The George Institute for Global Health

HMRI Hunter Medical Research Institute

The University of Newcastle Australia

NSW Government-Sponsored Clinical Trial: Management of Urinary Tract Infections by Community Pharmacists (Intervention study)

Research Protocol

The George Institute for Global Health in partnership with University of Newcastle, the Hunter Medical Research Institute and UTI research consortium

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Contents

1. Administrative information

1.1 Funding

NSW Health is funding the development, implementation, and monitoring of the trial through a grant awarded to a research consortium led by the Chief Investigator, Dr Sarah Dineen-Griffin from the University of Newcastle, titled *NSW Government-Sponsored Clinical Trial: Management of Urinary Tract Infections by Community Pharmacists*. This protocol is to undertake the Intervention Study.

Several other projects have been linked to this project. An ethics application for co-design has been approved by The University of Newcastle HREC (H-2023-0035). An application for a feasibility study has been approved by The University of Newcastle HREC (H-2023-0030). A separate sub-study has been approved by The University of Newcastle HREC (H-2023-0173) which will examine *Pharmacist Prescribed Antimicrobials for Urinary Tract Infections - Potential Indirect Effect on Local Rates of Antimicrobial Resistance*.

1.2 Roles and Responsibilities

1.3 Investigators

The George Institute for Global Health, UNSW Sydney

Name	Project Role	Position, Affiliation	Contact details
Prof David Peiris	Chief investigator (Intervention study evaluation)	Chief Scientist (acting), Director Global Primary Health Care Program	dpeiris@georgeinstitute.org
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Valerie Looi	Project Manager (Intervention study evaluation)	Project Manager, The George Institute for Global Health	vlooi@georgeinstitute.org.au

University of Newcastle

Name	Project Role	Role, Affiliation	Contact details
Dr Sarah Dineen-Griffin	Chief Investigator (for whole project)	Lecturer (Pharmacy), College of Health, Medicine and Wellbeing, University of Newcastle	sarah.dineengriffin@newcastle.edu.au

Hunter Medical Research Institute

Name	Project Role	Position, Affiliation	Contact details
Associate Professor Penny Reeves	Health Economist	Associate Director, Health Research Economics Hunter Medical Research Institute & Conjoint Associate Professor,	penny.reeves@hmri.org.au

		School of Medicine and Public Health, College of Health, Medicine and Wellbeing	

Additional Chief Investigators

Name	Position	Organisation
Emeritus Professor Shalom (Charlie) Benrimoj	Co-investigator	Emeritus Professor, The University of Sydney
Associate Professor Kris Rogers	Associate Professor in Biostatistics at University of Technology Sydney, Honorary Senior Research Fellow at The George Institute for Global Health	University of Technology Sydney/ The George Institute for Global Health
Emeritus Professor Julie Byles AO	Emeritus Professor, Research Centre for Generational Health and Ageing, College of Health, Medicine and Wellbeing & Director of the Centre for Women's Health Research & Gerontologist	The University of Newcastle & Hunter Medical Research Institute
Dr Indy Sandaradura	Staff Specialist in Infectious Diseases & Clinical Microbiology, Centre for Infectious Diseases and Microbiology Clinical Senior Lecturer, The University of Sydney School of Medicine	Centre for Infectious Diseases and Microbiology, Westmead Hospital and the Children's Hospital at Westmead
Dr Leanne Holt	Pro Vice-Chancellor Indigenous Strategy	Macquarie University
Dr Kylie Gwynne	Director of Research, Department of Health Sciences, Faculty of Medicine, Health and Human Sciences, and Member, Centre for Global Indigenous Futures	Macquarie University
Professor Kylie Williams	Head of Pharmacy, Faculty of Health	University of Technology Sydney
Dr Helen Benson	Senior Lecturer, Pharmacy, Faculty of Health	University of Technology Sydney
Ms Anna Barwick	Lecturer in Pharmacy, University of New England	University of New England
Associate Professor John Rae	Head, School of Dentistry and Medical Sciences	Charles Sturt University
Dr Joanna Moullin	Senior Research Fellow, School of Population Health Deputy Director WA Country Health Service (WACHS)-Curtin Research and Innovation Alliance Implementation Science Program Lead | Enable Institute	Curtin University
Ms Jan Donovan	Consumer representative	Independent

Research Staff and Students

Simone Diamandis	Project Manager and Doctoral Candidate	University of Newcastle
Mitchell Budden	Doctoral Candidate	University of Newcastle
Victoria Chisari	Doctoral Candidate	University of Technology Sydney

1.4 Steering committee

The Project Steering Committee for the study will comprise representatives from partner organisations. The role of the Project Steering Committee is to provide oversight to the study and advice on the development, implementation, and evaluation of the study.

Role	Person	Organisation
Chair	Ms Jan Donovan	Independent Chair
Committee Member	Dr Sarah Dineen-Griffin	Chief Investigator (Lead), The University of Newcastle
Committee Member	Emeritus Professor Charlie Benrimoj	Chief Investigator
Committee Member	Professor Charlotte Hespe	The Royal Australian College of General Practitioners NSW
Committee Member	Mr Chris Campbell	Pharmaceutical Society of Australia
Committee Member	Ms Catherine Bronger	Pharmacy Guild of Australia NSW
Committee Member	Dr Yann Guisard	Rural Doctors Network NSW
Committee Member	Mr Richard Samimi	Pharmacy Council NSW
Committee Member	Ms Jess Hadley	Pharmaceutical Defence Limited NSW
Committee Member	Dr Kylie Gwynne	Macquarie University
Committee Member	Mr Daniel Gilbertson	Deloitte Australia
Committee Member	Prof David Peiris	The George Institute for Global Health
Committee Member	Dr Elizabeth Deveny	Consumer Health Forum
Observer	Dr Jan Fizzell	NSW Ministry of Health
Secretariat	Ms Simone Diamandis	Research Project Manager

1.5 Glossary of abbreviations and terms

APDC	Admitted Patient Data Collection
CFIR	Consolidated Framework for Implementation Research
ED	Emergency Department
EDDC	Emergency Department Data Collection
EPA	Extended Practice Authority
GDS	George Data Systems
GP	General Practitioner
HREC	Human Research Ethics Committee
ID	Identification
MBS	Medicare Benefits Schedule
MMM	Modified Monash Model
NPT	Normalisation process theory
NSW	New South Wales
PSA	Pharmaceutical Society of Australia
PBS	Pharmaceutical Benefits Scheme
SEIFA	Socioeconomic indexes for area
TGI	The George Institute for Global Health
UoN	University of Newcastle
UTI	Urinary Tract Infection
UTIPP-Q	Urinary Tract Infection Pharmacy Pilot – Queensland

2. Protocol Synopsis

The aim of this overall research is to evaluate the clinical and economic impact and implementation of a service model (intervention) delivered by community pharmacists in NSW, and 5 pharmacies in ACT, managing UTIs for a specific patient cohort (women aged between 18 years and 65 years) presenting with symptoms consistent with an uncomplicated UTI.

Specific objectives are to:

1. Assess implementation uptake of the intervention including the reach, fidelity and adoption of the intervention in community pharmacies, participant characteristics, and variation in uptake by geographic region.
2. Assess the clinical and experience outcomes for patients managed and/or treated by community pharmacists.
3. Assess the safety of the intervention and identify any risks that need to be addressed for future implementation.
4. Evaluate acceptability and feasibility of the intervention to pharmacists, other care providers and participants using the service.
5. Identify contextual enablers and constraints to access, adoption, fidelity delivery, impact, sustainability, and generalisability of the intervention.

The service will be tested with the aim of understanding the effectiveness of the service, appropriate use of antibiotics, impact on use of other health service resources and impact on supporting self-care. The implementation process and potential for future sustainability of the intervention will be investigated using an implementation science framework [1-3].

The study will use a cohort study design to assess the clinical and economic and implementation of the intervention in NSW and ACT over a 10-month study period. The intervention is multicomponent including Pharmacist training and support and a Pharmacy consultation, using an IT program, applying a clinical management protocol. Pharmacies and pharmacists must meet the criteria of an 'approved pharmacy' and an 'approved pharmacist' outlined in the NSW Health Authority to participate.

