Imperial College London

Imperial College Healthcare NHS Trust

Promoting STatin Adherence with a Tailored Intervention (STATIN)

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Protocol authorised by:

Name & Role	Date	Signature

Study Management Group

Chief Investigator: Dr Gaby Judah
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Clinical Queries

Clinical queries should be directed to Dr David Wingfield (d.wingfield@imperial.ac.uk who will direct the query to the appropriate person.

Sponsor

Imperial College London is the main research Sponsor for this study. For further information regarding the sponsorship conditions, please contact the Head of Regulatory Compliance at:

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Funder

London Interdisciplinary Social Science Doctoral Training Partnership (LISS DTP)

This protocol describes the Promoting STatin Adherence with a Tailored INtervention (STATIN) study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the UK Policy Framework for Health and Social Care Research. It will be conducted in compliance with the protocol, the Data Protection Act and other regulatory requirements as appropriate.

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GLOSSARY OF ABBREVIATIONS

CVD	Cardiovascular Disease
TDF	Theoretical Domains Framework
BCTs	Behaviour Change Techniques
PIS	Participant Information Sheet
PPIE	Patient and Public Involvement and Engagement
CRN	Clinical Research Network
GP	General Practitioner

KEYWORDS

Statins, Dyslipidaemia; Medication Adherence; Behaviour Change Wheel; Digital intervention; Intervention Development;

STUDY SUMMARY

TITLE Promoting STatin Adherence with a Tailored INtervention (STATIN)

DESIGN Phase 1 - identifying why people don't take statins: We will conduct 15 to 17 interviews to explore patients' barriers to taking their statins as prescribed.

Phase 2 - co-designing a tailored yet scalable way to help people take their statins: We will run six workshops with different people, mainly from groups less likely to take prescribed statins. In these workshops, we will decide on the best solution and discuss how to adapt it for different people.

AIMS Primary aim: To develop a scalable intervention that can be individually tailored, using behavioural science to improve statin adherence.

Secondary aim: To determine the barriers and facilitators to statin adherence faced by different groups of patients in terms of:

A. Initiate the statin regimen as prescribed.
B. Implement their regimen as prescribed day to day.
C. Persist with their regimen for their prescribed duration.

OUTCOME MEASURES Primary outcome: co-designed intervention ready for feasibility testing and a full RCT

Secondary outcome: identified barriers and facilitators to patients' statin adherence.

POPULATION Adult patients who have been prescribed statins in the UK primary care workers that prescribe or manage, statin treatment

ELIGIBILITY

Patients:

