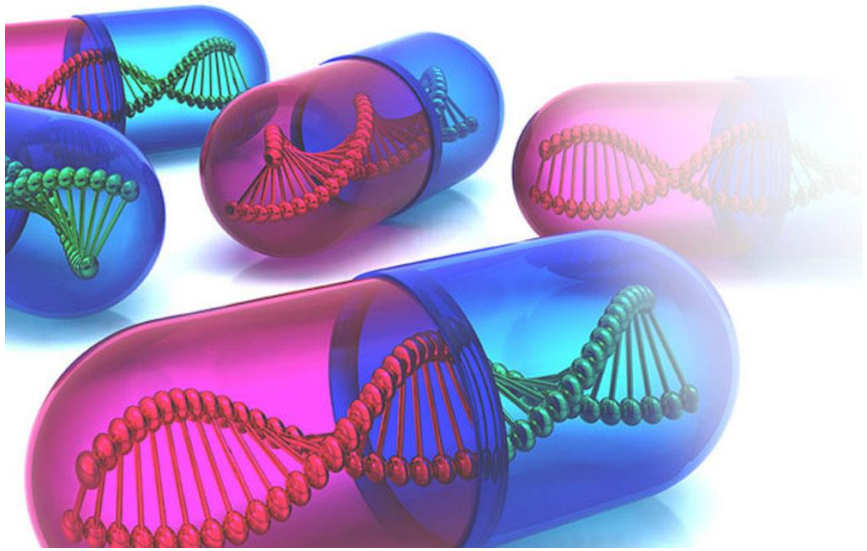
AWMGS

Weqas Annual Conference, 13th December 2023.

POCT applications in genetic testing

Genomic Strategies:

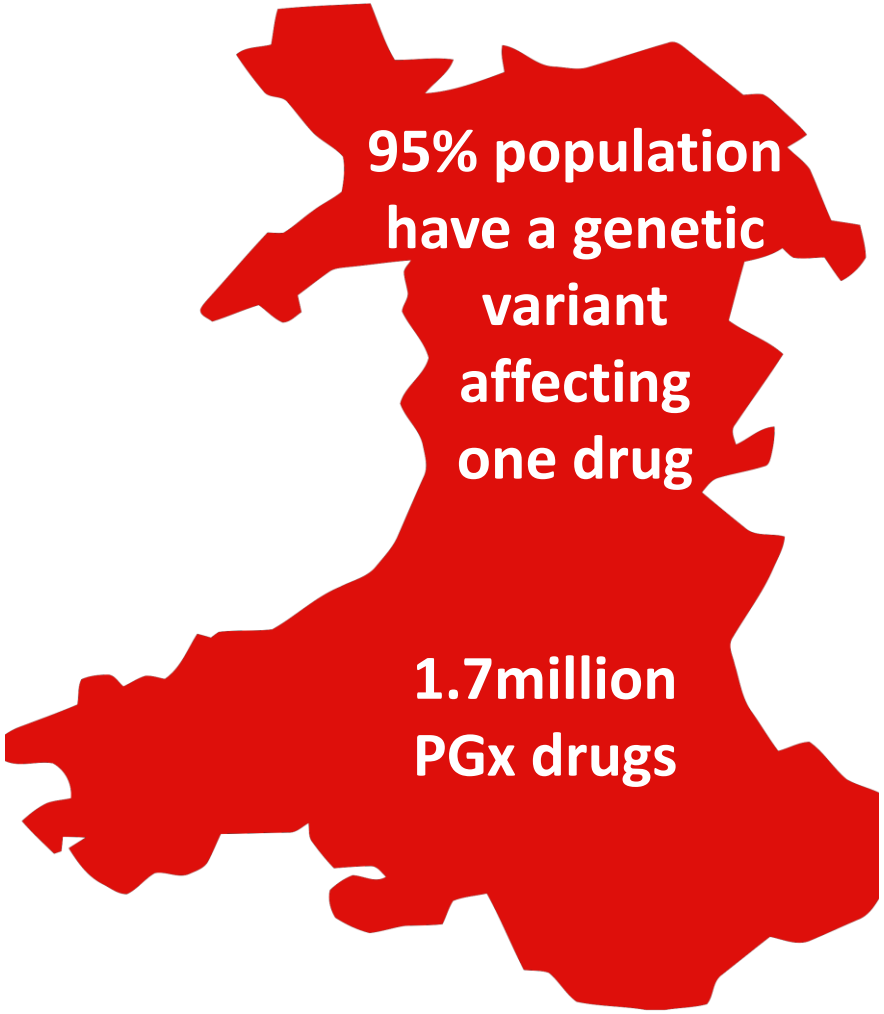


In Wales 200,000 new prescriptions could be adjusted based on the genotype. Up to 20%-30% of Adverse Drug Reactions could be prevented by pharmacogenetic testing.

Political awareness and a clear strategy is important to drive change within the healthcare system.

Pharmacogenomics (PGx)

- Pharmacogenomics is the study of how genetic changes affect an individual's response to drugs.
- ~20-30% of adverse drug reactions are due to genetic variation in drug metabolism genes.
- Cost the NHS £466 million annually.
- Most frequent drug groups include:
  - Cholesterol-lowering drugs, anti-coagulants and anti-platelet medication
  - Cancer treatment
  - HIV treatment
  - Pain medication
  - Hormonal contraception



Genomics for Precision Medicine Strategy

AWMGS

Llywodraeth Cymru
Welsh Government

About ▾ News ▾ Topics ▾ Consultation ▾ Legislation ▾ Funding

Home > About > Cabinet, Cabinet Secretaries and Ministers > Statements > Writte
Precision Medicine Strategy

