Session objectives

- Define the terminology around pharmacogenomics and how these relate to personalised medicine
- Identify the potential role of pharmacy within pharmacogenomics services and how it is has be implemented internationally
- Recognise current pharmacogenomic developments within England, Scotland and Wales.
- Describe why pharmacogenomics is important now and what the vision is for the future

Tonight's session

Session Chair

Sophie Harding – *Pharmacogenomics Lead, RPS*

Our guest speakers

Fleur van Gelder – *Community Pharmacist, Leiden, Netherlands*

Dr Alexandra Murray – *Consultant Clinical Geneticist and Clinical Director, All Wales Medical Genomics Service. Chair, Genomics Partnership Wales Workforce and Training Group.*

Professor Zosia Miedzybrodzka – *Lead Clinician, NHS Scotland Genomics Network. Professor of Medical Genetics, University of Aberdeen. Honorary Consultant Clinical Geneticist, NHS Grampian.*

Professor Kate Tatton-Brown – *Clinical Director and Head of the Genomics Education Programme, HEE. Consultant Clinical Geneticist, St George's University Hospitals NHS Foundation Trust*

ROYAL PHARMACEUTICAL SOCIETY

Demystifying Pharmacogenomics: Pharmacy's Role in Personalised Medicines

Sophie Harding

RPS Pharmacogenomics Lead

Getting familiar with the terminology

1. Genomics is the study of an organisms genome (its DNA) and how that information is applied.

2. Genetics the scientific study of genes and heredity—of how certain qualities or traits are passed from parents to offspring as a result of changes in DNA sequence.

3. Pharmacogenetics - how variation in one single gene influences the response to a single drug.

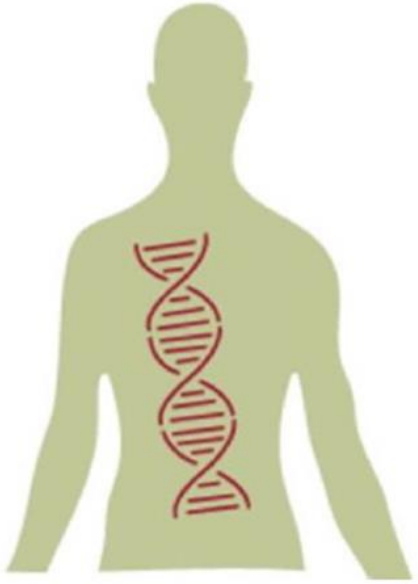
4. Pharmacogenomics (PGx) – study of how an individual's genetic information determines how an individual manages and responds to medicines.

5. Personalised medicine - individualising drug therapy in light of genomic, diagnostic and clinical information.

Personalised medicine

To personalise treatment and surveillance we can use genomic information...

from a person



from a person's cancer

from an infective organism

How is genomics delivering personalised medicine?

Gene therapies use new technology to deliver tailor-made genetic material into a patient's cells to treat disease

- e.g. CAR-T cell therapy for B-cell lymphoma and leukaemia

New targeted treatments based on ↑ understanding of genomic basis for disease & diagnosis

- Classification of cancer by genomic mutation has led to targeted and histology independent treatments

Repurposing existing medicines

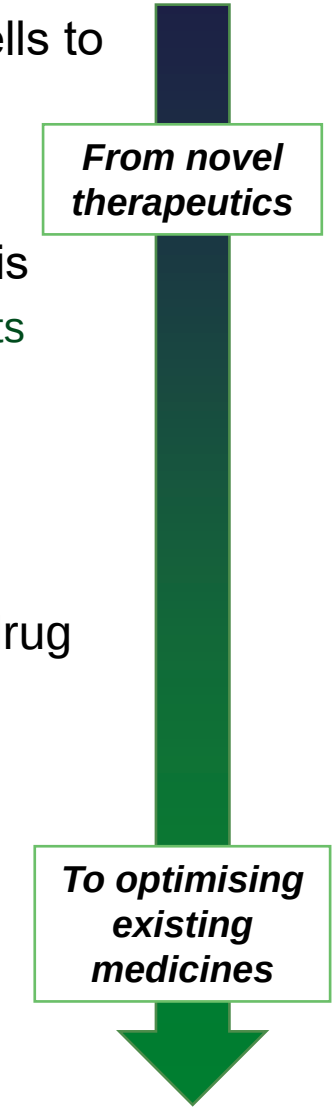
- e.g. Imatinib initially developed for CML, later found to be effective against *KIT*-positive GIST.