- Adult patients above 18 who have been prescribed statins

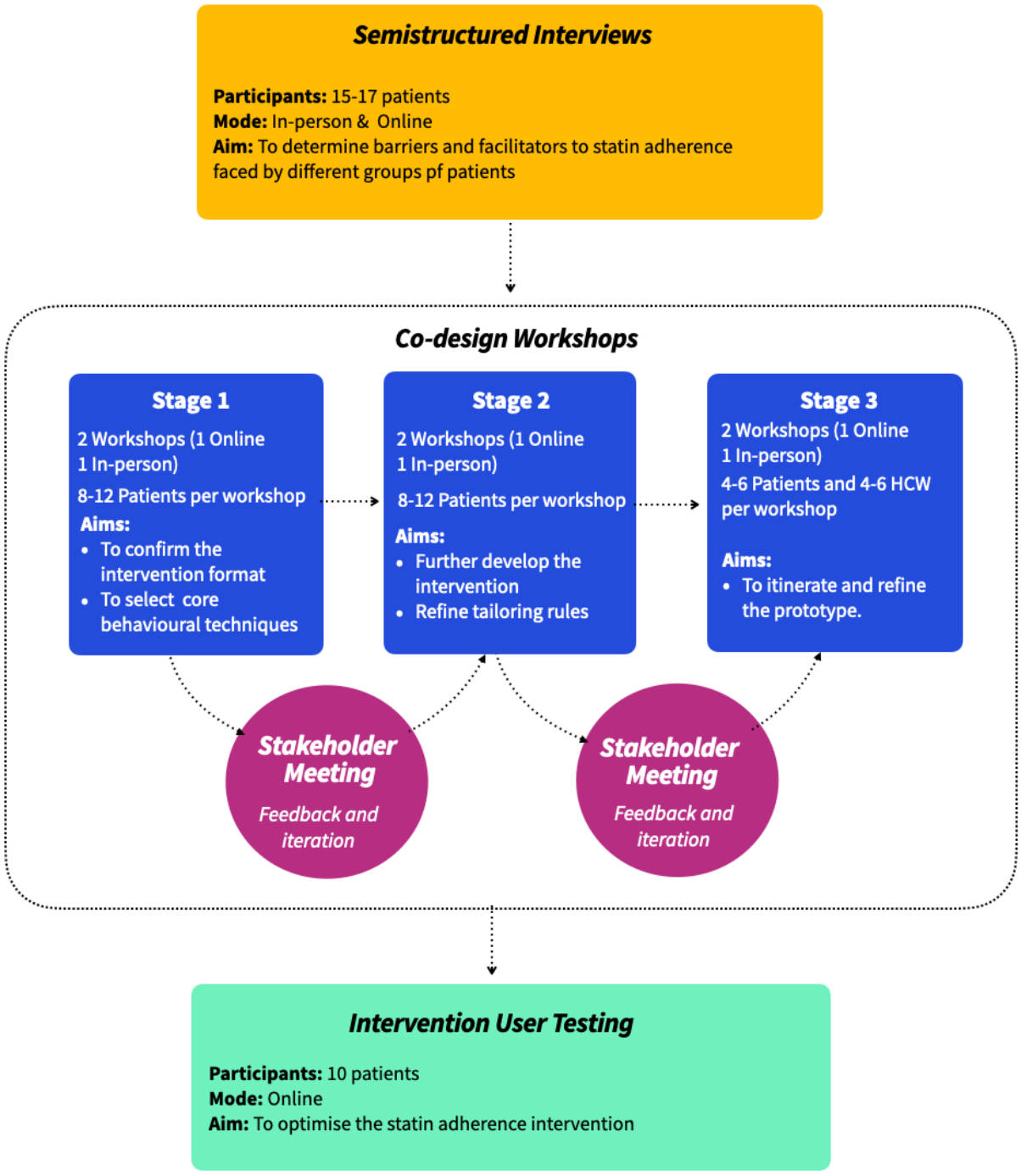
Healthcare workers:

- Clinical pharmacists, General Practitioners (GPs), practice nurses or healthcare assistants who regularly prescribe statins, or consult with, or advise patients on their statin therapy

DURATION 24 months

REFERENCE DIAGRAM

Figure 1: Project plan schematic.



1. INTRODUCTION

1.1 Background

Problem being addressed

Cardiovascular disease[1] (CVD) is the leading cause of death worldwide, accounting for 18.6 million deaths in 2019. In the UK, about 24% of the adult population takes statins, which translates to approximately 7 million people[2]. Globally, it is estimated that more than 200 million people at risk of or diagnosed with CVD take statins to reduce morbidity and mortality[3] However, statin adherence remains a major problem, with between 48% to 68% of patients being adherent in the first year of treatment[4, 5].

Medication adherence refers to the process of taking medication as prescribed[6] (6). It involves three phases: initiation, implementation, and discontinuation. *Initiation* is when a patient takes the first dose of medication, *implementation* is when the patient follows the prescribed dosing regimen, and *discontinuation* is when the patient omits the next and all the other following doses of medication without a prescriber's order[7]. *Persistence* is the period between initiation and discontinuation. Nonadherence to statins occurs when a patient fails to initiate their prescription, prematurely discontinues their intake, or adheres to their treatment less than 80% of the time[8].

Studies have shown that statin adherence varies among different groups of patients[9]. Specifically, ethnic minority groups and those from lower socioeconomic backgrounds have been found to have lower adherence rates, despite having a higher risk for cardiovascular disease[10, 11]. It's important for patients to adhere to their statin regimen, as nonadherence can increase the risk of cardiovascular events like heart attacks, strokes, and even death[12, 13]. It can also lead to higher healthcare costs, estimated to be 10-20% more for nonadherent patients, while improving adherence to 80% could save the NHS around £75 million each year[14].

Existing evidence

A wide range of factors have been associated with statin adherence, such as sociodemographic (age, gender), clinical (comorbidities, lifestyle) and psychological predictors[15]. Psychological factors may be the strongest and most modifiable and have typically been dichotomised as intentional or unintentional[16]; Intentional adherence barriers include concerns over side effects and lack of understanding about the value of the medication, and unintentional barriers include forgetfulness and fear of perpetual dependence. Whilst this binary model has helped consider adherence determinants broadly, behavioural theory can provide a more granular understanding of the causes of nonadherence[17].