Written Statement - Genomics for Precision Medicine Strategy

Last updated 12 April 2017 Share

Vaughan Gething, Cabinet Secretary for Health, Well-being and Sport

New genetic and genomic technologies are allowing us to develop a much more

….strengthen genomics and precision medicine services and research in Wales

Investment = £6.7 million over 5 years

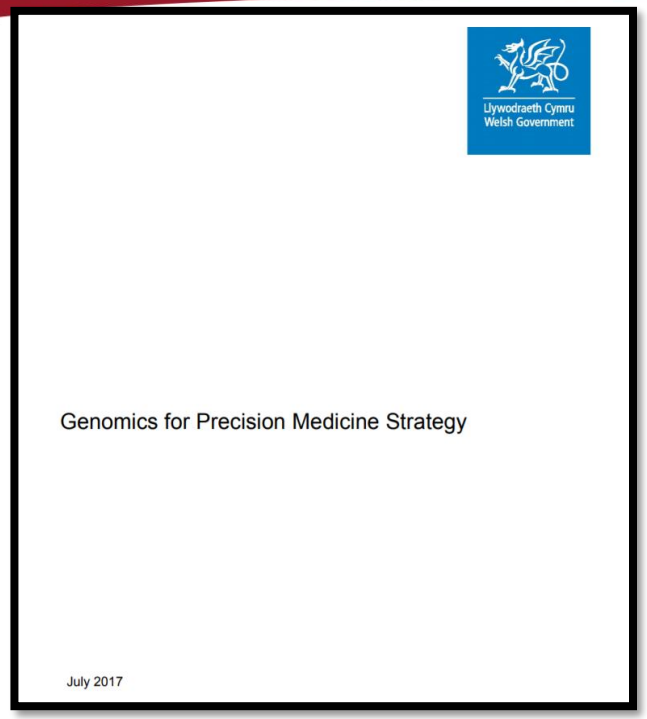
Genomic medicine has the potential to save costs and improve quality of care by targeting treatment, maximising benefit and reducing side effects

Partneriaeth Genomeg Cymru
Genomics Partnership Wales

Policy contexts - Wales

- ***Genomics for Precision Medicine Strategy*** notes the anticipated increase in the clinical utility and *requirement for pharmacogenetic testing in the near future*, and advises that services will be prioritised based on clinical need and Welsh expertise
- ***The Medicines Strategy for Wales*** (2018-2023) commits the AWMSG to work with the AWMGS with a particular focus on reducing the burden of ADRs

Genomics for Precision Medicine Strategy



To build infrastructure and capacity to deliver value based healthcare.

Actions:-

- Co-production
- Clinical and laboratory services
- Research and Innovation
- Workforce
- Strategic partnerships

The partners

Genomics Partnership Wales established 2018

Michaela John
Head of Programme
Genomics Partnership Wales

Nick O'Sullivan
Project Manager
Genomics Partnership Wales

Ryan Moreland
Project Support Officer
Genomics Partnership Wales

AWMGS

Our Programme Structure:

All Wales Chief Executives

SRO & Head of Programme

Governance Board

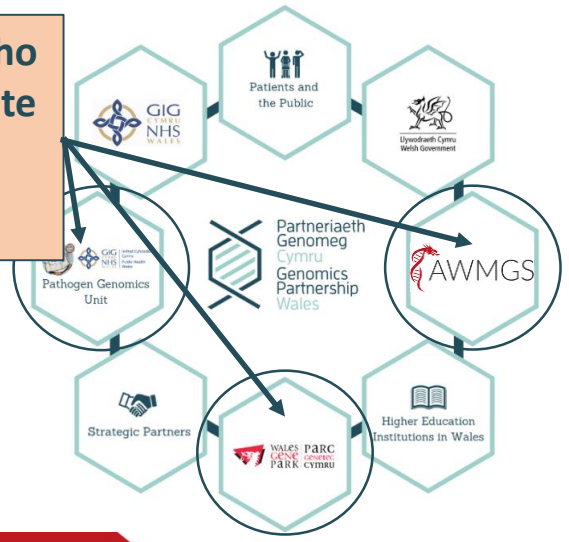
Patient & Public Sounding Board

Programme Board

New £15m genomics facility for Wales is given go ahead

29 October 2021

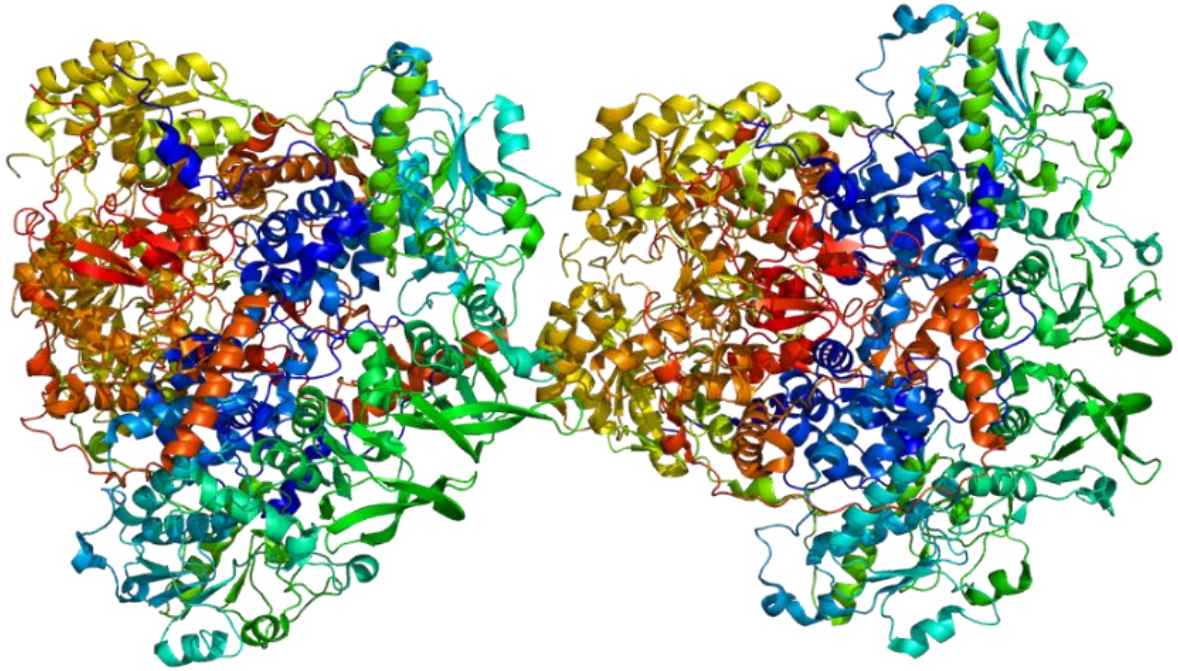
Partners who will co-locate



Pitch to Genomic Partnership Wales 2018/19: Prof. Dyfrig Hughes

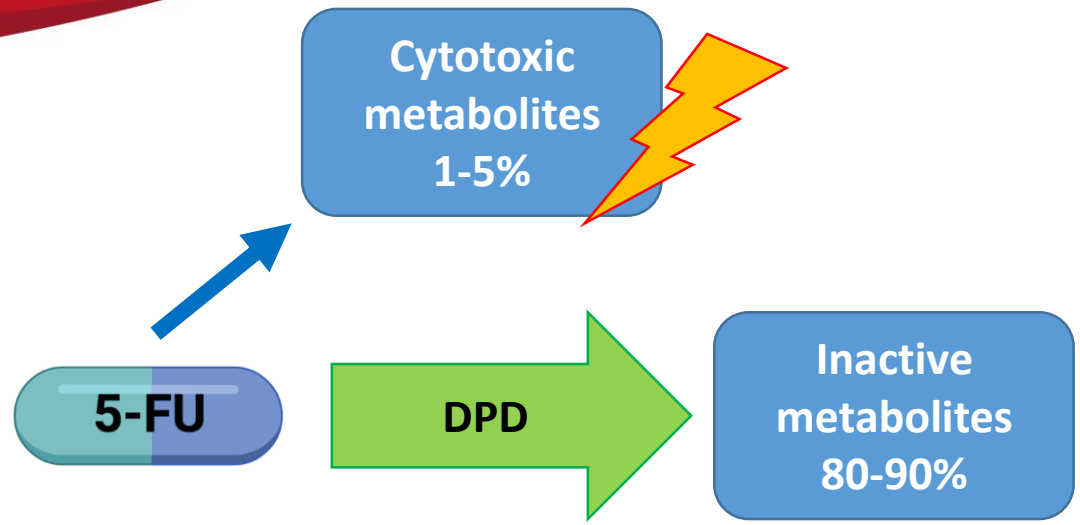
1. Define patient eligibility
2. Determine how germline genetic tests can be incorporated into treatment pathways
3. The All Wales Genomics Laboratory (UKAS accredited) will evaluate and validate the most appropriate testing technologies.
4. Establish clinical reporting systems.
5. Clinical interpretation will be established.
6. Health technology assessment. Patient and public involvement.
7. Healthcare engagement
8. Education and training

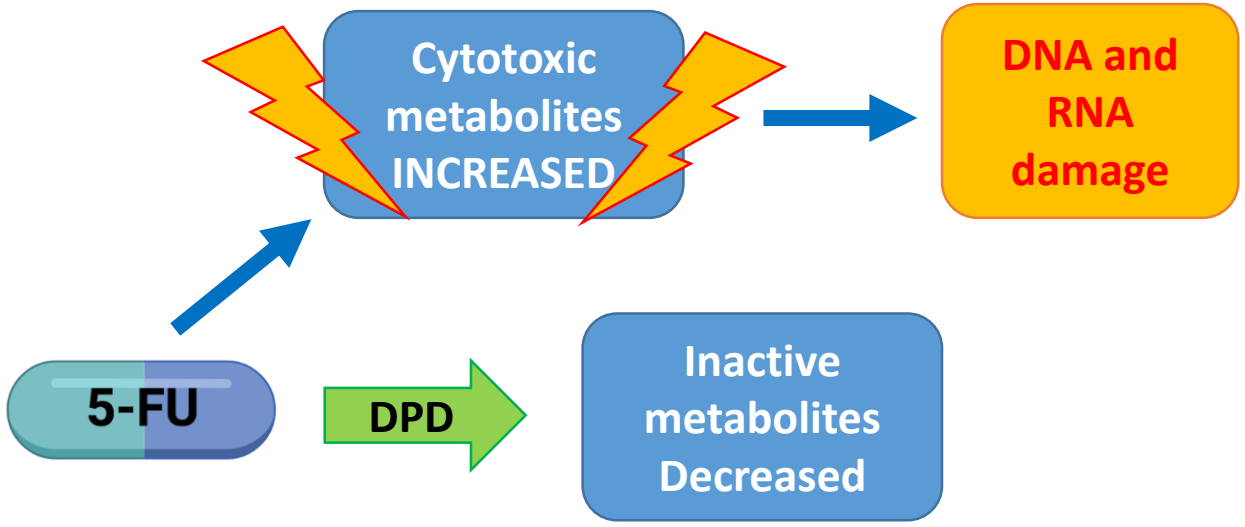
- **Chemotherapy agents: 5-fluorouracil, capecitabine, tegafur**
- **DPYD gene testing**



DPYD

- *DPYD* gene encodes for the enzyme dihydropyridine dehydrogenase (DPD).
- DPD is involved in metabolism of the chemotherapy agents 5-fluropyrimidine and capecitabine.
- Variants in this gene cause DPD deficiency.
- This leads to severe toxicity when treated with these chemotherapy agents.





Implementing DPYD testing

Pilot project Velindre Cancer Centre: Jan – May 2020

Aim: Well-governed DPYD testing process

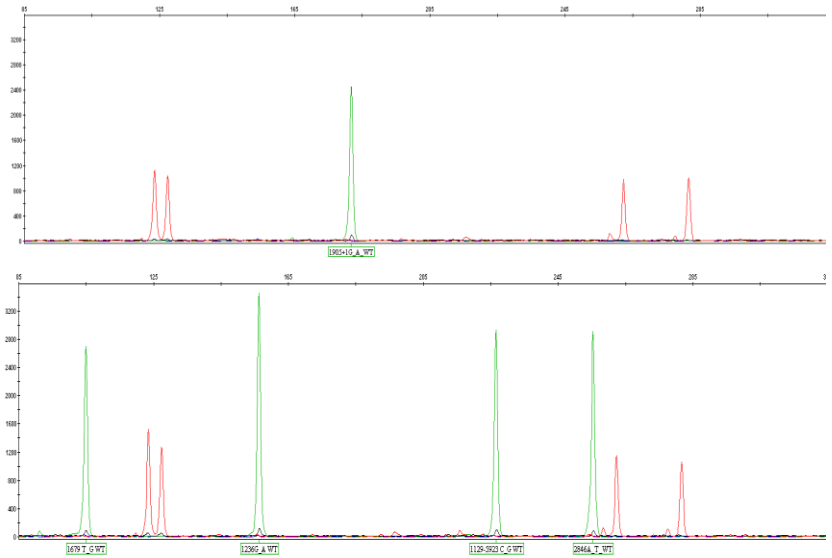
- VCC DPYD testing project
- Standardised, robust process
- Ensure routine testing
- Staff aware and confident in testing process.

