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A study to assess the usefulness of using genetics to improve prescribing

Submission date 14/06/2022	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 23/06/2022	**Overall study status** Ongoing	
Last Edited 18/11/2025	**Condition category** Other	

Plain English summary of protocol

Background and study aims

There is a growing understanding that the effectiveness and safety of many regularly prescribed medications can be influenced by common genetic changes. This is a concept known as pharmacogenetics (PGx). Despite this awareness, testing for these genetic changes is rarely done in the UK prior to prescribing. One reason for this is that it is not well understood what proportion of patients who have these genetic changes, also take the related medicines. This study aims to resolve this issue. By linking individuals' historical prescribing records with genetic data, this study will aim to better understand the clinical usefulness of genetic testing before prescribing and help to determine whether this should be done on a routine basis in the NHS.

Who can participate?

People aged over 18 years admitted to the Manchester University NHS Foundation Trust or attending an outpatient appointment, as a patient or relative, at the Manchester University NHS Foundation Trust.

What does the study involve?

Participants complete a short consent form and a sample of blood (3 ml) will be taken on the same day by a trained member of the research team. This will occur during their stay in MRI or during their outpatient appointment (if applicable). Basic demographic details will be collected during this time. This consent and sample/data collection process should take no more than 30 minutes. Beyond this, participants won’t be asked to do anything further for the study or attend any future study visits.

DNA will be extracted from the blood sample and stored in the Manchester Centre for Genomic Medicine, a specialist NHS genetics laboratory which performs genetic testing for the North West of England. The DNA sample will then be tested for about 75 genetic changes which are thought to be related to how well medicines work. All participants will have details about their past medical and drug history collected from the Greater Manchester Care Record (GMCR). Their medication data and genetic data will then be linked in a secure database. This data will be pseudo-anonymised, meaning that the researcher analysing the data will not know whose data they are looking at. Analysis of this final database will help researchers to understand the usefulness of pharmacogenetic testing.

What are the possible benefits and risks of participating?
Taking part in this study will help academics and clinicians understand whether this type of service should be rolled out in clinical practice. No genetic data will be reported to patients, as this type of pharmacogenetic information has not yet been approved for clinical use. Participants will not receive payment for taking part in the project.

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

When is the study starting and how long is it expected to run for?
October 2021 to January 2027

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr John McDermott, john.mcdermott@mft.nhs.uk

Contact information

Type(s)
Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
305751

Central Portfolio Management System (CPMS)
51741

National Institute for Health and Care Research (NIHR)
301748

Study information

Scientific Title
A cross-sectional trial assessing the clinical utility of pre-emptive pharmacogenetic testing in primary and secondary care: the Implementing Pharmacogenetics to Improve Prescribing (IPTIP) trial

Acronym
IPTIP

Study objectives
If a pre-emptive pharmacogenetic test were implemented, what proportion of patients would have their prescriptions adjusted based on the results?

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 25/02/2019, HRA and Health and Care Wales (HCRW, Castlebridge 4, 15 - 19 Cowbridge Rd E, Cardiff, CF11 9AB, UK; Tel: not available; approvals@hra.nhs.uk), ref: 22/PR /0012

Study design
Cross-sectional trial

Primary study design
Observational

Study type(s)
Screening

Health condition(s) or problem(s) studied
Pre-emptive pharmacogenetic testing

Interventions
This is an observational study recruiting across two study arms, inpatient (IPTIP-I) and outpatient (IPTIP-O). The information gathered at recruitment will be sufficient for the electronic platform to generate a study ID, allowing 3 ml of EDTA blood to be taken and labelled with the IPTIP study ID only. EDTA blood samples will then be transported to the Manchester Centre for Genomic Medicine via existing and secure clinical pathways for internal specimen transport. There, DNA will be extracted and quantified by the North West Genomic Laboratory Hub (NW-GLH), an NHS ISO15189 accredited laboratory. DNA samples will be labelled with the Study ID and stored at -20°C until genotyping. Genotyping will be undertaken using the AgenaTM iPLEX PGx 74 assay. This pre-designed assay targets frequent and clinically relevant variants across 20 pharmacogenes.

Following source data collection, with participant consent, study ID, identifiable demographic, and inpatient prescribing data will be shared with Graphnet CareCentric who operate the Greater Manchester Care Record (GMCR). These records will then be linked with outpatient prescribing data from within the GMCR and deposited as a pseudonymised dataset (labeled with

study ID only) available for analysis by the research team within Graphnet's secure data analysis environment. Participant genotype will then be added to the final dataset within the secure research environment, linked by the Study ID. The final pseudonymised dataset will contain the study ID, medicine history, participant genotype and metabolizer status. This will allow an assessment of the primary and secondary outcomes for the trial.

The proportion of patients with a genotype related to a medicine they are currently, or have previously been, prescribed. Genotype-phenotype relationships will be assigned where there is high-level PharmGKB evidence for clinical actionability (Levels 1A or 1B). Rates for the whole cohort will be presented but will be split by recruiting site and by age. These measures will be used to quantify the potential clinical utility of pre-emptive PGx testing in different settings, directly informing policy decisions around the implementation of PGx nationally.