The Theoretical Domains Framework (TDF) is a comprehensive framework of predictors of behaviour to understand adherence determinants, including beliefs about consequences of medication, environmental factors or social influences[17]. The TDF has practical application since it allows mapping determinants to Behaviour Change Techniques (BCTs) or the smallest active

ingredients that bring about change[18]. Using comprehensive frameworks to design statin adherence interventions could potentially improve their effectiveness which has been limited and inconsistent until today[19].

Our research group is doing theory-informed quantitative work to identify patients' barriers, but more research is needed to fill evidence gaps. Intermediate analysis (n=128) of our ongoing survey found that lack of trust in medical professionals, forgetfulness, costs, and difficulty obtaining repeat prescriptions were important constraints for patients. Evidence suggests these statin adherence barriers may differ across patient characteristics. For instance, patients in secondary CVD prevention might not take their medications because it reminds them of their illness[20] and patients of South Asian ethnicity have attributed coronary heart disease to "god's will", contributing to beliefs that they cannot control their disease[21]. Despite these findings, there is still little qualitative work exploring barriers to taking statins, especially in subgroups with lower adherence[15].

We are conducting a systematic review of existing studies to identify the barriers and facilitators to statin adherence for different groups of patients using the TDF. Our review's findings will help inform purposive sampling to fill evidence gaps in subgroups that tend to be lower in statin adherence and have been underrepresented in previous research (e.g. the underserved group). Study results will allow us to develop a solution tailored to the root causes of nonadherence using a theory and evidence-based approach. Theory has informed the development of medication adherence interventions for stroke survivors[22], hypertension[23], and cystic fibrosis[24], the latter leading to improved adherence over 12 months. However, a theoretical underpinning for interventions has not been considered in most statin adherence trials, potentially explaining why they have had limited and inconsistent success[19]. Moreover, statin adherence interventions with positive results have used complex and expensive approaches that make them unlikely to be implemented in broader populations[24].

Completed and ongoing research does not include a scalable, tailored, and theory-based intervention to improve statin adherence. One ongoing intervention is testing text message reminders to support statin adherence (ISRCTN13245243); however, without a clear theoretical rationale, only addresses forgetting, not other adherence barriers. Other statin adherence interventions with automated components exist but almost all of them have high risk of bias, none or small effect sizes and are poorly described, hindering their translation into practice[25]. Using mobileHealth (mHealth) interventions to promote statin adherence is promising from reviews, which have suggested effective intervention components (e.g. goal setting or information from a credible source)[26]. Given this potential cost-effectiveness, there have been multiple calls for rigorous and theory-based digital behavioural mHealth interventions focused on statin adherence[25, 26].

1.2 Study Rationale

Adherers to statins have 32% lower mortality, ischemic heart diseases, strokes or cardiovascular events than non-adherent patients[27]. Tailored interventions, e.g. multidisciplinary educational activities and counselling from healthcare workers, may be more effective than the one-size-fits-all approach[9, 28]. Individual face-to-face approaches address individual needs and barriers; however, they are not cost-effective or scalable, so cannot feasibly be used to improve statin adherence on a widespread level[29]

This study will combine our previous findings, primary research, and consolidation of existing evidence using behavioural theory to inform co-design of an intervention that is both tailored and scalable. Given the scalable design, the intervention is anticipated to lead to widespread patient benefit and NHS cost savings.

2. STUDY OBJECTIVES

Primary objective: To develop a scalable yet individually-tailored intervention to improve adherence to statins using behavioural science frameworks.

Secondary objectives:

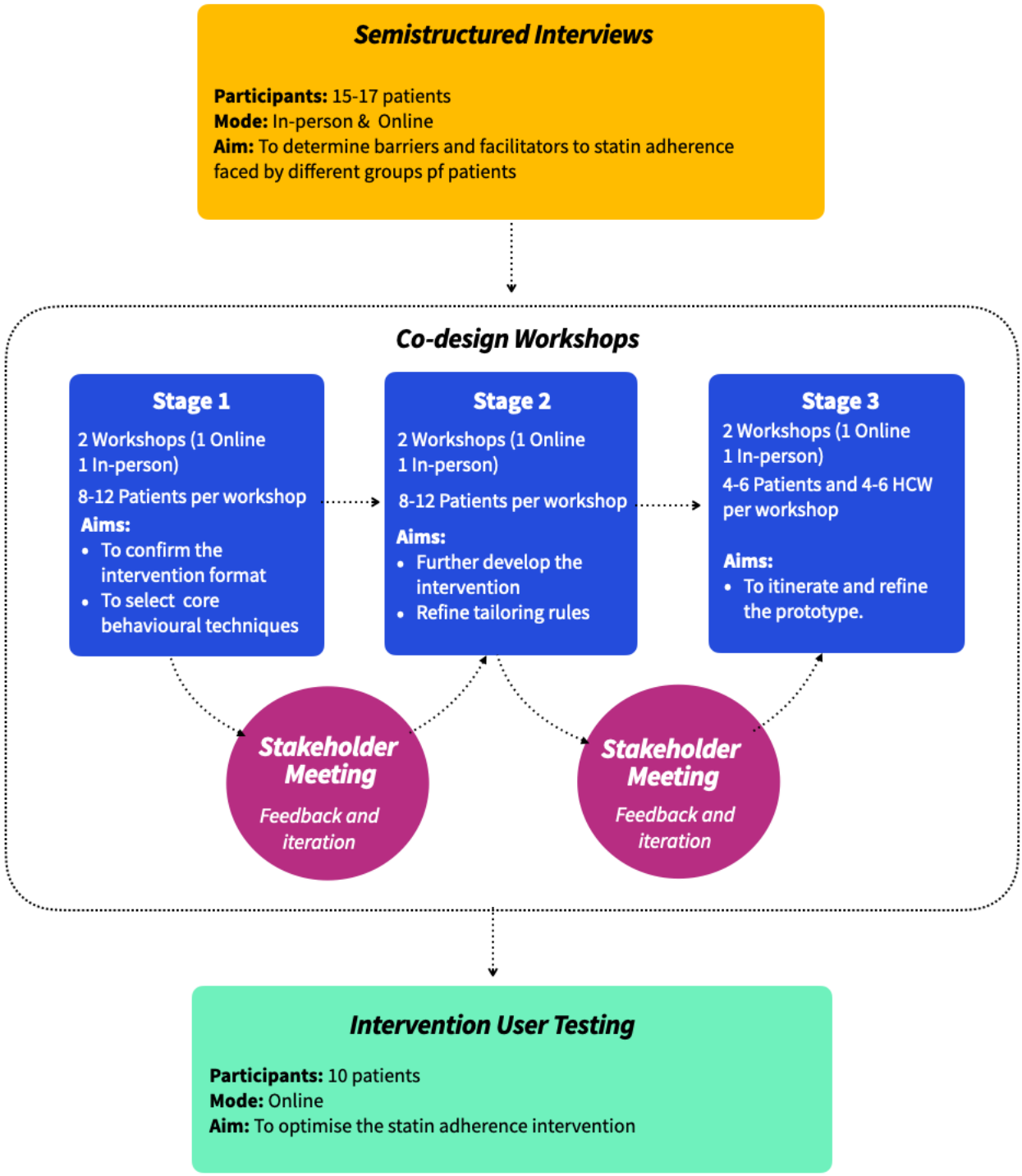
1. To determine the barriers and facilitators to statin adherence faced by different groups of patients in terms of:
    a. Initiate the statin regimen as prescribed.
    b. Implement their regimen as prescribed day to day.
    c. Persist with their regimen for their prescribed duration.

2. To co-design with patients and stakeholders a tailored yet scalable way to help people take their statin
3. To optimise the intervention by
    a. Exploring the acceptability and usability of the intervention content and functionalities
    b. Evaluating intervention engagement
    c. Identifying how the statin adherence intervention should be refined.

3. STUDY DESIGN

To better understand barriers and facilitators to statin adherence, the study will first conduct 15-17 semi-structured interviews with different groups of patients. The study's second phase will consist of a series of 2-hour workshops, each with 8-12 participants. The third phase will consist of intervention user testing with between 10-15 participants over the course of a month. A helpful visual summary of the study can be found in Figure 1:

Figure 1: Project plan schematic.



We will purposively invite patients taking statins to participate in our research, aiming to reach low-uptake groups with less good quality research investigating determinants. We will use a variety of recruitment strategies. We will first conduct searches of the medical records of Hammersmith and Fulham partnership to identify patients who have not been re-prescribed statins in 6 months (indicating non-adherence to statins) and participants that were prescribed statins but never collected their prescription to support recruitment of objectively measured non-adherent participants. We will also recruit a small number of adherent participants to assess the facilitators which could be incorporated into the intervention. We will also advertise our opportunity on online platforms and if necessary, will collaborate with charity and community groups to ensure that we can engage individuals who may be difficult to reach. More detail can be found in Section 4 of this protocol.

