Pee-In-Pot clinical evaluation-Microbiological Safety Profile

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Study group:

- Somerset NHS Foundation Trust Commercial team
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- Valerie Yick – Senior Infection Control Nurse, Somerset NHS Foundation Trust
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- Peter Harvey – Community Matron (Frome & West Mendip Hospitals), Somerset NHS Foundation Trust
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Independent scientific review: Dr Robert Porter, Consultant Microbiologist, Royal Devon University Healthcare NHS Foundation Trust.

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Infra-structure support: Somerset NHS Foundation Trust Quality Improvement team.

Protocol review: Drafted by Joseph John and reviewed by all working group parties.

Rationale and background:

Urinary tract infections (UTIs) represent a common cause of morbidity and mortality amongst patients, and represent a large proportion of patients admitted to hospital. They can substantially affect patient's quality of life and are a costly burden on health services. Urine microscopy, culture and sensitivity (MC&S) testing is therefore performed very frequently. Despite this, and despite the importance of gaining accurate test results, there is a high degree of variation in how urine specimen collection is performed. This variation risks inaccurate results, and the addition of unnecessary wasteful and expensive practices.

The Pee-in-Pot (PIP) innovation is intended to address practice variation, cost, and unnecessary plastic waste involved in the process of urine sample collection. Its shape provides a one-item solution for collection, dipstick testing, and decanting of exactly 10mL of urine into the appropriate 10mL boric acid container for laboratory testing. Its composition from thermofibre pulp makes it a more sustainable alternative to plastic, storing biogenic carbon from the atmosphere and undergoing disposal by maceration and flushing rather than incineration. Its clean but non-sterile nature allows it to be packaged and distributed more efficiently, and avoids sterile packaging.

The ability to safely and accurately test urine for MC&S using clean pulp has been demonstrated within Somerset in antenatal care. Comparison with similar units using sterile plastic pots for collection identified no clear difference in reportable culture rates between these units. Preliminary testing of the PIP in clinical areas gained favourable feedback from patients and staff, and once again no clear difference in urine culture results have been observed.

As a next stage in the evaluation of the PIP quality improvement intervention, we assessed the PIP against a standard of care sterile plastic collection device in a head-to-head format. We collected patient urine samples which were then be decanted into the usual boric acid tube, and into a second boric acid tube having been passed through the PIP. We have generated evidence that tested the hypothesis whether the PIP can be safely used as an alternative to sterile plastic for urine collection for MC&S.

Aim: To compare the performance of the Pee-in-Pot (PIP) urine collection container against the current standard of care (SOC) for performing mid-stream urine (MSU) microscopy, cultures and sensitivity (MC&S).

Objectives:

- Determine whether urine held within the clean, non-sterile, PIP has a different rate of reportable urine cultures compared to the SOC.
- Determine whether any identified variation in culture results would result in a change in clinical management.

Hypothesis:

We hypothesised that urine passed through the PIP before MC&S testing will provide comparable urine microscopy, culture and sensitivity results to that which has been tested according to usual best-practice defined technique.

Population:

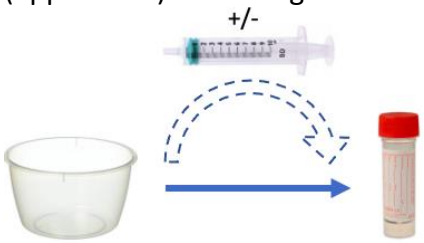
- Patients providing a routine mid-stream urine (MSU) sample for MC&S.

Intervention:

- MSU that has been collected using the SOC technique is passed into the PIP before being decanted onwards into the SOC boric acid tube.

Comparison (standard of care):

- MSU that has been collected using the SOC technique, into a sterile container and decanted into the SOC boric acid tube in the manner normally practiced. This is the technique as recommended by the local infection control team and based on the Royal Marsden Nursing Manual of Clinical Nursing Procedures recommendation (appendix 3). A visual guide is included in a separate file (appendix 5).



Design and setting:

- A head-to-head comparison of urine MC&S results for MSU specimens that have been passed through the PIP container, against those which have not been passed through the PIP.
- A single urine sample was produced by each patient, and this was sent as two separate labelled specimens for culture; one intervention (PIP) sample and one comparison (SOC) sample.
- The study was performed in the following settings:
    1. Antenatal clinic. *This provided high testing volumes.*
    2. Acute frailty unit. *This provided high testing volumes in a population with higher rates of asymptomatic bacteriuria and contamination.*
    3. Montecute (surgical) ward.
    4. Surgical decision unit.
    5. Fielding (medical) ward.

