Understanding the psychological determinants of medication adherence in patients taking anti-hypertensive and statin medication in the United Kingdom

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Safety Translational Research CentreSTUDY COORDINATION CENTRE: Imperial College London

Protocol authorised by:

Name & Role	Date	Signature

Study Management Group

Chief Investigator: Prof Peter Sever (Imperial College London),

Co-investigators: Dr Gaby Judah, (Imperial College London), Dr David Wingfield (Honorary Research Fellow – Imperial College London; GP at Hammersmith and Fulham Partnership) Mr Guy Martin (Imperial College London)

For general queries, supply of study documentation, and collection of data, please contact:

Study Coordinator: Dr Gaby Judah
Address: 10th Floor, QEQM Building, St Mary's Hospital, Praed Street, London, W2 1NY
Tel: 07866530031
E-mail: g.judah@imperial.ac.uk

Clinical Queries

Clinical queries should be directed to Dr Gaby Judah 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:

Joint Research Compliance Office
Room 221
Level 2, Medical School Building
Norfolk Place,
London W2 1PG
020759 41862
Tel: 020759 41862

Funder

Imperial College London, the Luff Foundation, and the National Institute for Health Research (NIHR) Imperial Patient Safety Translational Research Centre

This protocol describes the *"'Understanding the psychological determinants of medication adherence in patients taking anti-hypertensive and statin medication in the United Kingdom"* 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 NHS Research Governance Framework for Health and Social Care (2nd edition). It will be conducted in compliance with the protocol, the Data Protection Act 2018 and other regulatory requirements as appropriate.

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KEYWORDS

Hypertension
Statins
Medication adherence
Behavioural psychology
Habit formation

STUDY SUMMARY

TITLE "Understanding the psychological determinants of medication adherence in patients taking anti-hypertensive and statin medication in the United Kingdom"

DESIGN Cross-sectional evaluative study

AIMS To assess adherence to anti-hypertensive and statin medication in a UK population, identify and understand the psychological and behavioural barriers and facilitators to medication adherence in these patient groups, and identify potential interventions and strategies based around behavioural insight theory to improve medication adherence in these patient populations

OUTCOME MEASURES *Primary outcomes* – the behavioural and psychological determinants of medication adherence and non-adherence in UK patient populations on anti-hypertensive and statin medication

Secondary outcomes – validation of the self-reported medication adherence tools in UK patient populations taking antihypertensive and statin medications in primary care via direct adherence measures

POPULATION UK general population being treated for hypertension or taking statins.

ELIGIBILITY *Inclusion criteria* - all patients attending primary or secondary care service for the treatment of hypertension or hypercholesterolaemia who are willing to take part in the study. The semi-structured interviews, and questionnaire design and piloting stages will include patients attending a specialist hypertension clinic. The main data collection stage will be from patients recruited in primary care setting

Exclusion criteria - in the opinion of the investigator unsuitable or unable to adequately complete questionnaire e.g. due to inadequate level of English comprehension. In addition, patients on simvastatin will be excluded from the main data collection phase due to the inability of the urine test in being able to detect this particular statin.

DURATION Time period required for recruitment of target sample population – approximately 550 patients over 3-linked stages of the study, approximately 500 of whom will come from primary care. The main data collection period is anticipated to take 18 months, to finish on 31st January 2021.

1. INTRODUCTION

1.1 BACKGROUND

Hypertension is the largest contributor to global mortality (Lim 2013), and a major risk factor for heart disease and stroke. About 30% of the UK population suffer from hypertension (Joffres 2013). Anti-hypertensive medication reduces long-term morbidity and mortality, but medication adherence is a significant problem with around 50% of patients not fully adherent 1-year after starting treatment (Vrijens 2008).

Elevated serum levels of cholesterol, both total and low-density lipoprotein, are associated with an increased risk of cardiovascular disease (Ducharme 2008). Statins are amongst the most widely used classes of drugs globally (Chaplin 2015), and a number of studies have demonstrated that statins significantly reduce the risk of cardiovascular adverse events and mortality in adults both with and without established cardiovascular disease (Naci 2013, Aronow 2009, Baigent 2005, Brugts 2009, Taylor 2013, Minder 2013). Despite this strong evidence, studies estimate that approximately 50% of patients with CVD or its major risk factors demonstrate poor adherence to their prescribed medicines (Jimmy 2011). A cohort study conducted in over 229,000 patients reported a direct association between survival and adherence to statin therapy (Laufs 2011). Current estimates suggest that statin nonadherence generates US $44 billion avoidable health care costs in the USA (Gatwood 2014).