An SMS or email explaining the study with a link to Qualtrics platform where the participant information sheet (PIS),Consent Form, and a short pre-screening questionnaire will be sent to interested parties. After giving consent, people interested in participating will be asked to complete the pre-screening questionnaire (including age, gender, ethnicity, self-reported statin adherence, comorbidities, other medications, among others). This will enable purposive recruitment of participants with the characteristics previously identified. Primary care healthcare workers will be recruited through their surgery and other sources (e.g. the Clinical Research Network [CRN]).

Initially, 15-17 participants will be recruited to interview, using informational power as a guide to sample size calculation and considering the narrowing aim of filling information gaps[30]. Then, during the analysis, we will assess thematic saturation to determine if further recruitment is required ultimately.

Participants will be given the option to participate in an online or in-person one-on-one semi-structured interview that will last approximately 45 minutes. TDF informed the draft interview topic guide.

We have also planned to hold a total of 6 workshops, divided into 3 sets, with each set consisting of 2 workshops lasting for 2 hours. To ensure better representation, each workshop will have 8-12 participants, as recommended in our previous PPIE work. One set of workshops will involve both patients and healthcare workers. Each workshop set will have one online and one in-person workshop, with one scheduled during working hours and one during the early evening. During all workshops, discussions will combine whole and smaller group discussions in breakout rooms/separate spaces.

Workshops objectives are:

- *Stage 1 – Workshops:* confirm the intervention format and select broad behavioural techniques (BCTs).
- *Stage 2 Workshops:* further developing the intervention, including tailoring rules. Whole group discussions will be combined with prototype activities in smaller groups.

- *Stage 3 Workshops:* iterate and refine the intervention and will include patients and healthcare professionals to promote cohesive intervention co-creation.

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Between workshops, key stakeholder meetings (e.g. GPs, pharmacists) will assess appropriateness of the intervention, feasibility of implementation, and advise on intervention development. We will use the APEASE criteria[31] to assess Acceptability, Practicability, Effectiveness, Affordability, Side-effects, and Equity of versions of the intervention and intervention components. Solutions suggested at workshops will be refined for further co-design and iteration at subsequent workshops. Including key stakeholder, we will discuss evaluability of the intervention, to agree on evaluation outcomes, data collection methods, and feasibility study design. Alternating co-design workshops with patients, and meetings with clinicians, will ensure the intervention is appropriate and acceptable from patient and provider perspectives.

The intervention designed during the workshops will then be user-tested to optimise it. We aim to recruit between 10 and 15 participants to ensure sufficient representation and diversity. The focus will be on recruiting patients who were recently prescribed statins (those prescribed within the last three months) and those identified as nonadherent. Patients will be invited via SMS containing a link to an online pre-screening survey on Qualtrics. The survey will provide access to the Participant Information Sheet and Consent Form on the first page and a short pre-questionnaire that can only be completed after providing online consent. The pre-screening questionnaire retains the core structure of the previously approved REC version while incorporating modifications and additional questions to tailor SMS messages to participants' barriers and preferences. It captures clinical and demographic data, self-reported adherence levels (low adherence, discontinuation, and non-initiation), and barriers. Questionnaire responses will inform the intervention's tailoring to group-level needs, individual barriers, and messaging preferences (e.g., timing and frequency). Participants will receive personalised messages over one month.. SMS delivery will be monitored collaboratively by the research team and the care team. Follow-up data will be collected through a brief survey integrated within the SMS flow to assess usability using an adapted version of the System Usability Scale (SUS)[32], while digital log files will be used to monitor intervention engagement. After a month, participants will also be invited to participate in a one-hour in-person focus group with to explore factors influencing intervention acceptability, structured around the Theoretical Framework of Acceptability (TFA)[33], which includes seven constructs: affective attitude, burden, perceived effectiveness, ethicality, intervention coherence, opportunity costs, and self-efficacy. If participants cannot attend, they will be offered the option to have a video call via Zoom instead to share their insights. Focus groups will be conducted with approximately 5-8 participants each to facilitate meaningful discussions and capture a range of perspectives in the allocated time. If the number of participants exceeds the capacity for a single focus group or if additional insights are needed, more than one focus group will be organised.