Clinicians
Pharmacy
Project manager
AWMGS team

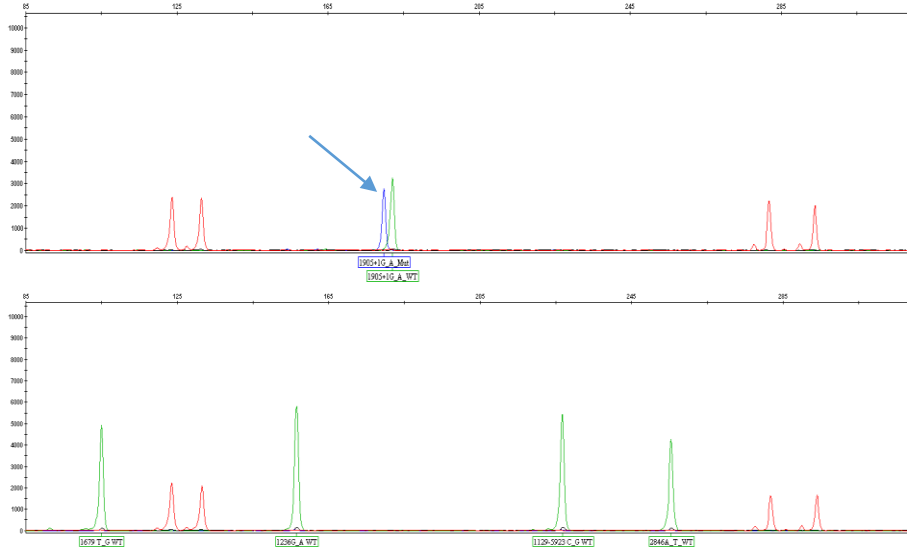
- ✓ Pathway
- ✓ Guideline
- ✓ Critical test on Chemocare
- ✓ Staff education events
- ✓ Patient information
- ✓ Trust intranet

AWMGS: single gene test

Normal Result



c.1905G>A heterozygote



DPYD Reporting

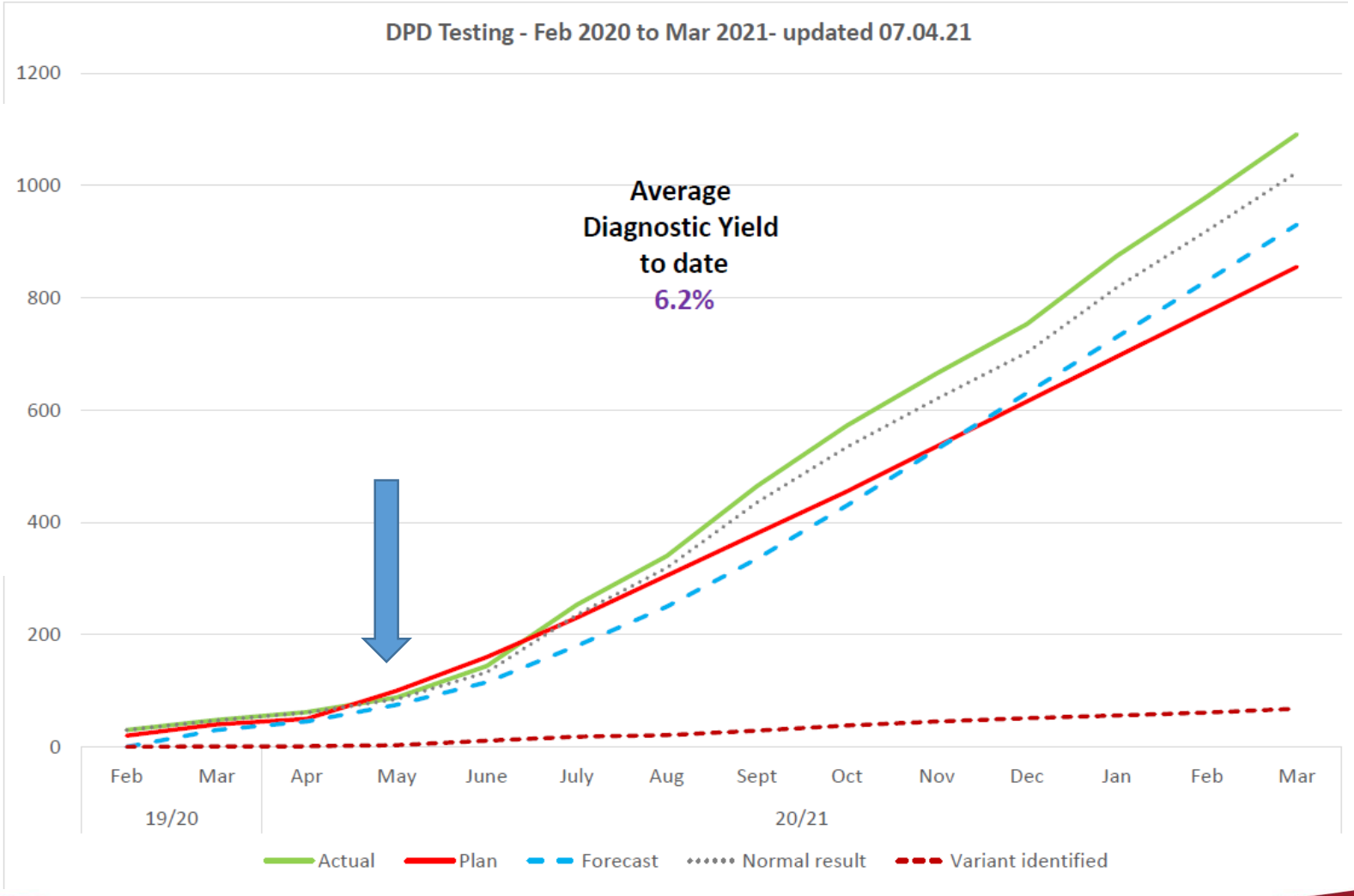
Result	Toxicity Risk	Treatment Recommendations (based in 100,000 genomes project and CPIC guidelines)
No variants detected	Not increased	
c.1905+1G>A heterozygote	Increased	Reduce starting dose to 50%; follow by titration of dose based on toxicity.
c.1905+1G>A homozygote	Increased	Do not use 5FU or capecitabine therapies.
c.1679T>G heterozygote	Increased	Reduce starting dose to 50%; follow by titration of dose based on toxicity.
c.1679T>G homozygote	Increased	Do not use 5FU or capecitabine therapies.
c.2846A>T heterozygote	Increased	Reduce starting dose to 50%; follow by titration of dose based on toxicity.
c.2846A>T homozygote	Increased	Reduce starting dose to 50%; follow by titration of dose based on toxicity.
c.1129-5923C>G; c.1236G>A heterozygote	Increased	Reduce starting dose to 50%; follow by titration of dose based on toxicity.
c.1129-5923C>G; c.1236G>A homozygote	Increased	Reduce starting dose to 50%; follow by titration of dose based on toxicity.
Compound heterozygote		To be reported on a case-by-case basis in alignment with CPIC guidelines.

