FULL/LONG TITLE OF THE STUDY

PPhoCUs: Polypharmacy, Pharmacists and Clinical Uncertainty – Understanding how pharmacist decision making can be improved in the context of polypharmacy

SHORT STUDY TITLE / ACRONYM

PPhoCUs: Polypharmacy, Pharmacists and Clinical Uncertainty

PROTOCOL VERSION NUMBER AND DATE

Version 1.1

Dated: 19/06/2024

RESEARCH REFERENCE NUMBERS

IRAS Number:	336527
SPONSORS Number:	2022-23-31
FUNDERS Number:	223501/Z/21/Z

SIGNATURE PAGE

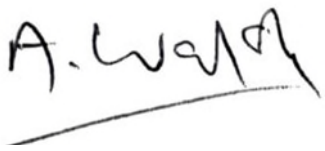
The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Date:
.18/04/2024

Signature: 

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Name (please print): ANTONY WALSH

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Position: Head of Research Ethics, Governance and Compliance.....
.....

Chief Investigator:

Date:
27/03/2024

Signature: 

.....

Name: (please print): TOMAZO KALLIS

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LIST of CONTENTS

KEY STUDY CONTACTS

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Sponsor	University of Exeter Dr Antony Walsh Head of Research Governance, Ethics and Compliance University Corporate Services, University of Exeter G14, Lafrowda House, St Germans Road, Exeter, EX4 6TL Tel: 01392 726621 res-sponsor@exeter.ac.uk
Funder(s)	NIHR School of Primary Care Research 'PhD for Primary Care Clinicians' Grant Ref: 223501/Z/21/Z
Key Protocol Contributors	Tomazo Kallis Prof Rupert Payne Dr Jenny Scott Prof Karen Mattick
Committees	Supervisory Group Contact: Prof Rupert Payne (r.a.payne@exeter.ac.uk) Patient Advisory Group Contact: Tom Kallis (t.j.kallis@exeter.ac.uk)

STUDY SUMMARY

Study Title	PPhoCUs: Polypharmacy, Pharmacists and Clinical Uncertainty - Understanding how pharmacist decision making can be improved in the context of polypharmacy
Internal ref. no. (or short title)	PPhoCUs: Polypharmacy, Pharmacists and Clinical Uncertainty
Study Design	The study will utilise both clinical observations and interviews across three initial phases: Phase 1: Clinical Observations (audio recorded) of polypharmacy structured medication reviews (SMRs). These

	will be SMRs delivered in a general practice setting, between a primary care clinical pharmacist and a patient currently prescribed ten or more medicines. Phase 2: Semi-structured qualitative interviews with practice-based clinical pharmacists. The sample of clinicians in this phase will represent a range of experience, ethnicities and geographical locations. Phase 3: Semi-structured qualitative interviews with patients to understand experiences of pharmacist-delivered care in primary care medication reviews. Patients will be actively recruited from phase 1 of the study.
Study Participants	Phase 1: Clinical Pharmacists and Patients in general practice settings Phase 2: Practice-based clinical pharmacists Phase 3: Patients with polypharmacy (prescribed 10 or more medicines)
Planned Size of Sample (if applicable)	Phase 1: A total of 70 recordings from 10 pharmacists based in multiple GP practices Phase 2: 15 – 20 Pharmacists Phase 3: 15 – 20 Patients
Follow up duration (if applicable)	N/A
Planned Study Period	July 2024 – October 2025
Research Question/Aim(s)	How can clinical pharmacist decision-making be improved when delivering patient-centred medication reviews in the context of complex polypharmacy and clinical uncertainty?

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
NIHR School of Primary Care Research Prof Steph Taylor Tel: 020 7882 2495	Financial support: 'PhD for Primary Care Clinicians' fellowship grant for Chief Investigator (£316,844) Grant Ref: 223501/Z/21/Z

s.j.c.taylor@qmul.ac.uk	QMUL Ref: WT 6473650 - QM03 - Kallis2023

ROLE OF STUDY SPONSOR

The study sponsor will ensure that the research team has access to resources and support to deliver the research as proposed and that responsibilities for management, monitoring and reporting of the research are in place prior to the study commencing. The sponsor will ensure that there is agreement on recording, reporting and reviewing significant developments as the research proceeds and approve any modifications to design, obtaining requisite regulatory authority approval.

The sponsor will assume responsibility for operating the management and monitoring systems of the research.

Prior to the study commencing the sponsor will be satisfied that:

- The research will respect the dignity, rights, safety and well-being of participants and the relationship with healthcare professionals.
- Where appropriate the research has been reviewed and approved by an NHS Research Ethics Committee and/or the Health Research Authority Approval Programme.
- The Chief Investigator, and other key researchers have the requisite expertise and have access needed to conduct the research successfully.
- The arrangements and resources proposed for the research will allow the collection of high quality, accurate data and the systems and resources will allow appropriate data analysis and data protection.
- Organisations and individuals involved in the research agree the division of responsibilities between them.
- Arrangements are in place for the sponsor and other stakeholder organisations to be alerted to significant developments during the study, whether in relation to the safety of individuals or scientific direction.
- There are arrangements for the conclusion of the study including appropriate plans for the dissemination of findings.

ROLE OF STUDY FUNDER

This study is funded through a ‘PhD for Primary Care Clinicians’ fellowship through the NIHR School of Primary Care Research. The research plan was developed de novo by the chief investigator (CI) and supervisory team before submission to the funding scheme. The fellowship was granted following a competitive process and review of the proposed research and its chief investigator. The funder will have no further role in the design, conduct or data analysis involved in the study. The funder may support with future dissemination and will be informed of any study outputs, including any resulting publications or conference proceedings.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Study Supervisory Group: A cross-institutional supervisory team of academic experts will provide support to the chief investigator over the study duration. The constitution and expertise of this group aligns to the research aim and objectives of the study. The group includes:

- Prof Rupert Payne, University of Exeter **(Principal Supervisor)**
  Professor of Primary Care and Clinical Pharmacology
- Dr Jenny Scott, University of Bristol
  Primary Care Senior Lecturer and Academic Pharmacist
- Prof Karen Mattick, University of Exeter
  Professor of Medical Education

The supervisory group meets with the chief investigator on a monthly basis, with one-to-one supervisory sessions between the principal supervisor and chief investigator occurring more frequently in the interim between whole group meetings. The role of the supervisory group is to:

- Provide appropriate governance and support to the chief investigator throughout the course of his PhD, centred around the delivery of the PPhoCUs research programme.
- Peer review and scrutinise planned research design, conduct, data analysis and interpretation, and any written outputs.
- Review study progress against agreed timeframes and milestones.

Patient Advisory Group (PAG): This group will seek to place a representation of the patient voice as an equitable contributor to the research design, conduct, analysis and dissemination. A group of 5 – 6 patients will be recruited to the group, including representatives that have lived experience of taking multiple medicines. Participants will be reimbursed for their time as per the NIHR INVOLVE recommendations and appropriate training and support will be provided to the group where applicable.