Inclusion criteria:

- All patients providing mid-stream urine samples in any of antenatal clinic, acute care of the elderly admissions ward, medical and surgical outpatients, paediatric ward.

Exclusion criteria:

- Catheter urine samples. *The best practice (Royal Marsden and local protocol) is to aspirate these from the catheter bag port and to transfer directly into a boric acid tube. Therefore neither a sterile pot nor a PIP are warranted.*

Consent:

Within the remit of this quality improvement project consent was not deemed to be necessary. All patients were offered the standard of care sterile plastic urine collection pot in which to urinate, and their sample was processed in the usual way. The additional step of

testing urine through the PIP was performed, however whilst these results were analysed, they were not added to the patient's record.

Primary outcome:

- The rate of **reportable** urine culture results, defined as specific organisms present at or above a threshold number of colony forming units (CFU). The definition of reportable urine culture results is outlined by the Southwest Pathology Service (SPS) standard operating procedure and/or UK Standards for Microbiology Investigation (SMI), "Investigation of Urine" guidance (1). Outcome measures are outlined in appendix 4.

Secondary outcomes:

- The rate of mixed growths
- Small particle counts; all small particles, bacteria, cellular casts, epithelial cells, granular casts, hyaline casts, red blood cells (urine), red blood cell casts, white blood cells (urine), white blood cells (casts).

Categorisation of data:

Patient sex was recorded. Patients were categorised into the following age groups except for those attending antenatal clinic and paediatrics:
Age 16-65
Age > 65

Antenatal clinic – no age categories applied.
Paediatrics – one age classification which is <16.

Statistical planning:

See appendix 2 for power calculation.

Study management:

The study start date :18th October 2023.

Day to day management of the study was undertaken by Mr Nick Burns-Cox, and a dedicated healthcare assistant (HCA). The HCA will visit each ward every morning to assess the following:

- PIP stock levels
- PIP storage, urine collection and the process of sending samples to the lab are in accordance with the study SOP. This is detailed in appendix 3.

Education about appropriate storage of the PIP device, and how to collect and transfer urine samples will be conducted by Tracey Doolan (infection prevention and control nurse).
Microbiology oversight will be performed by Rob Porter (clinical) and Andrew Walker (laboratory).
Statistical analysis oversight was performed by Andrew Mayne-Chief Data Scientist.

Monitoring and audit of the quality improvement project was conducted by the study management group based at Somserset NHS Foundation Trust, who meet regularly.

Interim data analysis:
After the study had been underway for 7 days, a preliminary data extraction took place. Raw data was shared with the statistical analysis team (AM) to ensure the following:

- It was is in a format that can be analysed
- All outcome measures were reported
- It was possible to distinguish between the SOC and PIP urine samples for each case.

Time scale:
The scheduled timescales led to study completion by February 2024 (5 month period).

Milestones	0 –1m	1-1.5m	1.5-4m	4-5m
Protocol completion				
Staff communication and training in clinical areas:				
Laboratory staff training:				
Data collection				
Data analysis				
Write-up				

Protocol review:
Independent opinion about microbiological aspects of the protocol were provided by Dr Robert Porter, consultant microbiologist and a member of the PiP Study Project Team.

Patient and Public Involvement and Engagement:
Patient feedback about the PIP was collated during previous testing. Patients typically commented that it was similarly easy to use in comparison with other urine collection containers, and that they viewed it favourably due to its reduced environmental impact.

Data management:
Each patient undergoing urine testing had the two urine tests sent to the laboratory. These two samples received separate laboratory IDs and were processed separately. The overall and clinical area-specific numbers of dual urine samples collected were monitored periodically until sample size criteria were met. At this point the study was discontinued and the dataset extracted by the laboratory manager (Andrew Walker). This dataset was pseudonymised prior to statistical analysis, with the paired urine samples having a common numerical identifier, followed by a letter P (PIP arm) or letter S (SOC arm). **Patient age and sex, and the clinical setting from which the urine sample was collected, are the only additional variables that were recorded.**

All study data were stored on a password-protected study specific folder on the secure Somserset NHS Foundation Trust server. All data was collected and stored in compliance with data protection guidelines and Trust clinical governance policy.

