

# Horizon Scanning Report: Identification of Urinary Tract Infection Technologies

**Authors:** Lucy Barrass, Abigail Roberts, Oluwatomi Arisa, Janet Kinnersley and Anne Oyewole

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**Professor Dawn Craig**  
*Director*

**T:** +44(0) 191 208 2259

**E:** [info@io.nihr.ac.uk](mailto:info@io.nihr.ac.uk)

[www.io.nihr.ac.uk](http://www.io.nihr.ac.uk)

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Research Innovation Observatory (NIHRIO),  
The University of Newcastle upon Tyne

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## Introduction

The NIHR Innovation Observatory's Medical Devices (MDx) team has completed the horizon scanning of the first of four clinical pathways, for the identification of technological innovations (e.g. products/interventions) that have the potential to reduce demand for antimicrobials through infection prevention, detection and or management intervention.

The innovation landscape presented for Urinary Tract Infections (UTIs) aims to inform decisions by NHSE & I's AMR Programme Board, and accelerate adoption of proven innovations that will enhance appropriate antimicrobial prescribing and improve patient outcomes. This report (accompanied with the complete Excel UTI dataset) provides important, immediately relevant data on key areas of development, to allow readers to evaluate the potential impact of these innovations and identify promising innovations for use in the NHS (or wider). To help with clarity and comprehensibility, the report has been organised and presented into three main sections:

1. Horizon scanning strategy – an overview of the search strategy devised to identify UTI technologies and related evidence
2. UTI technology landscape – the clinical trial, product pipeline and funding landscape result sections, each contain information (including visualised data) about the overarching global landscape of UTI technological innovations
3. Summary of key themes and emerging patterns, based on the results retrieved from the scan and market intelligence

It is hoped that the visualisations and accompanying narrative presented in this report (along with the complete Excel UTI dataset), inform understanding and shape discussions on the availability of UTI innovative technologies. The report also describes some of the key providers/developers in play for the international market and offers a snapshot of current products, including those with high innovation potential. Overall, our horizon scanning activities highlight that the evolution of UTI technology has the potential to offer significant opportunities in the NHS to deliver better outcomes.

## Methods

### Horizon Scanning

The horizon scan methodologies developed by the Innovation Observatory (IO) to identify the pipeline of UTI technologies, involved the identification of information sources that detected 'signals' for UTI technologies. The collection of primary and secondary sources identified, were systematically scanned using a combination of traditional scanning methods (manual), automated and novel AI/machine learning techniques.

## Collation of key Terms

Specific search strategies were formulated for the scans performed and combined MeSH/key terms identified with Boolean operators (where applicable). A comprehensive list of keywords and concepts was compiled by the IO's Information Specialist Team, based on the evidence reports provided by the AMR Programme Board, in addition to key publications/reports identified. The terms and concepts identified related to urinary tract, urinary tract infections (UTIs), antimicrobial resistance (AMR), diagnostic procedures, medical technology (including device, diagnostic and digital) and pathogenesis of UTI.

The set of systematic searches were performed between August and September 2021 and no date/period exclusions were applied to the searches (unless otherwise stated). Based on successive screening of sources (i.e. identification of UTI technologies), information was extracted and imported for further data processing.

Information sources used as part of these scans included (but are not limited to):

- [ScanMedicine](#), the IO's clinical trial database containing information from 11 registries across the globe (e.g. UK, Europe, USA)
- Regulatory agency sources (e.g. US FDA)
- Publications (including conference outputs)
- MedTech news websites (e.g. Fierce Biotech)
- Commercial websites and reports
- Academic institution webpages
- NICE medical technologies guidance

Inclusion criteria:

All technological innovations included in the scan had to meet the criteria for a medical technology (e.g. device, diagnostic test, digital or a combination) and be deemed to diagnose, monitor, screen for or prevent UTIs. All technologies were further classified (see below) and the collated information can be found within the UTI Dataset (Excel file accompanying this report):

Classification of UTI technologies:

- Type of technology (e.g. device, diagnostic test, digital or a combination)
- Clinical target (upper and/ or lower UTI)
- Clinical pathway (e.g. detection, prevention, monitoring, screening)
- Classification of test technology (e.g. phenotypic resistance tests, disposable tests)
- Care setting (e.g. primary care, secondary care, home)
- Target population (sex/age)
- Biological sample type
- Bacterial target
- Country of development

