NHS Digital Academy

hfma

Pharmacogenomics in general practice

Making prescribing safer and more effective

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Delivering value with digital technologies

Digital technologies such as digital medicine, genomics, artificial intelligence, and robotics have a huge potential to transform the delivery of healthcare and NHS organisations.[1]

These technologies can empower patients to participate actively in their care, with a greater focus on wellbeing and prevention. They also support the prediction of individual disease risk and personalize the management of severe or long-term conditions. In service areas that are not patient-facing, technology can streamline data processing tasks to enable staff to be more value added, or to reduce the WTE where the roles are only moving data around.

The HFMA, supported by NHS England Digital Academy (formerly part of Health Education England), is delivering a 12-month programme of work to increase awareness amongst NHS finance staff about digital healthcare technologies, and enable finance to take an active role in supporting the use of digital technology to transform services and drive value and efficiency.[2]

As part of the programme, the HFMA is publishing a series of case studies. Working with organisations who have started on the digital transformation journey, we will identify examples of good practice and highlight the challenges that services face. This will include specific challenges relating to NHS finance.

This case study describes how a digital system is enabling knowledge of the relationship between genes and medicines, so it can be used in primary care.

Summary

The *Pharmacogenomics roll out: gauging response to service (Progress)* study applies the science of pharmacogenomics in NHS primary care prescribing, using the known academic evidence that up to 95% of all individuals carry gene changes relevant to commonly prescribed medicines, meaning the medicine will have no effect on the condition it was prescribed for. Progress uses genetic testing by general practitioners (GPs) and uses a digital tool to convert the complex data outputs into easy-to-use red/amber/green (RAG) guidance for the GP to refer to when prescribing certain medicines. The plan is for the information to be available within existing healthcare record software. Professor William Newman and team[3] are undertaking the study with four general practice (GP) surgeries in north-west England, giving patients real-time benefit of the digital development.

Pharmacogenomics

What is pharmacogenomics? The Oxford Languages dictionary describes it as the branch of genetics concerned with the way in which an individual's genetic attributes affect the likely response to therapeutic medicines. Genetic testing of a person's DNA can identify differences in their genetic profile and their susceptibility to particular diseases or abnormalities. Over 95% of all individuals carry genetic variants relevant to commonly prescribed medications. In pharmacogenomics, the genetic testing reveals how a person will react to certain medicines. It is then possible to optimize their medicine therapy to achieve maximum effectiveness with minimal harm to the person's genetic profile.

Genetic testing

Every human has a genome – a profile of DNA where the pattern and variations of the structure give information about the person. In genetic testing, a blood, tissue or saliva sample is taken from the person and sent to a genetics laboratory to provide a map of the DNA. After processing, the results show the genes and identify if there are any are variants from the norm. Genetic testing can also identify specific genetic combinations that prevent the efficacy of a medicine.

[1] HFMA, *Introduction to digital healthcare technologies* July 2021
[2] HFMA, *Delivering value with digital technology* 2021
[3] The team members are listed at the end of this case study.

There is longstanding evidence that genetic testing identifies patients for whom a specific medicine will not have any impact[4]. Prescribing a medicine that will simply not work for a specific patient is costly to the NHS and importantly, to the patient. There may be a small placebo effect, but the delay in finding a treatment that will work could have significant implications.

Pharmacogenetics v pharmacogenomics

Pharmaco*genetics* looks at a single gene and the therapeutic value of the medicine, whereas pharmaco*genomics* looks at the impact of multiple genes. The two terms are often used interchangeably in the non-genetic community.

Many medicines have been studied in a one medicine to one gene format, and the evidence of the relationship is strong. However, few studies have looked at the impact of a panel of genes for a range of medicines. In the laboratory, a panel genetic test is more cost effective and efficient than a single genetic test and, for the health economy, a panel avoids repeating genetic tests for different medicines/ genetic factors. For the patient, having one panel of genetic tests speeds up the start of a treatment that will have a greater chance of working and also potentially prevents repeated appointments to start an effective treatment or to treat side effects.