100,000 Genomes Project: Validation and Reporting Guidance for DPYD Variants

DPYD testing – business as usual!

- All Wales roll-out May 2020
- One year on…..
  - 1091 tests at VCC
  - 68 variants
- Treatment plan personalised because of risk of side effects

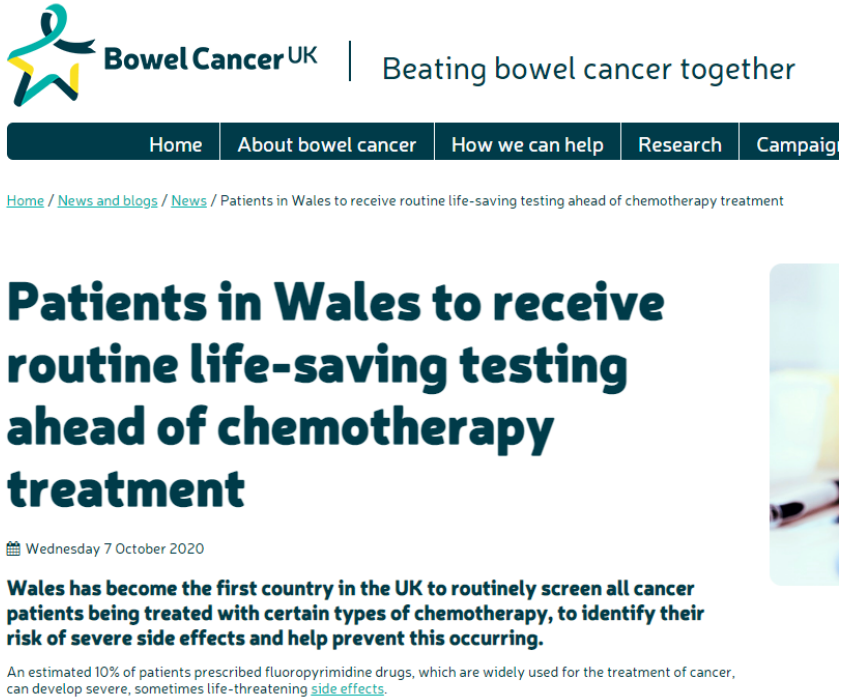
1st UK nation to offer as standard of care



DPYD gene service

- From **February 2020** to **December 2021** a total of **3,801 Welsh patients have undergone testing for DPYD variants**.

- The overall positivity rate for DPYD variants is 6.6%.
- 248 patients have been found to be heterozygous for one of the four common DPYD.
- Three patients have been homozygous or compound heterozygous for DPYD.



Bowel Cancer UK | Beating bowel cancer together

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Home / News and blogs / News / Patients in Wales to receive routine life-saving testing ahead of chemotherapy treatment

Patients in Wales to receive routine life-saving testing ahead of chemotherapy treatment

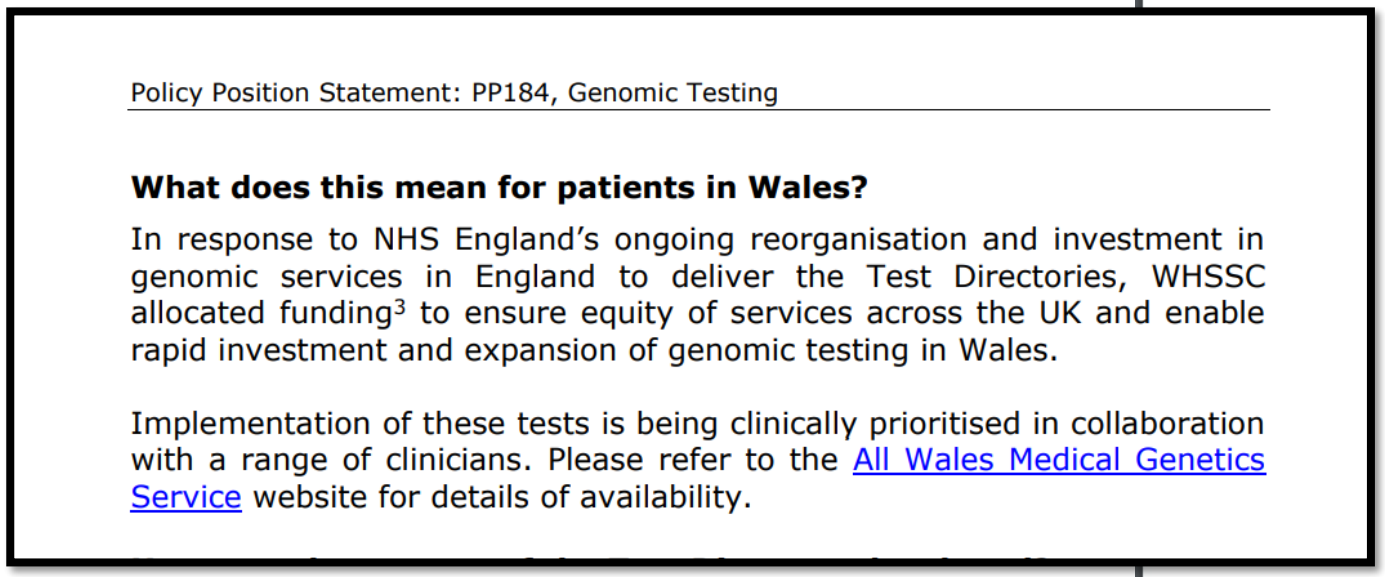
Wednesday 7 October 2020

Wales has become the first country in the UK to routinely screen all cancer patients being treated with certain types of chemotherapy, to identify their risk of severe side effects and help prevent this occurring.

An estimated 10% of patients prescribed fluoropyrimidine drugs, which are widely used for the treatment of cancer, can develop severe, sometimes life-threatening side effects.

