people but few had an understanding of ASB and its impact on the result, and several participants described continuing to use dipsticks despite clear instructions against doing so. The interpretation of a dipstick result varied depending on the index of suspicion for UTI, but only a negative result when there was a low clinical suspicion made them consider other causes for the illness. **These results highlighted the importance of training and support for diagnostic tests in the care homes setting. A lack of awareness of ASB and the impact of pre-test probability on test performance, and a limited appreciation of incorrect classification with false positives or false negatives could potentially risk misuse of any future diagnostic tests.**

8.3.3 Chapter 4

The justification for the age 65 threshold in the UK UTI diagnostic guidelines for using the urine dipstick is the prevalence of ASB in older people, thought to be particularly high in care homes. I presented the findings of a systematic review and meta-analysis of studies measuring the prevalence of ASB in settings relevant to the UK community context

published since 1990. Whilst there was considerable heterogeneity amongst the included studies, including differences in inclusion criteria and definition and measurement of ASB, the results confirmed that prevalence of ASB increases with age and is most prevalent in care homes (0.31, 95% CI: 0.25 to 0.36). **However, this estimate of ASB prevalence in care homes is lower and more precise than that cited in the UKHSA and SIGN guidelines. I suggested that there are likely unmeasured risk factors contributing to the 'care home' risk, and that a better understanding of these may allow a more nuanced decision as to whether an individual's risk of ASB precludes dipstick use in suspected UTI.**

8.3.4 Chapter 5

I presented the feasibility and acceptability results of DISCO UTI, a cohort study I designed and led of 81 care home residents recruited from 8 care homes in England. The cohort were followed up for a median of 255 days and during follow up there were 24 episodes suspected to be UTI by care home staff from 19 (23%) participants. The majority of the data and urine sample collection was successful. In the qualitative evaluation, care home and research staff highlighted the challenges around urine sample collection, which contributed to some of the missing urine samples. **Overall, the study was broadly feasible and acceptable, but I concluded that any future study in this setting would need a significant increase in dedicated research staff time to support it.**

8.3.5 Chapter 6

I described some of the exploratory results from DISCO UTI. Of the 24 episodes suspected to be UTI by care home staff, only 50% were associated with symptoms and signs of UTI. 9/24 (37.5%) of all possible UTI episodes experienced by this cohort could be considered as presenting with an 'acute functional decline'. 23/24 (95.8%) episodes had at least one course of antibiotics prescribed during the 28 day follow up. Some participants had significant bacteriuria in urine samples collected 14 and 28 days after symptom onset, possibly representing recurrent infection or a return to colonisation. Finally,the serial urine cultures from asymptomatic participants indicated that what is grown week to week is variable, which

may represent a dynamic microbiome or contamination from sampling. **This further complicates interpretation of isolated urine cultures in the context of non-specific symptoms like acute functional decline.**

8.3.6 Chapter 7

I presented the findings of the evaluation of three novel POCTs for UTI embedded in the DISCO UTI study. Due to delays in the introduction of the tests into the study and the low number of possible UTI episodes experienced by the cohort during the timeframe available for the research there was not enough data to be able to calculate meaningful diagnostic accuracy of the individual tests. However, an exploration of their potential usability in focus groups with care home and research staff demonstrated the value care home staff put on the simplicity of a test for UTI and the speed to a result. Research staff were able to highlight difficulties in reading results in some of the included tests that risked misinterpretation. **Overall, there was enthusiasm for the novel tests from care home staff. However, this evaluation demonstrated that there were a number of challenges to POCT testing for possible UTI in a diagnostic accuracy study within the care home setting that would need to be addressed in any future study.**

8.4 Synthesis of findings

8.4.1 Overlap between acute functional decline and UTI

In the DISCO UTI cohort **(Chapter 6)**, only 9/24(37.5%) of all care home suspected UTI episodes captured by the study presented with an acute functional decline in the absence of other symptoms. This is lower than I would have expected based on the association between acute functional decline and UTI described by care home staff **(Chapter 2)**, and from my own clinical experience. Potential reasons for this include:

- There is less overlap with acute functional decline and UTI than suspected.
- DISCO UTI did not capture all possible UTI episodes; this is suggested by the drop

off in number of episodes reported over time, and from the observations made by the research team in the qualitative evaluation. **(Chapter 5)**

- The eCRF was filled in by research nurses who may not have been able to easily establish whether changes in functional status had occurred, particularly if no member of staff who knew the participant was available. 3/24 (12.5%) episodes were recorded as 'Don't know' in the prompt about changes in activities in daily living. **(Chapter 6)**

- Care home staff identified other symptoms associated with UTI in participants who actually only presented with an acute functional decline, because they suspected UTI (confirmation bias).

- Care home staff changed their behaviour and reduced their reporting of suspected UTI in people experiencing acute functional decline because they were participating in research ("Hawthorne effect").[132]

In addition, in DISCO UTI we did not monitor participants for acute functional decline outside of episodes suspected to be UTI. It is therefore unknown whether there were other episodes of acute functional decline that occurred in the cohort during follow up that care home staff either felt were insignificant, or for which they considered there to be another more likely cause than UTI. For example, acute functional decline in the context of constipation would not have triggered a follow up visit. I reflect on alternative study designs in Section 8.5.3.

8.4.2 The scale of the problem of asymptomatic bacteriuria

In the systematic review **(Chapter 4)** I calculated the prevalence of ASB in older adult care homes to be 31% (95% CI: 25 to 36%). This is consistent with the baseline prevalence of ASB in the DISCO UTI cohort (32.5%) described in **Chapter 6**. As discussed in **Chapter 4**, this new estimate is lower and more precise than values quoted by current UK guideline documents. I argued that knowledge about true prevalence of ASB and potential impact

of risk factors may allow a clinician to make a more nuanced decision about the use of the urine dipstick in UTI diagnosis on an individual patient level. Whilst I was able to show in the systematic review that female sex is likely to be a risk factor for ASB, I was not able to compare pooled ASB prevalence between sexes in the care home setting. However, if ASB is as low as 8.7% as it was in the small number of male participants of DISCO UTI **(Chapter 6)**, it may even be possible that the dipstick has diagnostic utility for some male care home residents. Determining whether there are increased use cases for a cheap and widely available diagnostic test for UTI is justification for definitive prevalence studies in both community and care home settings. That said, it remains unclear whether considering ASB as binary state is useful for care home residents given the changes seen in the serial samples collected from the DISCO UTI cohort **(Chapter 6)**, and/or how much of it represents sample contamination.

8.4.3 Sampling challenges and implications for novel diagnostics

An important issue raised by both care home and research staff participating in DISCO UTI **(Chapter 5)** were the difficulties experienced with obtaining urine samples, particularly when someone was unwell. They described many hours sometimes over several days dedicated to the collection of urine and discussed how samples extracted from urine pads would be quicker, easier and would allow more people to access testing. Alternatively, blood samples would have been acceptable to participants in the DISCO UTI study **(Chapter 5)**, and care home staff percieved fingerprick samples to be the easiest to acquire **(Chapter 3)**. POCTs that can test a fingerprick blood sample may therefore have better uptake and be more universally accessible to care home residents. This would also remove the issue of ASB, which had the potential to impact the results of the novel POCTs evaluated in DISCO UTI **(Chapter 7)**.

8.5 Strengths and limitations of the thesis

8.5.1 Strengths

The overall strength of this thesis is the attempt to address this complex problem in a vulnerable population in a setting that is challenging to deliver research. Currently, acute functional decline in care home residents is often attributed to UTI, urine dipsticks are carried out against guideline recommendations and antibiotics are frequently prescribed. Care home residents may or may not receive benefit from these antibiotics, and some may experience harm. However, it will be difficult to challenge this cascade of events without research to develop the evidence base for alternative strategies that may improve antimicrobial stewardship, and ultimately improve care and outcomes for patients. My work has started to fill the evidence gaps, illuminating some of the interactions between acute functional decline, UTI and ASB, considering a potential role for point-of-care testing and assessing the feasibility of conducting research on this topic in UK care homes. My research was inclusive of people living with frailty and those lacking the capacity to consent for themselves, both historically poorly represented in research. The combination of the findings from the methodologically diverse studies including multiple stakeholders generated a richer understanding than that of each individual study alone. I have also provided informed, considered suggestions for further research in this area.

8.5.2 Limitations

The main limitation of this thesis is that none of the issues studied are clearly or consistently understood or defined in existing evidence and/or diagnosed in clinical settings.

- **Acute functional decline** is a clinical syndrome rather than a disease. Acute functional decline is also subjective, may be described or labelled in different ways, and may encompass a number of different phenotypes or clusters. The assumption that acute functional decline has an underlying cause that needs treatment is based on observational data from hospitals. We do not know the causes and prognosis of acute functional decline identified in the care home setting.

- **ASB** is inconsistently defined by international guidelines (Table 1.2) and, as evidenced in the systematic review in Chapter 4, is also inconsistently measured in research. It is also possible that some or all 'asymptomatic bacteriuria' detected in the papers included in the systematic review, and in DISCO UTI, is not colonisation of the urinary tract but contamination from the perineum.

- **UTI** has a clear laboratory definition but the gold standard reference test, urine culture and microscopy, is outdated and culture techniques may not be optimised for all potential uropathogens. The high prevalence of ASB in care homes means that culture alone is not recommended as a diagnostic aid, but instead should be used to guide antimicrobials.

Implications for this include that care home staff discussing acute functional decline in interviews in Chapters 2 and 3 may not all be reflecting on the same clinical syndrome. I also had to define both acute functional decline and ASB for DISCO UTI, but these definitions are not necessarily comparable to other studies. Additionally, in DISCO UTI, I did not attempt to determine how much of the 'possible UTI' was 'true UTI'. In other studies, researchers have created their own definition of 'true UTI' to avoid urine culture as an imperfect reference standard.