Online interviews, workshops will be conducted on Zoom, for which Imperial is licensed and will be recorded. Due to software limitations, both video and audio recordings are saved automatically as

separate files but video records of interviews will be immediately destroyed after the interview. In-person workshops will be audio-recorded, and online workshops will be video-recorded to ensure activities outputs are properly captured. Participants will be free to have their video off during the recording and take breaks if needed. In-person interviews and workshops will be audio-recorded.

Any data produced during interviews,workshops and user testing including recordings, transcriptions, sociodemographic data, consent forms, field notes, log files and survey responseswill be temporarily stored on a password-protected personal computer. It will then be backed up onto an encrypted folder at Imperial College OneDrive using Crypted Cloud to ensure security. Once saved, all data from password-protected personal computers will be deleted and stored exclusively on OneDrive.

Audio files from interview and focus groups recordings will be transferred securely to Page Six, a third-party transcript organisation, using SSL-encrypted transfers through a password-protected online system. Page Six will transcribe the interviews and the focus group into a pseudo-anonymised word file. This will also be saved securely onto the College's servers. Transcriptions will be scanned and saved to an encrypted Imperial College OneDrive folder. The organisation will return the transcripts securely to the research team. The team will review transcripts, then recordings will be erased permanently.

Pre-questionnaire and survey dataset, recordings transcripts with a unique identifier number rather than participants' names. The document linking the unique identifier codes to participant names will be stored securely in an encrypted folder with access restricted to the project team on the Imperial College OneDrive. When transcripts are checked, the document linking identifier codes will be destroyed, and data will be anonymised.

The total duration of the study will be 24 months.

3.1 Study outcome measures

The primary outcome will be a co-designed intervention ready for feasibility testing and a full RCT. The secondary outcome will be the identified barriers and facilitators to patients' statin adherence.

4. PARTICIPANT RECRUITMENT

A multiplatform recruitment strategy will be used to recruit for the interviews, workshops and user testing phases.

Patients:

Patients' recruitment will be mainly done at their primary care centre and user testing phase will rely exclusively on this method. The research team (including the Chief Investigator and Co-investigators) is working with the Hammersmith and Fulham Partnership, a GP Partnership of five practices, where Dr Wingfield, co-researcher of this project, is Head of Research and Development. Given our pre-defined criteria, Dr Wingfield's team will identify eligible patients using their health records (i.e. those prescribed statins, with purposive sampling of adherent and non-adherent patients using data on prescription requests). Then, a member of the direct care team will send an SMS to their registered numbers from the GP surgery to invite eligible participants to participate in the interviews, workshops and user testing. The SMS will include a secure link to the secure Qualtrics online platform where participants can access the pre- questionnaire. On the first page of the questionnaire, they will also find the Participant Information Sheet (PIS) and Consent Form. Participants only will be able to continue the survey if they confirm consent. Otherwise, they will be thanked for their interest but not shown the pre-screening survey.

If, after this first contact attempt, response rates are low, a member of the direct care team will call listed patients via telephone individually and invite them to participate in the study.

Email addresses and/or phone numbers will be provided by interested participants in the questionnaire, who will then be contacted by the research team if they are selected to take part. Participants that are non-selected will be informed via email or SMS once the recruitment has finished.

For interviews and workshops, patients will also be recruited through VOICE, an online network where public members can view and volunteer for opportunities to participate in research. To recruit participants, the researchers will post an advert on the website. Patients interested in participating in the study will have to respond to the advert themselves actively and will not be approached directly by research team members. The VOICE platform will re-direct participants expressing interest in our advert to the pre-screening survey containing the PIS and Consent Form.

The final method of recruitment of patients for interviews and workshops, will be through charities and local organisations such as The Abbey Centre, The Mosaic Community Trust or Open Age to ensure we find patients from certain backgrounds and conditions. The managing staff will send a formal invitation letter and the link to fill out the pre-screening survey via email to their members and any inquiries could be directed to the research team. Leaflets containing a study description and a QR code with the link to the pre-screening survey and research team's contact details (jr1322@ic.ac.uk / 07923832050) would also be printed out and shared in community events in case participants have any questions or require support accessing the survey. The link to the screening questionnaire would have the PIS and consent form as part of this, and all responses to the online screening questionnaire would go back to the research team.

After giving consent and completing the survey, participants will receive an email or a call to arrange their participation in the interview, workshop or user testing that will include the PIS again. We will

include the research team's contact details (jr1322@ic.ac.uk / 07923832050) should they have any questions before the interview/workshop.