From pilot to NHS commissioning

WHSSC commissioning approach altered in June 2020 to reflect GLH reorganisation & Test Directory

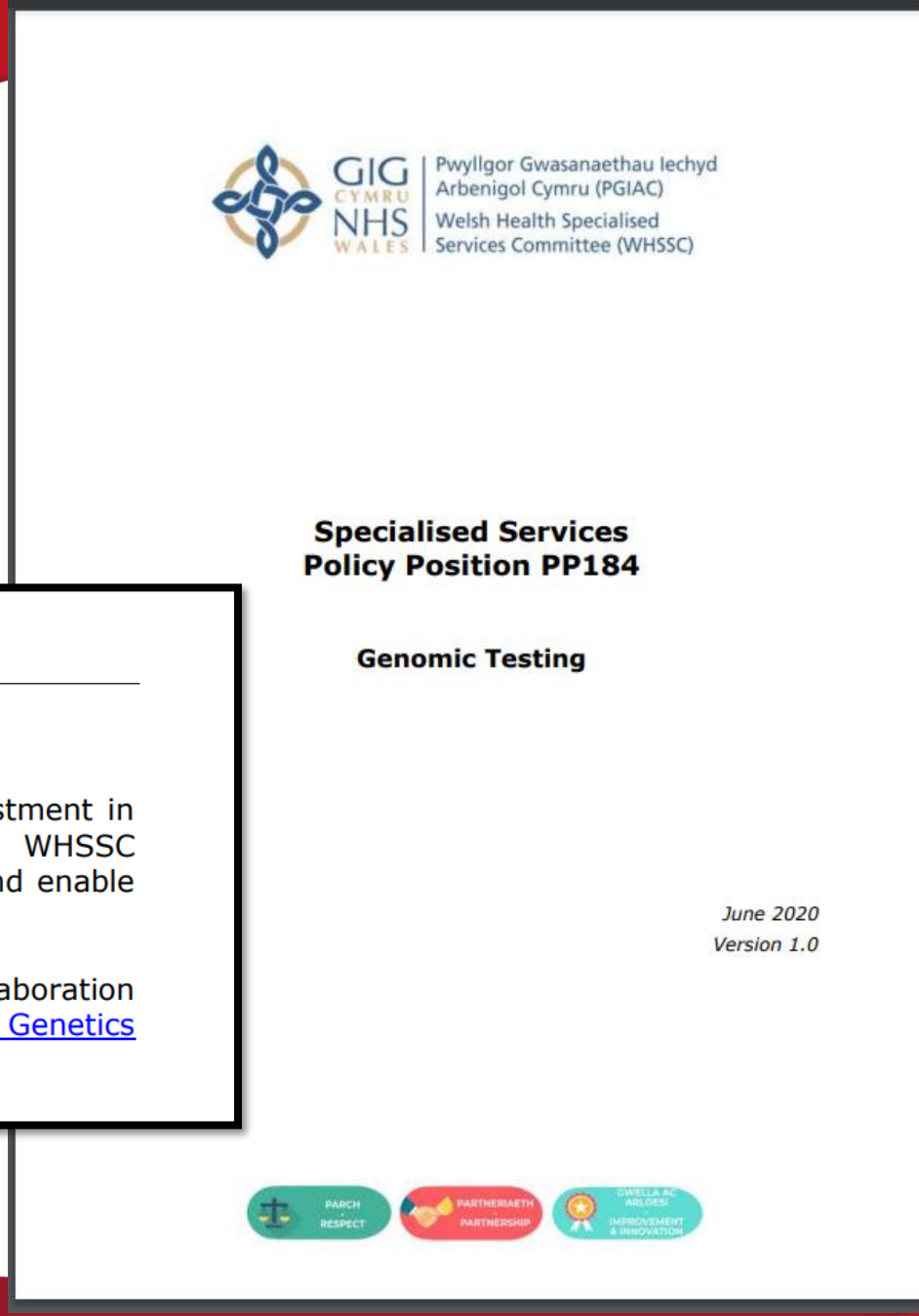


Policy Position Statement: PP184, Genomic Testing

What does this mean for patients in Wales?

In response to NHS England's ongoing reorganisation and investment in genomic services in England to deliver the Test Directories, WHSSC allocated funding[3] to ensure equity of services across the UK and enable rapid investment and expansion of genomic testing in Wales.

Implementation of these tests is being clinically prioritised in collaboration with a range of clinicians. Please refer to the All Wales Medical Genetics Service website for details of availability.



GIG CYMRU NHS WALES
Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)
Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Policy Position PP184

Genomic Testing

June 2020
Version 1.0

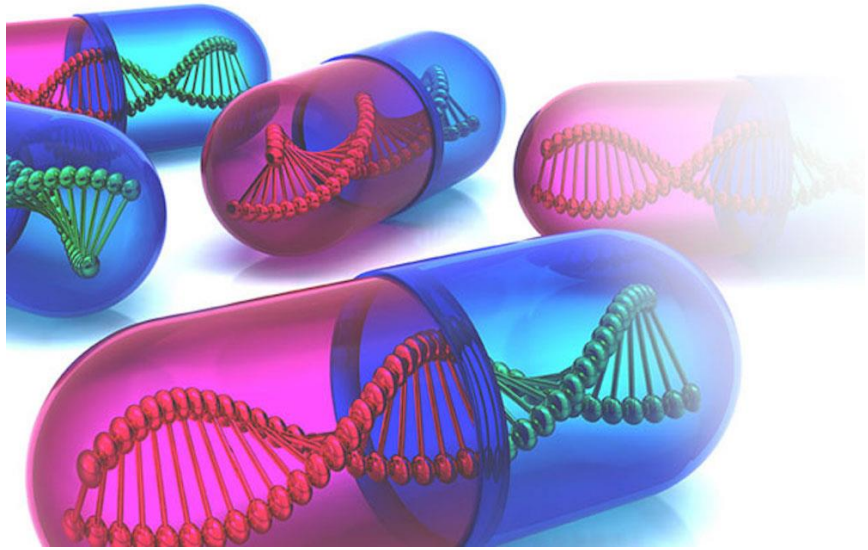
The Genomic Test Directory outlines the full range of genomic tests that are commissioned for the NHS in England. From 2021 it is updated annually.