8.5.3 Appraisal of the approaches taken

8.5.3.1 Qualitative interview study

The research questions answered in Chapters 2 and 3 were best addressed with qualitative methodology as this allowed in depth exploration of individuals experiences and perceptions of acute functional decline and POCTs. However, because I did not interview GPs and other healthcare professionals, it was not possible to fully appreciate how the care home staff experience interacts and is influenced by others in the same healthcare system. An alternative approach would have been a nationwide survey to care home staff and other healthcare professionals. However, I have had recent experience delivering a survey to care home staff on a different topic and had limited responses because it is hard to disseminate

without national networks and mailing lists.

8.5.3.2 DISCO UTI cohort study

A limitation of the DISCO UTI cohort study is its small size and missing data. Both of these arose as part of the challenges of delivering research in a care home setting. (See Section 8.6). An alternative study design would have been to broaden the scope of the events to be captured to include all episodes of acute functional decline. However, this would have been more labour intensive, would have cost more and would have been harder to know if episodes were missed. There is also the potential that the study could have influenced care home staff behaviour and lowered the threshold for suspecting UTI.

Another option would have been to recruit care home participants from primary care. Access to GP records could potentially provide better data on management and outcomes, compared to relying on the care home record. However, as described by research staff in **Chapter 5**, it sometimes took weeks for care home residents to decide if they wanted to participate. If the model was to reactively recruit at the start of an episode of acute functional decline/suspected UTI it is possible that the whole episode would be missed in the time taken for the participant to make a decision and/or contact a consultee.

Retrospective database research could be considered to look at diagnoses and outcomes of acute functional decline. However, care home residents are not easily identifiable in databases such as the Clinical Practice Research Datalink (CPRD) and acute functional decline is not something for which there is a clinical code and would therefore be difficult to search. Both of these latter approaches would also miss any episodes managed in house by care home staff, as described by participants in **Chapter 2**.

8.6 Barriers to delivering care home research and potential solutions

From my own clinical experience I have come to understand how hard it can be to work in the care home environment. In carrying out the work for my thesis, in particular the DISCO

UTI study, I have learned that designing and delivering research with care home residents and staff in the UK is also challenging for a number of reasons. However, I propose that there are some easily implementable solutions to address these issues, but that these require a culture change in care home research.

1) There is no incentive for care home staff to support research

There was little engagement from non-managerial care home staff in the DISCO UTI care homes. They were incredibly busy caring for sometimes very unwell and/or very demanding residents and research tasks that we needed support with (like identifying potential participants or helping collect a urine sample) were not a priority. Except for the qualitative interviews/focus groups, there was no reimbursement for time. There were also barriers to research put in by senior management within larger organisations - for example, refusing to sign a site agreement.

Possible solutions:

- Adequately reimburse care homes, ideally so that the staff actually doing the extra work get a boost in their pay, or allowing the home to be able to employ a supernumerary member of staff to carry out research-related tasks.

- Make research activity something that is valued by the Care Quality Commission (CQC) and by the public. This would provide a market force driving change.

2) Most care home staff do not have research experience

Research in the care home sector is relatively underdeveloped and there is a limited applicable evidence base, even though the care home population is vulnerable. However, effective care is vital to the sustainability of primary care and acute services. Most care home staff do not have a good working knowledge of research practices. For example, in DISCO UTI there was initially a requirement for managers in participating homes in the Thames Valley region to complete Good Clinical Practice (GCP) training. This

was not something any of them had done before, and proved to be such a barrier that I removed it with the agreement of the Sponsor.

Possible solutions:

- Set up a NHS trust as a single site, which then supports several care homes; this was the approach taken by Solent NHS Trust in the Wessex region for DISCO UTI. This takes most of administrative burden away from the care home, and would also reduce the delays incurred getting individual site agreements in place.

- Increase research training for care home managers, potentially supported and delivered by the RDN/ENRICH. As a consequence, even in research naive homes, management would have a better understanding of key research concepts before the beginning of a new study.

- Improve the engagement and outreach of the RDN/ENRICH, and ensure this is applied consistently across the country.

3) Care home residents need more time and support to make decisions.

Even participants who had capacity sometimes took several visits spanning several weeks to decide whether they wanted to take part in the DISCO UTI study. For those without capacity, we needed care home staff to make the first contact with the potential consultee to be able to discuss the study. This results in a longer recruitment time than studies in other healthcare settings.

Possible solution:

- Wishes around research participation should be considered when someone moves into a care home. If someone lacks capacity, an agreement signed with a family member to allow researchers to directly contact them would be beneficial, removing the administrative burden and the care home staff as gatekeepers.

4) Record keeping in care homes is variable and hard to access.

If staff had not had shifts recently, or did not know the participant well, it was sometimes difficult to get a clear description of some of the possible UTI episodes. We relied on care home staff to allow us access to the relevant part of the care home record, but even then events weren't always recorded consistently. Care homes use a variety of electronic record systems that often record healthcare interactions in the same area as personal care, and it can be difficult to navigate to the right information. Some care home systems do connect with some aspects of the GP electronic health record (eg. diagnoses and medications may be visible), but this is not the norm.

Possible solutions:

- Increase integration of GP records with care home records
- Work with care home electronic health record providers to standardise data entry so that it is easy to extract relevant information for research purposes.

8.7 Implications

8.7.1 Practice

GPs facing clinical scenarios similar to the case presented in **Chapter 1, Box 1** can be informed by several findings from this thesis. Firstly, a new appreciation of why care home staff may call a GP for help when they recognise a resident with acute functional decline; they too are experiencing diagnostic uncertainty and are anxious about potential deterioration. **(Chapter 2)** The staff member may have already been observing the resident for some time and have carried out some early investigations into possible causes of the acute functional decline. GPs may find it helpful to find out what has already been done, and providing support and reassurance where possible. Improved communication and training around the limitations of urine dipsticks may help disincentivise their use in care homes. Consistent messaging from primary care is important.

If a dipstick has been done by care home staff, the updated knowledge of the prevalence of ASB in care home residents can help with clinical interpretation. **(Chapter 4)** For now, it is best to consider the risk of false positives universally too high in this population for the dipstick to have diagnostic utility, although this may change with future research. (See Section 8.7.3) An isolated urine culture from care home residents who are asymptomatic or where there is low clinical suspicion for UTI is unlikely to be helpful. What grows in the urine can vary as much as weekly, including changes between ASB 'states'. **(Chapter 6)** However, AST results should still be used to guide/confirm appropriate antibiotic choices.

8.7.2 Policy/guidelines

The current UKHSA diagnostic decision tool for suspected UTI in older adults is based on outdated and flawed evidence that does not align with the findings of my more comprehensive systematic review. **(Chapter 4)** It is important that these guidelines are updated to reflect the new prevalence estimates of ASB. I have been working with the UKHSA on this review, and will discuss with them how these changes can be implemented. In the longer term, I suggest that it would be beneficial to develop a specific guideline on the diagnosis and management of UTI for care home residents due to the unique differences in their presentation and care compared to many community-dwelling older adults. (Table 1.4)

Urgent changes, like those suggested in Section 8.6, are needed at a policy level to better incentivise and support care homes to participate in research more generally, so that the evidence needed to best care for this population can be generated. Those at the most advanced age/frailty have typically been excluded from research that informs treatment and management of most acute and chronic conditions. As a result, many of the disease specific 'frailty guidelines' are based on expert consensus rather than research. As the population ages, more people will ultimately end up living in care homes, and healthcare professionals working in primary care will benefit from clear evidence-based guidelines to reduce clinical uncertainty.

8.7.3 Future research

8.7.3.1 Additional DISCO UTI analyses

There are several further exploratory analyses planned using DISCO UTI samples and data. Firstly, to explore urinary biomarkers that may be able to distinguish true UTI from ASB or contamination. This is particularly important in view of the complexity seen in serial urine cultures in DISCO UTI; tests for bacteriuria alone may be meaningless in this population. Secondly, to carry out a metagenomic analysis of bacterial DNA in samples collected; this may help to understand the relationship between the same bacteria isolated at different time points during the study (eg. when the participant was asymptomatic vs a possible UTI episode).

8.7.3.2 Further observational study in care homes on UTI

The aim of DISCO UTI was to inform an adequately powered observational study to meaningfully evaluate new approaches to UTI diagnosis. I think it is vitally important to continue research on this topic. However, for the reasons highlighted in Section 8.6, research in UK care homes is complex, labour intensive, and consequently, costly. My experience with grant applications is that it can be difficult to justify to a funding body the scale of the costs required to support a well planned, well staffed study involving UK care home residents. Alternative approaches to continue this work include:

1. Use established networks of research ready care homes with significant educational and delivery support. There are now new UK initiatives, like the Vivaldi network of over 600 care homes.[133] This network is able to collect routine data from participating care homes with NHS linkage without individual patient consent (opt out model). It is currently carrying out a pilot study to measure levels of common infections in care home residents.

2. Deliver the study in care homes outside of the UK. This would involve establishing collaborations with European partners and working with them to see how they are able to successfully recruit and follow up care home residents in larger numbers.

Evidence could then be translated to UK care homes.

3. Establish a large care home research database — like the CPRD — but capturing routine care home data. This would require standardising data capture from care homes; the DACHA study has started this process by establishing a minimum dataset for older adult care homes.[134] Ideally it would also need to be able to link to GP/HES data. This would only be helpful for UTI/acute functional decline if data were also captured at the symptom level.