The primary outcome will be self-reported 7-day symptom resolution rate. Secondary outcomes include rates of primary care utilisation, medication utilisation, hospital service utilisation, patient experience, and safety outcomes. Implementation outcomes will also be assessed to examine the fidelity, reach and adoption of the new service. Sub-group analyses will look at variation in outcomes based on participant demographics, geography, and clinical characteristics as well as pharmacy level characteristics. Semi-structured interviews with pharmacists and other stakeholders will be conducted to better understand barriers and facilitators to implementation of the service.

3. Introduction

3.1 Background to community pharmacy prescribing

On an international and national basis, the scope of practice for community pharmacists is evolving rapidly. The prescribing of antibiotics by pharmacists for females between the ages of 16 and 65 with uncomplicated Urinary Tract Infections (UTIs) has become usual practice in the United Kingdom, Canada and Queensland Australia [4-10].
The NSW and ACT Governments have recognised the expanded role community pharmacists could play. The broad goals of the initiative are to increase the community's access to primary care through:

1. Authorising pharmacists to administer a wider range of public health and travel vaccinations from 14 November 2022, including Japanese Encephalitis, Hepatitis A and Hepatitis B, Poliomyelitis, Typhoid and Zoster.
2. Funding a trial to evaluate allowing pharmacists to prescribe medication for urinary tract infections.

3. Supporting a state-wide trial where appropriately trained pharmacists can prescribe medications for certain conditions, such as skin ailments, ear infections, and hormonal contraception [11].

This study protocol refers to the second goal above.

Clinical data indicates that rapid and accurate diagnosis of UTI is essential to ensure timely and effective treatment [12]. Rapid diagnosis and effective early management can help reduce serious urinary infections [13]. There are approximately 2.4 million women aged 18-65 years in NSW [14]. UTIs are a common condition, and they are more common in women than in men. According to data from the Australian Institute of Health and Welfare, approximately 3 million cases of UTIs are diagnosed each year in Australia, and most of these cases are in women. UTIs accounted for 1.2% of all problems managed in Australian general practice in 2015-16 [15]. There were 76,854 hospitalisations for kidney infections and UTIs in 2017–18 [16]. The hospitalisation rate for kidney infections and UTIs among Aboriginal and Torres Strait Islander people is double the rate for other Australians [15]. The AIHW reported 109,612 emergency department presentations by principal diagnosis (diseases of the genitourinary system) in 2019–20 [17], however noting this is includes a wider range of conditions than UTIs alone.

International context - The evolution of a community pharmacy in Australia has mirrored international trends. In New Zealand (NZ) there has been an emphasis on integration, spanning primary care delivers and secondary care [18]. This has also occurred in the United Kingdom (UK), where pharmacists are seen as part of the integrated solution to patient and healthcare demands [18]. In the United States, pharmacists are being recognised as part of integrated teams, with opportunities provided by a proliferation of new models such as medical homes, and community-based care teams [19]. Canada, the UK and NZ are arguably advanced in terms of the enhancing pharmacist roles and scope of practice in areas such as minor ailment or common clinical conditions services, pharmacist prescribing, personalised medicines support and screening and chronic disease prevention [20].

The availability of UTI prescribing services by pharmacists varies by country [4-10]. Some countries have laws and regulations that allow pharmacists to treat and prescribe antibiotics for UTIs. In certain states of the United States, pharmacists can prescribe antibiotics for UTIs under certain conditions. In the United Kingdom, pharmacists can prescribe antibiotics for UTIs through a local extension of the national Minor Ailments Scheme. The UTI scheme is available in some areas through local commissioning; however, these vary greatly in eligibility criteria and method of diagnosis (to test or not to test) [21]. In Canada, most provinces have legislation which allow pharmacists to prescribe antibiotics for UTIs. Published studies of community pharmacy-led UTI services report the use of clinical assessment without the additional use of a urine dipstick test [5, 9, 22]. In Canada, most provinces have legislation which allow pharmacists to prescribe antibiotics for UTIs.

Overall, the impact of pharmacist prescribing services for urinary tract infections (UTIs) globally has been positive in terms of improving access to care, reducing the burden on primary care physicians, and decreasing the likelihood of antibiotic resistance. In several countries, the implementation of pharmacist prescribing services for UTIs has also been shown to improve patient outcomes [4-10]. For example, studies have shown that pharmacist prescribing for UTIs is associated with faster symptom resolution, improved patient satisfaction, and lower rates of treatment failure [4-10]. Furthermore, a systematic review published in the Canadian Pharmacists Journal also found that pharmacist prescribing for UTIs was associated with high rates of clinical improvement, low rates of retreatment and adverse effects and decreased health care utilisation [8]. However, it is important to note, the quality of studies is variable and there is an opportunity through this trial to generate more robust evidence and make an important contribution to international literature.

Australian context - Further to a two-year pilot program [10], the Queensland Government has implemented regulatory changes to allow Queensland community pharmacists, as usual practice, to manage UTIs through supply of antibiotics to a select patient cohort. From 01 October 2022, the Queensland Government Extended Practice Authority 'Pharmacists' (EPA) authorises a pharmacist who has successfully completed training in accordance with the EPA to sell a medicine listed in the EPA to an eligible patient, without the requirement for a prescription, for the treatment of a UTI [23].

The NSW and ACT Government have committed to examining the impact of the management of UTIs by community pharmacists under a clinical trial framework to capture robust outcome data to inform the future scope and role of community pharmacists. The implementation of a large-scale trial across NSW (and 5 pharmacies in the ACT) will help the State Governments in better understanding the impacts of pharmacist prescribing and supply within a specific patient cohort [24].

3.2 Aim and objectives

3.2.1 Aim

The overall aim of this study is to evaluate the clinical and economic impact and implementation of a service model (intervention) delivered by community pharmacists in NSW and 5 pharmacies in ACT, managing UTIs for a specific patient cohort (women aged between 18 years and 65 years) presenting with symptoms consistent with an uncomplicated UTI, over a 10-month study period.

3.2.2 Objectives

Specific objectives are to:

1. Assess implementation uptake of the intervention including the reach, fidelity and adoption of the intervention in community pharmacies, participant characteristics, and variation in uptake by geographic region.
2. Assess the clinical and experience outcomes for patients managed and/or treated by community pharmacists.
3. Assess the safety of the intervention and identify any risks that need to be addressed for future implementation.
4. Evaluate acceptability and feasibility of the intervention to pharmacists, other care providers and participants using the service.
5. Identify contextual enablers and constraints to access, adoption, fidelity delivery, impact, sustainability, and generalisability of the intervention.

4. Methods

4.1 Study hypothesis

The study hypothesis is that an intervention (UTI service) delivered by community pharmacists for women 18-65 years presenting with symptoms suggestive of an uncomplicated UTI will be feasible and acceptable to participants and providers, achieves high rates of self-reported symptom resolution rates at 7-day follow up and not be associated with safety risks.

4.2 Study design

The study hypothesis will be tested using a cohort study design, applying mixed methods (quantitative and qualitative research) to assess clinical and economic indicators, implementation, and patient experience. It builds on preparatory work commenced in 2023 to co-design the intervention and to assess implementation feasibility - ethics approval obtained from UoN H-2023-0035 and H-2023-0030 respectively.

4.3 Pharmacy recruitment

This state-wide study and as part of the contract with the NSW Government, the researchers are obliged to include any approved pharmacy and approved pharmacist in NSW that request participation. Furthermore, as part of our Contract with NSW Health, we have agreed to include 5 pharmacies in the ACT.

The NSW Ministry of Health have created an expression of interest (EOI) form on their website (https://www.health.nsw.gov.au/pharmaceutical/Pages/community-pharmacy-pilot.aspx) to which

pharmacies have been encouraged to complete if interested in participating. Similarly, the Pharmacy Guild of Australia (NSW Branch) and Pharmaceutical Society of Australia (NSW Branch) has undertaken a similar process in seeking EOIs to participate in the research. Details have been forwarded to the research team with consent. Pharmacies who submitted an expression of interest will be assessed to ensure they meet the eligibility criteria for the project.