AWMGS

National Genomic Test Directory

Colorectal Carcinoma	M1.1	Multi-target NGS panel - small variant (KRAS, NRAS, BRAF, MLH1, MSH2, MSH6, PMS2, POLD1, POLE, DPYD)	KRAS, NRAS, BRAF, MLH1, MSH2, MSH6, PMS2, POLD1, POLE, DPYD	Small variant detection	Panel	Known colorectal carcinoma, eligible for anti-EGFR therapy and / or BRAF status required as per NICE Guidelines algorithm for molecular testing for Lynch syndrome and or no IHC result for Lynch testing. Please refer to Rare & Inherited disease directory R210 Lynch syndrome for full eligibility criteria. Patient planned to receive fluoropyrimidine treatment
	M1.2	KRAS hotspot	KRAS	Small variant detection	Simple targeted mutation testing	Known colorectal carcinoma, eligible for anti-EGFR therapy, in rare cases where this cannot be delivered by panel testing NB will be subject to close audit
	M1.3	NRAS hotspot	NRAS	Small variant detection	Simple targeted mutation testing	Known colorectal carcinoma, eligible for anti-EGFR therapy, in rare cases where this cannot be delivered by panel testing NB will be subject to close audit
	M1.4	MSI Testing	N/A	Microsatellite instability analysis	Microsatellite instability	Known colorectal carcinoma, when MMR IHC not possible / not performed, as per NICE Guidelines algorithm for molecular testing for Lynch syndrome. Please refer to Rare & Inherited disease directory R210 Lynch syndrome for full eligibility criteria.
	M1.5	MLH1 promoter hypermethylation	MLH1	Methylation analysis	Targeted mutation testing	Known colorectal carcinoma, as per NICE Guidelines algorithm for molecular testing for Lynch syndrome. Please refer to Rare & Inherited disease directory R210 Lynch syndrome for full eligibility criteria.
	M1.6	Multi-target NGS panel - structural variant (NTRK1, NTRK2, NTRK3)	NTRK1, NTRK2, NTRK3	Structural variant detection	Panel	Patient's clinical status means they are eligible for an NTRK inhibitor in the event an NTRK rearrangement is detected
	M1.7	DPYD hotspot	DPYD	Small variant detection	Simple targeted mutation testing	Patient planned to receive fluoropyrimidine treatment Delivered via germline testing

Pharmacogenomics Test Evaluation Working Group Introductory Meeting



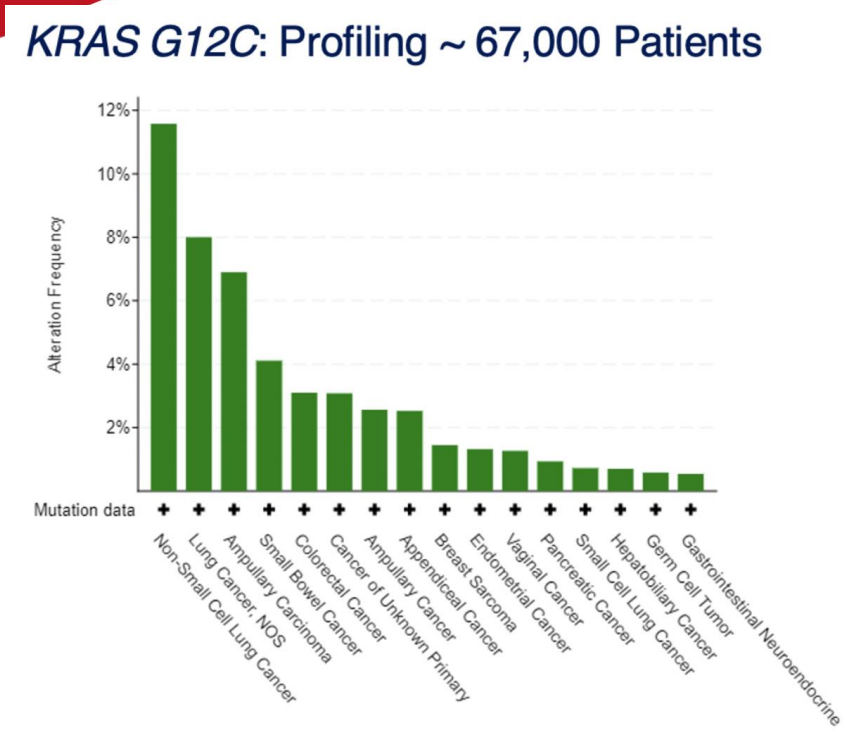
The ‘*first*’ drug-gene pair test commissioned in NHS Wales

Patient story: Patient X presented with rectal bleeding to their GP.

- Referred for endoscopy and diagnosed with rectal cancer, resection in 2019.
- Received adjuvant treatment which had to be halted due to a reaction to chemo as the patient was found to have a DPYD variant.
- Patient had a relapse. Due to the DPD variant, any 5FU treatment would have been risky. 5FU treatment is usually one of the main types of chemotherapy available for rectal cancer patients. As such, this patient had mostly exhausted their standard of care options.

- **2022** The genetic service and the medical oncology teams work together to identify suitable treatments in any potential clinical trial.
- The genetic service played a vital role in identifying a rare 'KRAS G12C' variant (which is present in less than 5% of colorectal cancers). This enabled us to enrol the patient into a clinical trial (drug = Sotorasib).
- The patient has had a **significant response** to this new trial treatment on the latest imaging.

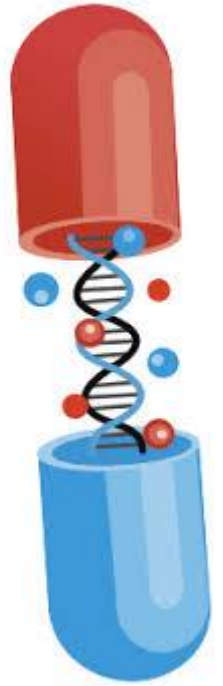
This is an excellent example of personalised care/pharmacogenomics and highlights the value of genomics in improving care for cancer patients.



Where next…

Adverse drug reactions (ADRs)

- Contribute to 6.5% of hospital admissions.
- Estimated to cost the NHS (across the UK) £466 million annually.
- Up to 20%-30% of ADRs could be prevented by pharmacogenetic testing



Working with UK Partners

- In 2020 - Wales signed as a partner the UK Government's strategy Genome UK: The Future of Healthcare

Genome UK: the future of healthcare (publishing.service.gov.uk)

- In March 2022 - Wales agreed to a set of shared commitments and principles to deliver better health outcomes across the UK over 2022-25

Genome UK: shared commitments for UK-wide implementation 2022 to 2025 - GOV.UK (www.gov.uk)

2020

AWMGS

HM Government

GENOME UK

The future of healthcare

3. Pharmacogenomics

Genetic variants in an individual can be used to predict the likelihood that a particular drug will (a) be effective and (b) cause unintended harm through an adverse reaction.