Key stages where the PAG will be involved include:

- Development and review of qualitative research protocols
- Development of patient and participant information materials in easy to read and accessible language
- Review of interview schedules and topic guides
- Analysis of interview transcript excerpts to ensure that themes identified are grounded in the data and are reflective of patient experiences of pharmacist-delivered in practice
- Development of patient-friendly communications at the end of the research project

PROTOCOL CONTRIBUTORS

This protocol was developed by Tomazo Kallis, who is a senior clinical pharmacist with extensive experience of working in PCN and GP practice settings. He is currently based at the University of Exeter as a Senior Clinical Research Fellow funded through the NIHR School for Primary Care Research Wellcome-funded 'PhD for Primary Care Clinicians' scheme. He has previous experience of qualitative interview research with pharmacists working in primary care, as well as clinical experience of delivering structured medication reviews for patients with significant polypharmacy. He will act as the Chief Investigator and will be the principal researcher responsible for core delivery of the research outlined in this protocol.

The NIHR SPCR were involved in the review of the proposed research at the application stage of grant funding, but will have no further input into research conduct, data analysis or final publication of journal articles or the resulting thesis.

A Plain English Summary was co-produced with patient representatives before this protocol was developed. These were members of the public from the Saltash Health Centre Patient Participation Group, separate to the PAG that will be formed to help further inform this research and iteratively develop this protocol.

The protocol will be peer reviewed by the supervisory group and by an external senior academic pharmacist.

KEY WORDS: General Practice, Polypharmacy, Pharmacists, Primary Health Care, Medication review, Uncertainty.

STUDY GANTT CHART

		2024										2025					
	Months	Jul-24	Aug-24	Sep-24	Oct-24	Nov-24	Dec-24	Jan-25	Feb-25	Mar-25	Apr-25	May-25	Jun-25	Jul-25	Aug-25	Sep-25	Oct-25
Phase 1: Audio Observations of SMRs																	
Recruitment of sites via CRN	3																
Engagement and set-up meetings	4																
Data collection	7																
Data Analysis	11																
Phase 2: Clinical Pharmacist Interviews																	
Topic guide development and testing	2																
Recruitment of participants	3																
Data collection	4																
Ongoing iterative review of topic guide	4																
Data Analysis	10																
Phase 3: Patient Interviews																	
Topic guide development and testing	2																
Recruitment via Phase 1	7																
Data collection	8																
Ongoing iterative review of topic guide	8																
Data Analysis	11																
Integrative analysis and synthesis of findings	5																

STUDY PROTOCOL

PPhoCUs: Polypharmacy, Pharmacists and Clinical Uncertainty

1 BACKGROUND

Polypharmacy and multimorbidity remain global challenges for national health systems, with inappropriate multiple drug prescribing being associated with avoidable hospital admissions, increased fall risks and poorer patient outcomes.[1,2] Polypharmacy is also strongly correlated with non-adherence, decreased functional status and cognitive impairment.[3] Although there is some evidence that robust medication review may reduce certain adverse outcomes[4], the evidence for interventions targeting polypharmacy is generally weak.[5] The reasons for limited effectiveness of medication reviews are varied, but increasing clinical complexity can compound clinical uncertainty, which is a barrier to deprescribing and increases the likelihood of clinicians opting to maintain the 'status quo.'[6] Furthermore, research suggests that pharmacist-delivered structured medication reviews (SMRs) can lack patient focus.[7] Although patient-centred care is vital for polypharmacy reviews and effective deprescribing, it is also recognised that increased complexity (and associated clinical uncertainty) decrease the ability to have true shared decision making with patients.[8,9] In General Practice, it is recognised that there is an emphasis on 'getting work done' as opposed to 'thoroughness' when it comes to medication review, to which both pharmacists and GPs acknowledge that pharmacists tend to be more thorough and more likely to deprescribe than other healthcare professionals when reviewing patients.[10,11]

A core thrust of recent national policy in England to address inappropriate polypharmacy has been the inception of the primary care network (PCN) pharmacist role in 2019 to deliver SMRs in the general practice setting.[12] A key group of patients eligible for an SMR is those with 'complex polypharmacy' defined in NHSE guidance as patients prescribed 10 or more drugs.[13] However, undergraduate and foundation pharmacist education does not fully prepare pharmacists for the delivery of care in general practice.[14] This has led to the development of the postgraduate 'Primary Care Education Pathway' through the Centre for Pharmacy Postgraduate Education. This 18-month pathway, alongside the requirement for regular clinical supervision in practice, is the only additional training that is currently mandated for PCN pharmacists to access as part of their role.

Current literature acknowledges that both GPs and pharmacists report a sense of clinical uncertainty when approaching multimorbidity linked to polypharmacy.[15] Although teaching programmes to support trainee GPs actively explore 'operating in a corridor of uncertainty' to make patient-centred decisions, this viewpoint is absent from core pharmacist training, with pharmacists citing a need for further support and training for professional decision making after qualifying.[16,17] There is an overt absence in the current published literature on how pharmacists manage clinical uncertainty in the context of reviewing polypharmacy. Nor is there currently guidance or policy advice available to support primary care clinical pharmacists in rationalising complex polypharmacy in the context of clinical uncertainty.

2 RATIONALE

Since 2019 and the advent of PCNs as a contracting mechanism to bring new and additional roles into primary care settings, 46% (£387million) of the total national budget for 18 new primary care roles has been spent solely on clinical pharmacists.[18] Pharmacists therefore represent a significant new addition to the primary care workforce within general practice. Traditionally, pharmacist undergraduate training is heavily grounded in scientific teaching as opposed to clinical practice, which in turn has led to the inception of postgraduate pathways to support pharmacist transitions into working in clinical settings. This emergent workforce has been tasked with reviewing patients with complex medication regimens and significant polypharmacy to help address the NHS England medicine optimisation priorities in an effort to reduce avoidable hospital admissions, harm from medicines and enhance cost savings where possible.[19]

Whilst it is recognised that pharmacists can reduce inappropriate prescribing, interventions with or without pharmacist involvement targeting polypharmacy lack a robust evidence base.[5] There is a significant gap between the current educational standards and the scale of the national policy ask for pharmacists deployed in PCNs and GP practices. It is therefore the objective of the PPhoCUs study to understand how pharmacists make decisions in primary care when reviewing polypharmacy in the context of the clinical uncertainty they may face. We will also seek to understand patient experiences of pharmacist-delivered care and shared decision-making in these encounters. The ultimate output of the PPhoCUs study will be understanding what factors can influence and enhance this shared decision-making process, giving rise to recommendations for postgraduate education or an intervention to better support pharmacists to deliver excellent polypharmacy reviews. The ambition is to provide pharmacists with additional support to deliver high quality interventions, resulting in enhanced patient outcomes and experiences.

The current study scope focuses on an understanding everyday clinical interactions and experiences through clinical observations and interviews. Focus groups and/or consensus exercises may form later stages of the PPhoCUs study predicated on the outcomes from the first three phases and leading to development of new interventions or educational recommendations – at this point, the Chief Investigator will apply to the relevant ethical authorities for an extension to this protocol.

