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

Submission date	<b>Recruitment status</b> No longer recruiting	[X] Prospectively registered		
14/06/2022		[X] Protocol		
<b>Registration date</b> 23/06/2022	<b>Overall study status</b> Completed	[X] Statistical analysis plan		
		[_] Results		
Last Edited	<b>Condition category</b> Other	Individual participant data		
08/05/2025		[X] Record updated in last year		

#### 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 October 2024

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

**Contact name** Dr John McDermott

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#### Contact details

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# Additional identifiers

EudraCT/CTIS number Nil known

IRAS number 305751

**ClinicalTrials.gov number** Nil known

#### Secondary identifying numbers

NIHR301748, IRAS 305751, CPMS 51741

# 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

Secondary study design

Cross sectional study

Study setting(s) Hospital

**Study type(s)** Screening

#### Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

#### 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 measure

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.

#### Secondary outcome measures

Current secondary outcome measures as of 16/10/2023:

1. Medicine exposure by British National Formulary (BNF) class will be presented with subanalysis 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 subanalysis 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.

Overall study start date 01/10/2021

**Completion date** 04/10/2024

# 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

#### Age group

Adult

#### Lower age limit

18 Years

Sex

Both

# **Target number of participants** 646

#### 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 03/10/2024

# Locations

#### **Countries of recruitment** England

United Kingdom

## Study participating centre

Manchester Royal Infirmary Cobbett House Oxford Road Manchester United Kingdom M13 9WL

#### Study participating centre

**St Mary's Hospital** Oxford Road Manchester United Kingdom M13 9WL

### Sponsor information

**Organisation** University of Manchester

Sponsor details Oxford Road Manchester England United Kingdom M13 9PL +44 (0)161 306 6000 doctoralacademy@manchester.ac.uk

**Sponsor type** University/education

Website https://www.manchester.ac.uk

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**

#### Publication and dissemination plan

Findings, positive or negative, will be published in open access peer reviewed journals and presented at international conferences. A dedicated PPIE dissemination strategy will be developed with the PPIE VOCAL team at the Manchester University NHS Foundation Trust.

#### Intention to publish date

01/10/2024

#### 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 HRA research summary	Details	Date created	<b>Date added</b> 28/06/2023	<b>Peer reviewed?</b> No	<b>Patient-facing?</b> No
<u>Protocol file</u>	version 5.3	21/09/2023	16/10/2023	No	No
<u>Statistical Analysis Plan</u>	version 5.3	21/09/2023	16/10/2023	No	No
Interim results article		17/10/2024	12/12/2024	Yes	No
<u>Protocol article</u>		06/05/2025	08/05/2025	Yes	No