Adverse reactions to medications account for 6.5% of UK hospital admissions and result in a median hospital stay of eight days. Admissions related to Adverse Drug Reactions (ADRs) cost the NHS an estimated £466m annually.[5]

Increasing routine genomic testing in the NHS particularly in England includes relevant targets to guide treatment or eligibility for clinical trials particularly in cancer. This ambition was set out in NHS England's 'Improving outcomes through Personalised Medicine'[6] vision published in 2016.

To further understand the opportunity to introduce pharmacogenomic panels for gene drug pairs for more common medicines, NHS England and NHS Improvement and Genomics England have established a pharmacogenomics working group, composed of experts from across the UK. This group has been reviewing the evidence to understand the implication of implementing targeted pharmacogenomic testing in the NHS and the approach to implementation including data and messaging requirements.

The Welsh Government's Genomics for Precision Medicine Strategy[7] notes the anticipated increase in the clinical utility and requirement for pharmacogenetic testing in the near future and advises that services will be prioritised based on clinical need and Welsh expertise. A commitment is made to release funding for genomic investigations through the substitution of more costly investigations, or the cost-avoidance of treatments where these will be ineffective or harmful. The Medicines Strategy for Wales[8] commits to reducing the burden of adverse drug reactions. A pilot study is underway to address and inform the challenges of implementing a national pharmacogenetics service in Wales. The outcomes of the pilot study will be to direct future testing strategy for patient benefit and identify further funding opportunities.

In December 2022, Welsh Government published the ‘Genomics Delivery Plan for Wales 2022-2025’ supporting the ambition to further expand the development of pharmacogenomics services in Wales

Eluned Morgan MS
Minister for Health and Social Services

Suzanne Rankin
Senior Responsible Officer, Genomics Partnership Wales

Developing an NHS pharmacogenomics service for Wales

- Develop a pharmacogenomics plan which will outline the processes for the effective implementation of the service, and which recognises the importance of multi-professional education and training, clinical pathway development, information technology and laboratory practice.
- Establish the ‘National Pharmacogenomics Group’ to ensure that there is a multidisciplinary, coordinated national approach with defined clinical and academic input to the development and introduction of pharmacogenetic services in Wales.

- Establish, within the All Wales Medical Genomics Service, a cost-effective pharmacogene panel service to cover multiple pharmacogenetic targets to inform the present and future prescribing needs.
- Develop appropriate decision-support tools for doctors and pharmacists within electronic health records.

National Pharmacogenomics Group (NPGG)

The National Pharmacogenomics Group (NPGG) was established in 2022 following endorsement of a white paper entitled ‘Pharmacogenetics in Wales’ by the All Wales Medicines Strategy Group (AWMSG) and the Genomics Partnership Wales (GPW) programme board.

Aims to ensure that there is a multidisciplinary, coordinated national approach with defined clinical input to the development and introduction of pharmacogenomic services within Wales.

Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

Partneriaeth Genomeg Cymru
Genomics Partnership Wales

Chair: Professor Dyfrig Hughes

Professor of Pharmacoeconomics, co-director of the Centre for Health Economics and Medicines Evaluation at Bangor University and Director of Impact and Engagement. He is also honorary professor at the Department of Molecular and Clinical Pharmacology, University of Liverpool.

Deputy Chair: Sian Morgan

Education and Training

More recently, in partnership with **Health Education and Improvement Wales (HEIW)**, **Bangor University** have developed a flexible eLearning module to increase pharmacogenomic understanding for the healthcare workforce in Wales. Pharmacy teams and the wider workforce across all care settings in Wales will play a crucial role in the implementation of pharmacogenomics across the health service.

HEIW has funded a part-time pharmacist lead for pharmacogenomics (Sophie Harding)

Some ongoing actions…

- **LEAD PHARMACIST:** PHARMACOGENOMICS PLAN FOR WALES (in draft). Will be shared for approval by the AWMSG in due course

- **DIGITAL HEALTH AND CARE WALES**: DHCW is working towards automating the process of mapping the raw genome data into phenotype (e.g. metaboliser status), and incorporating into clinical decision support tools and within electronic health records.

- **AWMGS** has designed a custom pharmacogenomics panel with Agena using the Veridose core kit on the MassArray system. This includes 80 variants across 18 genes, including DPYD and is currently being validated.

- Evaluation of effectiveness and value (**Bangor University**): DPYD publication (in draft)
- Public awareness (Wales Gene Park, GPW Patient Sounding Board, AWMSG Patient and Public Interest Group)

On the horizon…….

NICE National Institute for Health and Care Excellence

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

Clopidogrel genotype testing after ischaemic stroke or transient ischaemic attack

Final scope

August 2022

2.2 Technology properties

Point-of-care *CYP2C19* genotype testing

Point-of-care testing is a term that describes any analytical test done by a healthcare professional outside the conventional laboratory setting (MHRA 2021). For *CYP2C19* genotyping, these could be done in locations such as acute stroke centres or acute medical wards. In practice, some point-of-care tests may be done in local hospital laboratories to account for need to store reagents at low temperatures or to ensure quality control. Clinical experts highlighted that, if point-of-care tests are used outside of laboratories, it would be important to ensure that necessary training was provided and that ongoing quality assurance was done. Experience of test operator would also be an important consideration for data on point-of-care tests, who may in practice be operated by people with much less experience of doing tests than laboratory personnel.

OR/AND

Laboratory-based *CYP2C19* genotype testing

Genomic testing in the NHS is delivered through a network of 7 Genomic Laboratory Hubs (GLHs). The National Genomic Test Directory outlines the genomic tests that are commissioned for the NHS in England, specifying which tests are available and the patients who are eligible to access a test. *CYP2C19* genotype testing is not currently included in the Test Directory, which is updated annually.

Clinical experts have indicated that there are several technologies already in place in diagnostic genetic laboratories that could be used to implement this testing into routine service. These include both targeted variant detection and DNA sequencing-based approaches. The approach used would likely depend on considerations such as the number of *CYP2C19* alleles being tested for, scale of testing, and required turnaround times. The availability of specific genomic testing platforms available at a local level would also impact on what approach could be used, which can differ between GLHs. Some of the available potential testing approaches are outlined below:

NICE National Institute for Health and Care Excellence

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

Clopidogrel genotype testing after ischaemic stroke or transient ischaemic attack

Final scope

August 2022

National Pharmacogenomics Subgroup meeting.

NICE Guideline. Clopidogrel genotype testing after ischaemic stroke or transient ischaemic attack.

15th January 2024 11am-Midday

AWMGS

Thank you!

Diolch!