8.7.3.3 Furthering our understanding of ASB

Further studies are needed to determine how many of the ASB or positive UTI cultures collected from care home residents may be affected by perineal contamination. Knowing how much of the bacterial growth truly comes from the urinary tract is an important step in understanding the urine microbiome. Studies in which growth is compared from urine samples freely passed into a container, extracted from incontinence pads and (ideally) from suprapubic aspiration, as well as a perineal swab would help further this knowledge. Invasive tests are unlikely to be deemed acceptable for those lacking capacity, so this work may need to be done on a smaller group of care home residents who are able to consent for themselves.

8.7.3.4 Progressing rapid diagnostics for UTI suitable for care home use

We need to work with diagnostics companies to help educate them on the complexities of care home UTI diagnosis and ensure that new tests can account for these. For example, they are likely to need to involve a marker of inflammation (urinary or serum biomarker), not just evidence of bacteriuria. Tests that can provide rapid AST results would be helpful in targeting antibiotics sooner, rather than waiting for laboratory results. Novel diagnostics need to be tested in effectiveness trials to establish whether their use impacts relevant outcomes (improving antimicrobial stewardship, reducing need for multiple courses of antibiotics, admissions) rather than just diagnostic accuracy alone.

8.7.3.5 Considering alternative approaches to antimicrobial stewardship in care homes

It may be that we need to consider an alternative to finding a diagnostic test(s) that helps determine who has a 'true UTI'. Instead, it may be more helpful to consider which care home residents experiencing non-specific symptoms are likely to benefit from antibiotics, and in whom can we safely avoid their use. This could form the basis of an RCT, in which care home residents are randomised to usual care, or watch and wait (+/- delayed antibiotic prescribing). I was part of a team that explored this study concept with relevant stakeholders, including GPs and care home staff.[135]

8.8 Conclusions

With a growing care home population, a stronger and more rigorous evidence base is required to underpin healthcare for care home residents. Acute functional decline is a common problem experienced by care home residents, and is managed by care home staff and by GPs. Although little is known about the causes, natural history and outcomes of acute functional decline in the care home population, it is frequently attributed to UTI. Misattributing acute functional decline to a UTI carries risks, including a missed opportunity to investigate and treat the true cause, and exposing residents to unnecessary antibiotics driving AMR. Missing a UTI, however, also risks adverse outcomes like bloodstream infections, hospital admissions and death. Research is needed on new approaches that can reduce clinical uncertainty and improve antimicrobial stewardship in this setting. Without an investment in research driving change, the potential overdiagnosis of UTI and overuse of antibiotics will continue.

This thesis has started to address the current evidence gaps including how acute functional decline in care home residents is related to UTI and how ASB complicates the diagnosis for GPs and other healthcare professionals. I have shown how a lack of recommended, feasible rapid diagnostic tests currently contributes to clinical uncertainty. However, my work has also shown how the urine microbiome of care home residents is potentially more complex than anticipated, which complicates the interpretation of isolated urine cultures and may

impact the performance of novel UTI POCTs that are currently available. Given issues with sample collection and risk of contamination, we also need to consider testing alternative samples to freely passed urine.

More work is needed to understand the natural history of acute functional decline and pathogenesis of care home UTI so that we can better predict outcomes, target treatments and clinical support, and inform the development of further POCTs that could help with assessments in the future. However, this sort of research is complicated to deliver in care homes, most of which remain research naive. My work has identified a number of current barriers to care home research, but there are easily implementable solutions that could improve research delivery in the future. Ultimately, to successfully address this common yet complex problem, and other aspects of healthcare for care home residents, there will need to be a significant investment in resource, time, and a change in care home research culture. My ambition as a researcher is to work with other stakeholders to advocate for greater investment in care home research, play an active role in shaping the cultural changes that are needed, and thus challenge existing assumptions and practice to improve patient outcomes.

Appendix A

Contents of Appendix A relate to Chapters 2 and 3.

A.1 Interview topic guide

Review the Participant Information Sheet and answer any questions. Ensure participant has given informed consent, with audio recording if oral informed consent.

1. Introduction
Thank you for participating in our study. In this study we want to know more about how care home staff recognise it when residents are less well, whether bedside diagnostic tests would be helpful in care homes, and what you think about research studies happening in care homes in the future.

2. Background information
I will start off by collecting some background information about you. If you don't want to answer any of these questions, please let me know.

- How old are you?
- How would you describe your gender?
- How would you describe your ethnicity?
- Whereabouts in the country do you work?
- How would you describe the setting of the care home you work in? *Rural, Town, Inner city*
- What is your job title?
- What does your job involve?
- How many years' experience do you have in that role?
- Do you have any other experience of working in care homes in other roles? If so, what?

- Where did you receive the training for your role?
- Would you say that your work setting is: *Primarily residential home, Primarily nursing home, Mixture*
- Intermediate care beds No intermediate care beds
- Who runs the home you work in? *Private company, Voluntary/charity organisation, Local council*

3. Acute functional decline

We know that older people living in care homes sometimes experience episodes when they are less well than usual. Sometimes this is referred to as being 'off legs' or 'acute functional decline'. The next few questions are about these sorts of episodes.

- What sort of things do you monitor in your residents? *(Prompts if necessary: How do you know if someone is not their usual self? Mobility, appetite, pain, confusion, falls)*
- Do you have a particular term to describe this?
- How do your monitor *[participant's term for acute functional decline]*?
- What do you normally expect will happen if a resident is *[the things they monitor]*?
  - *Establish time frame, progression/recovery*
- Who is best at noticing a change? *(themselves, other team members, family)*
- Which of the *[the things they monitor]* do you feel is the most predictive of someone doing well/badly?
- How long or how severe does an episode of *[participant's term for acute functional decline]* for you to seek help?
- Who do you normally get help from? *(Nurse, manager, GP, paramedic)*
- What do you expect will happen after you seek help from *[answer above]*? Who else do you involve? What do they do next?
- Do you get any training on *[participant's term for acute functional decline]*? If so, what does this involve?
- Are there any protocols in place on *[participant's term for acute functional decline]*? If so, what do they cover?
- Do you feel confident recognising and managing these episodes of *[participant's term for acute functional decline]*? What would make you more confident?

- Are there any things that you would find helpful to improve the way you monitor and respond to *[participant's term for acute functional decline]*?

- Do you think that the COVID-19 pandemic has changed anything for you or the care home in the way in which you respond to these episodes?

4. Point-of-care testing
Point-of-care testing can be used to give diagnostic information at the patient's bedside. Common examples include urine dipsticks and blood glucose measurements. However, you can also do blood tests, tests for bacteria and viruses and some imaging –all with results available within minutes to hours. The next few questions are about your experience with point-of-care testing and how it could be used best in a care home setting.

- What (if any) is your previous experience or knowledge of using bedside diagnostic tests in care homes or other settings?

- Do you think that bedside diagnostic tests could be useful in your care home for helping to monitor or manage *[participant's term for acute functional decline]*?

- What extra value would a test add above what you already do?

- What would make doing a test worthwhile?

- What would you hope doing a test would achieve? *(indicating severity, justifying contact with healthcare, reassurance)*

- What would be key characteristics of a successful bedside diagnostic for use in a care home in terms of:

  - time taken to perform the test

  - time taken to obtain the result

  - cost

  - route of sampling

  - amount of sample required

  - amount of tests able to perform simultaneously (e.g. panel)

  - person able to do the test/training required

- Can you think of any positives of using bedside diagnostic tests in care homes?

- Can you think of any downsides to using bedside diagnostic tests in care homes?

- What would need to be in place for them to be used? *(protocols, training, time)*

5. Research in care homes

- What (if any) is your previous experience of being involved in research?
- What sort of things should a research team consider when planning research in a care home like yours?
- What do you think are the important priorities or questions that research in care homes should answer?
- What would make you more likely to want to help with the research?
- What would make you less likely to want to help with the research?
- Do you think that the COVID-19 pandemic has changed how you view research in care homes?

6. Closing

- Any other comments on this topic?

Thank participant and stop the recording.

Appendix B

B.1 Systematic review search strategy

Search strategy for Medline, as an example

Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present

1 Bacteriuria/ 7960
2 bacteriuria?.ti,ab,kf. 6609
3 1 or 2 10564
4 Asymptomatic Infections/ or Asymptomatic Diseases/ 9921
5 (asymptomatic or presymptom* or pre-symptom* or nonsympton* or non-symptom* or symptomless or inapparent* or latent or covert or subclinical or sub-clinical).ti,ab,kf. 343918
6 4 or 5 345805
7 afghanistan/ or exp africa/ or albania/ or andorra/ or antarctic regions/ or argentina/ or exp asia, central/ or exp asia, northern/ or exp asia, southeastern/ or exp atlantic islands/ or bahrain/ or bangladesh/ or bhutan/ or bolivia/ or borneo/ or "bosnia and herzegovina"/ or brazil/ or bulgaria/ or exp central america/ or exp china/ or colombia/ or "commonwealth of independent states"/ or croatia/ or "democratic people's republic of korea"/ or ecuador/ or gibraltar/ or guyana/ or exp india/ or indonesia/ or iran/ or iraq/ or jordan/ or kosovo/ or kuwait/ or lebanon/ or liechtenstein/ or macau/ or "macedonia (republic)"/ or exp melanesia/ or moldova/ or monaco/ or mongolia/ or montenegro/ or nepal/ or netherlands antilles/ or new guinea/ or oman/ or pakistan/ or paraguay/ or peru/ or philippines/ or qatar/ or "republic of belarus"/ or romania/ or exp russia/ or saudi arabia/ or serbia/ or sri lanka/ or suriname/ or syria/ or taiwan/ or exp transcaucasia/ or ukraine/ or uruguay/ or united arab emirates/ or exp ussr/ or venezuela/ or yemen/ 1314626
8 "organisation for economic co-operation and development"/ 500
9 australasia/ or exp australia/ or austria/ or exp baltic states/ or belgium/ or exp canada/ or chile/ or czech republic/ or europe/ or exp france/ or exp germany/ or greece/ or hungary/ or ireland/ or israel/ or exp italy/ or exp japan/ or korea/ or luxembourg/ or mexico/ or netherlands/ or new zealand/ or north america/ or poland/ or portugal/ or exp "republic of korea"/ or exp "scandinavian and nordic countries"/ or slovakia/ or slovenia/ or spain/ or switzerland/ or turkey/ or exp united kingdom/ or exp united states/ 3446864
10 european union/ 17503
11 developed countries/ 21284
12 8 or 9 or 10 or 11 3462645
13 7 not 12 1223531
14 exp animals/ not humans/ 5086995
15 13 not 14 1097809
16 3 and 6 2665
17 16 not 15 2499

B.2 Approach to decisions made about study quality using the JBI Critical Appraisal Checklist for studies reporting prevalence data.