NSW pharmacies

As of the 8 June 2023, the research team have received 1201 EOIs from pharmacies in NSW. The total number of pharmacies in NSW is 2010. Based on the feasibility study results, we expect between 800-1200 pharmacies and up to 4200 pharmacists to be recruited into the main study. However, these numbers may increase over time and if the above numbers are to be exceeded, we will notify the UoN HREC. As previously stated, the contractual arrangements with the NSW Ministry of Health oblige us to offer participation to all New South Wales pharmacies and therefore the maximum number of participants has not been set.

A formal recruitment letter will be sent via email to the pharmacies who submitted an EOI (Appendix 5), including the Participant Information Sheet and Consent forms for both Pharmacy and Pharmacist requesting involvement to be signed and returned electronically (Appendix 6-13). Consent will be sought at the pharmacy level from pharmacy owners, and from the individual pharmacists in those consented pharmacies, to participate in the study. Pharmacies and pharmacists must meet the eligibility criteria outlined below to participate in the study.

Pharmacies will be provided one week to accept or reject the offer. Pharmacies who do not respond to this first email call will be sent a second invitation via email, one week after the initial invitation. We will assume, if after a further three working days pharmacies have still not responded, they do not want to participate in the study. For pharmacies/pharmacists who indicate via email they would like further information or clarification, a follow up email and/or phone call will be made by a member of the research team using a standardised script (Appendix 14).

ACT pharmacies

ACT Health have released a request for EOIs to pharmacies to participate in the trial. The participants (5 pharmacies only based on the Contractual agreement with NSW Health) will be invited from the EOIs, to ensure a geographic spread of participation across 5 regions within the ACT. ACT Health will then provide the EOIs stratified by geographic region in the ACT, and the project statistician will randomly sample a pharmacy from each of the regions.

The ACT legislation process has been clarified with the acting Chief Pharmacist in ACT. Whilst in NSW the Chief Medical Officer signs an Authority for the change, a licence application will need to be made by participating pharmacies. The discretionary licence (available via PDF) would be issued to authorise the 5 pharmacies in the ACT to participate in the trial (Appendix 29). Further details on the licensing can be found on the ACT website: https://www.health.act.gov.au/businesses/medicine-and-poisons-licences-and-permits

Similarly, to NSW, consent will be sought at the pharmacy level from pharmacy owners, and from the individual pharmacists in those consented pharmacies, to participate in the study. Pharmacies and pharmacists must meet the eligibility criteria outlined below to participate in the study.

The pharmacies will be provided one week to accept or reject the offer. Pharmacies who do not respond to this first email call will be sent a second invitation via email, one week after the initial invitation. We will assume, if after a further three working days pharmacies have still not responded, they do not want to participate in the study. For pharmacies/pharmacists who indicate via email they would like further information or clarification, a follow up phone call will be made by a member of the research team using a standardised script (Appendix 14).

4.3.1 Pharmacy and pharmacist eligibility criteria

Pharmacies and pharmacists recruited must meet the eligibility criteria (defined below) to participate in the study, reflecting the criteria set by Authority under Section 10 Poisons and Therapeutic Good Act 1966 Clauses 170 and 171 of the Poisons and Therapeutic Goods Regulation 2208 (please see the NSW Health Authority – Appendix 1- signed by the Chief Medical Officer). All the pharmacies that have expressed an interest to participate will be sent a copy of the Authority. A summary is detailed below:

1. **Community pharmacies**
    - A community pharmacy in NSW or ACT must have a service room, consulting room, or area consistent with the following (as per the Authority):
        - "Ensures the room or area is not to be used as a dispensary, storeroom, staff room or retail area,
        - fully enclosed and provides adequate privacy (a divider or curtain in a dispensary, storeroom, staff room or retail area is not acceptable),
        - has adequate lighting,
        - is maintained at a comfortable ambient temperature,
        - has a hand sanitisation facility,
        - has ready access to a hand washing facility, and
        - has sufficient floor area, clear of equipment and furniture, to accommodate the person receiving the consultation and an accompanying person, and to allow the pharmacist adequate space to manoeuvre."

Pharmacies must have access to MedAdvisor to complete clinical record keeping for the purposes of the clinical trial assessment.

2. **Pharmacists**
    - A community pharmacist holding general registration employed or engaged in an eligible participating pharmacy in NSW and ACT and:
        - who has successfully completed the following training:
            - Australasian College of Pharmacy Uncomplicated Cystitis Treatment – Pharmacist Training [25]; or
            - Pharmaceutical Society of Australia Managing uncomplicated cystitis [26]; and
            - Training module(s) that have been approved by the Chief Heath Officer for the purposes of the clinical trial.

A pharmacist is eligible to participate if they hold general registration as a pharmacist with the Australian Health Practitioner Regulation Agency (AHPRA). Pharmacists with provisional registration (intern pharmacists) and pharmacists with conditions on their registration are not eligible to participate in the trial. The pharmacy must have at least one eligible pharmacist who is willing to provide their voluntary consent to participate, for the pharmacy to be eligible, and that there is always a pharmacist available to deliver the service during all opening hours of the pharmacy.

4.4 Participant recruitment

A flyer (Appendix 15) has been developed and approved by the NSW Ministry of Health to inform patients of the service and will be displayed in a prominent location in each participating pharmacy. Female patients will be opportunistically recruited in participating community pharmacies. Consecutive patients will be identified on presentation to the community pharmacy with symptoms suggestive of a UTI and either: requesting advice or medication or self-selecting a product for symptoms suggestive of a UTI. If meeting the below inclusion criteria, the pharmacist will offer the individual to participate in the study. Patients will be provided the Participant Information Statement and asked for their informed consent to participate in the study to be provided either via an electronic signature or on a printed hard copy version (Appendix 16-19).

4.4.1 Participant consent

All participants will require informed consent. Participants will be provided with hard copies of the patient information and consent forms for reading at the pharmacy. Participants will be provided with two consent forms (one for the study and a second form from Services Australia allowing access to MBS and PBS data). They will be given the option of separate consent. Once they have accepted, participants will then have the option of either providing electronic or wet ink signature consent. If they opt for electronic consent, the pharmacist will provide the participant with a location specific QR code for scanning on their mobile phone. This will open a secure webform hosted by the George Institute. The participant will then enter their personal details and be asked to review and tick the boxes as listed on the paper consent forms. They will then provide a finger signature on a signature panel on the screen and click submit for secure submission to The George Institute. The participant will be sent an SMS or Email confirmation message with a validation code which they will provide to the pharmacy and a copy of their signed participation information sheet and consent. If the participant opts for a wet-ink signature consent, the pharmacist will enter the information into the form on the participant's behalf and upload scanned copies of the paper form. Before consent may be obtained, pharmacists will provide an opportunity to ask questions.

If participants wish to withdraw from the study once it has started, they can do so at any time without having to give a reason. Withdrawing from the study will not affect their relationship with their employers, professional organisations, care providers or receipt of any care or treatment. Participants wishing to withdraw should notify their pharmacist or one of the research team. Once a participant decides to withdraw from the study, no further information will be collected from them. If they wish, their information will be removed from study records and will not be included in the study results, up to the point that we have analysed and published the results.

4.4.2 Participant inclusion criteria

Eligible patients will be females aged between 18 years and 65 years presenting to community pharmacies in NSW, and 5 pharmacies in the ACT, with symptoms associated with an uncomplicated urinary tract infection.

4.4.3 Participant exclusion criteria

Individuals who are not female and/or aged <18 years or >65 years.

4.5 Intervention description

The intervention is multicomponent.

4.5.1 Pharmacist training and support

Prior to service delivery, pharmacists will be prepared through a clinical training program (either through the Australasian College of Pharmacy or Pharmaceutical Society of Australia) to apply best practice standard of care. Furthermore, study specific training modules will be completed by pharmacists to ensure efficiency in the consultation process, patient consent, recruitment of patients, timely referral, and quality data collection.

4.5.2 Pharmacy consultation

The pharmacist will undertake a structured consultation with the patient in the community pharmacy guided by an IT program applying a co-designed clinical management protocol which considers the recommendations from the Australian Therapeutic Guidelines. The clinical management protocol has been subject to co-design between community pharmacists and senior general practitioners. This consultation is anticipated to take 10 minutes. Please refer to the Research Protocol for detailed information.

