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Programme on Adherence to Medication (PAM) randomised controlled trial

Submission date
28/10/2019

Recruitment status
No longer recruiting

Registration date
09/12/2019

Overall study status
Completed

Last Edited
27/02/2024

Condition category
Circulatory System

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Current plain English summary as of 01/12/2023:

Background and study aims
About 9.5 million people in England and Wales receive treatment for hypertension (high blood pressure) from their general practice. However, many people with hypertension and associated conditions (such as diabetes, heart disease and stroke) do not take their medication as prescribed. Not taking medication reduces how well such treatment works and increases healthcare costs; for example, unused medications cost the NHS in England several hundred million pounds per year.

Primary care practitioners have an important role in supporting patients to adhere to their prescribed medication. However, they have limited time to provide ongoing support for adherence, and their time is expensive.

A potential solution is for practitioners to deliver a very brief intervention during a consultation and to use a digital intervention such as text messaging, smartphone app or web-based intervention to support subsequent adherence. Digital interventions have several advantages: they can be fully automated; provide information that is highly tailored to the individual; be interactive; be available at any time; deliver support in real time; deliver support with high fidelity; and be easily updated. A two-component intervention comprising a very brief intervention from a primary care practitioner plus a digital intervention would be inexpensive to deliver, scalable and potentially cost-effective.

About 90% of UK adults and 67% of those aged 65 years and over use a smartphone, and 96% and 87% respectively use a mobile phone capable of text messaging.

We have developed an intervention comprising a very brief intervention delivered remotely by a practice nurse or healthcare assistant in primary care followed by a digital intervention (text messaging programme or smartphone app): the PAM (Programme on Adherence to Medication) intervention. We have shown the intervention to be acceptable, feasible and potentially effective in supporting medication adherence and reductions in blood pressure in patients prescribed treatment for hypertension, as an adjunct to usual care consultations.

The PAM trial will test whether the intervention helps people take their medicines as prescribed and reduces their blood pressure (i.e. whether it is effective) compared with usual care, and also whether it provides value for money. If the findings are positive, the intervention could be rapidly implemented in the NHS, with immediate and long-term benefits to patients and to the health service.

Who can participate?
Patients who have a diagnosis of hypertension (high blood pressure), have been prescribed at least one antihypertensive medication, and have poorly controlled blood pressure or gaps in collecting repeat prescriptions.

What does the study involve?
Participants are randomly allocated to the intervention group or the control group. The intervention group receive a very brief intervention (VBI) delivered remotely (by phone or videolink) by a healthcare practitioner, followed by a digital intervention (text messaging or smartphone app) for up to 14 months. The control group receive usual care only. Follow up is at 6 and 12 months. Participants will be asked to measure their own blood pressure, provide urine and blood samples, and complete questionnaires.

What are the possible benefits and risks of participating?
The potential benefits of participating are that participants allocated to the intervention group may find the intervention helpful in supporting them to take their medications as prescribed, which will be beneficial to their health. Participants allocated to the control group will not benefit from the intervention, but they may find that participation in general and measurement in particular (e.g. self-monitored home blood pressure measurement) may help them to take their medication as prescribed and control their blood pressure. Both groups of participants will also be contributing to evidence about the effectiveness and cost-effectiveness of the intervention. We believe that the risks of participating are low. At worst the intervention may not be effective, and some participants may find the measurement procedures burdensome. Participants are free to withdraw from the trial at any time, and procedures are in place to address any issues that arise.

Where is the study run from?
University of Cambridge (UK)
NHS Cambridgeshire and Peterborough Integrated Care Board (UK)

When is the study starting and how long is it expected to run for?
October 2020 to September 2024

Who is funding the study?
NIHR Programme Grants for Applied Health Research (UK)

Who is the main contact?
Prof Stephen Sutton srs34@medschl.cam.ac.uk

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Previous plain English summary:

Background and study aims
Almost 14.5 million people in the UK receive treatment for high blood pressure (hypertension) from their general practice, including many patients with other conditions such as diabetes,