Domain	Approach to decisions
1. Was the sample frame appropriate to address the target population?	Yes – if the sample frame includes those who could be representative of a primary care population. Unclear – if either not well described, or a niche population that may not be representative of the whole. No – if scoring this the study is unlikely to be eligible for the review.
2. Were study participants sampled in an appropriate way?	Yes – if random or consecutive sampling. Unclear – if not well described. No – if convenience sample or if case-control study.
3. Was the sample size adequate?	Yes - if sample size calculation given. Unclear - if no sample size calculation. No - if sample size calculated but did not recruit to target.
4. Were the study subjects and the setting described in detail?	Yes – if demographics and comorbidities of participants clearly described, along with relevant context for the setting. Unclear – if some characteristics of participants reported but not enough to build up a clear picture of who was included. No – if no details on participants or setting.
5. Was the data analysis conducted with sufficient coverage of the identified sample?	Yes – if subgroups of the sample identified and all respond at the same rate. Unclear – if unclear if subgroups or their response rate. No – if not all subgroups respond at the same rate. NA – if no relevant subgroups.
6. Were valid methods used for the identification of the condition?	Yes – if valid methods for measuring bacteriuria described. Unclear – if scant details on methods. No – if scoring this the study is unlikely to be eligible for the review.
7. Was the condition measured in a standard, reliable way for all participants?	Yes – if methods the same for all participants. Unclear – if unclear whether the same for all. No – if different methods used. This may be that some people were screened with a dipstick before culture. NB. If different methods for male and female participants described but this is in line with guidelines (ie. one sample for men, two for women) then this can be scored as Yes.
8. Was there appropriate statistical analysis?	NA for all; can calculate confidence intervals in our analysis.
9. Was the response rate adequate, and if not, was the low response rate managed appropriately?	Yes – if no dropouts. Unclear – if not well described. No – if large numbers of dropouts. NA – if dropping out/no response not possible due to study design.

B.3 Study ID and references for each included study

Abrutyn, 1991

J Elias Abrutyn et al. "E idemiology of Asymptomatic Bacteriuria in E P derly Women". In: *IAGS* 39 (1991), pp. 388–393. DOI: 10.1111/j.1532-5415.1991.tb02905.x. URL: https://agsjournals.onlinelibrary.wiley.com/doi/10.1111/j.1532-5415.1991.tb02905.x

Aguirre-Avalos, 1999

Guadalupe Aguirre-Avalos et al. "Asymptomatic Bacteriuria and Inflammatory Response to Urinary Tract Infection of Elderly Ambulatory Women in Nursing Homes". In: *Archives of Medical Research* 30.1 (1999), pp. 29–32. ISSN: 0188-4409. DOI: 10.1016/S0188-0128(98)00012-8

Akkus, 2024

Erman Akkuş et al. "Asymptomatic pyuria and bacteriuria are not risk factors for urinary tract infection in women with type 2 diabetes mellitus initiated SGLT2 inhibitors". In: *International Urology and Nephrology* 56.3 (2024), pp. 1165–1172. ISSN: 15732584. DOI: 10.1007/S11255-023-03798-5/TABLES/3. URL: https://link.springer.com/article/10.1007/s11255-023-03798-5

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B.4 Table of characteristics of each included study

See overleaf

Study ID		Country	Setting category	Study design	Included participants with only specific conditions	Microbiology methods	ASB definition		Participant age			% female	Total participants	Number with ASB	Prevalence	Risk factors (* = statistically significant)
Author	Year						Number of samples	CFU threshold	Min age	Max age	Mean/ median age					
Abrutyn	1991	USA	Care homes	Prospective Cohort	NA	Trypticase soy agar plates containing 5% sheep red blood cells and MacConkey agar plates. Incubated at 37°C for 24-48 hours.	Two samples	10^5 CFU/ml	60	99	81.9	1.00	865	134	0.15	***Place of residence**
Aguirre-Avalos	1999	Mexico	Care homes	Cross-Sectional	NA	Blood agar and eosin-methylene blue agar plates. Incubated at 37°C. Evaluated at 24, 48, and 72 h.	Two samples	10^5 CFU/ml	65	104	81	1.00	178	35	0.20	NA
Akkus	2024	Turkey	Outpatient clinic	Prospective Cohort	Diabetes	Blood agar and eosin methylene blue agar plates. Incubated at 37 °C for 24 h.	One sample	Any	34	87	62	1.00	143	37	0.26	NA
Aviles	1999	Mexico	Primary care/community	Cross-Sectional	NA	Blood agar, McConkey agar, HBT (human blood tween) agar and Saboraud dextrose agar plates. Incubated at 37ºC for 24 to 48 Hours. The HBT plates were incubated at 37ºC in partial tension of CO2 for 48 hours.	One sample	10^5 CFU/ml	28	82	missing	missing	165	29	0.18	NA
Balasiou	1997	Netherlands	Outpatient clinic	Cross-Sectional	Diabetes	Culture	Two samples	10^5 CFU/ml	18	77	42	1.00	63	6	0.10	NA
Beerepoot	2012	Netherlands	Outpatient clinic	Trial	NA	Dipslide	One sample	10^5 CFU/ml	missing	missing	missing	1.00	433	175	0.40	NA
Bengtsson	1998	Sweden	Primary care/community	Cross-Sectional	NA	Lactose bromthymol blue (modified Drigalski) agar plates.	One sample	10^5 CFU/ml	26	72	54.7	1.00	1359	72	0.05	Age
Biggel	2019	Belgium	Care homes	Cross-Sectional	NA	Cystine lactose electrolyte deficient agar (CLED, Becton Dickinson) and Columbia blood agar (OXOID) supplemented with 5% horse blood. Plates were incubated for 18–24 h at 37 °C.	Two samples	10^5 CFU/ml	67	104	86	0.80	198	80	0.40	***BES category** ***Continuous incontinence** ***Nursing home vs residential** ***Dementia** ***Female** ***Aged >85** ***Wheelchair bound** Diabetes Diuretic treatment Analgesia use
Bilsen	2023	Netherlands	Mixed	Case-control	NA	Routine culture media and incubated for 1 day	Two samples	10^5 CFU/ml	missing	missing	79	1.00	101	18	0.18	NA
Bonadio	2004	Italy	Outpatient clinic	Case-control	NA	Dipslide, and MacConkey agar and calcium nutrient blood agar	One sample	10^5 CFU/ml	missing	missing	missing	1.00	374	67	0.18	***HbA1c level** Age Duration of diabetes Glomerular filtration rate Urinary albumin secretion Kidney size
Bouvet	2014	Switzerland	Pre-operative	Prospective Cohort	NA	Culture	One sample	10^3 CFU/ml	16	97	69.1	0.61	504	182	0.36	NA
Boyko	2005	USA	Primary care/community	Prospective Cohort	NA	Culture	One sample	10^5 CFU/ml	55	75	missing	1.00	1017	46	0.05	***Diabetes** ***Duration of diabetes** ***Insulin treatment** Oral medication for diabetes Hba1c level