The intervention is provided under the NSW Health Authority allowing participating NSW pharmacists to supply medications as part of the trial. For the ACT, a discretionary licence will be approved for participating pharmacies.

The structured consultation is summarised in Box 1.

BOX 1

- Participant eligibility assessment, in which the pharmacist will assess if the patient meets the inclusion/exclusion criteria to participate in the study.
- Service offering, during which the pharmacist will explain the features of the study and will ask the patient if she/they is willing to participate.
- Provision of the Patient information sheet and informed consent form.
- Patient's clinical assessment. During the assessment the pharmacist will elicit relevant clinical information, including medical conditions, medication history and clinically assessed for the possibility of uncomplicated lower UTI, in line with diagnostic guidance and agreed treatment protocols. If the patient is a usual patient of the pharmacy, their medication dispensing history may be checked on the computer record, if not the patient medications will be asked. Further information may be obtained from the patients' Electronic Health Record (EHR). Viewing a patients EHR is legally and professionally allowed by pharmacists, with patient consent.
- Patient management by the pharmacist, or GP or ED referral. After the clinical assessment, the pharmacist will use agreed management protocols for:
    - Provision of self-care advice (e.g., symptom control, future prevention advice), and supply of antibiotics or referral to the GP, as appropriate. Trimethoprim, nitrofurantoin, cefalexin may be supplied under the service for this study and in accordance with the developed clinical management protocols and the Authority from NSW Health. Please refer to the management protocol (Appendix 2). If a medication is prescribed, the patient will be provided with the relevant Consumer Medicines Information and/or a self-care card.
    - Provision of follow up advice (e.g., expectation around duration of symptoms which should respond to appropriate antibiotic therapy within 48 hours; and to see GP urgently if their symptoms worsened or no improvement, if symptoms persist 48–72 hours after starting antibiotic treatment, symptoms reoccur within 2 weeks after finishing antibiotic treatment or symptoms develop that are not symptoms of an acute UTI [27]).
    - The pharmacist will share a record of the supply with the patient's usual treating medical practitioner or medical practice (via fax, secure messaging software, provision of a letter to the patient, or any other approved secure means by NSW Health), where the patient has one, following consent by the patient.
- The pharmacist will facilitate appropriate and timely referral, if required, according to the following categories:
    - Urgent referral – the patient's condition requires immediate medical attention by a medical practitioner or emergency department.
    - General referral – the patient's condition may be suitable for self-treatment, however medical review with a medical practitioner at the next available appointment is appropriate due to patient circumstances (comorbidity, chronic disease etc.)
    - Considered referral – the patient's condition is suitable for treatment by the pharmacist; however, referral is warranted if symptoms do not resolve within a defined time period.
    - The reason for referral must be clearly communicated verbally and in writing to the patient and provided with the appropriate referral documentation.
- The pharmacist complies with the 'Management Protocols', including that the pharmacist makes a record in MedAdvisor pharmacy software, or an approved system by the Ministry of Health, regarding the supply (as per NSW Health Authority).
- The pharmacist must keep a clinical record for 7 years that contains (as per NSW Health Authority):
    - sufficient information to identify the patient;
    - the date of the treatment;
    - the name of the pharmacist who undertook the consultation;
    - any information known to the pharmacist that is relevant to the patient's diagnosis or treatment (for example, information concerning the patient's medical history);
    - any clinical opinion reached by the pharmacist;
    - actions taken by the pharmacist;

- particulars of any medication supplied for the patient (such as form, strength and amount);
- notes as to information or advice given to the patient in relation to any treatment proposed by the pharmacist who is treating the patient;
- any consent given by a patient to the treatment proposed.

- The pharmacist will ask for the patients consent to be followed up by the research team at 7 days.

4.5.3 Implementation strategy

There will be follow up training and ongoing support as part of a translational/implementation strategy through the study period. Practice change facilitators will visit these pharmacies to provide ongoing support, answer any queries, ensure quality data is being collected, and collect implementation data. The implementation component of the study will be underpinned by the Consolidated Framework for Implementation Research (CFIR), in particular with the use of an adapted implementation model for community pharmacy. Implementation factors (barriers, causes and facilitators) and the Dougherty strategy classification systems, adapted to community pharmacy, will be used. Further details are provided in 4.6 below.

4.5.4 Considerations for the delivery of the intervention

Cost to patients

NSW - The cost of the consultation with patients ($20) will be paid for by the NSW Government to pharmacies, irrespective of the outcome of the consultation. The patient will meet out of pocket expenses for any medicines or products provided.

ACT - The cost of the consultation with patients will be paid for by the patient receiving the service to pharmacies, irrespective of the outcome of the consultation. The patient will also meet out of pocket expenses for any medicines or products provided.

Legislative considerations

NSW - The legislative approval required for the trial has been developed and executed by the NSW Ministry of Health (see Appendix 1).

ACT - The ACT legislation process has been clarified with the acting Chief Pharmacist in ACT. Whilst in NSW the Chief Medical Officer signs an Authority for the change, a licence application will need to be made by participating pharmacies. The discretionary licence (available via PDF) would be issued to authorise the 5 pharmacies in the ACT to participate in the trial (Appendix 29). Further details on the licensing can be found on the ACT website: https://www.health.act.gov.au/businesses/medicine-and-poisons-licences-and-permits

Professional indemnity for pharmacists

Pharmaceutical Defence Limited (PDL) is the major provider of professional indemnity and will cover pharmacists as part of their normal indemnity for delivery of this service (Appendix 20). Guild Business will cover the liability from the perspective of the pharmacy premises. The pharmacy and pharmacists consent forms have been amended to provide consent for the researchers to pass the names and addresses of the participants in the feasibility study for the purposes of indemnity cover.

4.6 Data sources

4.6.1 Community pharmacy data

During implementation of the intervention, information on health service delivery and program activities will be routinely captured in a case registration form by community pharmacists using the MedAdvisor application

which is built into pharmacy software systems. For the purposes of evaluation and study participants will be assigned a unique study identification number. Appendix 21 provides a list of data that will be collected in these extracts.

4.6.2 Participant self-reported data

Participants will be assessed at the registration visit (consultation) described above and this will include basic demographic and clinical information. Those assessed as eligible to participate in the trial will be followed up at Day 7 post registration to assess outcomes. This will include a brief survey administered by the George Institute either via SMS message or phone call with a link to a case report form using George Data Systems (GDS). Information will be collected on the primary outcome measure of symptom resolution rate, any additional care provided, changes to treatment and overall experience of care. Appendix 22 provides the case report form for the 7-day follow-up visit.

4.6.3 Implementation data

Practice change facilitators: The collection of the implementation data will be undertaken through visits/contacts (approximately monthly) within the resources available depending on the final number of community pharmacies participating, by practice change facilitators employed as part of the project. An open-ended discussion which, depending on the mode of contact, will vary between 10 to 20 minutes (see Appendix 23 for an implementation checklist to be used by practice change facilitators). Data will be collected using a pre-developed form in REDCap. Practice change facilitators will be trained by an implementation expert to undertake this work on models and frameworks of implementation science with an emphasis on the application of these to this specific study and the use of the checklist for data collection purposes.

Semi-structured interviews: The perspectives and experiences of community pharmacists and participants (patients) will be captured at 6 months and 10 months using semi-structured interviews. Perspectives of other stakeholders will also be sought including general practitioners, professional bodies including the Pharmacy Guild, Pharmaceutical Society of Australia and the Royal Australian College of General Practitioners, and NSW Health administrators (see Appendix 24 of Project Governance Structure).

A maximum variation sampling technique will be used to select a diverse range of pharmacies and patients for interviews, taking into consideration pharmacy level factors such as geography, pharmacy size and participant level factors such as age, geography, presence of comorbid conditions, income status. It is anticipated that around 50 interviews in total will be conducted, however, the final sample size will be determined when it is considered the research team have achieved thematic saturation and few new themes are emerging from the interviews.

For participants (patients), interview questions will focus on experiences of health care and awareness and perceptions of services (Appendix 25). They will take no longer than 45 minutes. For community pharmacists and other stakeholders', questions will focus on implementation and contextual factors which may influence program outcomes [28-31], sustainability, staff experiences and motivation to engage in the prescribing model (Appendix 26). These interviews will take up to 1 hour.