3 THEORETICAL FRAMEWORK

An overarching interpretivist approach will be taken when conducting this qualitative research, positing that there are multiple social realities that are phenomena of individual lived experience.[20] This in turn aligns with a relativist ontology, which accepts the subjective nature of 'truth' which can vary dependent on social contexts and in turn be shaped by perceptions and lived experiences of individuals.[21] Qualitative research logically follows as an employed methodology to discover new knowledge about the world, when this subjective view of how truth is understood is taken. The aim of utilising the proposed research methods is to generate rich data to:

1. Inform 'thick' descriptions of observed clinical pharmacist practice when confronted with polypharmacy and clinical uncertainty in primary care.[22]
2. Understand how clinical pharmacists make decisions when faced with clinical uncertainty in the context of polypharmacy.

3. Understand the patient experience of care delivered in polypharmacy medication reviews

The PPhoCUs studies will seek to understand the emic or 'insider perspective' of the participants in primary care medication reviews by using the different qualitative approaches of clinical observations and semi-structured interviews, in order to generate 'thick' descriptions of the phenomenon of inquiry.[23] The emic approach to naturalistic inquiry makes use of the researcher themselves as a data collection tool, to yield in-depth, nuanced and meaningful data from participants which considers not only the experiences shared, but the socio-cultural factors which may influence them also.

The majority of published research to date exploring clinician decision-making when prescribing or deprescribing is not underpinned by any conceptual theory, but instead takes a phenomenological, exploratory approach to define and characterise clinician behaviour.[24] Whilst a purely inductive approach could be argued to have a credence of fidelity to the data for analysis (in comparison to the imposition of a pre-determined framework or set of codes), a mixed approach, integrating a theoretical framework aligned to the research question in a deductive manner, whilst allowing inductively discovered themes to be identified, allows analysis to both 'follow the data' and align itself to the question being asked. The conceptual framework proposed by Hillen et al, which synthesises a range of factors which may affect clinical uncertainty tolerance will be used to inform interview topic guides and data analysis.[25] This model considers psychological and behavioural factors of the clinician undertaking the decision-making process, as well as encompassing external moderators, such as social, cultural or situational characteristics. As such, this framework provides the breadth of consideration of factors both internal and external to the clinician when they are confronted with clinical uncertainty. To allow for integration of data and findings between each of the research phases, this conceptual framework will inform the topic guides for both clinician interviews in phase 2 and patient interviews in phase 3.

4 RESEARCH QUESTION/AIM(S)

How can clinical pharmacist decision-making be improved when delivering medication reviews in the context of polypharmacy and clinical uncertainty?

4.1 Objectives

1. To understand how practice-based pharmacists approach clinical uncertainty when conducting reviews with patients who have complex polypharmacy. These data will be collected through audio recordings of medication reviews between pharmacists and patients with polypharmacy.
2. To understand what influences clinical pharmacists' decision making when encountering clinical uncertainty in patients with complex polypharmacy. This will be achieved through qualitative semi-structured interviews with pharmacists.
3. To explore patients' experience of care and person-centred decision making delivered by clinical pharmacists in general practice when reviewing polypharmacy. Semi structured interviews with patients will be used to identify themes and perceptions.

4.2 Outcome

The ultimate goal of the PPhoCUs study is to understand how pharmacists make clinical decisions when reviewing significant polypharmacy and faced with clinical uncertainty in primary care. Understanding both patient perceptions of care delivered and pharmacist beliefs/attitudes when working in the context of polypharmacy will be analysed alongside findings from naturalistic audio recorded data of these clinical encounters. Findings from this study may subsequently inform interventions to enhance primary care pharmacists' ability to work effectively in the context of clinical uncertainty and polypharmacy, or to enhance patient experiences and/or outcomes of pharmacist-delivered polypharmacy medication reviews.

5 STUDY DESIGN and METHODS of DATA COLLECTION AND DATA ANALYIS

The study will encompass multiple qualitative methods to meet the research objectives, including clinical observations of SMRs and semi-structured interviews with both patients and practice-based pharmacists. Audio recordings of pharmacist-patient interactions will be employed in the first phase to understand real-world delivery of pharmacist care in structured medication reviews. The data obtained from these recordings will be supplemented with in-depth qualitative interviews with pharmacists in phase 2 and patients in phase 3 to gain an insight into the perceptions of these two parties to the shared decision-making process.

5.1 Data Collection

Phase 1: Observations of patient-facing SMRs undertaken by clinical pharmacists in general practice

The first phase will entail the audio recording of SMRs (n=70) with patients who have significant polypharmacy (prescribed ten or more medications) in general practice settings. Ten different GP sites will be recruited across two comparator regions (see recruitment for further details) and a total of seven recordings taken by practice-based clinical pharmacists at each site. It is likely that only one pharmacist based at each of the GP sites will conduct the entirety of the seven recordings. Two distinct geographical regions will be used to sample from in order to enhance the variability of SMR interactions captured in the resulting dataset, and to enhance transferability of the study findings by capturing a diverse range of encounters. Audio recordings will be used (instead of video recordings) so that both face to face and remote/telephony SMRs can be analysed. After initial recruitment, pharmacists participating in the audio recording will be offered a briefing session with the chief investigator. In this briefing session, the CI will give information on the research background, explain the structure of the proposed study (including the role of the pharmacist) and provide an opportunity to take any questions. In advance of this meeting, pharmacists will be sent participant information sheets and the consent form. The briefing will also include a brief walk through of how to use the audio recording device needed to capture the clinical encounters in phase 1. Questions asked in each of these sessions will be collated into a master document and sent out to all participating pharmacists as an 'FAQ' document to ensure equitable information is provided to all pharmacists involved in this phase. Pharmacists will be formally consented to participate in phase 1 during this briefing. Participants will also be given the opportunity to consider the information shared and formally

consent in a reasonable time frame (2 weeks) following the meeting if they want to reflect on the information shared or discuss with members of their organisation.

Encrypted audio recorder devices meeting NHS standards for research will be used to record the clinical encounters. A total of four audio recorders will be available to the research team to provide to participating sites, meaning that they will need to be sent out and retrieved in a staggered, rolling fashion. Before sending the audio recorder to the practice site, the CI will ensure that any data files previously saved to the device have been removed and downloaded to the relevant secure location on the university server. An SOP for pharmacists involved with phase 1 will be shared with sites and explained in advance during the training session on how to use the audio recorder and what information needs to be transferred to the CI via NHSMail. The CI will remain available to participating pharmacists through phase 1 and have regular contact via e-mail and a direct line if there are any technical difficulties with using the audio recorder. The clean audio recorder will be transferred from the university to the participating site either via the researcher or a secure courier service. Ten 'Consent packs' for patients, including hard copies of the patient participation information sheet and consent form will also be sent with the audio recorder for the practice pharmacist to consent patients.

Once the audio recorder arrives at the GP research site, the pharmacist based at the practice can begin recording SMRs. Patients will be recruited by the practice staff. The site pharmacist will screen their clinics in advance for potential candidates for inclusion. Patients with significant polypharmacy will be contacted in advance e.g. sent a text message (via the clinical system or a third party application that the GP practice uses, such as mjog or AccuRx) informing them that the pharmacist conducting their review wishes to invite them to participate in the research. The text message (see supporting documents) will also contain a link to the patient-facing participant information sheet and will inform the patient that they are able to ask questions in advance.