A genetic panel test

A group of genes are tested at the same time. This allows the understanding of pharmacogenomic benefits for several medicines.

In 2023, a study called *Prepare*[5] was published in The Lancet, reviewing 6,944 patients from seven European countries, including the UK. This looked at a 12-gene pharmacogenetic panel and studied the side effects of a single medicine within a 12 week follow up period. The findings showed medicine that pharmacogenetic panel testing led to 30% less harmful medicine reactions than in the control group. But this study only looked at the reduction in side effects of the medicine and did not look at medicine effectiveness, so did not identify the patients who saw no benefit from the medicine.

In the NHS today, genetic tests are mainly used by secondary or tertiary care services in cancer, specific inherited diseases or other specialised services. GPs have limited access to genetic testing, meaning many prescribe medicines without access to using the genomic impact on benefits and side effects.

The Progress study

The Progress team, based at the Manchester Centre for Genomic Medicine includes experts in genomics and health informatics. The study investigates a group of medicines mainly prescribed in primary care and is funded by the NHS England network of excellence in pharmacogenetics and medicines optimisation[6]. Progress aims to demonstrate the practical application of pharmacogenomics.

Early on, the project identified three critical steps to prove the practical use of pharmacogenomic benefits within GP practices:

1. To identify the most appropriate genetic test to identify whether the medicine is effective and side effects can be avoided.
2. How to make the genetic information available to clinicians that need it, in the best possible language and as part of their usual ways of working.

[4] A range of introductory and detailed material is available from the international publications: *Introduction to pharmacogenomics — Knowledge Hub, The pharmacogenomics journal*, and Science Direct *Pharmacogenomics - an overview*

[5] The Lancet, *A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study,* June 2023

[6] NHS England genomic medicine service, *Pharmacogenomic and medicines optimisation NHS genomic network of excellence*

3. To test whether the approach works in practice. The study's work started in 2023 with four GP practices testing the practicality and success of the new process. Other GP practices will be added later in 2024.

Step two – making the information available - is sub-divided into ease of use and location of the information:

- The laboratory system scientific outputs are not easily used by a GP. They need clarity of result and instruction on the best course of action, without having to trawl through lengthy data findings. Simplicity is considered the key to widespread use. The information should answer the questions – 'do I give medicine a, medicine b, change the dose' and so on.
- NHS healthcare records sit in different software systems and the project did not wish to specify one, as this would create location-based access. The aim is for the genetic information to be stored securely and independently, making it available in existing healthcare records, which requires universal computer language.

The project is subject to research standards; but following an initial process development stage, is now actively applying the new process to all relevant patients in the GP practices rather than comparing with a control group, as it is the implementation process that is under investigation, rather than demonstrating the value of pharmacogenomics. This approach was chosen for speed, and to date the results have been welcomed by the participants.

Project scope

The *Progress team* selected general practice as 90% of medicines are prescribed in primary care. The focus is on four groups of medicines that have a direct relationship with specific genetic variants. They are prescribed to significant numbers of individuals and are often prescribed for long periods of time. The groups are:

- statins – prescribed for lipid management, to reduce cholesterol
- two types of anti-depressants:
  - selective serotonin reuptake inhibitors (SSRI)
  - tricyclic antidepressants (TCA)
- proton pump inhibitors - prescribed to reduce stomach acid reflux disease.

Within these medicine groups, those individuals with normal genetic makeup (without variants) can be up to 90% of patients, across the four main genes that are tested. This means that at least 10% of patients will not gain the required benefit from the medicine across the four gene panel, and for some individual genes the figure rises to 30% of patients.

A patient in the study is only prescribed one of these groups of medicines at a time, so although the genetic testing is for a panel of the genes that impact the successful use of all these medicine groups, the study only tests the potential for benefit one medicine at a time.

For the patients with the genetic variants that prevent any benefit from the prescribed medicine, the ongoing symptoms will continue, and the patient will have a longer waiting time to successful treatment. They may experience further symptoms or deterioration as the original condition is not managed. Some may also experience side effects from the medicines without any benefit. This can be addressed if information about the relevant medicine-associated genetic variant is known and acted upon.