Pharmacogenomics guides treatment decisions and dosing, using genomic data to predict drug response

- Can improve drug effectiveness and/or reduce risk of side effects e.g. abacavir & *HLA-B*5701*

Predicting drug resistance

- Serial sampling and genomic testing of tumours can detect early resistance to treatment
- Pathogen genomics predicts antimicrobial resistance e.g. multidrug resistant TB



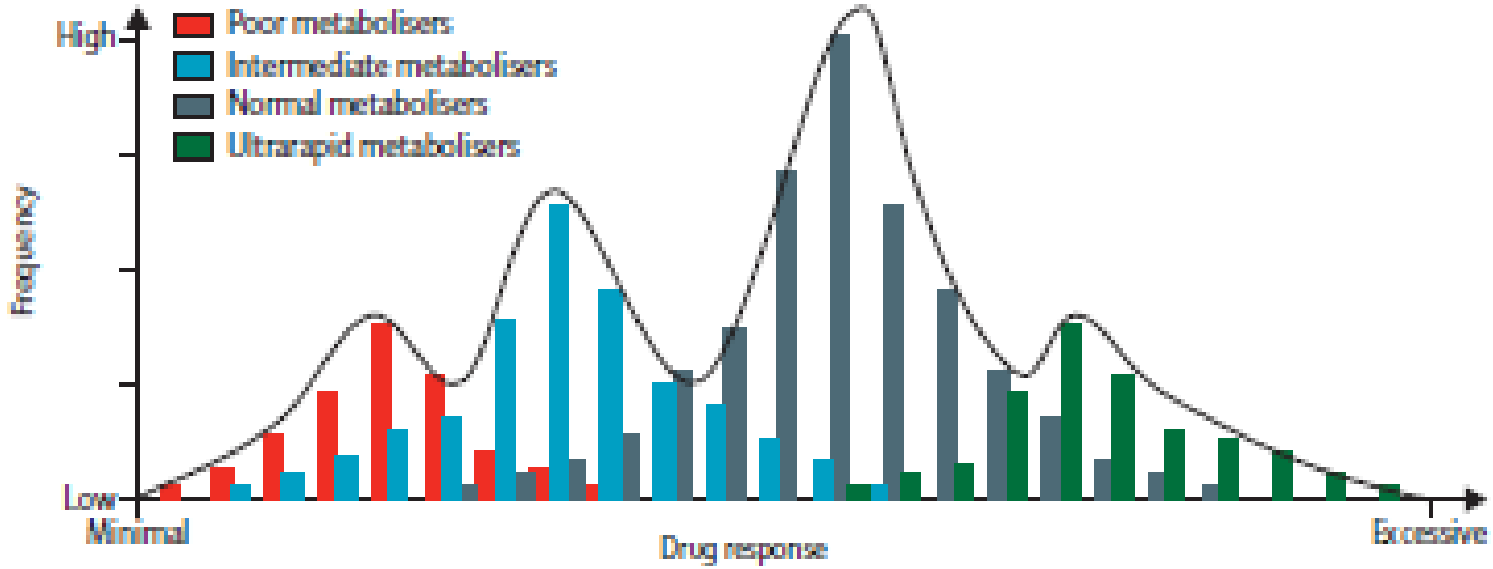
Ref: HEE/GEP slide deck

Pharmacogenomics

Pharmacogenomics **helps us to select the most suitable drug and dose to achieve a better therapeutic response**

Pharmacogenomics (PGx)

Pharmacogenomic variants affect an individual's response to a drug

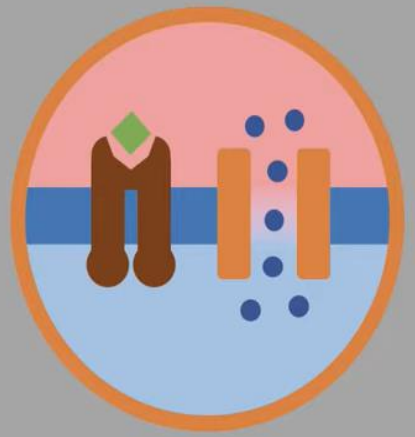


Roden et al (2019)

Ref: HEE/GEP slide deck

What determines our response to medication?