At the SMR appointment, the pharmacist will talk through the consent form with the patient and provide an opportunity for the patient to ask any questions before gaining informed consent. For face-to-face encounters, patients would be invited to read and sign a hard copy of the consent form. In the case of telephony SMRs, pharmacists will talk through each of the check points on the consent form verbatim and gaining verbal consent, recorded on the audio recorder for posterity and assurance. After informed consent has been obtained, the pharmacist will state on the audio recorder the GP practice, who they are (including name and role), the patients name, how the review is taking place (in person or remotely) and who is taking part in the review. The SMR will then proceed with the review recorded in its entirety. At the end of the review, the pharmacist and patient will both confirm they are still happy for the recording to be used for the research before the recorder is stopped.

A patient profile will be produced from the clinical system containing summary patient medical information for each of the SMRs. Pharmacists will be sent information on how to generate this. For each recording, a copy of the corresponding patient profile containing demographic information and prescribed medication will be generated by the GP practice research site and sent to the chief investigator via NHSMail. The pharmacist will use their NHSMail account to send the profile directly to the CI's NHSMail account to ensure end-to-end encryption. Once received by the CI, the profile document will reviewed and relevant data (age, ethnicity, major problems and prescribed medicines) extracted. The following table details the data that will be extracted from the patient profile and how it will be anonymised:

ORIGINAL REPORT FROM GP PRACTICE	RETAINED, EXTRACTED DATA
Age	5-year categories
Gender	Male/Female/other
Ethnicity	Categorised into superordinate census group (1. Asian or Asian British, 2. Black, Black British, Caribbean or African, 3. Mixed or multiple ethnic groups, 4. White, 5. Other)
Postcode	IMD quintile Rural/urban
Current and old problem list with Read codes	Text description using highest usable coding hierarchy Problems will be classed as "current" or "old", but no dates or Read/SNOMED codes will be retained
Medications – acute and repeat (12 months) - Medicine name (AMP) - Dosing instructions (free-text) - Quantity - Start date - Last issue date	- Convert AMP to VMP (generic name) - Simplify dosing (standard notation) - Categorise (e.g. 7, 14, 28, 56, more) - Weeks prior to review medicine started - Weeks prior to review medicine issued
Tests – any in past 12 months	Weeks prior to review test results available Blood tests extracted: - U&E: Na, K, eGFR CKD classification - FBC: WCC, Hb, plt - LFT: bili, ALT/AST, GGT, albumin - TFT: TSH - Ca - Vit D - Drugs: digoxin, lithium - INR (classify on thresholds) - Lipid: LDL, non-HDL, chol, ratio (classify based on thresholds) Tests will be classified as above, within or below reference range

Data extraction will be carried out by the CI using NHS systems (either on site at a GP practice or using NHS hardware e.g. an NHS laptop). Once the data have been extracted and anonymised, they will be stored on the dedicated Sharepoint site. An appropriate file number assigned to the extracted

data (as detailed in section 8.6) before saving to the relevant secure file location on the dedicated SharePoint location on University of Exeter servers.

Once seven recordings have been taken and corresponding patient profiles sent to the CI, the audio recorder will be collected either directly by the researcher or via a tracked, secure courier service. Audio recordings will only be transferred via the audio recording device. Audio recordings will be anonymised by the CI using NHS systems (either on site at a GP practice or using NHS hardware e.g. an NHS laptop) by redacting personally identifiable data via the use of audio editing software (i.e. patient demographic information, contact details, name, age, date of birth, GP surgery name/location).

Once effectively anonymised, the recordings will be stored on the University of Exeter hosted SharePoint site for transcription. Hard copies of consent forms will either be scanned and sent to the CI via NHSMail before being destroyed at the practice once safe receipt is confirmed or returned via the same mechanism as the audio recorder. Whilst the recorder is held by the research site practice, it will be stored securely in either a locked desk drawer or locked room when the clinician is not present.

Phases 2: Semi-structured interviews with primary care clinical pharmacists

Semi-structured interviews (n=15-20) will be conducted with pharmacists working in GP practice settings to understand their approach, priorities and beliefs when making decisions in scenarios of clinical uncertainty, when reviewing polypharmacy. Given that it is likely only ten pharmacists will participate in phase 1, pharmacists for this phase will be recruited separately to the first phase to allow for purposive sampling to capture a range of genders, primary care experience, qualification status and geographical location. Recruitment will take place through promotion through local and national professional networks (such as the Primary Care Pharmacy Association telegram groups) and social media posts on LinkedIn and X. Potential participants will freely contact the CI to express their interest and will be sent participant information sheets via e-mail. Pharmacists will then be invited to participate in an MSTeams interview at a time of their convenience. Phase 2 will seek to capture a diverse sample within the sampling frame (detailed in section 7), therefore demographic information will be captured at the start of the interview, which may allow for purposive sampling later in the phase if needed.

Upon formal invitation, participants will be sent the consent form and offered the opportunity to ask any questions in advance. Interviewees will be asked to return a copy of the signed consent form to the chief investigator before the interview takes place via e-mail. All interviews will be conducted by the CI and an MSTeams invite will be sent from the CI's university account to participants once a mutually acceptable time has been found. At the start of the interview, the CI will check if the participant has any questions and if they still consent to the interview proceeding. If written consent has not been received, the participant will be asked to complete the form and send to the researcher before the interview proper begins. By exception, if the interviewee is unable to send the consent form back to the researcher, the CI will talk through each of the check points on the consent form verbatim and undertake an e-consent process. The interview will be recorded via the MSTeams in-built functionality, as well as a back-up recording on an audio recorder device taken also.

Clinical vignettes will be used to stimulate discussion around clinical uncertainty, identifying areas of high self-efficacy and low clinician confidence, followed by general interview questions. The

vignettes will present a model patient in a hypothetical SMR to participants, including a list of drugs prescribed, chronic problems and background information to inform the scenario. These vignettes will be sent in advance of the interviews for consideration by participants and then discussed at the interview. Questions focussing on the scenarios will consider the pharmacists' thoughts about items they would wish to discuss during the SMR and any areas of uncertainty. The interview topic guide will be informed by the chief investigator's professional experience, peer discussion with the supervisory group and PAG, and Hillen et al's conceptual framework of clinical uncertainty tolerance.[25] Various items will be explored with interviewees, how participants rationalise clinical uncertainty (considering concepts central to the Hillen model, such as emotional, behavioural and cognitive processes), the shared decision-making process when reviewing polypharmacy and subsequent care planning. The interviews are expected to take in the region of 60 minutes. Questions listed in the topic guide will be completed in all interviews, but not followed by rote – instead allowing for time to be spent on areas pertinent to interviewees and to provide flexibility to create space for new areas of discussion that participants want to raise. Clinicians participating will be reimbursed £88, claimable via BACS invoicing – details of how to claim this will be shared with participants after the interview has concluded.

Phase 3: Semi-structured interviews with patients

Patients participating in the Phase 1 recorded sessions in will be invited to share their experiences of their SMR appointment using semi-structured interviews to provide in-depth insights. At the point of consenting for Phase 1, patients will be asked if they wish to participate in a follow up interview, with a £25 'thank you payment' provided on completion. Up to 15-20 participants will be purposively sampled using the characteristics listed in section 7 to provide a range of demographic and clinical characteristics. Once a patient has indicated they would like to participate, either via the written consent form or through verbal assent on the audio recording in phase 1, the CI will make contact with the patient via the email address or best contact method they provide. Patients not selected for inclusion, but who have opted to participate will also be contacted, thanking them for their interest and informing them that there will be no further follow up.