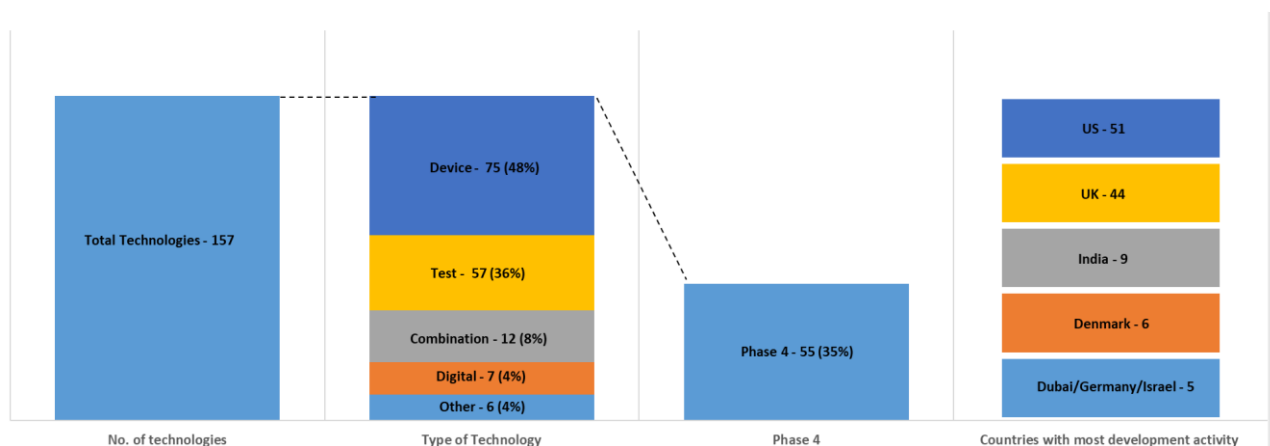
- Classification of development stage: Phase 1 (concept stage); Phase 2 (prototype/early-stage research/ preclinical); Phase 3 (technology validated/demonstrated in relevant environment e.g. clinical study); Phase 4 (commercialised i.e. regulatory approved or technology on the market)
- Regulatory status/market authorisation (including list of approved markets)

In addition to these fields, information related to sensitivity/specificity and limit of detection was captured for diagnostic technologies, as well as clinical trial information and published evidence, where available. Furthermore, intelligence relating to funding/investment, development or competition awards and patents that was available during the review of sources, was captured under 'Additional Comments' in the UTI dataset (accompanying Excel file).

## Results

### Product Pipeline

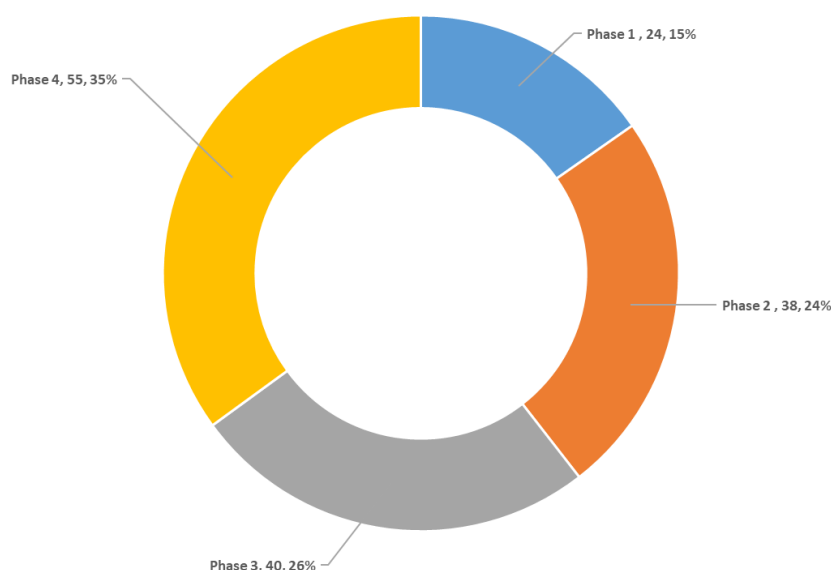
Our horizon scan of primary and secondary sources identified 157 technologies from across 24 countries. Whilst technological developments of UTI solutions are increasingly widespread across the world, our analysis (based on country of development) highlighted that the US (51, 32%), UK (44, 28%), and India (9, 6%) were the top countries for development activity (*Figure 1*). The US was found to develop a wide range of test technologies mainly for the detection of UTIs including multiplex tests (RT-PCR) and disposable tests (Lateral flow immunoassay). Innovations developed in the UK were concentrated on pathogen detection and Antimicrobial Susceptibility Testing (AST).