Data collection will be conducted by members of the research team who are experienced in qualitative research methods. These sessions will take place via telephone, videoconferencing (e.g., Zoom or MS teams), or face-to-face at a community pharmacy, depending on the participants' preference and feasibility due to COVID-19 restrictions and other factors at the time. All sessions will be audio-recorded and transcribed and detailed field notes recorded.

4.6.4 NSW Ministry of Health data

NSW Health will establish a public health register for the purposes of evaluating the trial. The NSW Public Health Act 2010 allows for the Minister for Health to establish public health or disease registers to follow up the care and treatment of patients; for infection control and disease outbreak investigations; disease risk factor monitoring in the population; monitoring the outcomes of population health interventions; and

monitoring exposure to chemicals or environmental risk factors. The Centre for Epidemiology and Evidence establishes and manages a range of ad hoc and ongoing registers.

4.6.5 Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) data

Participants will be requested at registration to provide consent to access their MBS and PBS data for the evaluation. The Services Australia approved patient and information consent form (Appendix 27) will be used to seek consent. Participants will have the option of authorising Services Australia to provide their claim history for MBS, PBS or both for a 2-year period from 12 months prior to registration to 12 months post registration.

4.7 Data management

Only authorised personnel acknowledged and approved by the Human Research Ethics Committees will have access to study data. All study files will be retained for a minimum of 15 years at respective study sites in accordance with the Australian Code for the Responsible Conduct of Research. The final evaluation dataset will be archived at the completion of the project resulting in a single primary data source being retained at the University of Newcastle.

4.7.1 Community Pharmacy Data

Participating pharmacies will record the patient consultation data in a software application (MedAdvisor) installed in each pharmacy. The data are stored centrally on a secure server hosted by MedAdvisor. MedAdvisor will generate an extract of community pharmacy data, and this will be transferred securely to the research team via one of the following ways:

1) Shared via an AWS S3 and The George Institute/University provided with an Access Key/Secret Access
2) Machine-to-Human e.g., a csv that is sent via secure message platform Kiteworks.

Data files will include patient identifiers (Medicare number, patient name, contact details and date of birth), the study identification number, and information collected at the registration visit. Upon receipt of data transfers, the George Institute research team will store the data files on secure servers (more detail below).

4.7.2 Participant self-reported data

7-day follow-up visit data will be collected on GDS case report forms hosted by the George Institute. Participants will be identified only by their study identification number and no identifying information will be collected on these forms.

4.7.3 Participant interviews

Participants will be asked during their consenting process if they may be contacted by the research team with an invitation to participate in an interview. It is not expected that interview topics will cause any harm or distress to participants. During interviews if a participant does experience discomfort from the topics discussed or recollection of their health care experiences, they can ask to stop or pause the interview or skip any questions. If patient/carer participants raise any concerns or have question about symptoms or their health care they will be directed to discuss this with their usual health care provider or a patient support line. To minimise inconvenience participants will be i) invited to complete the interview at a time best suited to them; ii) patients/carers will be offered a voucher of $20 in recognition of the time taken out of their usual day to participate. Private providers such as Pharmacists and GPs will be offered a $50 voucher for their time, while public health providers, and administrative and service managers will be interviewed within standard working hours, requiring no further compensation as standard practice.

4.7.4 Implementation data

Practice change checklists: Data from the checklists developed by Practice Change Facilitators will be entered into Redcap. A deidentified file including only pharmacy identification number will be securely sent by the UoN research team to the George Institute for analysis.

Interviews: Lists of patient participants that expressed they are willing to be contacted for an interview on the consent form will be generated. A diversity sample will be constructed from these lists to include a range of socio-economic status, living situation (independent/ other), morbidities and engagement with the initiative. Lists of health system administrators and providers will include those directly or indirectly involved in the initiative. The study team will contact eligible participants to invite them to participate and request a time for an interview/focus group. Non-responding eligible participants will be followed up a maximum of two times. At the scheduled interview all participants will be given a full explanation of the study by the research team and provided with an opportunity to ask questions. Consenting participants will be allocated the unique study ID number generated at the baseline registration visit. Interview data will include files of audio and video recordings and transcripts of interviews/focus groups. Audio or videoconference files of interviews will be transcribed verbatim by a professional transcription service after a confidentiality agreement has been signed.

4.7.5 NSW Health Data

The George Institute will provide NSW Health with a list of study participants recruited at each site. This will include a study identification number generated at registration into the trial and the following identifiers: name, date of birth, address. NSW Health will then extract information for these participants on the variables listed in Appendix 28. The data period will include 12 months prior to the study registration date up to the most recent data available in the NSW Health data collections. A deidentified file including only the participant study ID number will then be sent to the George Institute for Global Health using a secure file transfer protocol.

4.7.6 MBS/PBS data

A file of study participants including study identification number and the approved consent forms will be sent to Services Australia for obtaining the claims history for MBS and PBS data.

4.8 Data flow and storage

Table 1 summarises the data sources and flow:

Data	**Type**	**Source**	**Custodian**	**Flow**	**Ethics/ governance considerations**
Community Pharmacy registration data	Identified, + participant study ID	Community pharmacy (MedAdvisor)	- MedAdvisor -The George Institute (TGI) -The University of Newcastle (UoN)	-MedAdvisor send identified data to TGI and UoN	-University of Newcastle (UoN) HREC approval -Data access agreement between UoN, TGI and MedAdvisor
Participant 7-day follow-up data	Deidentified, + participant study ID	GDS form hosted by TGI	-TGI	-Data retained by TGI and not sent to other parties	-UoN HREC approval
Implementation data	Pharmacy ID Participant study ID	Community pharmacists and participants	-UoN -TGI	-Checklists entered into pre-prepared REDCap form	-UoN HREC approval

				-Interviews professionally transcribed and stored on UoN/TGI password protected server -Data retained by UoN/TGI and not sent to other parties	
NSW Health data	Deidentified, + participant study ID	TGI	-TGI -NSW Health	-TGI sends NSW Health a list of participants -NSW Health sends to Centre for Health Record Linkage (CHeReL) -CHeReL sends deidentified data with participant ID to TGI	-UoN HREC approval -NSW Health establishes a Public Health Register -Data access agreement between TGI and NSW Health
MBS/PBS	Identified data + participant study ID	Community pharmacy (MedAdvisor)	-TGI -Services Australia	-Pharmacy/ MedAdvisor sends paper/electronic Services Australia consent form to TGI --TGI prepares file including participant ID to send to services Australia with electronic/ scanned consent forms -Services Australia sends deidentified data with participant ID to TGI	-UoN HREC approval -Services Australia External Request Evaluation Committee

MedAdvisor is a ISO27001 credentialled company. This information security standard governs the company's handling of how personally identifiable information and health data is securely recorded and stored. Information is accessed by researchers via an extension of the company's information security management system and will be underpinned by a data sharing agreement. Functionally, researchers will be provided data via a secure machine to machine integration or a secure machine to human process. The company utilises the secure transfer software Kiteworks for this purpose. Pharmacy data is restricted within the pharmacy in alignment with the company's existing Pharmacy Licencing Agreement and the ISO27001 framework. The company offers on-premises software to support this data handling.

The George Institute policies pertaining to the secure transfer and storage of study materials and data will be followed. TGI's secure infrastructure is physically located in an ISO 27001 certified data centre in Sydney. Technical controls include access via encrypted network connections, multi factor authentication, data storage on encrypted disks, encryption of all offsite backups, discretionary access controls on project data folders, micro-segmented next generation firewalls, together with a Security Information and Event Management system monitoring network traffic and scanning for Indicators of Compromise. Associated procedural controls are captured in standard operating procedures and Work Instructions.

Pharmacies, pharmacists and patients will provide consent for data to be transferred from MedAdvisor to the research team.

4.9 Outcomes

Primary outcome: Self-reported 7-day symptom free rate: defined as the complete absence of urinary tract infection symptoms. This data will be collected by a researcher at 7-day patient follow up.