Upon formal invitation, participants will be sent the consent form and offered the opportunity to ask any questions in advance. Interviewees will be asked to return a copy of the signed consent form to the chief investigator before the interview takes place via e-mail. All interviews will be conducted by the CI and an MSTeams invite will be sent from the CI's university account once a mutually acceptable time has been found. At the start of the interview, the CI will check if the participant has any questions and if they still consent to the interview proceeding. If written consent has not been received, the participant will be asked to complete the form and send to the researcher before the interview proper begins. The interview will be recorded via the MSTeams in-built functionality, as well as a back-up recording on an audio recorder device taken also. If patients are unable to utilise MSTeams, telephone interviews may also be offered by exception, so as not to exclude patients from participating based on digital literacy. By exception, if the interviewee is unable to send the consent form back to the researcher, the CI will talk through each of the check points on the consent form verbatim and undertake an e-consent process.

The topic guide for use in the interviews with patients will be developed with input from the PAG, as well as being informed by both the uncertainty theoretical framework previously discussed and the data yielded in year phases. This will develop iteratively dependent on the results of phases 1 and 2, and as the interviews in this phase progress.

5.2 Data Analysis

Transcripts of all phases will be considered the 'raw data' for the data analysis phase of the study. The steps taken in data processing and analysis will be: transcription, familiarisation, coding, developing a framework, applying the framework to transcripts, charting and then interpreting the data.[26] Transcription of audio recordings of both clinical encounters and qualitative interviews will be carried out by either the chief investigator or a professional transcription service. If the researcher is able to carry out transcription, there will likely be greater familiarisation with the recorded content however, time limitations may necessitate the employ of an external transcription service if this is not viable within the study timeframes. Data will be processed and managed using NVivo and MSExcel software. For Phase 1 data, transcripts will be contextualised with data extracts from the relevant patient profile information, to give insights into which medications were routinely prescribed and any potential pharmaceutical problems versus which items were discussed during the course of the review.

Thematic analysis of transcripts using the framework method will be conducted to answer the research questions, drawing on Braun and Clarke's seminal work.[27] In concert with the uncertainty framework previously discussed for deductive interpretation, codes will also be identified inductively and developed contemporaneously during transcript analysis. For the first three interview transcripts, the CI and a second qualitative researcher will review and code separately, before meeting to discuss perceived codes and categories. This may be a single event per study or continue for subsequent transcripts if there are markedly different perceptions or differences of analysis that cannot be adequately reconciled at an early stage. An iterative approach to thematic analysis will take place, with emergent themes informing topic guide amendments if necessary, as the research develops. In such a way, analysis and data collection will occur in parallel, so that one may inform the other.

Interviews will continue in phases 2 and 3 until 'data saturation' has been reached. There are plural definitions as to what this might mean for a given qualitative study however, data saturation for this study will be considered reached when a minimum sample size has been met and no new themes have emerged in three consecutive interviews following this threshold being reached.[28] A minimum sample size will be set at 12 interviews for each of the interview phases.[29]

In Phase 1, all transcripts will be reviewed from the suite of 70 recordings yielded from across the research sites. High level themes and categories of behaviour will be identified, before selecting 15 transcripts to review in-depth, to the same level of detail as the Phase 2 and 3 transcripts.

Lincoln and Guba's quality standards for credibility, transferability, dependability and confirmability will be applied to ensure quality of research conduct and data yielded.[30] To meet these standards, the following approaches will be taken:

- Definition of a sampling strategy
- Ensuring data saturation

- Taking a reflexive approach by making adequate field notes when taking interviews and contemporaneous recording of thoughts, impressions and perceptions when collecting and analysing data in a field diary
- Outlining a clear methodology and transparently sharing this by registering the study on an open platform, sharing the final version of the study protocol
- Peer review of the study protocol and research findings
- Periodic debriefing of the chief investigator with the supervisory group during the study

5.3 Conclusion

The research will be considered concluded once the requisite data have been collected and analysed. For Phase 1, this will entail gathering 70 audio recordings and paired patient profiles, anonymising the data, transcribing and then analysing transcripts. For Phases 2 and 3, the research will be concluded upon recruiting sufficient pharmacists and patients respectively to thematic data saturation (anticipated to be c.15 – 20 participants for each phase), transcribing the interviews and concluding thematic analysis of these transcripts.

6 STUDY SETTING

Phase 1: SMRs will be recorded in the general practice setting where these naturally occur. Audio recording will be used to minimise intrusion on these encounters. Ten sites across two comparator regions will be used.

Phases 2 and 3: Interviews will be conducted via MSTeams at a time convenient to research participants. It will be recommended to interviewees ahead of the allocated time to be situated in an environment in which they are comfortable, not likely to be overheard (so that they speak freely) and free from extraneous noise (i.e. not in a public or noisy setting, such as café). The interviewer will be cognisant of the way he presents himself to both patients and clinicians. The chief investigator will wear informal dress whilst conducting interviews to better allow for a relaxed atmosphere for open discussions to take place in, as opposed to inadvertently creating power imbalances signalled through formal wear or ‘power’ clothing.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

This research will seek to include a diverse sample of pharmacists and patients in the three phases of work, across the dimensions of socioeconomic status (for patients), rurality, ethnicity and level of experience in primary care (for pharmacists). The use of two geographically distinct comparator sites (the south west peninsula and the west midlands) will seek to diversify the representation of patients across these dimensions, which is further expanded in section 7.2. To be eligible, patients will need to be registered at a GP practice at one of these two comparator sites and to meet the inclusion criteria listed below. Pharmacists registered with the GPhC and currently working

in a GP practice-based role in England will be eligible to participate given that they satisfy the inclusion and exclusion criteria listed in the subsequent sections.

7.1.1 Inclusion criteria

For Pharmacists (in Phases 1 and 2):

- Registered as a Pharmacist with the General Pharmaceutical Council
- Employed in the primary care sector, based in either a general practice or primary care network setting
- Currently delivering or able to deliver structured medication reviews

For Patients (in Phases 1 and 3):

- 18 years old or older
- Prescribed 10 or more medications on repeat
- Booked to have a structured medication review with a clinical pharmacist in primary care
- Able to freely give informed consent

7.1.2 Exclusion criteria

For Pharmacists:

- Pharmacists working in secondary care or community pharmacy settings
- Healthcare professionals who are not registered pharmacists
- Pharmacists with no experience or ability to deliver SMRs

For Patients:

- Under 18 years of age
- Patients who are unable to freely give consent or lack capacity
- End of Life Care patients
- Care Home Residents
- Patients identified by the host research site as being unsuitable for participation by virtue of being acutely or significantly unwell, difficulties in communicating, safety issues (e.g. noted on patient records or have overtly declined to be contacted by the practice) or welfare issues.

7.2 Sampling

Sites for participation in Phase 1 will be sampled from two comparator areas between the South West Peninsula (Cornwall, Devon and Somerset) and the West Midlands. Sites will be recruited through collaboration with the South West Clinical Research Network, targeting 'research' practices where possible (due to the level of work required by the practice based pharmacist) to include:

- Urban, Rural and Costal geographical contexts
- A variety of socio-economic locations, including areas of significant deprivation and those which are least deprived.
- Different ethnicity profiles for registered patients (this is anticipated to be achieved through the use of two distinct geographical comparator areas)

This approach will be replicated for sites in the West Midlands.