Study ID		Country	Setting category	Study design	Included participants with only specific conditions	Microbiology methods	ASB definition		Participant age			% female	Total participants	Number with ASB	Prevalence	Risk factors (* = statistically significant)
Author	Year						Number of samples	CFU threshold	Min age	Max age	Mean/ median age					
Brostrom	2002	Denmark	Primary care/community	Cross-Sectional	NA	Culture	One sample	10^5 CFU/ml	39	72	52.1	1.00	30	1	0.03	NA
Butler	1995	UK	Outpatient clinic	Cross-Sectional	Liver disease	Missing	One sample	10^5 CFU/ml	missing	missing	missing	1.00	115	25	0.22	NA
Coorevits	2017	Belgium	Primary care/community	Cross-Sectional	NA	Uricult dipslide with CLED and MacConkey agar incubated at 35 °C for 24h. Trypticase soy agar with 5 % sheep blood and a Schaedler agar incubated in ambient atmosphere and anaerobically at 35°C for seven days	One sample	10^5 CFU/ml	23	65	missing	0.85	101	6	0.06	NA
Cordero-Ampuero	2013	Spain	Pre-operative	Trial	NA	Culture	One sample	10^5 CFU/ml	missing	missing	76.75	0.62	471	46	0.10	NA
Del Rio	1993	Spain	Care homes	Trial	NA	Dipslide	One sample	10^4 CFU/ml	missing	missing	82	0.87	78	30	0.38	***Age** Urinary incontinence Bladder/prostate tumour Catheter Recurrent UTI Diabetes Immobilisation Prior pregnancy Number of pregnancies
Efe	2010	Turkey	Outpatient clinic	Case-control	NA	5% sheep blood agar and eosin methylene blue, incubated for 24 hours.	Two samples	10^5 CFU/ml	16	54	31	1.00	104	8	0.08	NA
Frazee	2015	USA	Primary care/community	Trial	NA	Standard quantitative urine culture	One sample	10^5 CFU/ml	missing	missing	missing	1.00	40	3	0.08	NA
Gazzani	2001	UK	Care homes	Cross-Sectional	NA	Culture	One sample	Not defined	64	101	86.7	0.84	161	77	0.48	NA
Georgiadou	2015	Greece	Outpatient clinic	Case-control	Rheumatoid conditions	Culture	Two samples	10^5 CFU/ml	missing	missing	51.8	1.00	498	46	0.09	***Autoimmune disease duration** ***Diabetes** Age Sexually active >2 children Recurrent UTI Type of autoimmune condition Immunosuppressive treatment Glomerular treatment rate
Giamerellou	1998	Greece	Care homes	Trial	NA	Quantitative urine culture using API System	Two samples	10^5 CFU/ml	missing	missing	82.8	0.73	455	106	0.23	NA
Gugino	1998	USA	Outpatient clinic	Case-control	HIV	Culture	One sample	10^5 CFU/ml	missing	missing	26.0	1.00	191	11	0.06	NA
Harding	2002	Canada	Outpatient clinic	Trial	Diabetes	Culture	Two samples	10^5 CFU/ml	missing	missing	missing	1.00	1900	135	0.07	NA
Hawn	2009	USA	Primary care/community	Case-control	NA	Blood agar, MacConkey, and CNA plates. Plates were incubated at 37uC for 48 hours	One sample	10^5 CFU/ml	missing	missing	37.4	1.00	1122	105	0.09	***Diabetes** ***History of bladder/kidney surgery** Age Ethnicity Kidney stones Kidney failure History of cystoscopy
Hedin	2002	Sweden	Care homes	Cross-Sectional	NA	Semi-quantitative cultures according to Swedish standards	Two samples	10^5 CFU/ml	missing	missing	84.6	0.75	237	55	0.23	***Urinary incontinence** Hospitalisation within last 3 months Antibiotics within last 3 months Not independently mobile Living in a single room

Study ID		Country	Setting category	Study design	Included participants with only specific conditions	Microbiology methods	ASB definition		Participant age			% female	Total participants	Number with ASB	Prevalence	Risk factors (* = statistically significant)
Author	Year						Number of samples	CFU threshold	Min age	Max age	Mean/ median age					
Hunold	2025	USA	Primary care/community	Cross-Sectional	NA	Culture	One sample	10^5 CFU/ml	missing	missing	69.6	0.62	162	18	0.11	***Female** Age Ethnicity
Ishay	2006	Israel	Outpatient clinic	Case-control	NA	Culture according to standard procedures (with reference)	One sample	10^5 CFU/ml	18	83	57.8	1.00	1246	29	0.02	***Creatinine** ***Microalbuminuria** ***Macroalbuminuria** Age HbA1c Duration of diabetes Body mass index
Jackson	2004	USA	Primary care/community	Prospective Cohort	NA	Culture	One sample	10^5 CFU/ml	55	75	missing	1.00	1017	46	0.05	NA
Karunajeewa	2005	Australia	Primary care/community	Prospective Cohort	Diabetes	Aerobic culture	One sample	10^5 CFU/ml	missing	missing	60.4	0.46	496	36	0.07	***Female** Age Type of diabetes Diabetes duration Body mass index Creatinine Urea Urinary albumin:creatinine ratio Fasting plasma glucose HbA1c Peripheral neuropathy Orthostatic hypertension
Kjölvmark	2016	Sweden	Care homes	Cross-Sectional	NA	Culture	Two samples	10^5 CFU/ml	missing	missing	missing	missing	116	38	0.33	Sex Age Urogenital disease Malignancy Diabetes COPD Incontinence Vaginal deliveries
Ko	2024	Korea	2) Primary care/community	Prospective Cohort	NA	UF-1000i flow cytometer	One sample	NA	40	69	52	0.51	8508	395	0.05	***Age** ***Female** ***Current smoker** ***Alcohol consumption** ***College graduate** ***Poor self-rated health** ***Creatinine** ***Albumin** ***Haemoglobin** High monthly income High activity Body mass index Impaired sleep Hypertension Diabetes Cardiovascular disease Chronic kidney disease Fasting plasma glucose White blood cell count Cholesterol CRP
Kocoglu	2007	Turkey	Care homes	Cross-Sectional	NA	5% sheep blood and eosin methylene blue agar, incubated at 37 degrees	Two samples	10^5 CFU/ml	missing	missing	74.9	0.29	34	6	0.18	***Diabetes** ***History of invasive urological procedure** Age Sex Inappropriate antibiotic use Incontinence
Koseda-Dragan	1998	Poland	Outpatient clinic	Cross-Sectional	Rheumatoid conditions	Chapman's, McConkey's and Sabouraud's agar.	Two samples	10^4 CFU/ml	missing	missing	missing	1.00	85	14	0.16	NA

Study ID		Country	Setting category	Study design	Included participants with only specific conditions	Microbiology methods	ASB definition		Participant age			% female	Total participants	Number with ASB	Prevalence	Risk factors (* = statistically significant)
Author	Year						Number of samples	CFU threshold	Min age	Max age	Mean/ median age					
Kunin	1993	USA	Outpatient clinic	Cross-Sectional	NA	MacConkey and blood agar plates incubated for 48 hours at 37 hours	One sample	10^5 CFU/ml	missing	missing	23.6	1.00	388	12	0.03	NA
Leihof	2021	Denmark	Mixed	Prospective Cohort	NA	Flexicult agar plate for cultivation overnight	Two samples	10^5 CFU/ml	60	missing	missing	missing	193	14	0.07	NA
Martín Álvarez	2000	Spain	Primary care/community	Case-control	NA	Culture	One sample	10^2 CFU/ml	19	82	54	missing	116	3	0.03	NA
Martínez-Vélez	2016	Spain	Pre-operative	Cross-Sectional	NA	Culture	One sample	10^5 CFU/ml	missing	missing	73.4	0.78	215	11	0.05	NA
Matteucci	2007	Italy	Outpatient clinic	Case-Control	NA	Semiquantitative urine culture was performed using a 10-µl calibrated loop and chromogenic medium	Two samples	10^5 CFU/ml	22	91	62.7	0.49	602	43	0.07	***Female** ***Age (in controls)** Duration of diabetes Body mass index Blood pressure Creatinine Fasting plasma glucose HbA1c Urine albumin excretion Retinopathy
Matthiopoulou	2023	Greece	Outpatient clinic	Case-Control	Diabetes	Columbia blood and MacConkey agar plates	Two samples	10^5 CFU/ml	missing	missing	70.4	0.61	437	88	0.20	***Age** ***Body mass index** ***Duration of diabetes** ***HbA1c** ***UTI within last year** ***Recurrent UTI** ***Regular sexual contact** ***B12** Family history of Type 2 diabetes Prior antimicrobial use CRP
Meiland	2006	Netherlands	Mixed	Prospective Cohort	Diabetes	Quantitative urine culture (with reference)	One sample	10^5 CFU/ml	missing	missing	51.1	1.00	644	110	0.17	NA
Mendoza	2002	Chile	Outpatient clinic	Case-control	NA	Blood agar, MacConkey agar, and in parallel with CPS ID 2 medium. A calibrated 10-microliter loop was used for colony counting,	Two samples	10^5 CFU/ml	missing	missing	62.9	1.00	100	18	0.18	In T2 diabetes patients: ***Duration of diabetes** HbA1c Fasting blood glucose Chronic complications of diabetes Treatments for diabetes
Mims	1990	USA	Mixed	Prospective Cohort	NA	MacConkey, colistin-nystatin-ampicillin (CNA) and blood agar plates and incubated for 24 hours	Two samples	10^5 CFU/ml	missing	missing	missing	0.00	238	29	0.12	NA
Nastos	2011	Greece	Mixed	Cross-Sectional	NA	McConkey and blood agar plates	One sample	10^5 CFU/ml	missing	missing	missing	missing	509	137	0.27	Sex
Nicolle	2012	Multicentre - 12 countries	Not stated	Trial	Diabetes	Culture	One sample	10^5 CFU/ml	missing	missing	52.9	0.52	371	24	0.06	NA
Ouslander	1996	USA	Care homes	Trial	NA	Culture using standard laboratory techniques	One sample	10^5 CFU/ml	missing	missing	85	0.71	214	91	0.43	Sex
Papazafiropoulou	2010	Greece	Outpatient clinic	Cross-Sectional	Diabetes	Blood and MacConkey agar plates. The plates were incubated at 37°C aerobically for 48 hours.	Two samples	10^5 CFU/ml	missing	missing	65.45	0.48	200	29	0.15	***Microalbuminuria** ***Coronary artery disease** ***Female**