Secondary outcomes

- **Primary care utilisation:** MBS records will be used to measure use of general practice services prior up to 12 months pre- and 12 months post the registration date. MBS claims for pathology items will also be included.

- **Medication utilisation:** Antibiotic prescribing during the trial will be assessed. PBS records for prescribed antibiotics will be analysed to assess claims made in the 12 months prior to registration to the pharmacy trial and over the next 12 months post registration.

- **Hospital utilisation**: Admitted Patient Data Collection (APDC) data will be used to assess hospitalisation trends over the 12-month interval before and 12 months after initiation of the program:
    - avoidable (or "potentially preventable") hospital admissions per 100 persons
    - avoidable hospital admissions per 100 persons for genitourinary conditions[1]
    - acute hospital admissions per 100 persons
    - length of stay for acute hospital admissions per 100 persons
    - bed days for acute hospital admissions per 100 persons

- **Emergency presentations**: Emergency Department Data Collection (EDDC) data will be used to assess emergency and urgent care presentation trends over the 12-month interval before and 12 months after initiation of the program:
    - total presentations per 100 persons;
    - presentations per 100 persons for genitourinary conditions

- **Experience:** Self-reported patient experience. A series of questions on patient experience will be used to determine patient experience, collected by a researcher via a survey at 7-day patient follow up. The perspectives and experiences of a sample of patients will be captured at 6 months and 10 months through semi-structured interviews.

- **Safety outcomes**: Adherence rates to treatment protocol (assessed by practice change facilitators conducting regular pharmacy monitoring), rates of switching to alternative antibiotics by GP, rates of ED and hospital admission for UTI related complications.

- **Implementation outcomes**: Implementation outcomes will also be assessed to examine the fidelity, reach and adoption of the new service, and barriers and facilitators to implementation. Other implementation outcomes to be assessed include:
    - Numbers of patients supplied antibiotics by pharmacists
    - Numbers and types of antibiotics supplied
    - Numbers of patients provided self-care advice
    - Numbers of patients referred to another health professional
    - Reasons for patient referral to another health professional
    - Supply of first-line antibiotics for UTI/Total antibiotic supply for UTI
    - Estimated duration of consultation
    - Patient follow-up rates
    - Patient adverse events

[1] The following ICD 10 codes: N00-N08 Glomerular diseases; N10-N16 Renal tubulo-interstitial diseases; N17-N19 Acute kidney failure and chronic kidney disease; N20-N23 Urolithiasis; N25-N29 Other disorders of kidney and ureter; N30-N39 Other diseases of the urinary system; N70-N77 Inflammatory diseases of female pelvic organs; N80-N98 Noninflammatory disorders of female genital tract; N99-N99 Intraoperative and postprocedural complications and disorders of genitourinary system, not elsewhere classified

- Antibiotic use and completion of course

- **Economic outcomes:** Results from the economic analysis will be expressed as (1) net benefit in terms of implementation costs and cost savings arising from more efficient treatment pathways; and (2) cost-consequence results accounting for patient experience measures, relevant safety outcomes and implementation measures. This will be assessed using multiple data sources including MBS records for 12 months pre and post intervention.

4.10 Data analysis

A mixed methods analytic approach will be applied.

4.10.1 Quantitative analysis

Descriptive statistics will be calculated for all study variables. Continuous variables will be reported using the appropriate measure of central tendency. Categorical variables will be summarized as proportions. Analyses will be conducted using SAS and R. The primary and secondary outcomes will be analysed with multivariable regression models adjusted for age, comorbidity count, hospitalisation in the 12 months prior to enrolment and Socio-Economic Indexes for Areas (SEIFA). Interim descriptive analyses of the 7-day follow up participant data will assess symptom resolution rates, use of other health care professionals including emergency department presentations and adverse events. Sub-group analyses will be conducted to examine variation in outcomes for the cohort will be assessed based a range of demographic and clinical characteristics. A separate ecological study will be conducted to assesses antimicrobial resistance.

4.10.2 Qualitative analysis

Self-reported patient experience will be examined at 6 and 10 months using qualitative methods. Interview transcripts will be imported into NVivo for thematic analysis. Initial open coding of transcripts will be undertaken iteratively by members of the research team. Themes and care quality measures will be presented to the broader research team and program implementers for final consensus.

4.10.3 Economic analysis

The analysis will be conducted from a health service perspective (base case) and a societal perspective including direct and indirect costs from the health-consumer's perspective - out of pocket expenses for any medicines or products provided, waiting time and travel time to attend treatment, productivity gains or time lost from work.

The scope of the within-study cost analysis is constrained by the design of the cohort study. Cost items associated with the co-design process, research and evaluation will be excluded. Resource use associated with the 2 components, pharmacy enrolment, training and support and pharmacy consultation, will be prospectively identified, measured and valued. In measuring resource use associated with delivery of the intervention, data will be collected from the research team, from the enrolled pharmacies and from the enrolled patients. Labour time will be measured using opportunity costs and valued based on Pharmacy Industry Award rates of pay, and average earnings for patients.

Health care resource use will be captured per the secondary outcomes of the study. Primary care resource use will be measured from MBS records and valued based on current Medicare Benefits Schedule listed prices. Medication use will be valued using Pharmaceutical Benefits Schedule listed prices, over-the counter medication will be valued using market prices. Hospital utilisation will be measured using the APDC and EDDC and valued based on Independent Health and Aged Care Pricing Authority (IHACPA) National Efficient Price tariffs.

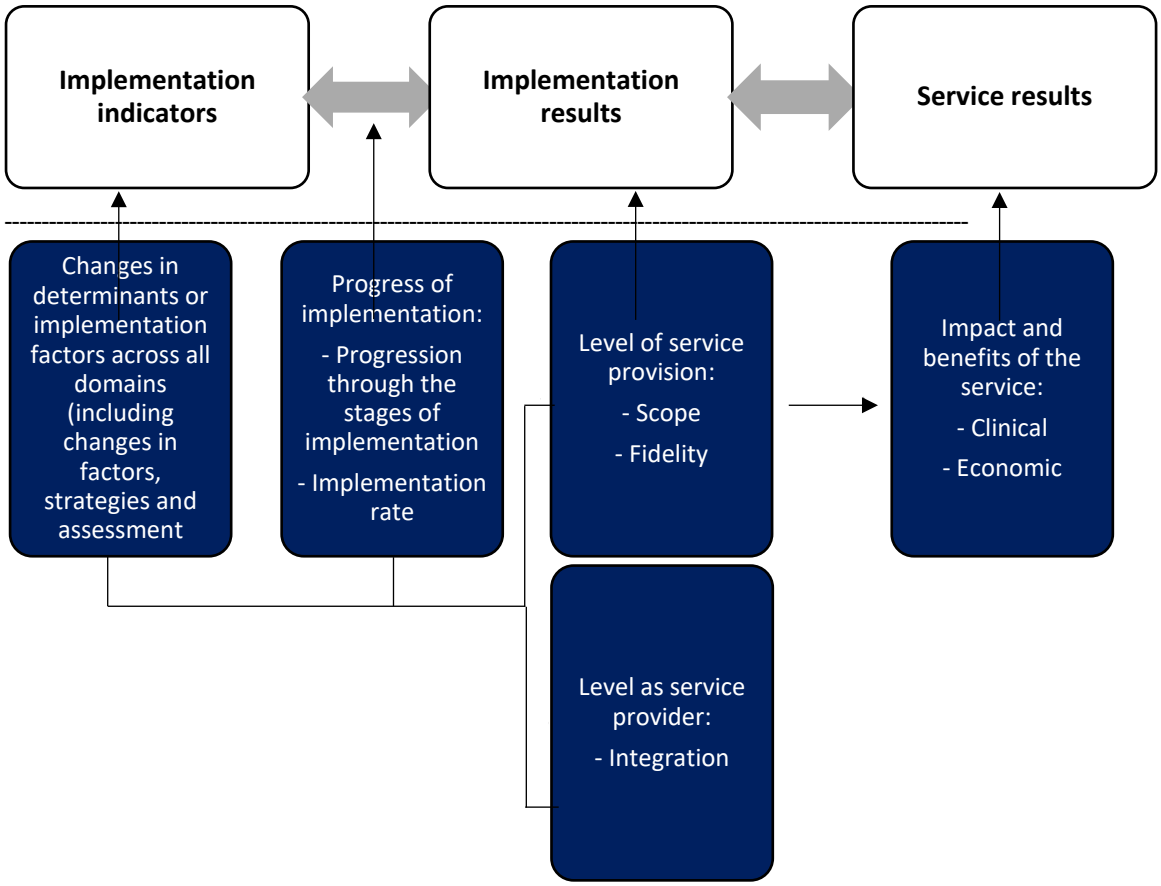
Results from the economic analysis will be expressed as (1) net benefit in terms of implementation costs and cost savings arising from more efficient treatment pathways; and (2) cost-consequence results accounting for patient experience measures, relevant safety outcomes and implementation measures.