For Pharmacists participating in the semi-structured interviews in Phase 2, a purposive sample will be taken following public recruitment via social media and national professional networks to include a mix of:

- Experience, both in terms of total years qualified and time spent practicing in a GP/PCN setting
- Geographical locations across England
- Ethnicities
- Qualifications (e.g. post graduate diploma, subsequent MSc beyond initial training, advance clinical practitioner status, prescriber status)

Patients will be sampled for participation in semi-structured interviews directly from the cohort that participated in the phase 1 clinical observations. Whilst the agency of the researcher will be limited as to which patients can be included (dependent on what medications take place with which patients on a given day, and which patients consent to follow up with an interview), it is anticipated that there will be a mix of the following criteria to sample from:

- Socio-economic status
- Location (rural, urban)
- Ethnicity
- Number of routinely prescribed medicines

7.2.1 Size of sample

Sample size will vary for each phase of the proposed research:

Phase 1: 70 Audio recordings of SMRs between primary care clinical pharmacists and patients with polypharmacy

Phase 2: 15 – 20 Pharmacists (final number dependent on data saturation)

Phase 3: 15 – 20 Patients (final number dependent on data saturation)

It is anticipated that there will be significant variation between SMRs, dependent on clinician experience, mode of delivery (face to face vs. remote), practice population and region, which will be accounted for in the sampling frame, but also necessitates the high volume of data in phase 1. The triangulation of data by considering 'real-world' phenomena, the views of pharmacists and the experiences of patients accounts for the overall study design into three phases, with the latter two dependent on data saturation of themes identified by the researcher.

7.2.2 Sampling technique

General practice sites will be purposively sampled with the support of the Clinical Research Network to ensure a range of socioeconomic, rural/urban settings in differing locations and ethnic contexts are represented in the sampling frame. Having a mix of these social settings and backgrounds will enrich the quality of data yielded and enhance any potential transferability of findings at a national level, as opposed to only having a narrow section of society represented in the included participants.

Clinical pharmacists will also be purposively sampled to ensure a diverse representation of the desired characteristics listed in section 7.2. Participants in phase 2 will complete a demographic questionnaire and as the study progresses, pharmacists with characteristics not accounted for in the sample will be proactively targeted for inclusion. Although there will be some scope to purposively sample, this will be somewhat limited by the uptake rate of an invitation to follow up and participate in phase 3, and the patients included in the phase 1 research. However, the most important characteristic for inclusion in the patient interviews will be the lived experience of being prescribed multiple medicines and having experienced a medication review with a pharmacist.

7.3 Recruitment

Phase 1: General Practices

The South West Clinical Research Network (CRN) will support the recruitment of GP practices sites with engaged clinical pharmacists to participate in the research. This will be achieved through ongoing regular meetings with the CRN and the adoption of the PPhoCUs study to the NIHR portfolio. Discussions with the Southwest CRN indicate that there are strong links with other national research networks, which will allow for GP practices from the West Midlands to be recruited also as a comparator site. A Research Information Sheet for Practices (RISP) will be developed by the CI to support with the initial recruitment of practice sites. After initial engagement via the CRN, the CI will liaise directly with the practice based pharmacist (and other relevant parties if so desired, such as

prescribing lead or practice manager) to offer an initial briefing session and to provide more information.

Phase 2: Clinical Pharmacists

Primary care clinical pharmacists will be recruited via public advertisement of the PPhoCUs study via the CI's social media networks on LinkedIn and X, as well as via dissemination through national communication networks, such as the Primary Care Pharmacy Association (PCPA) telegram groups. Potential participants will freely contact the CI to express their interest and will be sent participant information sheets via e-mail. Later in the phase, particular pharmacist characteristics may be purposively sampled for to ensure a range of characteristics listed in the sampling frame are represented in the included clinicians. Once selected for inclusion, prospective participants will be sent a consent form to read, complete and return via e-mail before the interview date and offered the opportunity to ask any questions or meet informally in advance of the interview.

Phase 3: Patients

Patients will be recruited directly for participation in semi-structured interviews from Phase 1. The practice-based pharmacist will offer the patient a follow-up interview and the opportunity to participate in phase 3 as an additional part of the consent process. If the patient consents, they will be asked to provide the best contact method to engage with the research – preferably via e-mail. The CI will then screen the relevant patient profile and, if necessary, make contact with the patient after the audio recording and patient profile have been received back from the research site. Further information will be provided is needed, along with the opportunity to ask questions about the interviews and proposed research. Written consent will be sought again before commencing the interviews, but an e-consent process will be taken if the patient is unable to send a copy of the signed consent from in advance of the MSTeams interview.

7.3.1 Sample identification

The CRN will support with the identification of GP practices to participate as research sites in phase 1. The sampling frame criteria listed in 7.2 will be shared with the CRN before active recruitment, to ensure that there is a range of representation across these criteria in the recruited practices. Patients participating in phase 1 will be targeted for recruitment into phase 3 and offered a £25 thank you payment for participation. The pharmacists conducting the audio-recorded SMRs in phase 1 will be responsible for offering patients the opportunity to participate in phase 3 as part of the consent process. Interested patients will then be screened via the use of their patient profile by the CI before being invited to arrange an interview for the phase 3 research.

Pharmacists will be recruited using public advertising via social media platforms and national professional communication groups. Permission has been sought from the PCPA to advertise recruitment into the study via their telegram group, which has been granted. It is anticipated that a generous reimbursement rate of £88 for pharmacists participating in the research will encourage interest.

7.3.2 Consent

Participation in any of the phases of research in the PPhoCUs study will be contingent upon participants giving informed consent freely and being offered the opportunity to ask questions about the proposed research if so desired. In all cases, participant information sheets will be shared with prospective participants in advance of consent being requested. Informed consent will demonstrate that the participant has read and understood the provided information and is aware that there will be no repercussions for not participating in the research.

In phase 1, pharmacists at research sites will be required to assess capacity of patients to consent to participate in the study, in the same manner as they would be expected to when consenting patients for clinical procedures or treatments.

Participants are free to withdraw their consent during the clinical observation recording or interview and for a limited period of time after the data has been collected, dependent on stage of research. Phase 2 and 3 participants will have up to 7 days to withdraw consent for their data being used in the study, after which the transcripts will be processed and analysed, unable to be withdrawn from the overall dataset. Either pharmacist or patient in phase 1 may withdraw their consent to participate in the research during audio recording or immediately afterwards. There is only a limited capacity for a ‘cooling off’ period in the first phase, given the need to also process a patient profile sent via NHSMail and the added complication of removing data from an audio recorder at the research site.

Written consent will be sought from participants wherever possible in each phase of the study. Where it is not possible to obtain written consent, an e-consent process will be available by exception, which will mirror the written consent forms.