Many studies have previously investigated predictors of adherence and non-adherence in populations taking antihypertensive and statin medication (Warren 2013, Wei 2013, Mann 2007). Common factors associated with good adherence include knowledge about the condition being treated and the medications themselves, positive health beliefs about the necessity of medication and perceived behavioural control. Factors associated with poor adherence include forgetfulness and concerns over medications and side-effects. Despite this there is a paucity of literature looking at adherence to antihypertensive and statin medication within the UK population and health system; both of which will be important factors in framing behavioural barriers and facilitators to adherence. A study performed in Sunderland found that medication related side-effects are most strongly predictive of intentional non-adherence, followed by inconvenience. Forgetfulness was also found to be predictive on non-intentional non-adherence (Khan 2014). Conscientiousness, perceived behavioural control, past adherence and intention has also been shown to predict future adherence (Quine 2012).

Findings of key relevant literature from other health systems and populations are summarised below:

- In a Hong Kong population advanced age, unemployment and good self-perceived health status were associated with good hypertension medication adherence; whereas being married and having other health co-morbidities was associated with optimal blood pressure control (Kang 2015)
- In elderly patients from Korea with hypertension, memory issues resulting in un-intentional non-adherence is a major issue (Park 2012)
- In Chinese female migrants to the USA a lower perceived benefit of hypertensive medication is predictive of non-adherence (Li 2007)
- In rural Indian and Iranian populations with hypertension, greater adherence is associated with regular physical activity and non-smokers/drinkers in addition to those who perceived high susceptibility, severity and benefit (Venkatachalam 2015, Kamran 2014)
- In Pakistan knowledge about hypertension is a significant predictor of adherence (Saleem 2012)
- In Peru beliefs about harm from medications or concerns regarding the medication is associated with low adherence to antihypertensives. Patients whose ideas of necessity outweighed their concerns were more likely to be adherent (Fernandez-Arias 2014)
- In the Seychelles adherence in patients with uncontrolled hypertension can be predicted by increased literacy and the ability of patients to correctly report the number of pills to be taken daily (Hungerbuhler 1995)
- In the US, a study of patients taking statin medication found that the reasons most commonly cited for discontinuation were side effects (specifically muscle pain), followed by cost and perceived lack of efficacy. Risk factors for non-adherence

included low household income, experience of muscle pain side effects and those taking other medication for cardiovascular disease (Wei 2013).

- Mann 2007 found that short expectations of length of treatment, perceived low risk of a heart attack, being Hispanic and younger age were all independently associated with poor adherence in another study conducted in the USA.
- A study of Australian patients aged over 45 years old found that adherence to statins was lower in patients who were employed, had a higher level of education, were current smokers or reported moderate to very high levels of psychological distress. The strongest predictor of poor adherence in this study was speaking a language other than English at home (Warren 2013).
- There has been significant work looking at medication adherence in African Americans with hypertension within the US healthcare system; interestingly lower educational attainment was related to higher adherence in men, but lower adherence in women (Braverman 2009). In addition, in males younger age, depression and low-self-efficacy were associated with self-reported non-adherence (Lewis 2012a, Lewis 2012b), whilst those with greater happiness exhibit greater adherence behaviours. The most commonly reported reasons for missing medication are forgetfulness, being too busy, travel, sickness, disruption of daily routines and an inability to get to a pharmacy. Another study has demonstrated that in older adults' factors at the individual, relationship, health care system, and environmental or policy level also affect adherence. These factors include memory, knowledge, attitudes and beliefs, side effects, social support, interaction with healthcare providers and the cost and convenience of medication filling (Holt 2014).

Through identification of the psychological and behavioural determinants of non-adherence, the results from this study will facilitate the design, evaluation and implementation of targeted interventions to improve medication adherence and clinical outcomes, drive patient-centric care and reduce waste.

1.2 RATIONALE FOR CURRENT STUDY

Hypothesis:

There are common psychological and behavioural barriers and facilitators that influence medication adherence in patient populations on antihypertensive and statin treatments in the UK. These may directly impact on medication adherence and thus blood pressure control, cholesterol levels and general cardiovascular health. Identifying these factors and developing strategies to address them may help medication adherence and subsequent blood pressure control, cholesterol levels and clinical outcomes.