So far, the *Progress study* has found that across the four medicine groups, 20% of patients tested have had the gene variant resulting in a prescription change.

Financial focus

The prescribing cost of these four medicine groups is significant – nearly £439 million in primary care alone. Identifying up to 20% of the national cost of these medicines could enable up to £88m to be redeployed to more effective treatments[7]. This value is based on the Prescription cost analysis for

[7] This analysis does not consider the income received from prescription charges. For greater accuracy, this analysis should also consider the cost of the genetic testing.

England[8] which shows the basic price of the medication without other fees. The pharmacy dispensing time for the 44m items could also be redeployed. **Table 1** shows extracted information for the four medicine groups.

Table 1: NHS Business Services Authority: the national number of items and costs for medication groups in the *Progress* Study[9]

	Total		20% Saving	
	Number of items prescribed (m)	**Cost 2022/23 (£m)**	**Number of items prescribed (m)**	**Cost 2022/23 (£m)**
Statins	80.5	100.1	16.1	20.0
Selective serotonin reuptake inhibitors	46.3	94.3	9.3	18.9
Tricyclic antidepressants	18.3	52.3	3.7	10.5
Proton pump inhibitors	73.2	192.5	14.6	38.5
Total cost (England)	218.5	439.3	43.7	87.9

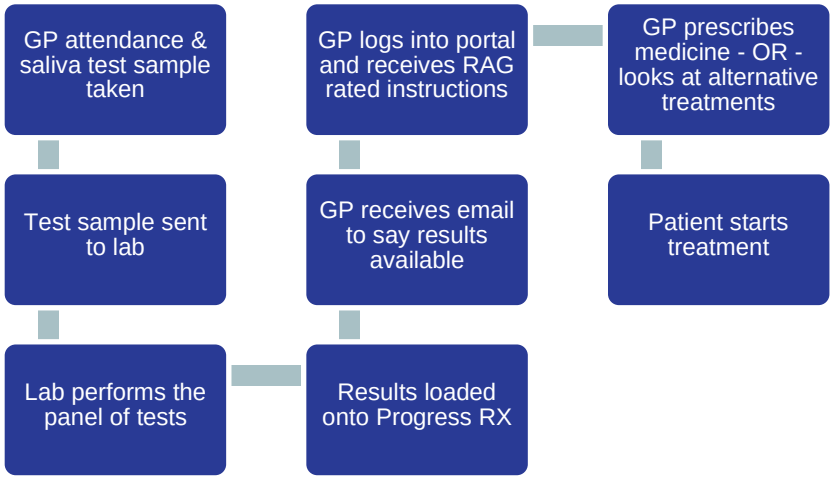
There will be ongoing cost savings to the NHS as patients already having had the panel of tests will not need separate genetic testing for other medicines in the panel: the information will already be available on their health record. Professor Newman has already received a thank you letter from a GP where this situation has occurred, enabling tailored prescription of a second medicine.

Process focus - for GP, laboratory, and patient

The *Progress* study has established a simple process between GP and laboratory, as shown in **figure 1**. The patient attends the GP. The GP then arranges for a saliva sample for the genetic test. The laboratory receives and tests the sample, with the digital output from the system loaded into the software *Progress RX*. This has an online portal, and within a week of the test the GP receives an email to say the genetic test result is available. They can then use the pharmacogenomic information to follow up with the patient, either writing the prescription of the originally planned medicine or prescribing an alternative treatment.

[8] NHS Business Services Authority, *Prescription cost analysis for England, 2022/23*, updated July 2023
[9] The PCA data includes medicine costs from all prescribing locations. This will include hospital prescribed medicines.

Figure 1: illustration of the process for the *Progress* study



Clinically set criteria agreed with the GPs determine which patients become part of the project: those with an emergency clinical need for medication are not part of the *Progress study*. Patients can be prescribed the medication while the genetic testing is processed so there is no delay in starting treatment for those who will benefit. When genetic test results show a relevant genetic variant predicting that an individual will not benefit from the medicine, the prescription will be amended, or the treatment plan altered.