Healthcare workers:

Potential participants will be approached through our clinical contacts, e.g. from an email signed by Dr Wingfield (co-investigator) sent to staff at Hammersmith and Fulham Partnership communication or through the CRN. Interested healthcare professionals will be sent a formal email letter of invitation with the PIS and consent form attached, and they will be asked to return the consent form signed if they agree to participate.

4.1 Pre-recruitment evaluations

Patients will complete a pre-screening survey after giving consent to ensure purposive selection before interviews, workshops and user testing. This will request baseline information and ask potential participants to confirm their email addresses. S survey questions will include age, gender, ethnicity, self-reported statin adherence, comorbidities, whether they have previously had a cardiovascular event, other medications and length of time prescribed statins. No pre-recruitment evaluations will be conducted on healthcare workers.

Once participants submit their responses, name and email fields in the dataset will be eliminated and substituted with a six-digit code. A separate document will be created to link the codes with the respective names and emails, as it will be imperative to contact the participants regarding their selection or non-selection, as well as provide information about the next steps in the research. The document linking the unique identifier codes to participant names will be stored securely in an encrypted folder with access restricted to the project team on the Imperial College OneDrive and will be deleted once interviews and workshops are finished and their transcripts checked.

4.2 Inclusion Criteria

Inclusion criteria will be as follows:

Patients:

- Adult patients 18+ who have been prescribed statins.

Healthcare workers:

Clinical pharmacists, General Practitioners (GPs), practice nurses or healthcare assistants who regularly prescribe statins, or consult with, or advise patients on their statin therapy.

4.3 Exclusion Criteria

Exclusion criteria will be as follows:

Patients:

- Age >18
- Patients that have never been prescribed statins
- Cognitive impairment
- Pregnant women
- Severe life-limiting condition
- Did not speak English if a translator cannot be arranged for them
- Did not consent to participate

Patients whose statin treatment has been discontinued by a healthcare professional due to documented medical reasons, such as adverse reactions or other clinical considerations.

Healthcare workers:

- Healthcare providers working only on secondary care
- Healthcare providers without experience in prescribing statins, managing, or advising patients on following statin therapy.

4.4 Withdrawal Criteria

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Participants can withdraw consent at any stage of the project. Individuals can withdraw verbally by contacting researchers directly (tel: 07923832050), or in writing via email (jr1322@ic.ac.uk). Once transcriptions are checked and anonymised it will not be possible to remove individual responses, as the recordings will have been deleted. However, before this point, participants can remove consent, and if they have already participated in an interview that has not been transcribed, their data will not be transcribed and will be deleted.

5. ADVERSE EVENTS

5.1 Definitions

Adverse Event (AE): any untoward medical occurrence in a patient or clinical study subject.

Serious Adverse Event (SAE): any untoward medical occurrence or effect that:

- **Results in death**
- **Is life-threatening** – *refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe*

- **Requires hospitalisation, or prolongation of existing inpatients' hospitalisation**
- **Results in persistent or significant disability or incapacity**
- **Is a congenital anomaly or birth defect**

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

5.2 Reporting Procedures

All adverse events should be reported. Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

5.3 Non-serious/Serious AES

5.3.1 Non-serious AEs

All such events, whether expected or not, should be recorded- it should be specified if only some non-serious AEs will be recorded, any reporting should be consistent with the purpose of the trial end points.

5.3.2 Serious AEs

An SAE form should be completed and emailed to the Chief Investigator within 24 hours. However, relapse and death due to CVD and hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs.

All SAEs should be reported to the North East - York Research Ethics Committee where in the opinion of the Chief Investigator, the event was:

- 'related', ie resulted from the administration of any of the research procedures; and
- 'unexpected', ie an event that is not listed in the protocol as an expected occurrence

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES SAE form for non-IMP studies. The Chief Investigator must also notify the Sponsor of all related and unexpected SAEs.

Local investigators should report any SAEs as required by their Local Research Ethics Committee, Sponsor and/or Research & Development Office.

Contact details for reporting SAEs
Dr Gaby Judah
Email: g.judah@imperial.ac.uk
Tel: 02033126666
Please send SAE forms to: RGIT@imperial.ac.uk
Tel: 0207 104 8070 (Mon to Fri 09.00 – 17.00)

6. ASSESSMENT AND FOLLOW UP

As this study is cross-sectional, no follow-up or assessment will be necessary. However, it will be possible for interview participants to also register to take part in the workshops if they wish. The end of the study will be on 01 March 2026. No changes to the individual's care or any other assessments will be needed following this study. Any incidental findings during the study set-up or implementation will be notified to the participants' clinical care team who will then take action accordingly

Participants from any stage of the study will be given an opportunity to voluntarily submit their email addresses if they wish to receive copies of the study results following analysis. These will also be stored, with consent, on a password-protected computer and backed up on a password-protected university server.