**Figure 1. Key Insights into UTI Innovations**

157 UTI technological innovations including medical devices, diagnostic tests, digital technologies (or a combination), were identified from across 24 countries. Development activity was largely concentrated in the US (32%) and UK (28%).

All devices identified as part of this scan have been classified based on their stage of development (Phases 1-4), with Phases 3 and 4 indicative of late/mature stage of development. The majority of the devices were in the late/mature stage of development i.e. on or near ready to market, as shown in [Error! Reference source not found.](#). Overall, 26 of the 55 products in Phase 4 (mature phase) have obtained regulatory approval in 1 or more jurisdictions, with 37% of technologies in Phase 4 awarded EU approval (CE Mark).



**Figure 2. Doughnut chart representing the development stages of UTI technologies**

In total, 157 UTI technologies were identified in the Innovations Observatory's scan. The technologies have been classified by stage of development: Phase 1 (i.e. concept) – 24, 15%; Phase 2 (i.e. prototype/early-stage research including preclinical studies) – 38, 24%; Phase 3 (i.e. product validated/demonstrated in relevant environment/clinical study) – 40, 26%; Phase 4 (i.e. product ready to launch/regulatory approved) – 55, 35%.

The vast majority of UTI technologies that were identified were reported to be developed for healthcare professionals use only, however there are a small number of innovative solutions (6) in the pipeline that are adapted for use by unqualified individuals (e.g., the general public) and include device and diagnostic innovations such as TestCard, MinuteFul UTI and Digital Dipstick. Despite the prevalence of UTIs being the highest amongst women, almost 96% of the innovations in our product pipeline scan are indicated for both genders, with a small number (6) specifically for women and a single innovation specifically for men (Flexible cystoscopes, Maulana Azad Medical College). One technology in development, a clinical decision support system for the diagnosis of UTIs, pneumonia or bacteraemia, has been specifically designed by the University of Sydney for use in children who are presenting with a fever. This technology, which utilises a diagnostic algorithm, is being developed to improve appropriate antibiotic use by calculating the likelihood of serious bacterial infection and displaying it to the physician using interactive software. This technology aims to ensure children who have a serious bacterial infection receive the appropriate treatment immediately.

Urinary catheters frequently lead to catheter-associated urinary tract infections (CAUTI), accounting for a high proportion of hospital-associated infections, which are becoming more difficult to treat due to growing antibiotic resistance. An emerging strategy for the prevention of CAUTI that is being explored, is the development of 'Next-Generation Urinary Catheters', through the application of novel materials. The natural mechanism of these novel materials (such as elastomer, hydrogels, silver nanoparticles and nitric oxide), are showing the potential to kill or reduce bacterial attachment. Alternative innovative technology being implemented to address CAUTI includes the application of surface acoustic wave technology that has been developed by NanoVibronix. The technology which is named 'UroShield', works by generating and propagating low frequency, low intensity ultrasonic surface acoustic waves throughout the catheter, which interferes with the attachment of bacteria. In the UK, we have identified 8 developers including Camstent Limited, University of Aberdeen and Mofgen Limited, who are developing 'Next-Generation Urinary Catheters' that are focused on preventative approaches. Next-Generation Urinary Catheters are promising options for addressing the challenge of CAUTI, and could significantly reduce hospital costs (related to CAUTI), decrease length of hospital stay and decrease mortality. These innovative catheter solutions are showing markedly improved outcomes compared with standard catheters in clinical evaluation studies.

### **Innovations for Older Adults**

Our pipeline scan of technological innovations (prevention, detection and monitoring) for older adults (65+) living at home or in care homes identified a small number of innovations in the pipeline internationally. In total 5 technologies were identified that are specifically designed for the elderly population and or a care home setting. Innovations included point of care tests (POCTs) developed by Academical Medical Center (University of Amsterdam) and Waterscope both designed to bring rapid UTI testing into care homes. Another innovative solution is a home monitoring device designed by Imperial College London to detect infections such as UTIs, by monitoring environmental and physiological data of people with dementia within their own homes. Two other innovative devices designed by Buskerud and Vestfold University College and Chang Gung University, detect UTI biomarkers in adult diapers. These analytical devices perform urinalysis using a colorimetric approach and may be viable rapid UTI screening systems.