heart disease and stroke. Treatment for high blood pressure usually consists of one or more blood-pressure-lowering medicines, known as antihypertensives. Many patients will also be prescribed other medicines including statins (to lower cholesterol) and glucose-lowering medicines. Taking medication as prescribed can significantly reduce risks, complications and early deaths associated with these conditions. However, many people with these conditions do not take their medication as prescribed. This reduces how well such treatment works, leading to increased heart attacks and strokes. It also means that a lot of medicines are wasted, which costs the NHS several hundred million pounds a year. GPs and nurses can support patients in taking their medication, but they have limited time and their time is expensive. There is, therefore, a need for low-cost interventions that support patients to take their tablets as prescribed.
A promising approach is to use digital interventions such as text messaging and smartphone 'apps' that are accessible from mobile phones. Such interventions have several advantages: they can be fully automated; they can provide information that is highly tailored to the individual; they can be interactive; they can be available at any time; they can deliver support in real-time; the content can be easily updated; and, once they have been developed, they are relatively inexpensive to deliver.
The researchers are proposing that a digital intervention could be used in combination with a brief intervention from the practice nurse or healthcare assistant. Practitioners would give brief medication adherence advice and support to patients during consultations such as blood pressure checks and annual reviews. As part of this, they will 'signpost' patients to a digital intervention which would support them to take their medicines between visits to the practice. With the help of patients, practitioners and other experts, and informed by a review of existing evidence, the researchers will develop a new intervention that has two parts: (i) a very brief medication adherence intervention (lasting under five minutes) delivered by a nurse/healthcare assistant, who then 'signposts' the patient to (ii) a digital intervention designed to provide ongoing behavioural support between practice visits. The researchers will test whether the intervention helps people take their medicines as prescribed and reduces their blood pressure (i. e. whether it is effective) compared with usual care, and also whether it provides value for money and utility of health. If the findings are positive, the intervention could be rapidly implemented in the NHS, with immediate and long-term benefits to patients and to the health service.

Who can participate?
Patients who have a diagnosis of high blood pressure (HBP), or comorbidities of HBP, such as type 2 diabetes or high cholesterol, are prescribed at least one antihypertensive medication, and have poorly controlled HBP or gaps in collecting repeat prescriptions

What does the study involve?
Participants are randomly allocated to the intervention group or the control group. The intervention group receive a 1-minute very brief intervention (VBI), followed by a 12-month text message and/or smartphone app intervention. The control group receive usual care only. Follow up is at 12 months.

What are the possible benefits and risks of participating?
The VBI delivered by the health care professionals has been designed to support medication adherence and to register patients into the text messaging or app intervention. The researchers will use this information to make recommendations to health care providers in primary care about how best to support people take their prescribed medications by delivering very brief advice. The text messaging service and app intervention has been designed to reflect research which suggests digital interventions may enhance medication adherence by providing ongoing support following practitioners' consultations. This intervention will be available to provide advice on taking medications and support patients to self-monitor their medication taking. It is

anticipated that this element of the digital intervention will increase patients' satisfaction with the continuous care they receive from the practice. If feasible, this low-cost intervention could reach people even in the most deprived areas. Practitioners may not directly benefit from the study, but if successful, this intervention may benefit people with long-term health conditions and help other practitioners to achieve practice QOF targets. Furthermore, medication non-adherence reduces the effectiveness of treatment and increases the cost to the NHS from hospital admissions, additional consultations, referrals, investigations and medicine wastage. If this scalable intervention is effective it will most probably be a cost-effective intervention for the NHS. This is a behavioural intervention and does not involve the test of any medical device /equipment or drugs. Thus, in the researchers' view, this is a low-risk study.

Where is the study run from?
University of Cambridge (UK)

When is the study starting and how long is it expected to run for?
October 2020 to October 2023

Who is funding the study?
Programme Grants for Applied Research (UK)

Who is the main contact?
Dr Katerina Kassavou, kk532@medschl.cam.ac.uk

Study website
https://www.phpc.cam.ac.uk/pcu/research/research-groups/bsg/research-themes/medication-adherence/pam-programme-on-adherence-to-medication/

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
268471

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
268471 v0.2 20-10-19, CPMS 43962, IRAS 268471

Study information

Scientific Title
Randomised controlled trial of a very brief practitioner-delivered intervention plus a digital intervention to support medication adherence in people prescribed treatment for hypertension in primary care: the Programme on Adherence to Medication (PAM) trial

Acronym
PAM

Study objectives
Current study hypothesis as of 01/12/2023:
The aim of this trial is to estimate the effectiveness and cost-effectiveness of the PAM intervention to improve medication adherence and reduce blood pressure compared with usual care, to inform a decision on whether to implement the intervention in primary care

Previous study hypothesis as of 22/10/2020:
This trial aims to assess the effectiveness and cost-effectiveness of the PAM intervention to support blood pressure control and medication adherence in primary care.

Previous study hypothesis:
Is PAM (cost) effective to support adherence to antihypertensive medications and improve blood pressure as an adjunct to primary care?

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/10/2020, Cambridge East Independent Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048181; CambridgeEast.REC@hra.nhs.uk), ref: 19/EE/0354

Study design
Parallel group multi-centre individually randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Efficacy

Participant information sheet
https://cambridge.eu.qualtrics.com/jfe/form/SV_eG4vCL5yilD4jzw

Health condition(s) or problem(s) studied
Supporting medication adherence in patients prescribed treatment for hypertension

Interventions
Current interventions as of 01/12/2023:

Intervention group: A very brief intervention (VBI) delivered remotely (by phone or video call) by a practice nurse or healthcare assistant followed by a digital intervention (text messaging or smartphone app), in addition to usual care.