Study ID		Country	Setting category	Study design	Included participants with only specific conditions	Microbiology methods	ASB definition		Participant age			% female	Total participants	Number with ASB	Prevalence	Risk factors (* = statistically significant)
Author	Year						Number of samples	CFU threshold	Min age	Max age	Mean/ median age					
Raz	2001	Israel	Care homes	Prospective Cohort	NA	Culture	Two samples	10^5 CFU/ml	63	99	83.658883	0.90	197	85	0.43	***Reduced mobility** ***Dementia** ***Urine incontinence** ***Bowel incontinence** Age Sex Diabetes Ischaemic heart disease Cerebrovascular accident COPD Malignancies Chronic catheter Haemoglobin White blood cell count Albumin Creatinine
Ribera	2006	Spain	Outpatient clinic	Prospective Cohort	Diabetes	Culture	Two samples	10^5 CFU/ml	missing	missing	68.3	0.63	457	91	0.20	NA
Rodhe	2006	Sweden	Primary care/community	Cross-Sectional	NA	CLED-agar according to Swedish standards	Two samples	10^5 CFU/ml	missing	missing	84.7	0.68	432	64	0.15	**Female** In females: ***Reduced mobility** ***Urinary incontinence** ***Oestrogen treatment** Living in serviced flats Diabetes History of stroke Diuretic treatment Reduced mental capacity Reduced functional status Faecal incontinence Genitourinary symptoms Frequency Antibiotic treatment in previous 3 months
Rodríguez-Pardo	2021	Spain	Pre-operative	Trial	NA	Culture	One sample	10^5 CFU/ml	missing	missing	84.3	0.71	594	152	0.26	***Female** ***Urinary incontinence** ***Charlson index score** Age Body mass index Obesity Cardiac failure Peripheral vasculopathy Diabetes Dementia Chronic bronchopathy Cirrhosis Chronic renal failure Rheumatoid arthritis Immunosuppressors Malignancy Anticoagulant treatment Antiplatelet treatment
Samuels	2024	USA	Primary care/community	Cross-Sectional	NA	Standard urine culture	One sample	Not defined	missing	missing	missing	1.00	272	3	0.02	Age
Savvala	1998	Greece	Outpatient clinic	Cross-Sectional	Diabetes	Culture	One sample	10^5 CFU/ml	missing	missing	61	1.00	363	60	0.17	NA
Semetkowska-Jurkiewicz	1996	Poland	Outpatient clinic	Cross-Sectional	Diabetes	Hoperich method	One sample	10^4 CFU/ml	25	76	55	0.49	900	71	0.08	NA

Study ID		Country	Setting category	Study design	Included participants with only specific conditions	Microbiology methods	ASB definition		Participant age			% female	Total participants	Number with ASB	Prevalence	Risk factors (* = statistically significant)
Author	Year						Number of samples	CFU threshold	Min age	Max age	Mean/ median age					
Şener	2013	Turkey	Care homes	Prospective cohort	NA	Blood-based and MacConkey agars. Cultured plates were incubated under aerobic conditions at 37°C for 18 to 24 hours.	Two samples	10^5 CFU/ml	missing	missing	74.6	0.60	606	146	0.24	***Female** ***Age** ***Length of stay in nursing home**
Senior	1999	Scotland	Outpatient clinic	Case-control	Rheumatoid conditions	CLED agar plate. In addition, 1 ml pipetted into a sterile petri dish and mixed with 12 ml molten cool Urea Agar Base medium containing clindamycin (5 mg/l).	One sample	10^4 CFU/ml	21	80	58.838	0.86	76	25	0.33	NA
Sotiropoulos	2005	Greece	Outpatient clinic	Case-control	NA	Culture	Two samples	10^5 CFU/ml	missing	missing	62.13	1.00	713	45	0.06	***Diabetic microvascular complications** ***Past urinary tract infection** Age Diabetes duration Diabetes treatment Sexually active Sexual intercourse/month Creatinine HbA1c
Sousa	2014	UK, Portugal and Spain	Pre-operative	Prospective Cohort	NA	Culture	One sample	10^5 CFU/ml	21	96	68	0.63	2497	303	0.12	***Age** ***Female** ***Obesity** ***ASA score** Diabetes Knee location
Sundvall	2014	Sweden	Care homes	Cross-Sectional	NA	Cystine-lactose-electrolyte deficient agar (CLED) and a Columbia blood agar base. Plates were incubated overnight (minimum 15 h) at 35-37°C. CLED plates were incubated in air, and Columbia plates were incubated in 5% CO2	One sample	10^5 CFU/ml	63	100	86.4	0.70	396	128	0.32	NA
Turan	2008	Turkey	Outpatient clinic	Prospective Cohort	Diabetes	Blood agar and eosine methylene blue agar were used for routine urine cultures. Plates were incubated aerobically for 24 h at 37°C	Two samples	10^5 CFU/ml	26	80	56.7	0.74	123	22	0.18	***HbA1c** ***Duration of diabetes** ***Glycosuria** ***Pyuria** Age Sex Body mass index Glomerular filtration rate Microalbuminuria
Varli	2011	Turkey	Outpatient clinic	Cross-Sectional	NA	Blood agar and eosin methylene blue agar used for routine urine cultures. Plates were incubated aerobically for 24 h at 37 °C	Two samples	10^5 CFU/ml	65	93	72.4	0.63	625	39	0.06	***Female** Age Number of prior UTI History urolithiasis Urinary incontinence Number of births Prior genitourinary surgery
Ye	2014	Canada	Outpatient clinic	Prospective Cohort	Liver disease	Culture	One sample	10^8 CFU/ml	missing	missing	57.2	0.37	99	5	0.05	NA
Yoo	2009	UK	Outpatient clinic	Cross-Sectional	Diabetes	Culture	One sample	Not defined	missing	missing	missing	missing	100	10	0.10	NA

Study ID		Country	Setting category	Study design	Included participants with only specific conditions	Microbiology methods	ASB definition		Participant age			% female	Total participants	Number with ASB	Prevalence	Risk factors (* = statistically significant)
Author	Year						Number of samples	CFU threshold	Min age	Max age	Mean/ median age					
Zhanel	1995	Canada	Outpatient clinic	Prospective Cohort	Diabetes	Blood agar and MacConkey agar plates. Plates were incubated at 35°C for 18- 24 hours	Two samples	10^5 CFU/ml	16	94	45.7	1.00	1072	85	0.08	***Non insulin dependent diabetes** ***Duration of diabets** ***Current diabetes treatment** ***No diabetic complications** ***Ketoacidosis** ***Aboriginal origin** Age Weight History of UTI Renal function Retinopathy Neuropathy Renal disease Peripheral vascular disease Heart disease Enteropathy

Appendix C

C.1 Electronic Case Report Form for Baseline Visit

See overleaf

BASELINE VISIT

Record ID

_____

Date of baseline visit

_____

INFORMED CONSENT/CONSULTEE DECLARATION

Is the participant able to consent for themselves to take part in this study?
- ◯ Yes
- ◯ No, they have a consultee

Has the participant/consultee read and understood the latest information sheet and had the opportunity to ask questions about the study?
- ◯ Yes
- ◯ No

Please ensure the participant/consultee has read the relevant information sheets and you have answered any questions, before moving on.

Has the participant freely given informed consent OR is there a complete Consultee Declaration Form?
- ◯ Yes
- ◯ No

If the participant has capacity, informed consent must be given before any study specific procedures take place. If the participant lacks capacity a consultee must have completed a Consultee Declaration Form before any study specific procedures take place.

Name of GP practice:

_____

Tick to confirm that GP letter has been sent:
- ☐ Yes

DEMOGRAPHIC DATA

How long has the participant lived in a care home?
- ◯ Less than 6 months
- ◯ 6 months - 1 year
- ◯ 1 - 2 years
- ◯ 2 - 3 years
- ◯ > 3 years
- ◯ Don't know

Age (years)

_____

Gender identity
- ◯ Male
- ◯ Female
- ◯ Other _____

Is this the same gender that was assigned at birth?
- ◯ Yes
- ◯ No

What was the gender assigned at birth?
- ◯ Male
- ◯ Female

Do they have the same urological anatomy as the gender assigned at birth?
- ◯ Yes
- ◯ No

Most recently recorded height (cm)

_____

Most recently recorded weight (kg)

_____

Ethnicity

◯ Asian or Asian British
◯ Black British, Caribbean or African
◯ Mixed or multiple ethnic groups
◯ White
◯ Other ethnic group _____

MEDICAL HISTORY

Please review the care home record and medicines administration record (MAR chart)

Relevant medical diagnoses:
(Please tick all that apply):

☐ Dementia (Alzheimer's disease, other dementias including vascular dementia, mixed dementia, unspecified dementia)
☐ Diabetes (Type 1 or Type 2)
☐ Chronic kidney disease (CKD)
☐ Benign prostatic hyperplasia/hypertrophy (BPH or prostatism)
☐ Irritable bladder/overactive bladder
☐ Recurrent urinary tract infection (UTI)
☐ Prostate cancer
☐ Other cancers/malignancies
☐ None of these apply

Please count the total number of different oral medications the participant takes regularly:

◯ 0-4
◯ 5-9
◯ 10 or more

Does the participant regularly take/use any of the following:
(Please tick all that apply)

☐ SGLT2 inhibitors ('flozins' eg. dapagliflozin, empagliflozin)
☐ Daily antibiotics for infection prevention (eg. nitrofurantoin, trimethoprim, cefalexin, pivmecillinam)
☐ Methenamine hippurate
☐ Prednisolone
☐ DMARDs (eg. methotrexate, sulfasalazine, hydroxychloroquine, leflunomide, azathioprine)
☐ Topical oestrogen (eg. estradiol vaginal tabs, estriol intravaginal cream, Ovestin, Gynest, estriol pessaries, Imvaggis)
☐ Finasteride OR tamsulosin
☐ Solifenacin OR oxybutynin OR tolterodine OR fesoterodine OR mirabegron
☐ None of these apply

Has the participant had any courses of antibiotics in the last 6 months?

◯ Yes
◯ No
◯ Don't know

Date Antibiotic Indication (if documented)

_____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____

FRAILTY

Please record information about frailty according to the participant and/or the care home staff.

Clinical frailty scale
(Please note - if score 8 or 9, the person may not be suitable for inclusion in this study. Please consult exclusion criteria.)