No interim analysis was performed.

Data Confidentiality:

All participant data has been held in a link-anonymised format, with personal identifiable data only accessible to personnel with training in data protection who require this information to perform their duties. Participants' research and sample data was identified by unique study ID numbers and all data has been held on password-protected computers. Only delegated members of the QIP team have access to personal identifiable data. To comply with the Data Protection legislation information was collected and used fairly, stored safely and not disclosed to any unauthorised person. This applied to all data held. The study group preserved the confidentiality of participants taking part in the study and ensured the EU General Data Protection Regulations (GDPR) in conjunction with the UK Data Protection Act 2018.

The following individuals had access to participant's personal data during the study:

- Laboratory team processing urine samples, and urine sample report.
- Data analyst, who will pseudonymise the dataset for analysis.

All other team members only had access to analysed anonymous data.

Data Storage and Archiving:

All electronic data will be stored on an encrypted, password protected server at Somerset NHS Foundation Trust, with regular file backup. The server is stored in a dedicated secure facility. Data transfer to this server will be via password protected encrypted NHS email, or using a password protected encrypted USB storage device. Archiving will be undertaken as per current standard Somerset NHS FT protocols and procedures. Study data will be stored at the sponsor site for 5 years, in keeping with sponsor site research and development standard operating procedures.

Risks of bias:

- Clinical team bias. The attached guidance outlines the means of collecting, decanting and sending off urine for the study. The concept of clinical equipoise driving the need for this study was explained to staff involved. Clinical staff bias was therefore not felt to be a significant risk to the internal validity.
- Unequal biomedical scientist scrutiny of culture results. New practices might undergo additional scrutiny from laboratory biomedical scientists, as part of external validation exercises. The SPS laboratory operates a Kierstra automated system, however. This automated system means that the scientists who process urine samples were blinded as to whether they came from a PIP sample or a SOC sample. Scientists were presented with a high-definition photo image to analyse for

microscopy, with an associated laboratory number. This did not indicate whether the specimen came from a PIP or not. The same was true for the scientists processing the urine culture and analysing its results.
- Research team bias. By deciding upon outcome measures and statistical analysis in advance, and by gaining independent microbiology advice and statistical analysis, we aimed to reduce the risk of researcher bias in both study design and results interpretation.

Adverse event recording and reporting:
Given that urine was collected using the previously used standard of care method, and that PIP culture results are not be visible on the patient's record, the risk of an adverse event related to this study was extremely low. In the event of an adverse event due to deviation from protocol, the study group was set up to be convened within 72 hours, the incident discussed, and any necessary mitigating measures planned. This in theory included discussing the safety of continuing the study.

Benefits to patients:
The potential benefits to patients are:
- Standardisation of the urine collection leading to more accurate test results
- Reduced environmental impact of healthcare by making this common test less environmentally harmful. This will have downstream public health benefits.
- Reduced financial strain on health services by providing a cheaper alternative, releasing financial resource for other health-related purposed.

Risks to researchers:
There were no anticipated risks to the researchers. There was a small risk that the increased workload placed upon clinical staff (producing and labelling an additional urine sample) could have made it more challenging to complete their usual duties. Responsible oversight to ensure that this did not occur lay with the senior nurse in each clinical environment. Laboratory staff might have found that the increased workload made it more challenging to complete their usual duties. Oversight of this was provided by Mr Andrew Walker, SPS laboratory manager.

Dissemination/implementation of research
Results were written up and are to ne submitted for publication in a peer-reviewed journal (BMJ) . Abstracts will be submitted to national and international conferences (nursing and medical). Written information in the form of a letter outlining the key findings of the study will be sent to all participants and any stakeholders.

End of study
The study completed when data for all participants had been collected, analysed and interpreted in the form of write-up and presentation as outlined above in the Gantt chart.

Appendix 1. References.