Control group: Usual care only.

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Previous interventions as of 22/10/2020:

Intervention group: usual care PLUS a very brief intervention (VBI) facilitated by a practice nurse or health care assistant followed by a 12-month text messaging programme or smartphone app.
Comparator group: usual care only.

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Previous interventions:

The intervention group will receive a 1-minute very brief intervention, followed by a 3 months text message and/or a smartphone app intervention. The control group will receive usual care only.
Follow up will be at 12 months. Randomisation will be stratified by primary care professionals only.

Intervention Type
Behavioural

Primary outcome measure
Current primary outcome measure as of 01/12/2023:

Systolic blood pressure obtained from self-monitored home blood pressure measurements at 12-month follow up

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Previous primary outcome measure as of 22/10/2020:

Blood pressure measured using A&D Upper Arm Blood Pressure Monitor at 12 months follow up

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Previous primary outcome measure:

Systolic blood pressure measured using electronic monitoring devices at baseline and at 12 months follow up

Secondary outcome measures

Current secondary outcome measures as of 01/12/2023:

1. Medication adherence measured by chemical adherence testing of urine samples, self-report questionnaires and prescription data from practice records, at 12-month follow up
2. Diastolic blood pressure obtained from self-monitored home blood pressure measurements at 12-month follow up
3. Full lipid profile and HbA1c for patients with high cholesterol and type 2 diabetes, respectively, at 12-month follow up
4. Health related quality of life using EQ-5D-5L and resource use questionnaire at 6-month and 12-month follow up
5. Process evaluation using audio recordings of the baseline consultation, log files recording use of the digital interventions, qualitative interviews with practitioners and patients, and self-report questionnaires at 12-month follow up

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Previous secondary outcome measures as of 22/10/2020:

1. Medication adherence measured by biochemical testing of the urine and by self-reports (i.e. two items from the MARS questionnaire and two additional single-item measures) at 12 months follow up
2. Full lipid profile and glucose levels for a subsample of patients, measured using blood samples at 12 months follow up
3. Quality of life measured using EQ-5D-5L, and resource use using a self-reported questionnaire at 12 months follow up
4. Process evaluation using an audio recording of the VBI, digital log files during the 12-month intervention, interviews and self-reported questionnaires at 12-month follow up

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Previous secondary outcome measures:

1. Medication adherence measured by urine samples, two self-reported items, and MARS at baseline and 12 months follow up
2. Quality of life measured using EQ5-D at baseline and at 12 months
3. Process evaluation using digital log files and audio-files during the 3-months intervention, and self-reported questionnaires at baseline and 12 months

Overall study start date
05/10/2020

Completion date
30/09/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 01/12/2023:

Patients will be included if they satisfy all the following criteria:
1. Has a diagnosis of hypertension (high blood pressure)
2. Have been prescribed at least one antihypertensive (blood pressure lowering) medication
3. Any Blood Pressure reading higher than 140/90 mmHg OR gaps in collecting repeat prescriptions
4. Can understand English and is able to provide informed consent
5. Has a mobile phone and is familiar with sending and receiving text messages
6. The practice nurse or healthcare assistant is not aware of any other reason why the patient should be excluded

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Previous inclusion criteria as of 22/10/2020:

Patients will be included if they satisfy all six criteria:
1. Have a diagnosis of hypertension (high blood pressure)
2. Have been prescribed at least one antihypertensive (blood pressure lowering) medication
3. Have a most recent blood pressure reading higher than 140/90 mmHg or gaps in collecting repeat prescriptions
4. Can understand English and is able to provide informed consent
5. Have a mobile phone and is familiar with sending and receiving text messages
6. The practice nurse or health care assistant is not aware of any other reason why the patient should be excluded.

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Previous inclusion criteria:

Patients will be included if they:
1. Have a diagnosis of high blood pressure (HBP), or comorbidities of HBP type 2 diabetes cholesterol
2. Are prescribed at least one antihypertensive medication
3. Have poorly controlled HBP or gaps in collecting repeat prescriptions
4. Are able and use mobile phones
5. Have the capacity to provide informed consent

Participant type(s)
Patient

Age group

Adult

Sex
Both

Target number of participants
542

Total final enrolment
578

Key exclusion criteria
Current exclusion criteria as of 01/12/2023:

Patients will be excluded if:
1. They have BP > 200/100mm Hg or postural hypotension (>20mm Hg systolic drop)
2. They have a diagnosis of dementia or other cognitive difficulties that could affect study participation
3. They have had a recent severe life-threatening event or are under treatment for another long-term health condition (e.g. cancer)
4. They are taking part in another medication adherence intervention or digital intervention for behaviour change
5. Their BP is not managed by their GP practice