Decision uncertainty will be accounted for using parametric and non-parametric bootstrapping to generate uncertainty intervals around the net benefit result.

4.10.4 Implementation outcomes analysis

The implementation component of the study will be underpinned by the Consolidated Framework for Implementation Research (CFIR) [32-35], in particular the use of an adapted implementation model for community pharmacy [1, 2, 36-44]. Implementation factors (barriers, causes and facilitators) (Appendix 3) and the Dougherty strategy classification systems (Appendix 4), adapted to community pharmacy, will be used [1, 2, 36-44]. This will build on the trial outcomes to determine scalability of the intervention. The evaluation framework is set out in Figure 1. The CFIR domains and sub-domains will also be used to organise the data. Descriptive statistics be produced for all implementation outcomes. Links between implementation barriers and facilitators, their cause and implementation strategies will be visually represented using Sankey diagrams. A predictive resolution percentage will be calculated using random forest method for predicting effective strategies for all implementation barriers.

Figure 1 Implementation Evaluation Framework adapted from Moullin, et al. [1]



4.11 Management of serious adverse events

The establishment of a Data Safety Monitoring Board (DSMB) will be an essential step in ensuring the safety and integrity of a research study or clinical trial. The DSMB will be an independent committee responsible for the ongoing monitoring of the study and making informed decisions regarding participant safety. One of the primary functions of the DSMB will be to review and evaluate any serious adverse events that occur during the study. Serious adverse events refer to unexpected or severe adverse reactions, complications, or other medically significant incidents experienced by participants. Furthermore, the DSMB will be responsible for assessing the overall safety profile of the study. It will analyse the frequency and severity of adverse events, identify any emerging patterns or trends, and evaluate whether the study intervention poses any risks that outweigh its potential benefits. The DSMB will also review the safety data in relation to the study's objectives

and may make recommendations to modify or discontinue the study if warranted. The DSMB will report its findings and recommendations to the UoN Health Research Ethics Committee (HREC). The DSMB's report to the HREC will include information on serious adverse events, their assessment, and any recommendations regarding participant safety or modifications to the study protocol. During the period before the establishment of the DSMB, the responsibility for reviewing and reporting serious adverse events falls to the Project Steering Committee. The Project Steering Committee comprises individuals involved in the management and oversight of the study, including principal investigators, study coordinators, and other relevant stakeholders. While the Project Steering Committee assumes this role temporarily, its objective is to ensure that any serious adverse events are promptly addressed, and appropriate measures are taken to protect participant safety.

5. Ethical Considerations

5.1 Research ethics approval

This research protocol was submitted to the University of Newcastle HREC for ethical review and received approval on 27 June 2023 (H-2023-0119). Following HREC approval, The Services Australia External Request Evaluation Committee has reviewed the request for MBS and PBS data linkage, and approval has been received (13 July 2023).

5.2 Protocol adherence

Except for changes to eliminate an immediate hazard to participants, the approved protocol will be followed as specified. Any significant protocol deviation will be documented, and notification sent to the HREC as soon as possible.

5.3 Protocol Amendments

Any significant change in the study protocol will require an amendment. The Chief investigator will submit this to the University of Newcastle HREC for review and approval. The approval letter, signed by the HREC Chair, will refer specifically to the investigator, the protocol number, the protocol title, the protocol amendment number, and the date of the protocol amendment. The protocol amendment may be implemented only after it has been approved by the HREC. If the revision is an administrative change (such as the addition or removal of committee members), a letter explaining the change(s) along with a copy of the amended pages(s) of the protocol will be submitted to the HREC for their information.

5.4 Notification of study closure

In addition to interim reports as required by the HREC, the Coordinating Principal Investigator will complete a final report notifying the HREC of the conclusion of the study. This report will be made within 3 months of completion or termination of the study.

5.5 Records retention

The Site investigator (or The George Institute for Global Health, on behalf of the Investigator) shall retain and preserve one copy of all data generated during the study for 15 years following study closure.

5.6 Confidentiality

All data collected for the purposes of the study will be kept confidential and will only be accessible by Study Personnel. Data will be maintained in accordance with the National Privacy Act 1998 and the NSW Health Records and Information Privacy Act 2002.

5.7 Dissemination Policy

Results will be published in the academic literature and presented at national and international conferences, media articles and newsletters. Publication of the main report from the study will be in the name of the research group, with each individual study investigator named personally at the end of the report.

6. Appendices

A list of appendices will be added as attachments to this application:

Appendix 1	NSW Health UTI Authority
Appendix 2	Clinical Management Protocol
Appendix 3	Implementation Barriers, Facilitators and Causes
Appendix 4	Dougherty strategy classification systems
Appendix 5	Pharmacy recruitment letter
Appendix 6	Participant Information Statement (Pharmacy – NSW)
Appendix 7	Consent Form (Pharmacy – NSW)
Appendix 8	Participant Information Statement (Pharmacist – NSW)
Appendix 9	Consent Form (Pharmacist – NSW)
Appendix 10	Participant Information Statement (Pharmacy – ACT)
Appendix 11	Consent Form (Pharmacy – ACT)
Appendix 12	Participant Information Statement (Pharmacist – ACT)
Appendix 13	Consent Form (Pharmacist – ACT)
Appendix 14	Indicative script for initial contact with identified pharmacies
Appendix 15	NSW Health Consumer Flyer
Appendix 16	Participant Information Statement (Patient – NSW)
Appendix 17	Consent Form (Patient – NSW)
Appendix 18	Participant Information Statement (Patient – ACT)
Appendix 19	Consent Form (Patient – ACT)
Appendix 20	PDL Professional Indemnity Letter
Appendix 21	Patient consultation data collection form (MedAdvisor)
Appendix 22	Patient follow up data collection form (GDS)
Appendix 23	Implementation checklist
Appendix 24	Project governance structure
Appendix 25	Interview questions (Patients)
Appendix 26	Interview questions (Community pharmacists and other stakeholders)
Appendix 27	Services Australia approved patient and information consent form
Appendix 28	Routinely collected datasets available in NSW Health data
Appendix 29	ACT Health Medicines Poisons Therapeutic Goods New Licence Application