Despite UTIs having high prevalence in the older adult population and UTI innovations for this population considered an unmet need, our appraisal of market intelligence highlighted two major diagnostic problems facing developers:

- Older adults presenting with a genuine UTI who do not have urinary tract symptoms (i.e. present with non-specific symptoms such as anorexia, confusion and a decline in functional status)
- Older adults presenting with symptoms unrelated to the urinary tract who are found to have asymptomatic bacteriuria and may then mistakenly be diagnosed with a UTI



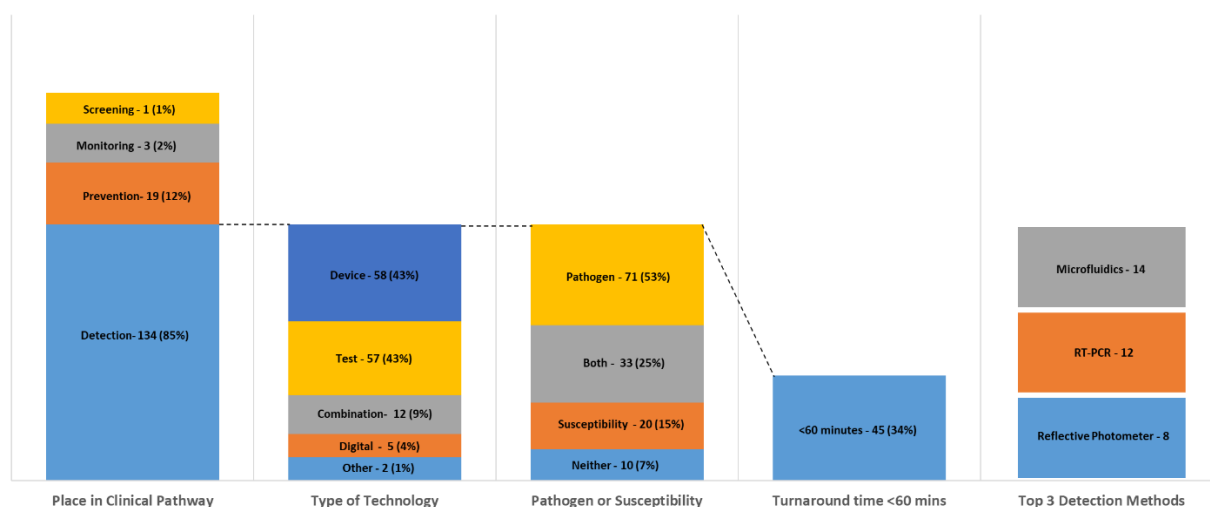
The complexity of diagnosing UTIs in older adults is a key contribution to the small number of technologies identified in the pipeline of innovations. The lack of diagnostic and monitoring modalities for UTI in older adults will continue to place a large burden on the healthcare system, as current standard of care is reliant on clinical monitoring, which is susceptible to diagnostic delays, over and under treatment.

## Detection Innovations

With the prevalence of UTIs continuing to rise, combined with the emergence of antibiotic resistance, there has been a greater demand for technology-enabled solution that assist with the challenges of UTI, in particular new and efficient detection technology. Our analysis revealed that detection of pathogens was the most prevalent type of technology in development for UTI (85%), with the majority of UTI innovations found to be applicable across 2 or more care settings (86, 55%) including GP surgeries, hospitals, nursing homes and other community settings. The need for 1) rapid and accurate diagnostic solutions and for 2) prompt and informed clinical decisions on appropriate antibiotic therapy, is well recognized globally. Current gold standard urine culture diagnostics take 24-48 hours to yield results, however adaptations of traditional methods and innovative methods appear to be driving technological advancements in UTI diagnostic solutions.

As shown in *Figure 3*, a high proportion of detection technologies consist of diagnostic tests or diagnostic devices (medical devices which have the ability to act as a diagnostic). A closer look at the data revealed that the pipeline of innovations contained a wide range of existing (e.g. PCR, fluorescence *in situ* hybridization, immunoassays and mass spectrometry) and novel technologies (biosensors and microfluidics), of which a small fraction appear to be in use within the NHS at present (e.g. Roche Urisys 1100, TestCard, URILYZER 100 PRO). Emerging technologies identified appear to focus on expediting diagnosis via direct pathogen detection from urine samples, and include rapid AST and POCT. For example, the Health Research Institute of the Balearic Islands (Spain) have developed the origami biosensors that detect UTIs caused by *E. coli* at the bedside in less than 7 minutes, showing promising potential as a rapid POCT. To combine gold standard techniques with POCT, the KTH Royal Institute of Technology are in the process of developing miniature, digital culture plates which may offer similar accuracy to traditional culture method. Furthermore, Korean scientists at Ulsan National Institute of Science and Technology (UNIST) have engineered a diagnostic POCT device based on the toy 'fidget spinner', which has the potential to manage the detection of UTIs in different clinical settings.