8 ETHICAL AND REGULATORY CONSIDERATIONS

8.1 Assessment and management of risk

Over the course of the PPhoCUs studies, it will be imperative to align methodologies and conduct to the UK Policy for health and social care research, in order to protect members of the public and professionals involved in the research.[31] A number of potential risks have been identified, which will require appropriate management and mitigation:

1. **Data Management.** A secure chain of data handling from the point of collection at research sites to being received, processed and stored by the CI at the University of Exeter will need to be in place to ensure that recordings of clinical encounters, patient summaries and interview recordings are handled and stored in an appropriate manner. At any point of data transfer or storage, there is a risk of inappropriate access from members extraneous to the research team or participants, if not managed accordingly. Field recordings will be taken using an encrypted audio recorder that meets NHS standards, with passwords reset and data cleared from hardware between different sites. Dissemination and retrieval of hardware containing encrypted data will be via a secure courier service or the CI himself. Audio files from phase 1 will be processed by the CI on NHS servers to remove any patient identifiable information from the recording. Generation of patient profiles to support clinical encounter recordings will be undertaken by practice staff and sent directly to the CI via the use of secure NHSMail. Patient profiles will have data extracted from them on NHS servers. The data extracted from patient

profiles and anonymised audio recordings from phase 1 will be stored on a dedicated, secure, restricted access SharePoint site for the duration of the study, which only the chief investigator and data custodian will have access to. Recordings for transcription from phases 2 and 3 will also be stored on the SharePoint site, hosted on University of Exeter servers, in line with the sponsor's Research Data Management policy.[32] The Phase 2 and 3 recordings will only be stored for up to 90 days after recording to allow anonymised transcriptions to be made. After this period, the recorded interview files will be deleted. Access to the SharePoint site will be granted to members of the supervisory team or sponsor representative on a 'minimum necessary use' basis by the CI. Further information on data protection is provided in section 8.6.

2. **Participant disclosures.** The research topic is unlikely to provoke recall of traumatic events or upsetting memories during qualitative interviews however, due to the unpredictable nature of responses from participants, this is not a risk that can be eliminated entirely. The interviews will be conducted by the CI who has experience of working in mental health settings and is familiar with signs and non-verbal cues that may indicate participants are in distress or significantly upset. The interviewer will proactively work to avoid and minimise any upsetting topics of discussion however, if a participant does become distressed, they will be offered the opportunity to terminate the interview at any point. There is also a risk of disclosures of undeclared clinical negligence or intentional harm to patients. Whilst this is significantly unlikely, the CI has a professional obligation to report any instances of pharmacist misconduct to the General Pharmaceutical Council, which will be included in the participant information sheet.
3. **Time incumbency.** Given the current pressures and demands on the health system in the UK, it is recognised that an hour-long interview is not an insignificant time commitment for practice-based pharmacists. The CI will make every effort to ensure that interviews take place at a time that is convenient to participants and do not impinge on daily clinical practice. The £88 incentive for pharmacists recognises the time commitment made by participants to contribute to this research study.

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

Health Research Authority (HRA) approval will be sought before the commencement of any research activity detailed in this protocol. As part of this approval process, a favourable NHS Research Ethics Committee (REC) decision will need to be in place also. The ethics application will be submitted via IRAS before the application is booked through the online booking service. The participant information sheets, consent forms, social media post wording, topic guides and other relevant documents will be submitted for review as part of this process.

All correspondence with the REC will be retained for information. The REC will be informed when the study ends. An annual progress review will be submitted to the REC annually within 30 days of the anniversary date on which the favourable opinion was given, until the study has ended.

Regulatory Review & Compliance

The Chief Investigator will ensure that appropriate approvals and confirmations are in place with the participating primary care organisations before sites commence enrolment of patients and

pharmacists into the proposed research. Specific arrangements on how to gain approval from participating organisations will be in place and comply with the relevant guidance for NHS sites.

For any amendment to the study, the Chief Investigator, in agreement with the sponsor, will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (both the NHS sites and the research team based at the University of Exeter) so they can put the necessary arrangements in place to implement the amendment to confirm their support for the study as amended.

Amendments

Any proposed substantial or non-substantial amendments to the study will be shared with the HRA and REC for consideration after discussion with the supervisory team and the sponsor. The sponsor will decide whether an amendment is substantial or non-substantial for the purpose of submission to the REC. Once approved, any participating sites, the research team and the supervisory group will be notified of any amendment details. The amendment history will be documented through retention of all documents pertaining to application for amendment and correspondence with the relevant stakeholders (i.e. the sponsor, REC, research sites) over the course of application and implementation of any amendments. This will also be tracked in appendix 3 of this document, detailing any amendments and changes to the protocol.

8.3 Peer review

As part of the funding application for the PPhoCUs study, the research programme was developed by the Chief Investigator and a collaborative of cross-institutional academics, which now form the supervisory group. The Wellcome-funded NIHR PhD for Primary Care Clinicians programme accepts projects that are developed de novo (as this plan of research was) as well as a pre-published list of available research projects. The research programme underwent extensive peer review as part of the grant application process both on the review of the submitted overview and subsequent interview of the chief investigator. Whilst the supervisory team played a key role in reviewing this document, a final draft was shared with a senior pharmacist academic (external to the immediate group and the institutions at which the chief investigator and supervisors are based) for peer review and commentary.

8.4 Patient & Public Involvement

Patient and public involvement with the proposed research will be critical to ensure that the planned research is meaningful to patients and adequately informed by representatives of patients who might receive pharmacist-delivered care. The PAG will be constituted of patients from a variety of geographical locations who have lived experience of being prescribed multiple medication. The key stages of the planned study that the PAG will be involved with are:

- Co-development of Plain English Summaries and patient-facing materials (e.g. participant information sheets) in easy to read and accessible language

- Review of research design, including this protocol
- Analysis and review of themes identified from audio recordings and interview transcripts to ensure these are reflective of patient experiences of pharmacist encounters in practice
- Development of patient-friendly communications at the end of the research project

The PAG will meet routinely over the course of the study, 3 – 4 times a year dependent on need and stage of the research.

8.5 Protocol compliance

The PPhoCUs study will seek to only conduct research activities in accordance with this protocol. However, accidental deviations can occur at any time. If these occur, they will be documented and reported to the supervisory group and to the sponsor. If a minor deviation occurs to deal with unforeseen circumstances occur, it may not be considered a serious breach of protocol. All deviations will be recorded and reviewed during routine supervisory group meetings. Frequently occurring deviations may call for immediate action and for an extraordinary meeting of the supervisory group for consideration, to understand whether they constitute a serious breach if not adequately addressed. If deviations meet the standard for a substantial amendment to be made to the protocol, the relevant HRA application will be submitted.

8.6 Data protection and patient confidentiality

All research team members will comply with the requirements of the General Data Protection Regulation (UK-GDPR) and Data Protection Act (DPA 2018) regarding data collection, storage, processing, and disclosure of personal information.

NHS organisations require a minimum of 256bit encryption for data security when audio recording clinical encounters. To satisfy this requirement, Olympus DS-9500 audio recorders will be used to record clinical observations in Phase 1. These recorders will have password protection for both audio recording and retrieval of recorded data. Passwords will be set by the chief investigator and shared only with the participating pharmacists in Phase 1 immediately prior to the research site commencing their audio recordings. The password will be communicated via NHSMail directly to the pharmacist based at the research site. Passwords will be reset between each site the recorder is used at. Patient profiles accompanying recorded data will be transferred from the host GP practice to the chief investigator using end-to-end NHSMail. Identifiable data from patient profiles will not leave NHS systems – the chief investigator will extract data from the patient profiles (patient age, ethnicity, major problems and drugs prescribed) which will not contain personally identifiable information. These extracted data will be stored on the Sharepoint hosted on the University of Exeter server under an anonymised encounter number.