Ease of use focus

The project identified that clinicians' uncertainty about genomic outputs was one of the main blockers to successful use of pharmacogenomics in primary care. They already have significant cognitive load and did not need to add to it with further complex data. Front line clinicians were therefore actively involved in the design of the *Progress RX* software, which is used to turn the genetic laboratory results into easy-to-use information.

Each patient's information is marked using the RAG recognised categorisation, which tells the GP the result and the next step.

RAG scale for GP ease of use

- Red: stop the medicine, or do not prescribe the medicine – meaning it is predicted to have no benefit or a high risk of adverse side effects – due to that patient's genetic makeup.
- Amber: there are indications of concern – further information may be needed/ the medicine may have limited but some benefit.
- Green: means the medicine is suitable for use.

The GP practices in the study found this straightforward and reported that they included it in prescribing decision-making more quickly than expected, and with more confidence. The positive feedback confirms the success of the study has changed the clinicians' prescribing process.

The information is immediately available in the centralised portal to all clinicians who have access. This currently only includes the GP practices in the study but will become wider with further roll out.

The portal location raised some queries, as GPs reported they would rather it was imported into their existing patient information systems. The study aims to achieve this, and by doing so also prevent the need for additional systems training.

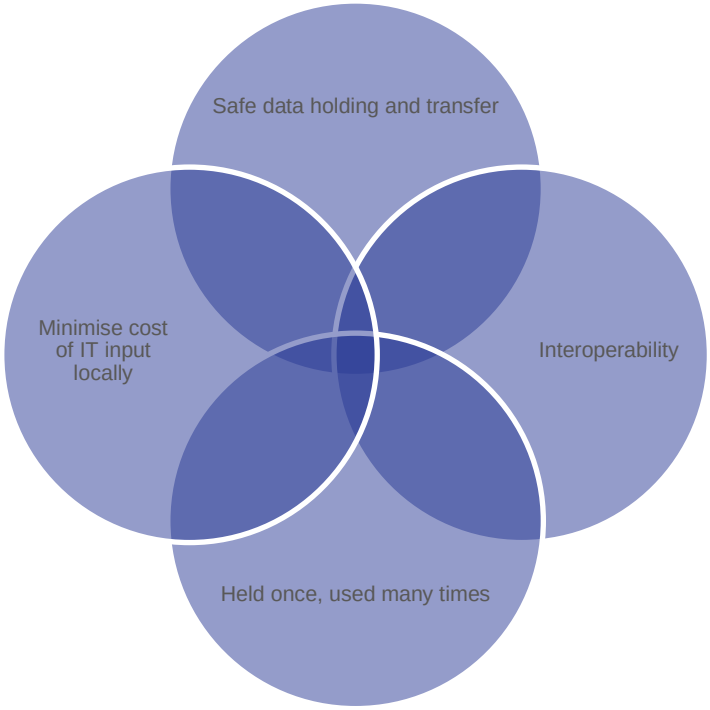
Digital focus

Figure 2 shows the digital factors of this project, which ensure that data:

- is held safely
- is in one location
- can have repeated access-based use, and
- is interoperable – ensuring future scale up of the process is facilitated.

Genetic information does not change over time, so it can become a permanent part of the person's health record. Occasionally the guidance around testing or the RAG scoring may change, and so updates may be needed: but as these are done centrally within *Progress RX*, the local impact is minimal.

Figure 2: the four digital factors for the Progress study



During the study, *Progress RX* has received information from the genetic laboratory in a direct data load, although the intention is for automation. Scott Watson, health informatics lead for *Progress*, reported that a further long-term objective is for the data to be held in the central unified genomic record (UGR) for all individuals in England. The creation of the UGR is being developed by NHS England genomics unit, separately to the *Progress* study but with close working communications. It is intended that the URG will also link directly to the clinical decision-making tools already used by patient facing services.