**Figure 3. Key Insights into Detection Innovations**

134 UTI technological detection innovations including medical devices, diagnostic tests, digital technologies (or a combination), were identified from across 22 countries. Most common detection methods were Microfluidics (10%), RT-PCR (9%) and Reflective Photometer (6%).

Globally, there remains a growing interest in technologies with the potential to expedite UTI diagnosis using enhanced screening, molecular pathogen identification, and rapid AST. Most developments to date have been targeted toward decreasing the turnaround time and enhancing automated processing in the clinical laboratory. In total we identified 40 rapid solutions which reported to provide results in 30 minutes or less (sample to results). Of these 12 had a turnaround time of 16-30 minutes, 7 could report to produce results in 6 – 15 minutes, whilst 21 could provide results in under 5 minutes. The detection strategies implemented in these rapid solutions include biosensors which along with the shortened assay time, only require a small sample volume, are high throughput and highly portable. We have also observed the integration of smartphone technology into detection platforms (e.g. TestCard, Minute UTI, smaRT-LAMP, University of Bath Smartphone UTI test). It is worth noting that most of these emerging technologies have not been rigorously tested in large-scale clinical settings and or are not in a format that facilitates use on a large scale (e.g. clinical laboratory). Therefore, further consideration for system integration is needed for widespread clinical adoption. Also, different technologies might prove to be optimal for different clinical settings. For example, the improved diagnostic potential of immunological-based lateral flow assays over conventional dipsticks could be adequate for community settings. Biosensor or microfluidic systems capable of integrated pathogen identification and AST may provide the greatest clinical benefit for complicated UTI.

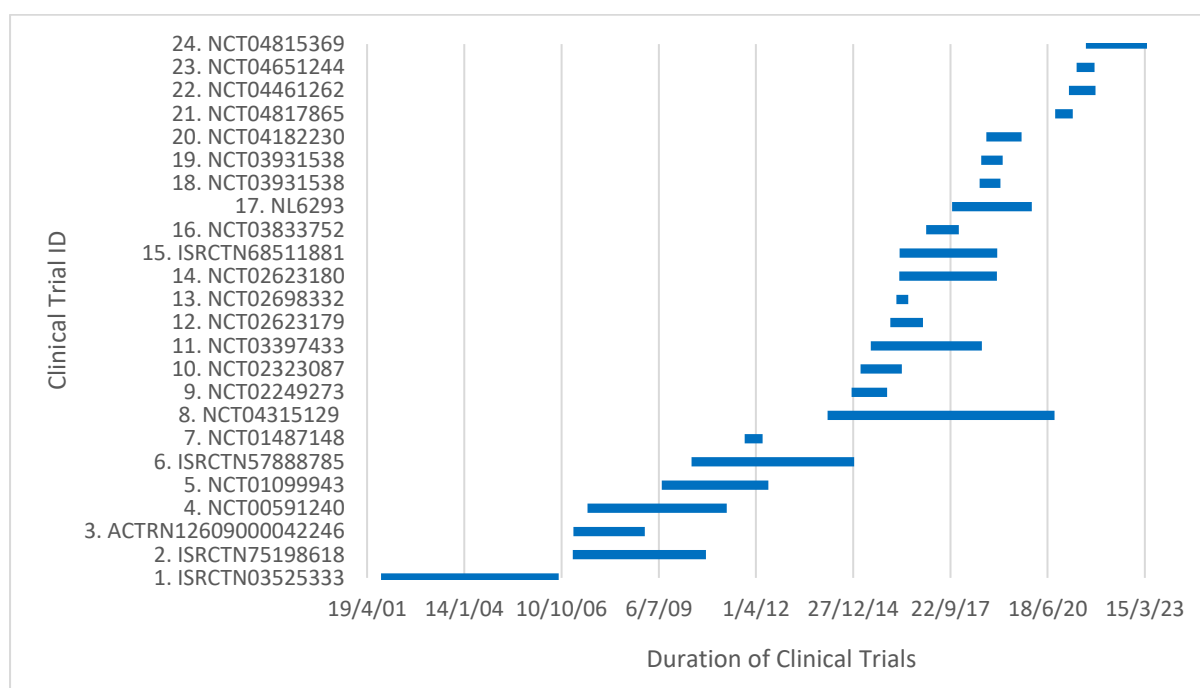
Overall, we have observed a significant growth in the development of new and emerging technological advancements in UTI innovations. Technological developments focus on rapid, diagnosis, AST and preventing infection through catheters. These new technologies present a promising opportunity towards improved antimicrobial stewardship and patient outcomes.