1. PHE. UK Standards for Microbiology Investigations [Internet]. gov.uk. 2019 [cited 2023 Aug 14]. p. 1–51. Available from: https://www.gov.uk/government/publications/smi-b-41-investigation-of-urine

Appendix 2: Statistical Power Calculation

1. Based on this information with a 2% error margin and 95% confidence interval

The size of the control and experiment group is the same. (t-test)

Sample sizes of MSU Suggested.xlsx

2. Baseline Mid Stream Urine Specimen Positive Culture rates (Table 1)

Baseline MSU Rates.xlsx

Appendix 2 – power calculation

for the actual sample size calculation, a difference in proportions test was used (two independent proportions):
9.1 - Two Independent Proportions
which allowed us to estimate the required number of samples so that the confidence interval for the difference in proportion was within +-2.5%. For the actual comparison, a confidence interval based on the McNemar test was used.

Appendix 3: SOP for storage and use of the PIP

SOP - PiP Trial

Storage of PiP's

1. Main Stores
    - Boxes must be stored in a clean and dry environment.
    - PiP's boxes must remained sealed
    - Whole boxes must be delivered to the wards/departments
    - Store staff must not handle PiP's

2. Wards / Departments
    - PiP's must not be stored in a sluice/ dirty utility
    - PiP's must be stored in a clean area
    - Prior to handling PiP's, hands must be cleaned to reduce the risk of cross contamination
    - Once a cardboard box is opened, PiP's must be stored in a covered container preferably plastic with a lid
    - PIP's must be stored inverted within the container

Procedure for obtaining a Midstream Specimen of Urine (MSU)

- Gain consent and explain the procedure to the patient
- Ensure a private location to obtain a sample
- Ensure that the patient has had a wash and that there is no visual contamination of the genital area
- Ask the patient to clean their hands with soap and water
- Pass the patient the sterile bowl and advise them not to touch the top or inside of the bowl.
- Ask the patient to void the first stream of 15-30mls of urine into the toilet
- Then, place the sterile container into the stream of urine without interrupting the flow. Advise to fill half of the sterile bowl
- The rest of the bladder can be emptied into the toilet.
- The healthcare worker should don a pair of non-sterile gloves and take the sample to a clean surface within the sluice/ dirty utility

Send 2 urine samples to the lab

- Request testing on Ordercomms and type '*PiP trial*' into the clinical details

Sample 1 directly from the Sterile bowl

- If required dipstick the urine
- Transfer the urine from the sterile bowl into a 30ml red top urine collection bottle (boric acid)
- Label 30 ml red top urine collection bottle with the Ordercomms request sticker

- The remaining urine will be transferred to a PiP

Sample 2 from a PiP

- Collect a PiP from the store room
- Clean hands prior to touching the PiP
- Hold the PiP underneath and do not to touch the spout, top or inside of the PiP
- If a dipstick was previously required, test from the non-spouted side
- Decant 10mls of urine from the spouted side of the PiP into a 10ml red top urine collection bottle
- Label the bottle with a patient sticker from the medical notes and NOT an ordercomms sticker
- Place remaining urine into the sluice hopper
- The PiP can then be macerated or disposed of in line with the trusts waste management policy if no macerator within the department
- Remove gloves & clean hands

Sending to the lab

- Add the Ordecomms request sticker to the blue micrology bag
- Place BOTH samples into the bag and send to the lab
- Send to the lab at the earliest opportunity

Appendix 4. Categorisation of urine culture and cytometry results

Primary outcome

Reportable culture results	Reported as	Note
Escherichia coli	Present/absent	
Enterococcus sp.	Present/absent	
Streptococcus Group B	Present/absent	only reportable for samples from antenatal, otherwise to be considered contaminant
Proteus mirabilis	Present/absent	
S. saprophyticus	Present/absent	
Coliforms	Present/absent	
Pseudomonas aeruginosa	Present/absent	
S. aureus	Present/absent	

Secondary outcomes

Contamination	Reported as	Note
Mixed growth	Present/absent	
Streptococcus Group B	Present/absent	only reportable for samples from antenatal, otherwise to be considered contaminant
coagulase negative staphylococci	Present/absent	
Candida species	Present/absent	
Other Streptococci	Present/absent	

Small particles	Reported as	Note
All Small Particles	Count	
Bacteria	Count	
Cellular Casts	Count	
Epithelial Cells	Count	
Granular Casts	Count	

Hyaline Casts	Count
RBC (Urine)	Count
RBC Casts	Count
WBC (Urine)	Count
WBC Casts	Count