7. References

1. Moullin, J.C., D. Sabater-Hernández, and S.I. Benrimoj, *Model for the evaluation of implementation programs and professional pharmacy services.* Res Social Adm Pharm, 2016. **12**(3): p. 515-22.
2. Moullin, J.C., et al., *A systematic review of implementation frameworks of innovations in healthcare and resulting generic implementation framework.* Health Research Policy and Systems, 2015. **13**(1): p. 16.
3. Moullin, J.C., et al., *Development and testing of two implementation tools to measure components of professional pharmacy service fidelity.* J Eval Clin Pract, 2016. **22**(3): p. 369-77.
4. Thornley, T., et al., *Evaluation of a community pharmacy-led test-and-treat service for women with uncomplicated lower urinary tract infection in England.* JAC Antimicrob Resist, 2020. **2**(1): p. dlaa010.
5. Stewart, F., et al., *Building capacity in primary care: the implementation of a novel 'Pharmacy First' scheme for the management of UTI, impetigo and COPD exacerbation.* Prim Health Care Res Dev, 2018. **19**(6): p. 531-541.
6. Peiffer-Smadja, N., et al., *Preventing and Managing Urinary Tract Infections: Enhancing the Role of Community Pharmacists-A Mixed Methods Study.* Antibiotics (Basel), 2020. **9**(9).
7. Sanyal, C., et al., *Cost-effectiveness and budget impact of the management of uncomplicated urinary tract infection by community pharmacists.* BMC Health Serv Res, 2019. **19**(1): p. 499.
8. Wu, J.H., et al., *Community pharmacist prescribing of antimicrobials: A systematic review from an antimicrobial stewardship perspective.* Can Pharm J (Ott), 2021. **154**(3): p. 179-192.
9. Beahm, N.P., D.J. Smyth, and R.T. Tsuyuki, *Outcomes of Urinary Tract Infection Management by Pharmacists (R(x)OUTMAP): A study of pharmacist prescribing and care in patients with uncomplicated urinary tract infections in the community.* Can Pharm J (Ott), 2018. **151**(5): p. 305-314.
10. *Nissen, L, Lau, E, & Spinks, J (2022) The management of urinary tract infections by community pharmacists: A state-wide trial : Urinary Tract Infection Pharmacy Pilot - Queensland (Outcome Report). Queensland University of Technology, Brisbane, Qld. Available at: https://eprints.qut.edu.au/232923/.*
11. *NSW Health. (2022). Pharmacy reform to expand community health care. Accessed via: https://www.health.nsw.gov.au/news/Pages/20221113_00.aspx.*
12. Arienzo, A., et al., *A new point-of-care test for the rapid detection of urinary tract infections.* Eur J Clin Microbiol Infect Dis, 2020. **39**(2): p. 325-332.
13. Abernethy, J., et al., *Epidemiology of Escherichia coli bacteraemia in England: results of an enhanced sentinel surveillance programme.* J Hosp Infect, 2017. **95**(4): p. 365-375.
14. *Australian Bureau of Statistics. (2021). New South Wales Census. Accessed via: https://www.abs.gov.au/census/find-census-data/quickstats/2021/1.*
15. *Britt H, Miller GC, Henderson J, Bayram C, Harrison C, Valenti L, et al. General practice activity in Australia 2015–16. General practice series no. 40. Sydney: Sydney University Press; 2016.*
16. *Australian Commission on Safety and Quality in Health Care. (2021). Fourth Australian Atlas of Healthcare Variation. Accessed via: https://www.safetyandquality.gov.au/our-work/healthcare-variation/fourth-atlas-2021/chronic-disease-and-infection-potentially-preventable-hospitalisations/24-kidney-infections-and-urinary-tract-infections.*
17. *Australian Institute of Health and Welfare. (2021). Emergency department care 2019–20: Australian hospital statistics. Table 4.5: Emergency department presentations(a) by principal diagnosis in ICD-10-AM(b) chapters, states and territories, 2019–20. Accessed via: https://www.aihw.gov.au/getmedia/433caea4-03ff-4569-96ac-042f2844f29c/Emergency-department-care-2019-20.xlsx.aspx.*
18. *Ministry of Health (2016). Pharmacy Action Plan 2016 to 2020. Available at: https://www.health.govt.nz/publication/pharmacy-action-plan-2016-2020 (accessed 21 November 2018). .*
19. *Smith, M., Bates, D.W. and Bodenheimer, T.S., (2013). 'Pharmacists belong in accountable care organizations and integrated care teams.' Health affairs (Project Hope), 32(11), pp.1963–1970. .*
20. *Pharmacy Guild of Australia. (2017). Pharmacists in 2025. Accessed via: https://www.guild.org.au/__data/assets/pdf_file/0022/45454/PGA_CP2025_intro-paper.pdf.*
21. *Pharmaceutical Services Negotiating Committee. PSNC Services Database. https://psnc.org.uk/services-commissioning/services-database/.*
22. Booth, J.L., et al., *Antibiotic treatment of urinary tract infection by community pharmacists: a cross-sectional study.* Br J Gen Pract, 2013. **63**(609): p. e244-9.
23. *Queensland Government. (2019). Medicines and Poisons Act Extended Practice Authority 'Pharmacists'. Accessed via: https://www.health.qld.gov.au/__data/assets/pdf_file/0027/1108944/epa-pharmacists.pdf.*

24. *NSW Health. (2022). Research Grant: Clinical trial examining management of urinary tract infections by community pharmacists. Accessed via: https://www.medicalresearch.nsw.gov.au/community-pharmacists-uti-management-clinical-trial/.*
25. *Australasian College of Pharmacy. (2022). Uncomplicated Cystitis Treatment – Pharmacist Training. Accessed via: https://www.acp.edu.au/uti-training/.*
26. *Pharmaceutical Society of Australia. (2022). Managing uncomplicated cystitis. Accessesed via: https://my.psa.org.au/s/training-plan/a110o00000JPST0AAP/managing-uncomplicated-cystitis.*
27. *Pharmaceutical Society of Australia. (2020). Treatment guideline for pharmacists. Cystitis. Accessed via: https://www.psa.org.au/wp-content/uploads/2022/12/Treatment-guideline-for-pharmacists-cystitis.pdf.*
28. Greenhalgh, J. and A. Manzano, *Understanding 'context' in realist evaluation and synthesis.* International journal of social research methodology. **ahead-of-print**(ahead-of-print): p. 1-13.
29. Paparini, S., et al., *Evaluating complex interventions in context: systematic, meta-narrative review of case study approaches.* BMC medical research methodology, 2021. **21**(1): p. 1-22.
30. Matheson, A., et al., *Evaluating a community-based public health intervention using a complex systems approach.* Journal of public health (Oxford, England), 2018. **40**(3): p. 606-613.
31. Datta, J. and M. Petticrew, *Challenges to evaluating complex interventions: a content analysis of published papers.* BMC public health, 2013. **13**(1): p. 568-568.
32. Damschroder, L.J., et al., *Conceptualizing outcomes for use with the Consolidated Framework for Implementation Research (CFIR): the CFIR Outcomes Addendum.* Implementation Science, 2022. **17**(1): p. 7.
33. Kirk, M.A., et al., *A systematic review of the use of the Consolidated Framework for Implementation Research.* Implementation Science, 2016. **11**(1): p. 72.
34. Skolarus, T.A., et al., *Assessing citation networks for dissemination and implementation research frameworks.* Implementation Science, 2017. **12**(1): p. 97.
35. Damschroder, L.J., et al., *Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science.* Implement Sci, 2009. **4**: p. 50.
36. Moussa, L., et al., *Data-driven approach for tailoring facilitation strategies to overcome implementation barriers in community pharmacy.* Implementation Science, 2021. **16**(1): p. 73.
37. Varas-Doval, R., et al., *Evaluating an implementation programme for medication review with follow-up in community pharmacy using a hybrid effectiveness study design: translating evidence into practice.* BMJ Open, 2020. **10**(9): p. e036669.
38. Crespo-Gonzalez, C., et al., *Community pharmacists' perspectives about the sustainability of professional pharmacy services: A qualitative study.* J Am Pharm Assoc (2003), 2021. **61**(2): p. 181-190.
39. Varas-Doval, R., et al., *Systematic review of pragmatic randomised control trials assessing the effectiveness of professional pharmacy services in community pharmacies.* BMC Health Serv Res, 2021. **21**(1): p. 156.
40. Crespo-Gonzalez, C., et al., *Sustainability of innovations in healthcare: A systematic review and conceptual framework for professional pharmacy services.* Res Social Adm Pharm, 2020. **16**(10): p. 1331-1343.
41. Hossain, L.N., et al., *Qualitative meta-synthesis of barriers and facilitators that influence the implementation of community pharmacy services: perspectives of patients, nurses and general medical practitioners.* BMJ Open, 2017. **7**(9): p. e015471.
42. Pérez-Escamilla, B., et al., *Using network analysis to explore factors moderating the implementation of a medication review service in community pharmacy.* Res Social Adm Pharm, 2022. **18**(3): p. 2432-2443.
43. Moussa, L., V. Garcia-Cardenas, and S.I. Benrimoj, *Change Facilitation Strategies Used in the Implementation of Innovations in Healthcare Practice: A Systematic Review.* Journal of Change Management, 2019. **19**(4): p. 283-301.
44. Garcia-Cardenas, V., et al., *The complexity of implementation factors in professional pharmacy services.* Res Social Adm Pharm, 2018. **14**(5): p. 498-500.