## Clinical Trial Landscape

ScanMedicine, IO's clinical trials tool was utilised to gain access to clinical trial data from 11 registries from across the globe (including UK, Europe, USA, Australia, Japan and Brazil). The clinical trial search excluded trials out of scope e.g. non-medical technology interventions (e.g. supplements), as well as trials where the evaluation of medical technologies was not the primary intervention (e.g. drug trials).

*Figure 4*, depicts the changing clinical trial landscape covering trials registered between 2001 – 2021 and provides a holistic perspective of the evolving clinical research ecosystem, including activity by trial start date and the duration of trials to completion. In total, 27 trials were identified which meet the inclusion criteria for the scope of this work (*Figure 4*). There were 3 trials (CTRI/2019/04/018460, CTRI/2018/09/015678, ACTRN12611000344998) that were omitted from the data visualisation, as no information was provided on the primary study completion date. The clinical trial landscape indicated a focus on novel detection methods (10, 37%), assessment of catheters and catheter biofilms (5, 19%) and digital technology or computer-based systems to aid clinical decision making in relation to UTI's (4, 15%). 26 of the clinical trials identified were undertaken with adults, with 1 trial including children less than 5 years old (ACTRN12609000042246). The Australian study, sponsored by English biotech company Camstent Ltd, compares a computer decision support system with a structured febrile assessment tool or standard care. The study which is ongoing, aims to evaluate which method provides the most appropriate diagnosis and antibiotic prescription for children under 5 with pneumonia, UTI or bacteraemia.

The coverage of trials involving UTI technologies (diagnostic, digital and devices) comprised North America (40%), Europe (33%), Asia (15%), Oceania (7%) and South America (4%). On a national level the US (11), UK (6) and Denmark (3) were revealed as the countries with the most clinical trial activity over the last 20 years.



**Figure 4. Evolving clinical trial Landscape**

The clinical trial landscape (activity and duration) for UTI technological innovations.

Our global clinical trial scan showed that most trial activity focused on the application of technological innovations for the general population. Whilst only 2 trial were identified which specifically evaluated technologies in the elderly population and or care homes home setting, a number of the trials and innovations identified in the trial landscape, may have wider application to this population. A trial completed in 2019 by the University of Sydney evaluated point of care diagnostics to guide appropriate antimicrobial therapy of UTIs in nursing homes (NL6293). A new trial led by Pathnostics (NCT04815369, completion 2023) is evaluating if Guidance® UTI Clinical Pathway, compared to traditional pathways, will reduce the proportion UTI-related adverse events within nursing homes (NCT04815369). Guidance® UTI pathway utilises molecular testing for UTI, Pooled AST, and polymicrobial infections and has the potential to reduce use of broad-spectrum antibiotics and improve health related patient outcomes.

A study led by Imperial College London, evaluating a novel Smart Catheter biosensor for early detection of CAUTIs has recently been completed (2020). The study (NCT04315129) aimed to validate the accuracy and speed of pre-emptive CAUTI diagnosis through continuous urinary biochemical monitoring. The validation of this biosensor with patient-derived samples will help to determine the robustness of this novel biosensor, and demonstrate its practical clinical use for providing early diagnosis of developing infections. In addition to the development of technologies, we also identified innovative biological collection products under evaluation. A study undertaken by Pathnostics (ISRCTN68511881) evaluated the use of 2 urinary collection devices which aim to reduce contamination of urine samples. This study, which was completed

in 2018, was undertaken in a primary care setting (GP surgeries) and has the potential to improve the levels of contamination in urine samples collected.

### **Patent Landscape**

The data from our international patent scan revealed that there were 8,502 patent applications in the field of UTI technological innovations. North America accounted for 61% of the patent landscape, followed by Europe (11%) and Asia (2%). The leading countries of patents filings were the US (4,161), China (141) and Canada (28). Our data analysis also revealed that 37.5% of patent applications have worldwide patent protection through the World Intellectual Property Organization (WIPO). Since the 1950s, patents have gradually increased, with an average of 351 new annual patent applications in the last decade. Growth in UTI innovation patents appeared to peak in 2019 and 2020 and has been slower in 2021, which is likely due to the impact of the pandemic. Leading patent topics included biomarkers of UTI (such as proteins, enzymes and molecular markers), absorbent sanitary items implanted with detective strips, lateral flow tests, and medical devices paired with diagnostics (e.g. catheters and urostomy bags).