The research team will co-produce an accessible lay summary of the study for dissemination through patient groups, charities (e.g. Age UK) and social media, as well as study participants, those involved in co-design and the clinical care team from the research sites.

The developed intervention will be shared with study participants, and everyone involved in co-design and user testing (email summary, and invitation to a demonstration meeting with a recording shared afterwards). Findings will be also presented at well-attended Imperial seminars, regular engagement activities and education activities for community groups, patients and carers.

The present research will result in a developed intervention. Following subsequent testing of this intervention it is expected to conduct a larger roll out the intervention to a wider population. Findings will be translated into policy reports to support evidence-based policy making.

6. STATISTICS AND DATA ANALYSIS

Data from the interviews will be analysed qualitatively using thematic analysis; mapping identified beliefs onto the 14 domains of the TDF. These beliefs will be stratified according to high, moderate or low barriers or facilitators to the behaviour. A second researcher will independently code a sub-sample of 20% of the transcripts, and a Cohen's kappa value will be calculated to assess inter-rater reliability. Any discrepancies will be resolved through consultation.

Transcriptions of the workshop discussions and any other data submitted during the activities (e.g. comments or questions in chat boxes), will be analysed and synthesised in order to refine the intervention design further and to document justification for the intervention rationale Synthesised data will be discussed during stakeholders' meetings to ensure the intervention is appropriate and acceptable from patient and provider perspectives. Social, physical, cultural, economic and organisational aspects of healthcare and patient contexts will be considered during intervention design.

In user testing, anonymised data from focus groups will be analysed using thematic analysis. Using an inductive approach, focus group transcripts or interviews will be coded and then grouped into broader themes deductively. Descriptive statistics will summarise the quantitative data collected from digital log files and follow-up questionnaires. A mixed methods approach will combine qualitative and quantitative findings to address the study objectives. Findings will then be integrated into improvement strategies to refine the statin adherence intervention.

7. REGULATORY ISSUES

7.1 Ethics approval

The Chief Investigator has obtained approval from the [North East – York] Research Ethics Committee (REC) and Health Research Authority (HRA). The study must also receive confirmation of capacity and capability from each participating NHS Trust before accepting participants into the study or any research activity is carried out. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

7.2 Consent

Consent to enter the study will be sought from each participant only after the PIS is shared, read through and time allowed for consideration. The right of the participant to refuse to participate without giving reasons must be respected. Online Participant Consent Forms will be embedded into the screening Pre-questionnaire, and will need to be completed before the questionnaire can be accessed. After completing the process, participants will receive copies of the Consent Form and Pre-questionnaire responses via email. All participants are free to withdraw at any time but after anonymisation their individual responses will not be able to be deleted. This can be undertaken by participants contacting Javiera Rosenberg (jr1322@ic.ac.uk). The right of the participant to refuse to participate without giving reasons will be respected, as will their right to withdraw from the study at any time.

7.3 Confidentiality

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act. Data will be pseudonymised.

7.4 Indemnity

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

7.5 Sponsor

Imperial College London will act as the main sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

7.6 Funding

This study is funded by London Interdisciplinary Social Science Doctoral Training Partnership (LISS DTP). Participants in interviews will be paid £25 as a token of thanks. Patients will be paid £50 for participating in each workshop and will receive £5 working from home online expenses or £10 for in-person workshops to cover subsistence costs for time spent away from home. Pharmacists/nurses will be paid £72 and GPs £176 for the 2-hour workshop according to CRN guidelines. Focus group participants will be compensated £25 for their time.

7.7 Audits

The study may be subject to audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the UK Policy Frame Work for Health and Social Care Research.

8. STUDY MANAGEMENT

The day-to-day management of the study will be co-ordinated through the PhD student Javiera Rosenberg (jr1322@ic.ac.uk).

9. PUBLICATION POLICY

A robust publication policy is envisaged with aggregated unidentifiable data published in peer review journals and in presentations. To ensure widespread dissemination of the work presentation to stakeholders will also involve non-traditional means such as blog posts. This work will also be incorporated into a PhD thesis. No identifiable data will be used in any publication.

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