Aims:

To assess adherence to anti-hypertensive medication and statins in a UK population, identify and understand the psychological and behavioural barriers and facilitators to medication adherence in these patients, and identify potential interventions and strategies based around behavioural insight theory to improve medication adherence in patients prescribed antihypertensive or statin medications.

Research Questions:

- What is the self-reported and objectively measured rate of anti-hypertensive and statin medication non-adherence in a UK patient population?
- What are the psychological and behavioural barriers to medication adherence?
- What are the psychological and behavioural facilitators of medication adherence?
- Can identified behavioural and psychological constructs be used to predict medication non-adherence?

2. STUDY OBJECTIVES

Primary Objectives:

- To develop an evidence-based questionnaire to assess the determinants of medication adherence in a UK patient population in both primary and secondary care
- To determine the psychological determinants of medication adherence and non-adherence in UK patient populations on antihypertensive or statin therapies in both primary and secondary care

Secondary Objectives:

- To assess the self-reported and measured rates of medication non-adherence in a UK population prescribed antihypertensive or statin therapies
- To validate self-reported medication adherence tools in a UK patient population on anti-hypertensive or statin therapy via direct medication adherence measures.

3. STUDY DESIGN

This study takes place in three linked stages:

1. Semi-structured interviews:
    a. Formalised semi-structured interviews with hypertensive patients attending an anti-hypertensive clinic (approx. 15 patients)
    b. Understand the patients' experience of taking medication
    c. Elicit the barriers and facilitators of medication adherence
2. Questionnaire design and piloting:
    a. Inductive (thematic) framework analysis of semi-structured interviews
    b. Formulation of questionnaire to assess the barriers and facilitators of medication adherence based upon the Theoretical Domains Framework and Health Belief Model of behaviour
    c. Testing and refinement of pilot questionnaire on sample adherent and non-adherent populations (approx. 30 patients)
3. Main data collection and testing:
    a. Assessing the determinants of medication adherence through testing the association between the psychological and demographic factors measured by the questionnaire, and self-reported and objectively measured medication adherence and blood pressure control in patients attending primary care for the management of hypertension or hypercholesterolaemia.)

Through the identification of the key psychological determinants of medication adherence this will provide the framework for the design, evaluation and implementation of a behaviour change intervention to improve medication adherence.

Semi-structured interviews:

Semi-structured interviews of patients attending the Peart Rose clinic will be performed. Whilst the focus will be on allowing patients to freely express their experience of taking medication, a structured topic guide will be used to direct the interviews as required to help elicit barriers and facilitators of adherence. Patients will be recruited until saturation (<10% statement duplication), which from previous similar studies is likely to be approximately 15-20 patients. The interviews will be analysed thematically to guide questionnaire item generation.

Questionnaire design and piloting:
Questionnaire items will be constructively aligned to the Health Belief Model and Theoretical Domains Framework of behaviour and generated following an inductive analysis of the semi-structured interviews and literature review. The pilot questionnaires will then be tested on a sample patient population of 30 patients and refined via calculation of ceiling and floor effects, inter-item correlation and Cronbach's Alpha internal consistency measures. The pilot questionnaire items will also be assessed for read ability and comprehensibility using a validated method to ensure it is appropriate for the target population.

Main data collection and testing:
In order to validate the questionnaires, and to assess the association between medication adherence and its' behavioural and psychological determinants approximately 500 patients will be recruited from primary care through established processes via the NIHR North West London Clinical Research Network. The following will be data will be collected:

- Objective measure of medication adherence – a urine sample will be collected and subsequently tested for anti-hypertension and statin medication metabolites to give a valid and reliable direct measure of medication adherence within the past 24hrs. After the end of the study, the urine samples will be destroyed by the lab in accordance with the Human Tissue Authority's Code of Practice.
- Self-reported measures of medication adherence – validated tools for assessing medication adherence and medication taking habit will be used
- Questionnaire – completion of questionnaire assessing psychological determinants of medication adherence to either anti-hypertensives or statins. Approximately 300 patients will be recruited to complete the questionnaire on anti-hypertensive medication adherence, and 200 to complete the questionnaire on statin adherence. Participants will be encouraged to complete the questionnaire at the GP surgery at the point of recruitment and consent. However, if they are unable to do so, they can be given the option to complete the questionnaire at a later date, either by an emailed link, or as a paper version which can be returned with a stamped addressed envelope. If participants do not return the questionnaire within a week, the researcher may telephone participants up to three times, to remind them to complete the questionnaire. Phone numbers will only be collected for those participants who wish to complete the questionnaire at a later date, and will not be stored beyond the end of the study. If participants do not return the questionnaire within four weeks of consent, their urine samples will be destroyed in accordance with HTA guidelines.Demographic information – including age, sex, marital status, co-morbidities, medication history, socio-economic factors. We will also store the reason for attendance at the GP surgery (i.e. whether or not the visit is related to blood pressure/cholesterol or medications), as this may affect the adherence or questionnaire responses.

Eligible patients attending the surgery will be recruited opportunistically. To supplement this recruitment strategy, a poster will be displayed in the reception of the GP surgery, to direct any patients who may be interested in the study to the research team. The patient list of the GP surgery may also be reviewed to identify eligible patients. These patients will be telephoned to ask if they may be interested in taking part in the study, and if so, to invite them to come into the surgery to complete the study procedures.

If patients are found to be non-adherent to their medications according to the urine test, this has implications for their health and care. In order not to single out those who were not fully adherent, urine test results for all participants will be sent to their physicians. This will be accompanied by an explanatory letter about the research. The test results will indicate all

prescribed statin and antihypertensive medications, and whether or not metabolites of these medications were detected in the assay.

3.1 STUDY OUTCOME MEASURES

Primary outcomes – the psychological determinants of medication adherence and non-adherence in a UK patient population established on anti-hypertensive or statin therapy.

Secondary outcomes – validation of the self-reported medication adherence tools in a patient population established on anti-hypertensive or statin therapy via direct adherence measures.

4. PARTICIPANT ENTRY

4.1 INCLUSION CRITERIA

All patients attending either primary or secondary care for the treatment of hypertension or hypercholesterolaemia who are willing to take part in the study.

The semi-structured interviews, and questionnaire design and piloting stages will include patients attending a specialist hypertension clinic. The main data collection stage will be from patients recruited in primary care setting.

4.2 EXCLUSION CRITERIA

Those patients who in the opinion of the investigator are unsuitable or unable to adequately complete questionnaires or take part in the semi-structured interviews e.g. due to inadequate level of English comprehension. Patients taking simvastatin will be excluded from the main data collection, due to the urine test being unable to detect this particular statin.

5. STATISTICS AND DATA ANALYSIS

An analysis assessing the psychological and demographic predictors of adherence will be performed using a backwards stepwise regression method (and repeated with the objective and self-reported adherence measures as the independent variable). Associations between the self-reported and objective adherence measures will also be tested using correlation analysis.

Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

6. REGULATORY ISSUES

6.1 ETHICS APPROVAL

The Chief Investigator has obtained approval from an NHS Research Ethics Committee. The study must be submitted for Site Specific Assessment (SSA) at each participating NHS organisation. The Chief Investigator will require a copy of the organisations approval letter

before accepting participants into the study. 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.

6.2 CONSENT

Consent to enter the study will be sought from each participant after a full explanation has been given, an information leaflet offered and time allowed for consideration. Potentially eligible patients will be given the information sheet and the opportunity to ask any questions. Informed consent for completion of the questionnaire and urine test will be taken at the time of completion as is standard practice for this type of cross-sectional survey. Signed participant consent will be obtained. All participants are free to withdraw at any time from the study without giving reasons and without prejudicing further treatment.

6.3 CONFIDENTIALITY

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act 2018.

6.4 INDEMNITY

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

6.5 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.

6.6 FUNDING

This study is being funded by The Luff Foundation and Imperial College London, and Imperial College London NIHR Patient Safety Translational Research Centre. Support may also be provided by the NIHR North West London Clinical Research Network through adoption to the NIHR Portfolio.

6.7 AUDITS

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor, the Research Ethics Committee and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care (2nd edition).

7. STUDY MANAGEMENT

The day-to-day management of the study will be co-ordinated through Dr Gaby Judah

8. PUBLICATION POLICY

The results of the study will be published in full in a suitable peer-reviewed medical journal and be entered for presentation at an appropriate international conference.

9. REFERENCES

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