### **Key Providers**

Internationally, industry (small or medium-sized enterprises and large enterprises), research institutions, funding agencies, clinical laboratories, hospitals and other healthcare organisations continue to play a key role in the development of innovative UTI interventions. We identified over 120 developers during our global scan, largely based across North America and Europe. Key developers included Sysmex, OmiX Research and Diagnostics Laboratories, Imperial College London, University of Southampton and University of Bristol.

In general, innovations developed by biotechnology companies were found to be at the late/mature stage of development (i.e. clinical validation or ready to market), whereas products developed by laboratories or research institutions were at the early stage of development (i.e. prototype/ early-stage research). The large number of academic research institutions (UK and International) in the UTI technological landscape highlights their strong focus on the Global AMR strategy. These institutions are building on their research strength and driving the development of technological advancements in the UTI field, as reflected in the wide range of innovative solutions (over 40), captured in this technological landscape.

At a national level, the UK continues to play a leading role in the development of innovative UTI solutions, which predominately focus on rapid diagnostics. Imperial College London have a development portfolio of 5 UTI technologies which is attributed to their multidisciplinary approach to antimicrobial research, which involves collaborations with internal and external stakeholders. The University of Bristol have received several research grants to develop novel AMR technologies, which has led to the formation of the spin-off company Vitamica. The company is developing a novel diagnostic technology to test pathogenic bacteria for susceptibility to antibiotics within one hour. With a considerable number of 'innovative active' developers in the UK (35) contributing advanced UTI technologies to the global technological

landscape, this presents a significant opportunity for the NHS (and wider) to consider the clinical, financial, infrastructural, logistical, and organisational provisions to improve preparedness for the potential adoption of future innovations, which provide the greatest clinical benefit for UTIs.

The rapid development of new and emerging UTI technologies in healthcare, undoubtedly increases the complexity and challenges of identifying the most potentially promising technologies. From our dataset, we identified technologies with high potential that have attracted investment and or have been shortlisted for development awards and competitions, based on available information at the time of extraction from the information source. Technologies (presented in *Table 1*) include the application of existing (e.g. mass spectrometry) and novel (e.g. microfluidic and biosensor) technologies to pathogen identification and AST.

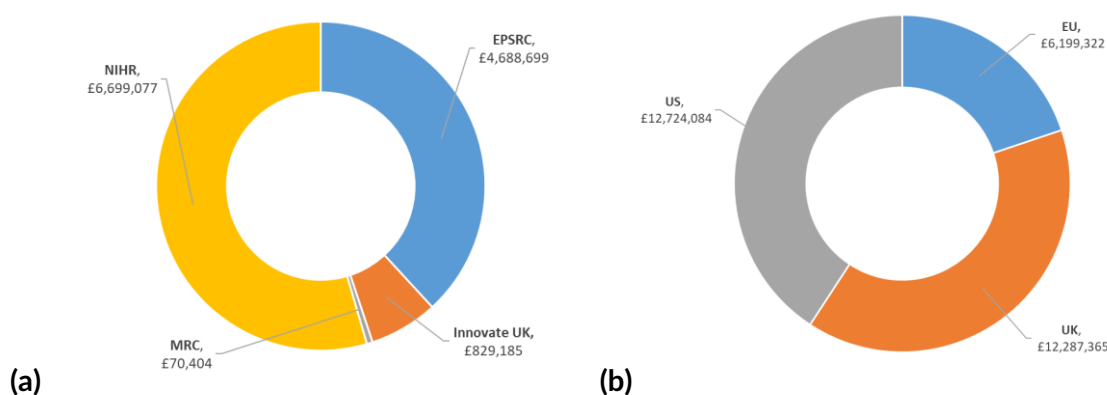
**Table 1 New and emerging UTI technologies with high potential**