Audio recorders will be transferred between the university and relevant research site either via the chief investigator or through the use of a secure courier service. The physical audio recorders will have recorded audio removed and anonymised by the CI before being sent on to new research sites. Anonymisation will take place on NHS systems via the use of audio-editing software to remove any patient identifiable information from the encounter recording. Anonymised audio recorded files will be saved with a 7-character randomised alphanumerical filename to the dedicated SharePoint site for the purposes of transcription for the duration of the study. Extracted data from patient profiles will be anonymised and labelled with an encounter number unrelated to any patient details to link the record to the relevant audio file before being saved to the project SharePoint. A password-protected mastersheet on the secure SharePoint site will contain a list of filenames of audio recordings and anonymised patient profile filename to which each recording corresponds.

All data for the study will be stored on a dedicated SharePoint site hosted by the University of Exeter, in line with the university's research storage guidance. SharePoint has the functionality to grant access on varying levels of membership to users. Access to data will be granted on a 'minimum required access' basis for members of the research team. In the first instance, this will be restricted to the chief investigator alone, but may be granted to members of the supervisory team if required. The sponsor may also be granted access if there are any ethical, governance or regulatory concerns. Anonymised transcripts of the Phase 1 recordings and associated data extracts will be stored for 10 years in accordance with consent that was freely given to participate in the study, to allow for research beyond the scope of the proposed study to interrogate the data further using different methods (e.g. conversation analysis) or research questions. The anonymised audio recordings from Phase 1 will be retained only for the duration of the study to allow for transcription. The CI will destroy Phase 1 recordings once transcripts have been made.

Interviews in Phases 2 and 3 will be conducted using MSTeams, hosted on the Chief Investigator's University of Exeter Microsoft account. By exception, interviews in Phase 3 may occur via telephone (audio recorded with the Olympus DS-9500 device) if patients are unable to access MSTeams, so as not to exclude patients from participating based on digital inequalities. These interviews will be recorded, with the recordings being retained for 90 days to allow for transcription before being deleted. Interviews will be transcribed by either the chief investigator on university hardware or using a professional approved transcription service. Any external transcription services employed will require secure data transfer and storage facilities, and will be asked to sign confidentiality agreements in advance.

Data excerpts may be shared with the PAG for elements of data analysis, but these will have any identifying data removed and raw interview transcripts or audio recordings will not be shared.

Only members of the immediate PPhoCUs research team will have access to any patient identifiable data. In the event of data being disclosed that is deemed inappropriate or where patient safety might be of concern, the chief investigator will inform the supervisory group and report any concerns immediately to the sponsor.

The data collected will remain the property of the University of Exeter. Prof Rupert Payne will be the data custodian for the data collected in this study.

8.7 Indemnity

Public Liability Insurance and Employer's Liability Insurance is provided by Aviva Insurance Ltd through the sponsor, with full details available at:
https://www.exeter.ac.uk/departments/cgr/insuranceauditandrisk/insurancepolicies/public/

Personal professional indemnity arrangements, the Clinical Negligence Scheme for General Practice and any employer-granted vicarious liability will be applicable for staff working in or employed through general practices and primary care networks.

No arrangements have been made for the payment of compensation in the event of harm to the research participants where no legal liability arises.

8.8 Access to the final study dataset

For the duration of the study, access to the final dataset will be restricted to the immediate research team (i.e. the chief investigator and the supervisory team). This is due to the nature of the in-depth qualitative data that will be gathered over the course of the interviews and sensitive nature of audio recorded health encounters. If there are any ethical, governance or regulatory concerns, the sponsor will be granted access also.

Informed consent will be sought for the use of anonymised data to be used in the final study write up and any resulting publications. As part of this consent process, participants in Phase 1 of the study will be asked to give explicit consent for the retention of anonymised transcripts for 10 years, to allow for future research beyond the scope of the proposed study to answer different research questions or use methodologies not employed in the PPhoCUs study (e.g. Conversation Analysis). The retained data will be stored in accordance with the General Data Protection Regulation (GDPR) and Data Protection Act (DPA). Future use of this dataset will be restricted to researchers granted permission from the principal supervisor based at the University of Exeter, Prof Rupert Payne. The retained dataset will be anonymised and not contain patient identifiable information.[33]

9 DISSEMINIATION POLICY

9.1 Dissemination policy

The protocol and research information will be made publicly available on the OSF registry. The analysis of the data arising from the study will be combined into a final thesis as part of the Chief Investigator's PhD submission. This will be placed into the University of Exeter's Open Repository (Open Research Exeter, ORE) for public access. The study data will be owned by the University of Exeter. It is also anticipated that each phase will give rise to an accompanying formal publication in a peer-reviewed journal. As a predicate of NIHR funding, all research published will be made publicly available via open access.

Other outputs will include:

- Conference presentations

- Social media updates via X and LinkedIn
- Blogs posted on Institutional webpages
- Plain English Language summaries (co-produced with the PAG)
- Policy briefings targeting pharmacy professional groups and national bodies

The outputs from this study will seek to inform and engage:

- Primary Care Clinical Pharmacists and Pharmacy Technicians
- Patients with significant polypharmacy
- Professional groups including the Royal Pharmaceutical Society, Centre for Pharmacy Postgraduate Education and Primary Care Pharmacy Association
- Higher Education Institutions and Academics currently offering postgraduate pharmacy education
- National bodies and policy makers, such as the General Pharmaceutical Council

9.2 Authorship eligibility guidelines and any intended use of professional writers

Authorship rights will be granted in line with the International Committee of Medical Journal Editors (ICMJE) recommendations. This recommends authorship is based on:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work
2. Drafting the work or reviewing it critically for important intellectual content
3. Final approval of the version to be published
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.[34]

The Chief Investigator and members of the supervisory team will be granted authorship rights on any resulting publications. There is no intention to make use of professional writing services.

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11. APPENDICIES

11.1 Appendix 1- Required documentation

- **Chief Investigator CV**
- **Participant information sheet for patients (Phases 1 and 2)**
- **Participant information sheet for pharmacists (Phase 1)**
- **Participant information sheet for pharmacists (Phase 3)**
- **Consent form for Phase 1 (Pharmacists)**
- **Consent form for Phase 1 (Patients)**
- **Consent form for Interviews (Same for Phase 2 and 3)**
- **Example AccuRx Text message wording**
- **Pharmacist SOP for audio recording**
- **Example social media post wording for Phase 2**
- **Invitation to participate wording for pharmacists (Phase 2)**
- **Invitation to participate and Decline wording for patients (Phase 3)**
- **Example Interview topic guide for patients**
- **Example Interview topic guide for pharmacists**
- **RISP**
- **NIHR Wellcome Funding Letter**
- **Organisation Information Document Template**
- **Schedule of Events Cost Attribution Template (SoECAT)**

11.2 Appendix 2 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1	1.1	16/06/2024	TK	Section 5.3 added to clarify the definition of the conclusion of the research, as per HRA request.