The *Progress* RX portal is a transactional service that holds the genetic information in a safe, centralised data repository. The end user's software accesses this preventing the need for local data holding and data duplication. The *Progress* study is being developed in accordance with the appropriate NHS authorised information governance and security standards. However, achieving information governance authorisation for each organisation has been time-consuming and required persistence and significant effort. The clinical team reported that the varied approach to information governance regionally will impact the speed of roll out for pharmacogenomics.

Previous research projects have not brought the pharmacogenomic information into live healthcare records, so creating interoperable data is important. The code, scripts and programming language is designed to interface with any GP system or hospital EPR, for as Professor Newman says 'There is no foreseeable prospect of a single electronic patient record in the NHS'.

Progress has successfully tested the links to the Optimise RX clinical decision support software that is used in the majority of UK GP practices[10]. In the hospital sector, a parallel study by the same team has achieved proof of concept that *Progress* RX interfaces with the EPIC electronic patient record software. The plan is for national roll out of the interface to other software products, making the tool available to all healthcare organisations. This may also prevent the need for local charges for new software or upgrades.

Next steps

Following the first reviews of the process, the study has instigated some changes to streamline the process and to make it even easier to use:

[10] Digital health, *FDB's OptimiseRx achieves savings of £300 million for the NHS*, 2023

- The saliva test will change to a cheek swab in response to patient feedback about convenience of test method.
- The study is moving to clinical packets of the testing materials that the patient can use to take the swab at home, and then post the sample to the laboratory.
- GPs have requested that the genetic output is converted by the digital system and available in the GPs' local system, as the process of opening emails and going to the portal adds time to the process.
- Electronic consent forms are being developed, to streamline the process.
- Codeine (used for pain relief) will be added to the list of four medicine groups.
- An additional approximately 20 GP practices will be added to the project in 2024.
- Expansion to GP practices in other regions will expand the benefits and ensure location-specific factors in north-west England do not skew the results.
- The *Progress* team are working with NHS England and The Global Alliance for Genomics and Health to develop data standards to support the standardised storage and messaging of pharmacogenomics results.

As an implementation study (rather than a research study), *Progress* is able to share the results while further roll out of the scheme is in progress. Information about the study can therefore be accessed from the NHS England supported Network of Excellence in pharmacogenomics and medicines optimisation.

Pharmacogenomic knowledge is being considered by NICE for in-hospital prescribing of clopidogrel after a transient-ischaemic attack (TIA) or an ischaemic stroke. For clopidogrel, pharmacogenomic knowledge shows that genetic variation is present in 30% of patients, preventing benefit from the medicine. This means genetic testing for all patients in the context of stroke could save or redeploy £150m recurrently.

The aspiration is that in five to 10 years, patients in England will benefit from their full genetic picture being available to all clinicians in England. This will ensure the known pharmacogenomic relationship between medicines and genes can be a part of all prescribing decisions, minimising side effects and non-effective medication and enabling appropriate treatment to be started earlier. A successful digital solution is an essential part of this target.

The Progress study team

- William Newman, professor of translational genomic medicine, University of Manchester
- Scott Watson, genomics informatics director, NHS North-West Genomic Medicine Service Alliance
- John McDermott, NIHR clinical research fellow, University of Manchester
- Videha Sharma, clinical innovation lead, Pankhurst Institute, University of Manchester
- Jessica Keen, pharmacy lead, NHS North-West Genomic Medicine Service Alliance

About the HFMA

The Healthcare Financial Management Association (HFMA) is the professional body for finance staff in healthcare. For nearly 70 years, it has provided independent and objective advice to its members and the wider healthcare community. It is a charitable organisation that promotes best practice and innovation in financial management and governance across the UK health economy through its local and national networks.

The association also analyses and responds to national policy and aims to exert influence in shaping the wider healthcare agenda. It has particular interest in promoting the highest professional standards in financial management and governance and is keen to work with other organisations to promote approaches that really are 'fit for purpose' and effective.

The HFMA offers a range of qualifications in healthcare business and finance at undergraduate and postgraduate level and can provide a route to an MBA in healthcare finance. The qualifications are delivered through HFMA's Academy which was launched in 2017 and has already established strong learner and alumni networks.

HFMA

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