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Investigation of the use of a genetic-led approach for the management of multiple medications in the ageing population

Submission date
27/04/2021

Recruitment status
No longer recruiting

Registration date
28/09/2021

Overall study status
Completed

Last Edited
19/05/2023

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Polypharmacy is the use of multiple medications (three or more) and is common in older individuals and/or people with multiple conditions. In these populations, medicines are frequently associated with adverse drug reactions, including falls, impaired cognition and reduced quality of life. Definitely avoidable adverse drug reactions collectively cost about £100 million annually, contribute to about 1700 deaths per year and are directly responsible for an additional around 700 deaths per year. Evidence demonstrates that over 40% of adverse drug reaction-related hospital admissions may be preventable.
Pharmacogenomics (PGx) is the study of how an individual's genetic make-up affects their response to drugs and aims to provide information to improve the safety and effectiveness of drug treatment. Pharmacogenomic information can be considered actionable if it leads to a change in prescribing decisions, such as alternative medications or dosing. PGx has been shown to be effective for preventing the potential side effects of polypharmacy. As a strategy for optimizing medication usage, PGx is becoming an important element of precision medicine with a significant potential impact on older people with polypharmacy.
This study aims to investigate the use of a PGx-led approach to the management of polypharmacy. The aim is to assess the frequency of pharmacogenomic actionable changes in a patient's DNA, study the impact on de-prescribing, adverse drug reactions and the effect on the number and length of hospital admissions and General Practice (GP) visits. In addition, the study aims to use smart devices to capture patient-reported outcomes to monitor the impact of deprescribing, dose alteration or provision of alternative medications.

Who can participate?
Patients aged 50 years or over, taking three or more medications for cardiovascular (heart) health, pain (musculoskeletal), gastroprotection or mental health

What does the study involve?
Participants will be asked to complete a questionnaire at the start of the study. This questionnaire will ask about health and wellbeing, how the participant copes with their illnesses and what treatments and other health services they use. Participants are asked to donate a

sample, either saliva or blood, from which DNA will be extracted. Researchers will look at markers in the DNA which are known to be associated with how the body processes medications. The participant's general practitioner and pharmacist will review this DNA information in conjunction with the participant's medications and discuss with the participant if any changes in medication are recommended based on the DNA markers. The participant will have the opportunity to proceed with recommended changes or stay on the current regime. Participants will then be asked to complete questionnaires at 1 month, 3 months, 6 months and up to one year after the DNA testing, to record health and wellbeing, and how they cope with their illnesses and treatments. Information on the number of appointments and treatments a participant has in the year before and the year after DNA testing will also be recorded.

What are the possible benefits and risks of participating?
Participants may benefit from longer appointments with their named doctor or pharmacist. Participants may benefit from having medications simplified and their risk of adverse drug reactions reduced.
Risks to participants include giving up time to complete questionnaires. If participants become unwell or experience any unwanted effects, they should inform their GP. If they think that this happened because they have received their medication to be taken in a different way or even if they have been prescribed a new drug, then they should also inform the research team because they need to record and report any incidents like this. It is possible deprescribing or increasing medication dose could cause side effects or hospital admission if there is an adverse drug effect. If a blood sample rather a buccal/saliva sample is taken, this can cause discomfort and bruising.

Where is the study run from?
Congenica Ltd (UK)

When is the study starting and how long is it expected to run for?
January 2021 to November 2024

Who is funding the study?
1. Congenica Ltd (UK)
2. Innovate UK

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
295387

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 295387, CPMS 49485

Study information

Scientific Title
Healthy aging pharmacogenomics & polypharmacy

Acronym
HAPPY

Study objectives
Polypharmacy, the use of multiple medications (3 or more) at the same time is common amongst older individuals and/or in people with multiple co-morbidities. In these populations, medicines are frequently associated with adverse drug reactions (ADRs), falls risk and may have a negative impact on both cognition and quality of life. There are an estimated 237M medication errors per year in the NHS (England), with 66M of these potentially clinically significant. "Definitely avoidable" adverse drug reactions collectively cost ~£100M annually, contribute to ~1700 deaths /year and are directly responsible for an additional ~700 deaths/year. Evidence demonstrates that over 40% of ADR-related hospital admissions may be preventable.
Pharmacogenomics (PGx), the study of how genes affect an individual's response to drugs, aims to provide information to improve the safety and effectiveness of drug treatment. Pharmacogenomic information can be considered actionable if it leads to a change in prescribing decisions, such as alternative medications or dosing. PGx has been shown to be effective for preventing potential side effects of polypharmacy. As a strategy for optimizing medication usage, PGx is becoming an important element of precision medicine with a significant potential impact on older people with polypharmacy.
This research study aims to investigate the use of a PGx-led approach to the management of polypharmacy. The aim is to assess outcomes e.g., actionable PGx DNA sequence variants, de-prescribing, reduced ADRs and effect on number and length of hospital admissions and General Practice (GP) visits. In addition, the researchers will aim to use SMART devices to capture patient-

reported outcomes to monitor qualitative impacts of deprescribing, dose alteration or provision of alternative medications and to assess the clinical implementation pathway of PGx in primary care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/08/2021, North West - Preston Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8206; preston.rec@hra.nhs.uk), REC ref: 21/NW/0166

Study design
Multicenter interventional non-randomized study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Patients on three or more medications for cardiovascular disease, mental health, pain and gastroprotection

Interventions
Patients who are over 50 years of age taking three or more medicines will be identified. This study will focus on patients on medication for cardiovascular disease, mental health, pain and gastroprotection.