Developer	Technology	Product Description	Location
Pattern Bioscience	Digital Culture™ technology	Single-cell analysis with AI pattern recognition to bypass time-consuming culture steps. At phase 2 in development, with funding from CARB-X and AMR Diagnostic Challenge Fund. Product can be used across UTI, RTI and blood stream infection (BSI)	US
Vitamica	Unknown	Start-up Vitamica, with links to University of Bristol, have received NIHR funding for development of a novel AST for UTIs, using Sub-cellular Fluctuation Imaging (SCFI)	UK
Bioamp Diagnostics	DETECT	Rapid test for ESBL using Enzyme Trigger-Enabled Cascade Technology, currently at phase 3 in development with Longitude Prize and NSF funding	US
OmixResearch	OmiX rapAMR CARBA / ESBL / Colistin / CAZ - AVI	Omix Research have received Longitude prize for funding for development of a number of rapid molecular antibiotic resistance tests for UTIs currently in phase 3 of development	India
BiosparQ	Cirrus® D20	Real-time bacterial profiling (pathogen and susceptibility) using mass spectrometry. Can be used across a range of applications, including detection of UTI. Currently in phase 3 development with Longitude Prize funding	Netherlands
Imperial College London	Smart Catheter	A Novel Biosensor for Early Detection of Catheter Associated UTI, clinical trial completed July 2021	UK
Module Innovations	USENSE / ASTSENSE	First Indian Biotech company to be funded by CARB-X. Funding related to POCT for diagnosis and AST in UTI	India

## Funding Landscape

Our scan of international funding databases (consisting of the UK, EU and the US), identified 62 projects related to UTI technological innovations. Our scan included both active and completed projects and covers a range of results collated between 2003-2021. Our data showed that the large majority of funding was awarded to research grants. On a national level, we identified several UK agencies funding the acceleration of innovations in the UTI field, including the EPSRC and Innovate UK (Figure 5a). In the US, funders investing in the development of UTI innovations included the National Institutes of Health (NIH) and Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X). Our data revealed that the highest number of funded projects were located in the US (28) and the National Science Foundation (NSF) (as a single agency) awarded the highest number of projects (14, 23%) in the US, followed by the National Institute for Health Research (NIHR) (9, 14%) in the UK. The US and the UK represent a high level of research and innovation activity in the field of UTI innovations, and overall they contributed the largest proportion of funding for research and innovation (Figure 5b). Overall, the NIHR contributed the largest proportion of funding, investing £6,699,077 (21%) into UTI innovations which mainly consisted of research grants, followed by the European Commission who awarded £6,157,104, (20%). Our data shows that funding awards mainly focused on AST and POCT for the diagnosis and monitoring of UTI.

PhenUTest UK is an innovative AST technology that has recently received funding from Innovate UK (£257,322) due to its ability to determine antimicrobial susceptibility within 30 minutes using state of the art technology. This technology has the potential to ensure patients receive the correct antibiotic treatment at the first GP visit. In the US, DETECT a rapid point of care diagnostic test has received funding from the NSF (£224,996) as it uses a dual-enzyme trigger-enabled cascade technology to allows for rapid identification of pathogens for first-line antibiotic prescription.



**Figure 5. Doughnut charts representing the funding allocation for UTI technologies**

In total, 62 funded projects for UTI technologies were identified in the Innovations Observatory's scan. (a) Represents the breakdown of funding allocated to these projects by research organisation in the UK (EPSRC,



Innovate UK, MRC, and NIHR) and (b) demonstrates the amount of funding allocated internationally consisting of the UK, EU, and US. Please note that 6 projects have been omitted from the funding landscape visualisation due to incomplete information (including amount of funding award and or location of project).

## Conclusions

Advances in UTI innovations has the potential to generate significant benefits including rapid diagnosis and improved clinical decision making on treatment. Our horizon scan provides valuable and relevant insights into the global scale of UTI development activities covering a diverse range of technology types (devices, diagnostics and digital). Solutions in the pipeline include existing and new methods (e.g. microfluid technology) with a variety of applications automated/semi-automated portable analysers for POCT, phenotypic resistance tests and AST. The two key 'innovation' themes emerging from our scan and review of market reports are:

1. Innovations focussed on rapid and accurate UTI diagnosis
2. Innovation focussed on rapid detection of antibiotic sensitivity

Whilst a large number of technological solutions show promising potential for adoption and widespread use, it is important to note that the 'optimal' use of each UTI innovations will vary depending on the clinical setting.

The findings from our scan provide important, immediately relevant data on the pipeline of innovations for UTIs, which will continue to grow due to technological advancements and the increase demand from healthcare systems worldwide. The data and insights provided will allow members of the NHSE/I and the AMR Programme Board (and wider), to evaluate the potential impact of these technologies against their priorities and anticipate some of the consequences for policy actions, service delivery and health economics.

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Room 3.12, 3 Science Square,  
Newcastle Helix,  
Newcastle upon Tyne NE4 5TG