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Previous exclusion criteria:

Patients will be excluded if they:
1. Have a diagnosis of dementia or other cognitive difficulties that could affect study participation
2. Have had a recent severe life-threatening event or are under treatment for another long-term health condition (e.g. cancer)
3. Take part in another medication adherence and/or digital intervention

Date of first enrolment
01/11/2020

Date of final enrolment
30/03/2022

Locations

Countries of recruitment
England

United Kingdom

Wales

Study participating centre
University of Cambridge
Primary Care Unit
Department of Public Health and Primary Care
East Forvie Building
Cambridge
United Kingdom
CB2 0SR

Sponsor information

Organisation
University of Cambridge

Sponsor details
Research Governance Office
School of Clinical Medicine
University of Cambridge
Cambridge Biomedical Campus
Box 111, Hills Road
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United Kingdom
CB2 0SP
+44 (0)1223 769291
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Sponsor type
University/education

Website
https://researchgovernance.medschl.cam.ac.uk

ROR
https://ror.org/013meh722

Organisation
NHS Cambridgeshire and Peterborough Integrated Care Board

Sponsor details
Gemini House
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Cambridgeshire Business Park
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England
United Kingdom
CB7 4EA
-
alexander.phillips3@nhs.net

Sponsor type
Hospital/treatment centre

Website
https://sites.google.com/nihr.ac.uk/cpresearch

Funder(s)

Funder type
Government

Funder Name
Programme Grants for Applied Research

Alternative Name(s)
NIHR Programme Grants for Applied Research, PGfAR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Current publication and dissemination plan;
Planned publication in high-impact peer-reviewed journals

Previous publication and dissemination plan as of 14/08/2023:
Planned publication of the main trial in a high-impact peer-reviewed journal. This programme's lead researcher and the first author is Dr Aikaterini Kassavou, katerina, kassavou@gmail.com. Dr Kassavou will lead the publications and dissemination plan for the WS4 and WS5; that is the results for the main randomised controlled trial, including the intervention effectiveness and cost-effectiveness, as well as the mixed methods process evaluation. For more information see https://osf.io/qfgx7/

Previous publication and dissemination plan as of 08/12/2022:
Planned publication of the main trial in a high-impact peer-reviewed journal. This programme's lead researcher and the first author is Dr Aikaterini Kassavou, katerina.kassavou@gmail.com. Dr Kassavou will lead the publications and dissemination plan for the WS4 and WS5; that is the results for the main randomised controlled trial, including the intervention effectiveness and cost-effectiveness, as well as the mixed methods process evaluation.

Previous publication and dissemination plan as of 09/05/2022:
Planned publication of the main trial in a high-impact peer-reviewed journal. The lead researcher and first author Dr Aikaterini Kassavou will lead the publication and dissemination plan for the main trial, including the intervention effectiveness and cost-effectiveness, and the process evaluation.

Previous publication and dissemination plan from 29/11/2021:
Planned publication of the main trial in a high-impact peer-reviewed journal.

Previous publication and dissemination plan:
Planned publication in a high-impact peer-reviewed journal. The protocol is currently under ethics review. It will be available for publication after the study is approved from ethics and when recruitment is underway.

Intention to publish date
30/09/2024

Individual participant data (IPD) sharing plan
Current Individual participant data (IPD) sharing plan as of 01/12/2023:
The current data sharing plans for this study are unknown and will be available at a later date

Previous IPD sharing statement as of 08/12/2022:
The datasets generated during and/or analysed during the current study are/will be available upon request from the lead and first author Dr Aikaterini Kassavou (katerina.kassavou@gmail.com).
Type of data: primary data for systolic blood pressure and biochemical medication adherence
When the data will become available: after publication in peer-review journals
What access criteria data will be shared including with whom: data will be shared with researchers conducting secondary analysis of RCTs (e.g. meta-analysis).

Previous IPD sharing statement as of 29/11/2021:
The datasets generated during and/or analysed during the current study are/will be available upon request from the lead and first author Dr Aikaterini Kassavou (kk532@medschl.cam.ac.uk).
Type of data: primary data for systolic blood pressure and biochemical medication adherence
When the data will become available: after publication in peer-review journals
What access criteria data will be shared including with whom: data will be shared with researchers conducting secondary analysis of RCTs (e.g. meta-analysis).

Previous IPD sharing statement:
The datasets generated during and/or analysed during the current study are/will be available upon request from Aikaterini Kassavou (kk532@medschl.cam.ac.uk).
Type of data: primary data for systolic blood pressure and medication adherence

When the data will become available: after publication to peer-review journals
What access criteria data will be shared including with whom: data will be shared with researchers conducting secondary analysis of RCTs (e.g. meta-analysis).

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1	15/09/2020	24/01/2022	No	No
HRA research summary			26/07/2023	No	No