Genetic Variation in Receptors and Transporters

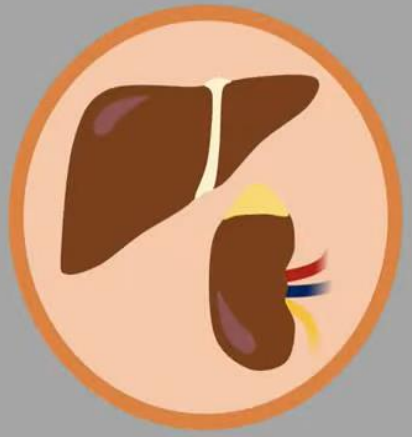


Genetic Variation in Metabolism

Diet (e.g. Grapefruit juice)

Old or young age

Sex

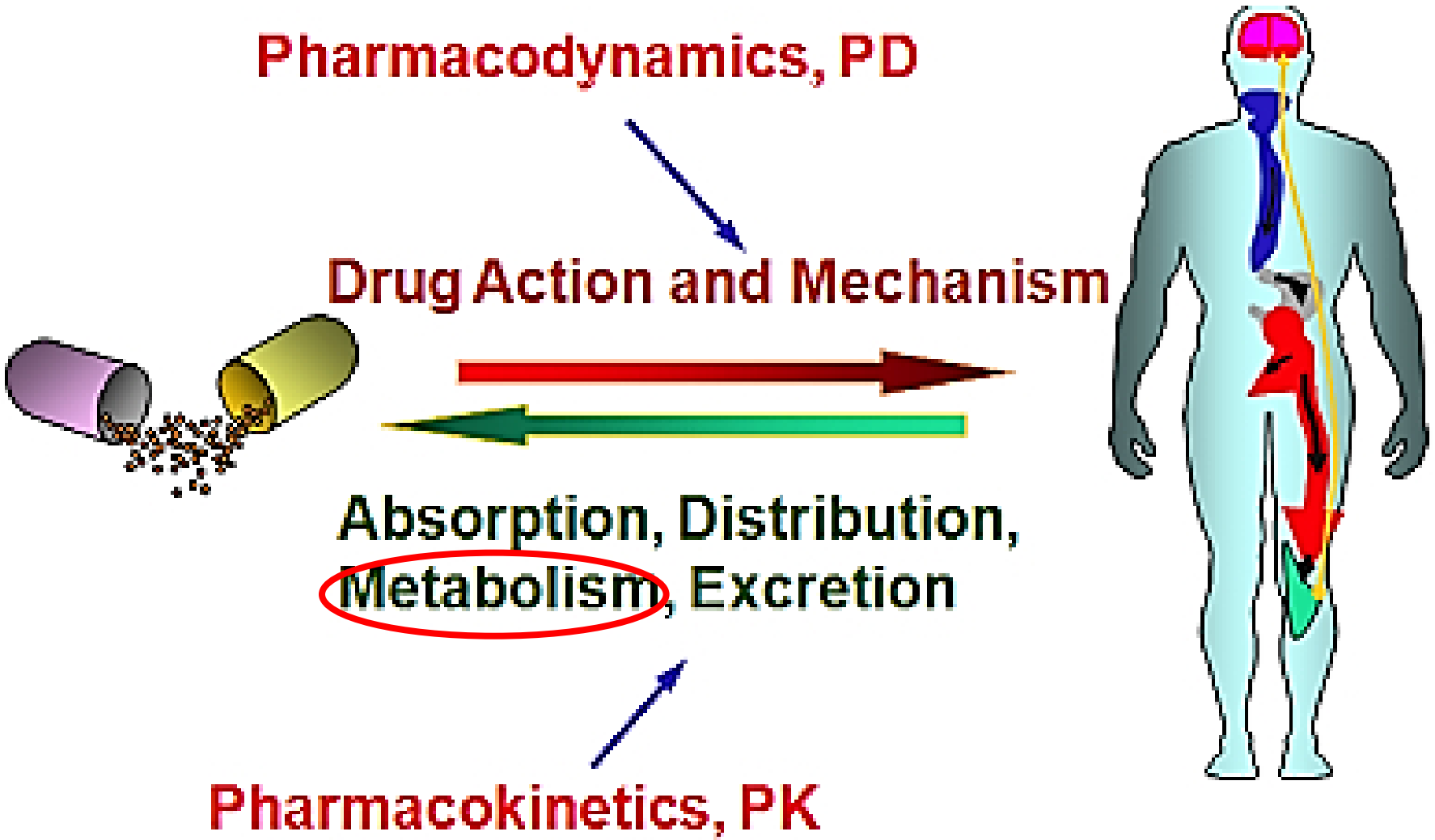


Comorbid Diseases (Liver and Kidney diseases)