Saliva samples will be collected for DNA extraction and PGx testing looking at pharmacogenomic gene variants associated with commonly used drugs prescribed in general practice.

On receipt of the PGx data the study lead GP from each site will review the results +/- with their pharmacist and where genetic variants are identified as part of the study which may impact the medication the patient is taking the patient will be invited for a medication review to inform them about the implications of the genetic data and how that might lead to an actionable effect such as dose reduction (deprescribing) or dose increase or changing to an alternative medication. This study uses medications with a marketing authorization in the UK, prescribed in accordance with the terms of that authorization. Pharmacogenetic data from the patient will be used to suggest changes to prescribing within the confines of the authorization, based on guidelines from the Clinical Pharmacogenetics Implementation Consortium (CPIC), the Dutch Pharmacogenetics Working Group (DPWG) and the Food and Drug Administration (FDA) and in the context of the patient history. The clinical decision for prescribing for each patient is however the physician's responsibility.

Baseline, quality of life and drug adverse side effects will be recorded, followed by 1, 3, 6, 12 month follow-ups post any PGx recommended and accepted change.

Data will be collected about the number of appointments and treatments including hospital A/E admissions in the year before the PGx data is collected and again in the year after the study the same data will be reviewed.

Intervention Type
Mixed

Primary outcome(s)
1. The number of patients with DNA variants indicating an actionable change in currently prescribed medication, measured using pharmacogenomic genotype data at the time of the medication review questionnaire
2. The number of recommended prescription changes per patient, measured based on pharmacogenomic genotype data at the time of the medication review questionnaire
3. Prescription changes (e.g. dose increase/decrease) recommended as a result of pharmacogenomic data at the time of the medication review questionnaire
4. The number of pharmacogenomic prescription changes actioned, recorded at the time of the medication review questionnaire
5. The reasons for acceptance or discounting of pharmacogenomic prescription changes, recorded at the time of the medication review questionnaire

Key secondary outcome(s))
1. The number of adverse drug reactions reported by patients pre- and post-receipt of pharmacogenomic data, measured using questionnaires pre-testing and at 1, 3, 6 and 12 months post-testing
2. The type of adverse drug reactions reported by patients pre- and post-receipt of pharmacogenomic data, measured using questionnaires pre-testing and at 1, 3, 6 and 12 months post-testing
3. The number of actionable pharmacogenomic variants which do not impact a patient's currently prescribed medications, measured using pharmacogenomic genotype data at the time of the medication review questionnaire
4. Anxiety measured using EQ-5D questionnaire at baseline, 1, 3, 6 and 12 months after consent
5. General practitioner and pharmacist confidence in the use of pharmacogenomic data, measured using a questionnaire at baseline, 1, 3 and 6 months
6. Service use review (e.g. hospital admissions, GP appointments) measured using GP records at baseline and 1 year

Completion date
30/11/2024

Eligibility

Key inclusion criteria
1. Over 50 years of age
2. Taking three or more medications for cardiovascular health, pain (musculoskeletal), gastroprotection and mental health
3. Agree to follow up after pharmacogenomic analysis

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
50 years

Sex
All

Key exclusion criteria
1. Do not have the capacity to consent to take part in the project
2. Suffering from terminal cancer or terminal disease
3. Pregnant
4. Suffering from severe mental illness
5. Under the age of 50 years
6. Are not able to understand English or translated material
7. Do not agree to follow up after pharmacogenomic analysis and in particular those patients who have actionable pharmacogenomic data

Date of first enrolment
01/09/2021

Date of final enrolment
01/07/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Longcroft Clinic
5 Woodmansterne Lane
Banstead
United Kingdom
SM7 3HH

Study participating centre
Shipley Medical Practice, Affinity Healthcare
Alexandra Road

Shipley
United Kingdom
BD18 3EG

Sponsor information

Organisation
Congenica Ltd

Funder(s)

Funder type
Industry

Funder Name
Congenica Ltd

Funder Name
Innovate UK

Alternative Name(s)
Technology Strategy Board

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Participant level data will not be made available (only in agglomerated format). Data will be held by the sponsor for 10 years.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol file	version 0.5	07/07/2021	06/08/2021	No	No