◯ 1. Very Fit - People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.
◯ 2. Well - People who have no active disease symptoms but are less fit than category 1. Often, they exercise or are very active occasionally, e.g. seasonally.
◯ 3. Managing Well - People whose medical problems are well controlled, but are not regularly active beyond routine walking.
◯ 4. Vulnerable - While not dependent on others for daily help, often symptoms limit activities. A common complaint is being "slowed up", and/or being tired during the day.
◯ 5. Mildly Frail - These people often have more evident slowing, and need help in high order IADLs (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.
◯ 6. Moderately Frail - People need help with all outside activities and with keeping house. Inside, they often have problems with stairs and need help with bathing and might need minimal assistance (cuing, standby) with dressing.
◯ 7. Severely Frail - Completely dependent for personal care, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).
◯ 8. Very Severely Frail - Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.
◯ 9. Terminally Ill - Approaching the end of life. This category applies to people with a life expectancy < 6 months, who are not otherwise evidently frail.

SUPPORT WITH ACTIVITIES OF DAILY LIVING/MOBILITY

	Independent	Performs with assistance
Eating	◯	◯
Dressing	◯	◯
Bathing	◯	◯

Mobility

◯ Walks without walking aids
◯ Walks with walking aid (stick, frame etc)
◯ Unable to walk but is transferred in/out of bed/chair
◯ Bedbound

NORMAL URINATION/CONTINENCE PATTERNS

Please record information about the participant's usual urination/continence patterns according to the participant and/or the care home staff.

Awareness of needing to pass urine

◯ Aware of when needs to pass urine
◯ Sometimes aware of when needs to pass urine
◯ Never aware of when needs to pass urine
◯ Don't know

Support using the toilet

◯ Usually able to use the toilet/commode independently (including mobilising, managing clothing and getting on/off WC)
◯ Usually needs support using the toilet/commode
◯ Usually unable to use a toilet/commode
◯ Don't know

Does the participant USUALLY have any of the following symptoms:

- Frequent urge to urinate, strong and immediate need to urinate, and/or frequent urinary incontinence
- Poor urine stream, difficulty starting or maintaining a urine stream, continues to leak urine after finishing passing urine, inability to completely empty the bladder Please tick yes if ANY of these symptoms are normal for them.

◯ Yes
◯ No
◯ Don't know

URINE SAMPLE

All participants need a baseline urine sample

Sample collected

☐ Yes

Date collected

_____

Time collected

_____

_____
(If the sample was collected longer than 6 hours ago, please consider a fresh sample.)

Any issues with sample collection?

_____
(Eg. multiple visits required, reason for no sample collected)

How was the urine sample collected?
(Where possible, this should be a clean catch mid-stream urine sample - which means that the urine is collected in a sterile container and that the first part of urine is avoided.)

◯ Clean catch, mid-stream
◯ Clean catch, not mid-stream
◯ From container placed in commode/toilet
◯ From a pad
◯ Other, please state _____
◯ Dont know

Is the sample likely to be contaminated by foecal matter?

◯ Yes
◯ No
◯ Don't know

Was the participant given support with the sample collection?

◯ Yes - care home staff
◯ Yes - research team
◯ No
◯ Don't know

Was the sample stored in the fridge between collection and posting?	◯ Yes ◯ No ◯ Don't know
Please tick to confirm urine sample has been posted	☐ Yes

Date posted

_____

(Please note, the sample will need to be divided into two tubes and posted to Microbiology Cardiff, Public Health Wales using the provided packaging. Samples may only be posted Monday - Thursday. Samples collected after post collection from Thursday through to Monday morning must be refrigerated and posted on Monday.)

Royal Mail tracking number

_____

C.2 Topic guide for interviews with care home staff, study participants and consultees

Review the Participant Information Sheet and answer any questions. Ensure participant has given informed consent.

1. Introduction

Thank you for participating in our study. In this study we want to know more about your experience of supporting/taking part in DISCO UTI and about any changes we should make when scaling up the study in the future.

CARE HOME STAFF

2. Background information

I will start off by collecting some background information about you. If you don't want to answer any of these questions, please let me know.

- What is your job title?
- How many years' experience do you have in that role?
- Have you been involved in research prior to DISCO UTI? *If so, what? Any research training?*
- How old are you?
- How would you describe your gender?
- How would you describe your ethnicity?

3. Supporting the study

I will now ask you some questions about supporting DISCO UTI at your care home.

- What did you think about the study when you first heard about it? Did you understand why the study was being done? Did you this the research was answering an important question?
- If a manager – what were the things that made you decide that the care home should support this study? Was there anything that put you off the study? How you do you suggest we approach care homes about this study in the future?
- Did any perceptions change once the study started?
- Could you describe to me the main tasks you had to do as part of supporting this study?

- How did you feel about carrying out those tasks?
- Were there any tasks that were particularly straightforward/challenging to do?
- Did you feel that you had enough time to carry out the tasks?
- Did you feel that you had enough training to carry out the tasks?
- How did you find supporting the research team to identify eligible residents?
- How did you find supporting residents to collect urine samples?
- How did you find contacting the research team when you suspected a UTI in a participant?
- What do you think that residents/their families thought about taking part in the study?
- Are there any aspects of the study that you think worked well? (for the care home, for the residents)
- Are there any aspects of the study that you think worked less well? (for the care home, for the residents)

RESIDENTS (+/- FAMILY MEMBERS/FRIENDS) and CONSULTEES

2. Taking part in the study

- Can you remember first hearing about the research study? If yes, what did you think about the study when you first heard about it? Did you understand why the study was being done? Did you this the research was answering an important question? Did any perceptions change once the study started?
- The first thing that happened was that someone spoke to you about the study and provided you with an information sheet *(show copy as a prompt).* Can you remember this? What did you think about the information sheet? How did you find reading it? Are there any things about it that you think could be improved? *Prompts – volume of information, size of font. Would you have preferred information in another format eg. video?*
- The next thing that happened was that you signed a consent form. Prompt with example. Do you remember this? How did you find the consent process?
- You provided a urine sample at the beginning of the study. Do you remember this? How did you find providing a sample? Did you have help?
- You/some people gave weekly samples for 4 weeks. How did you find this? Was the frequency of sampling acceptable? What if someone had asked you to give a sample

every day, or for longer? What is the optimum sampling frequency?

- (If relevant) You had a possible urine infection during the study – this meant that you had a visit at the beginning, 2 and 4 weeks later. How did you find these visits? Did you mind giving the additional urine samples?

- Have you ever had experience of urine infections? If yes, what did you used to do to treat them? *Eg. homely remedies when younger.*

- You met a research nurse on a regular basis during the study. How did you find this?

- Were there any parts of the study that were particularly straightforward/challenging for you/the person you know to do?

- What do you think the care home staff thought about the study?

- What do you think your family or friends thought about the study?

- If a consultee: How did you find acting as a consultee? Have you ever done anything similar previously?

ALL

4. Improving the study design for the future

I will now ask you some questions about how we should learn from DISCO UTI to develop a larger study in the future.

- Are there any aspects of the study that you think could be improved for a future study? *(Prompts: Frequency of urine sampling, work asked of care home staff, training, feedback, size of study)*

- Do you have any suggestions about additional related questions that we should answer as part of a future study? (Alternative: what are the important things about UTI in care homes that we should be researching?)

- If the future study were to take place in the care home you work/live in, how would you feel?

- For residents/consultees: Would you want to take part in the larger study? Why/why not?

Closing

- Any other comments on this topic?

Thank participant and stop the recording.

C.3 Topic guide for focus group with research staff

Ensure each participant has given informed consent before starting the focus group.

1. Introduction

Thank you all for taking the time to be part of this focus group today. You were all invited because you have been involved in delivering DISCO UTI as part of the research team.

The aim of this session is for us to explore what you thought about delivering the study. We aim to use the results to improve the design and delivery of future studies in care homes. We would like everyone to have an equal voice and to hear honest opinions from all of you. Please feel free to share your opinion even if it differs from what someone else has said.

Just to remind you that the focus group is audio recorded. I would ask that we keep what we discuss in the focus group today confidential, and respect each other's opinions.

Does anyone have any questions before we start?

2. Background information

Can we start by doing some introductions, just so we can all understand who is here?

- Please could you all state your name and what your job role is? Please also say whether you have done any research in care homes previously.

3. Supporting the study

I will now ask you some questions about delivering DISCO UTI.

- How did you find identifying/setting up care home sites?
- How did you find identifying eligible residents?
- What do you think residents thought of the study?
- How did you find the consent process?
- How did you find identifying consultees?
- What do you think consultees thought of the study?
- How did you find completing the consultee declaration form?
- How did you find supporting residents to collect urine samples?
- How did you find dividing urine samples and posting them?
- What made collecting urine samples more or less challenging?

- Did the care homes contact you when they suspected a UTI in a participant? If not, why not?

- What did you think of the eCRF?

- Can you think of any ways the eCRF could have been improved?

- Are there any aspects of the study that you think worked well? *(for you, for the care home, for the residents)*

- Are there any aspects of the study that you think worked less well? *(for you, for the care home, for the residents)*

4. POCTs

Most have you have used each of the POCTs we have evaluated as part of this study.

- What do you think of each test?

- How easy or not were they to use?

- How did you find recording the results?

Ask these questions by test: Utriplex, Lodestar DX, Astrego PA-100.

5. Improving the study design for the future

I will now ask you some questions about how we should learn from DISCO UTI to develop care home studies for the future.

- What are the lessons you have learnt from carrying out DISCO UTI?

- Are there any aspects of DISCO UTI that you think could be improved for a future similar study? (Prompts: Frequency of urine sampling, work asked of research team, care home staff, training, feedback, size of study)

- What do you think are the most important things for research teams to be aware of when working with care homes?

6. Closing

- Before I close this meeting, are there any other comments or questions?

Thank participants and stop the recording.