In addition to the primary outcome, baseline characteristics will be presented. Medicine exposure by British National Formulary (BNF) class will be presented with sub-analysis by age group, sex, and the presence of recorded co-morbidities. Analysis will be presented for the whole cohort, and separately for inpatient and outpatient arms.

Genotype and metaboliser frequencies, derived using Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines, will be presented for the whole cohort. These frequencies will then be analysed by age, sex, and ethnicity. Analysis will be presented for the whole cohort, and separately for inpatient and outpatient arms. Statistical differences in genotype based on demography, or recruiting site, will be tested via ANOVA or independent t-test. Genotype frequencies will be compared against an independent control cohort, generated as part of an ongoing trial, genotyping 1500 patients from the TARDIS Trial. This will allow for comparison as to whether the dataset generated in this fellowship is consistent with others around the country, so clarifying generalizability.

Finally, the predictive value of patient variables, such as age, co-morbid status, or ethnicity, for exposure to medicines where pharmacogenetic guidelines exist will be determined. This will be used to assess whether these variables, either in isolation or in combination, could be used to define a targeted screening approach for pharmacogenetics.

Intervention Type
Genetic

Primary outcome(s)
The proportion of patients with an actionable genotype related to a medicine they are currently, or have previously been, prescribed. Genotype-phenotype relationships will be assigned where there is high-level PharmGKB evidence for clinical actionability (Levels 1A or 1B). This will be expressed as a percentage of the whole study cohort (i.e. number of individuals with an actionable variant receiving a corresponding medicine/the total study cohort). Sub analyses will be undertaken by age and comorbid state. For the inpatient cohort (IPTIP-I) hospital prescriptions will be assessed at a single timepoint during the admission following recruitment. For both cohorts (IPTIP-I and IPTIP-O), Historical GP medicine records will be accessed at a single timepoint after recruitment has closed. Genetic data will be generated for all participants once recruitment has closed.

Key secondary outcome(s))
Current secondary outcome measures as of 16/10/2023:
1. Medicine exposure by British National Formulary (BNF) class will be presented with sub-

analysis by age group, sex, and the presence of recorded co-morbidities. Analysis will be presented for the whole cohort, and separately for inpatient and outpatient arms. This will be presented as a percentage of individuals within the whole cohort, or given sub-group, exposed to a particular medicine class.
2. Genotype and metaboliser frequencies, derived using CPIC guidelines, will be presented for the whole cohort. These frequencies, presented as percentages, will then be analysed by age, sex, and ethnicity.
3. Clinical outcomes based on the presence of clinically relevant variants (primary outcome measure) measured using analysis of the patient's healthcare record.

For the inpatient cohort (IPTIP-I) hospital prescriptions will be assessed at a single timepoint during the admission following recruitment. For both cohorts (IPTIP-I and IPTIP-O), Historical GP medicine records will be accessed at a single timepoint after recruitment has closed. Genetic data will be generated for all participants once recruitment has closed.

Previous secondary outcome measures:
1. Medicine exposure by British National Formulary (BNF) class will be presented with sub-analysis by age group, sex, and the presence of recorded co-morbidities. Analysis will be presented for the whole cohort, and separately for inpatient and outpatient arms. This will be presented as a percentage of individuals within the whole cohort, or given sub-group, exposed to a particular medicine class.
2. Genotype and metaboliser frequencies, derived using CPIC guidelines, will be presented for the whole cohort. These frequencies, presented as percentages, will then be analysed by age, sex, and ethnicity.

For the inpatient cohort (IPTIP-I) hospital prescriptions will be assessed at a single timepoint during the admission following recruitment. For both cohorts (IPTIP-I and IPTIP-O), Historical GP medicine records will be accessed at a single timepoint after recruitment has closed. Genetic data will be generated for all participants once recruitment has closed.

Completion date
01/01/2027

Eligibility

Key inclusion criteria
1. Participants must be admitted to the Manchester University NHS Foundation Trust or attend an outpatient appointment, as a patient or relative, at the Manchester University NHS Foundation Trust
2. Participants must have the capacity to independently consent
3. Patients must be over the age of 18 years

Participant type(s)
Mixed

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Patients unable to independently consent
2. Patients under the age of 18 years

Date of first enrolment
04/07/2022

Date of final enrolment
01/01/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Manchester Royal Infirmary
Cobbett House
Oxford Road
Manchester
England
M13 9WL

Study participating centre
St Mary's Hospital
Oxford Road
Manchester
England
M13 9WL

Sponsor information

Organisation
University of Manchester

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
An anonymised version of the genetic dataset will be stored in a data repository with no limitations on access or use. Genotype data will be deposited in the Figshare repository (https://figshare.com/) at the end of the study following publication. Data will be open access and will be entirely anonymised, with no study ID. There are no restrictions on access to the data.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		06/05/2025	08/05/2025	Yes	No
HRA research summary			28/06/2023	No	No
Interim results article		17/10/2024	12/12/2024	Yes	No

Protocol file	version 5.3	21/09/2023	16/10/2023	No	No
Statistical Analysis Plan	version 5.3	21/09/2023	16/10/2023	No	No