Appendix D

D.1 Antimicrobial Susceptibility Testing results for isolates from samples collected from participants experiencing possible UTI

			AST						
Participant	Visit	Organism	Nitrofurantoin	Trimethoprim	Pivmecillinam	Fosfomycin	Cefalexin	Co-amoxiclav	Ciprofloxacin
1	Onset	Escherichia coli	S	S	S	S	S	S	S
5	Day 14	Pseudomonas aeruginosa							
	Day 14	Enterococcus faecalis							
6	Day 14	Aerococcus urinae							
	Day 14	Aerococcus sanguinicola							
8	Onset	Klebsiella pneumoniae	-	R	S	-	S	S	S
	Day 14	Klebsiella pneumoniae	-	R	S	-	S	S	I
	Day 28	Klebsiella pneumoniae	-	R	S	-	S	S	S
9	Day 14	Escherichia coli	S	S	S	S	S	S	S
10	Day 14	Escherichia coli	S	S	S	S	S	S	S
	Day 28	Escherichia coli	S	S	S	S	S	S	S
	Day 14	Klebsiella oxytoca	-	S	S	-	R	R	S
	Day 28	Escherichia coli	S	R	S	S	R	S	I
	Day 28	Klebsiella oxytoca	-	S	S	-	R	R	S
12	Day 28	Enterococcus faecalis							
13	Day 14	Escherichia coli	S	R	R	S	R	R	R
	Day 14	Escherichia coli	S	R	R	S	R	R	R
	Day 28	Escherichia coli	S	R	R	S	R	R	R
	Day 14	Escherichia coli	S	R	R	S	R	R	R
	Day 28	Escherichia coli	S	R	R	S	R	S	R
15	Day 28	Escherichia coli	S	S	S	S	S	S	S
18	Onset	Escherichia coli	S	S	S	S	R	S	R
	Day 14	Escherichia coli	S	S	S	S	R	S	R
	Day 28	Escherichia coli	S	S	S	S	R	S	R
19	Onset	Escherichia coli	S	S	S	S	S	S	S

Key	
R	Resistent
I	Susceptible, increased exposure
S	Susceptible, standard dosing regimen
-	Agent is unsuitable for treatment of infections caused by the organism

D.2 Antimicrobial Susceptibility Testing results for isolates from samples collected from asymptomatic participants at baseline

			AST						
Participant	Visit	Organism	Nitrofurantoin	Trimethoprim	Pivmecillinam	Fosfomycin	Cefalexin	Co-amoxiclav	Ciprofloxacin
A	Baseline	Klebsiella pneumoniae	-	S	S	-	S	R	R
B	Baseline	Escherichia coli	S	S	S	S	S	S	S
C	Baseline	Escherichia coli	S	S	S	S	S	S	S
D	Baseline	Klebsiella pneumoniae	-	S	S	-	S	S	S
E	Baseline	Klebsiella pneumoniae	-	S	S	-	S	S	S
F	Baseline	Aerococcus sanguinicola							
	Baseline	Streptococcus mitis/oralis							
G	Baseline	Escherichia coli	S	S	S	S	S	S	S
H	Baseline	Klebsiella pneumoniae	-	R	S	-	S	S	S
I	Baseline	Enterobacter hormaechei	-	S	S	-	S	R	S
J	Baseline	Klebsiella pneumoniae	-	R	S	-	S	S	S
K	Baseline	Escherichia coli	S	S	S	S	S	S	S
K	Baseline	Klebsiella pneumoniae	-	S	S	-	S	S	S
L	Baseline	Klebsiella pneumoniae	-	S	S	-	S	S	S
M	Baseline	Citrobacter koseri	-	S	S	-	S	S	S
	Baseline	Escherichia coli	S	S	S	S	S	S	S
N	Baseline	Klebsiella pneumoniae	-	S	S	-	S	S	S
O	Baseline	Escherichia coli	S	S	S	S	S	S	S
P	Baseline	Escherichia coli	S	S	S	S	S	S	S
Q	Baseline	Escherichia coli	S	R	S	S	S	S	I
R	Baseline	Escherichia coli	S	R	R	S	R	R	R
S	Baseline	Escherichia coli	S	R	S	S	S	S	S
T	Baseline	Proteus mirabilis	-	R	S	-	S	S	S
U	Baseline	Proteus mirabilis	-	R	S	-	S	S	S
V	Baseline	Escherichia coli	S	R	S	S	S	S	S
W	Baseline	Escherichia coli	S	S	S	S	S	S	R
X	Baseline	Escherichia coli	S	R	S	S	S	S	I
Y	Baseline	Enterococcus faecalis							
	Baseline	Escherichia coli	S	R	R	S	S	R	S
Z	Baseline	Escherichia coli	S	S	S	S	S	S	S

Key

R	Resistent
I	Susceptible, increased exposure
S	Susceptible, standard dosing regimen
-	Agent is unsuitable for treatment of infections caused by the organism

Appendix E

E.1 Topic guide for the focus group with care home staff

Ensure each participant has given informed consent before starting the focus group. Start recording.

1. Introduction

Thank you all for taking the time to be part of this focus group today. You were all invited because you work in a care home that is participating in the DISCO UTI study, which is looking at improving identification of urinary tract infections in care home residents.

The aim of this session is for us to explore what you think of several new rapid tests for UTI. We will briefly show you how each of them works. We would like everyone to have an equal voice and to hear opinions from all of you. Please feel free to share your opinion even if it differs from what someone else has said. There are no right or wrong answers.

Just to remind you that the focus group is audio recorded. I would ask that we keep what we discuss in the focus group today confidential, and respecting each other's opinions.

Does anyone have any questions before we start?

2. Background information

Can we start by doing some introductions, just so we can all understand who is here?

- Please could you all state your name and what your job role is?

3. Discussion of tests

We will now look at each of the tests one by one.

Utriplex

This detects the presence of 2 proteins in the urine sample that are raised in a urine infection. You dip the end into a urine sample for 30 seconds then leave it for 5 minutes before reading

the result. A positive result is when you can see two lines, as shown on your sheet. It is like reading a pregnancy test or Covid lateral flow test.

DEMONSTRATION OF TEST. Tests will also be passed around to participants to try on samples of water.

- What are your first impressions of the test?
- Is there anything you would like us to clarify?
- What do you think about how to use the test?
- What do you think about how to read the result?
- Are there any aspects of the test which seem easy to use?
- Are there any aspects of the test which seem more challenging?
- Do you think this test would be good to use in a care home? Why? Why not?

Lodestar DX

The Lodestar test detects DNA from 6 common UTI-causing bacteria. You put a small amount of a urine sample mixed with a reagent to each of these small tubes. You place in the analyser and press start. Results take approximately 35 minutes. If any of the bacteria are present in the sample the lights turn on the dashboard – as shown on your sheet.

DEMONSTRATION OF TEST. There are also 2 pipettes to be passed around so participants can have a go at transferring water sample to the test tubes.

- What are your first impressions of the test?
- Is there anything you would like us to clarify?
- What do you think about how to use the test?
- What do you think about how to read the result?
- Are there any aspects of the test which seem easy to use?
- Are there any aspects of the test which seem more challenging?
- Do you think this test would be good to use in a care home? Why? Why not?

Astrego PA-100

The Astrego test can detect the presence of bacteria in a urine sample, and if it finds any can then tell you whether it is susceptible to common antibiotics. You pipette a small amount of

urine into the cassette and put it into the machine. After 15 mins it will tell you whether bacteria are present and after another 20-30 mins it will tell you the sensitivities. These come up on the screen. Samples have to be less than 30 minutes old and you can't use it if someone is already taking antibiotics.

DEMONSTRATON OF TEST. Cartridges and pipettes to also be passed around to try using with water samples.

- What are your first impressions of the test?
- Is there anything you would like us to clarify?
- What do you think about how to use the test?
- What do you think about how to read the result?
- Are there any aspects of the test which seem easy to use?
- Are there any aspects of the test which seem more challenging?
- Do you think this test would be good to use in a care home? Why? Why not?

4. Comparisons and UTI testing more generally

In this final section we will think about comparing the tests and testing for UTIs with new tests more generally.

- Now you have looked at all the tests, how do you think they compare to each other?
- How do you think they compare to what you currently do when you suspect a UTI in a resident?
- Do you think you would use any of these tests if they were introduced to your care home? Why/why not?
- Are there any adjustments that would need to be made to make them suitable?
- How would you use? (prompts: to decide whether to call a GP, to provide information to a healthcare professional)
- Do you think they would be better used by another healthcare professional? If so, who and when?
- What would make you confident in the test result?
- What things would make you more or less likely to use a new UTI POCT?
- If you were going to use it, what kind of training and support would you want?

- Are there any other things that should be taken into consideration when developing a UTI POCT for use in care homes?

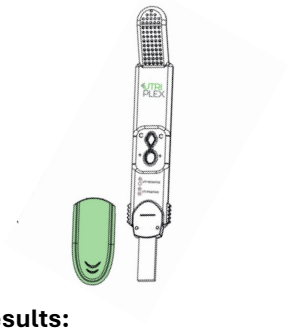
5. Closing

- Before I close this meeting, are there any other comments or questions?

Thank participants and stop the recording.

E.2 Reference sheet provided to care home staff during the focus group

UTRIPLEX



Results:



Negative Positive

Key points:
- Results take 5 minutes
- Detects proteins in urine that are associated with infection

LODESTAR



Results:



RED light – positive for the bacteria
GREEN light – negative for the bacteria

Key points:
- Results take 35 minutes
- Detects common bacteria that cause UTI
- Have to mix and pipette urine into small tubes

ASTREGO



Results:



Results come up on the screen

Key points:
- Results if negative for bacteria after 15 minutes
- If positive it takes another 20-30 mins to give antibiotic sensitivities
- Have to pipette urine into cassette
- Can't use if already on antibiotics

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