Drug-Drug Interactions

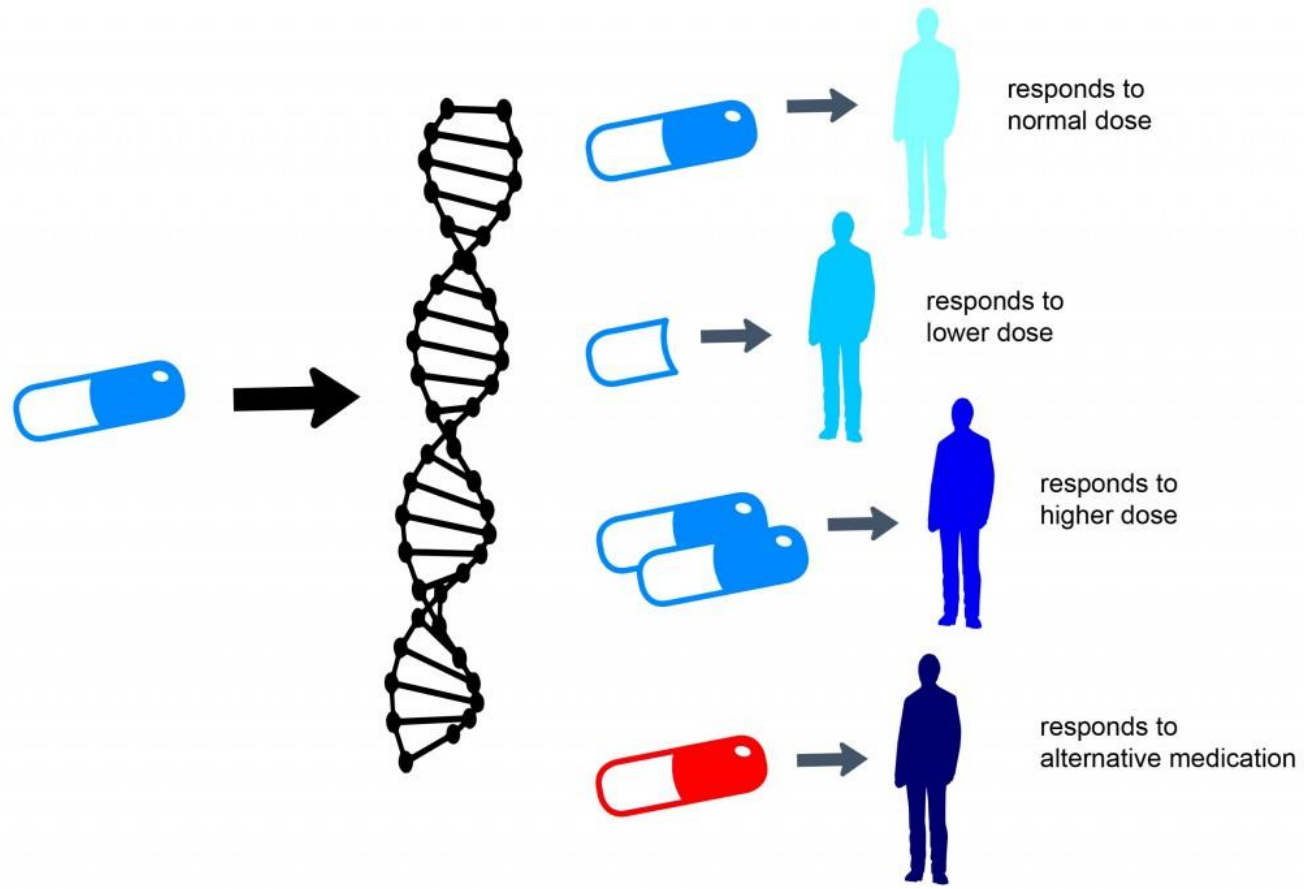
https://medicurioblog.wordpress.com/2020/04/06/pharmacogenomics/

Pharmacokinetics versus Pharmacodynamics



Slide taken from Uni of Exeter lecture slides for Pharmacogenomics module

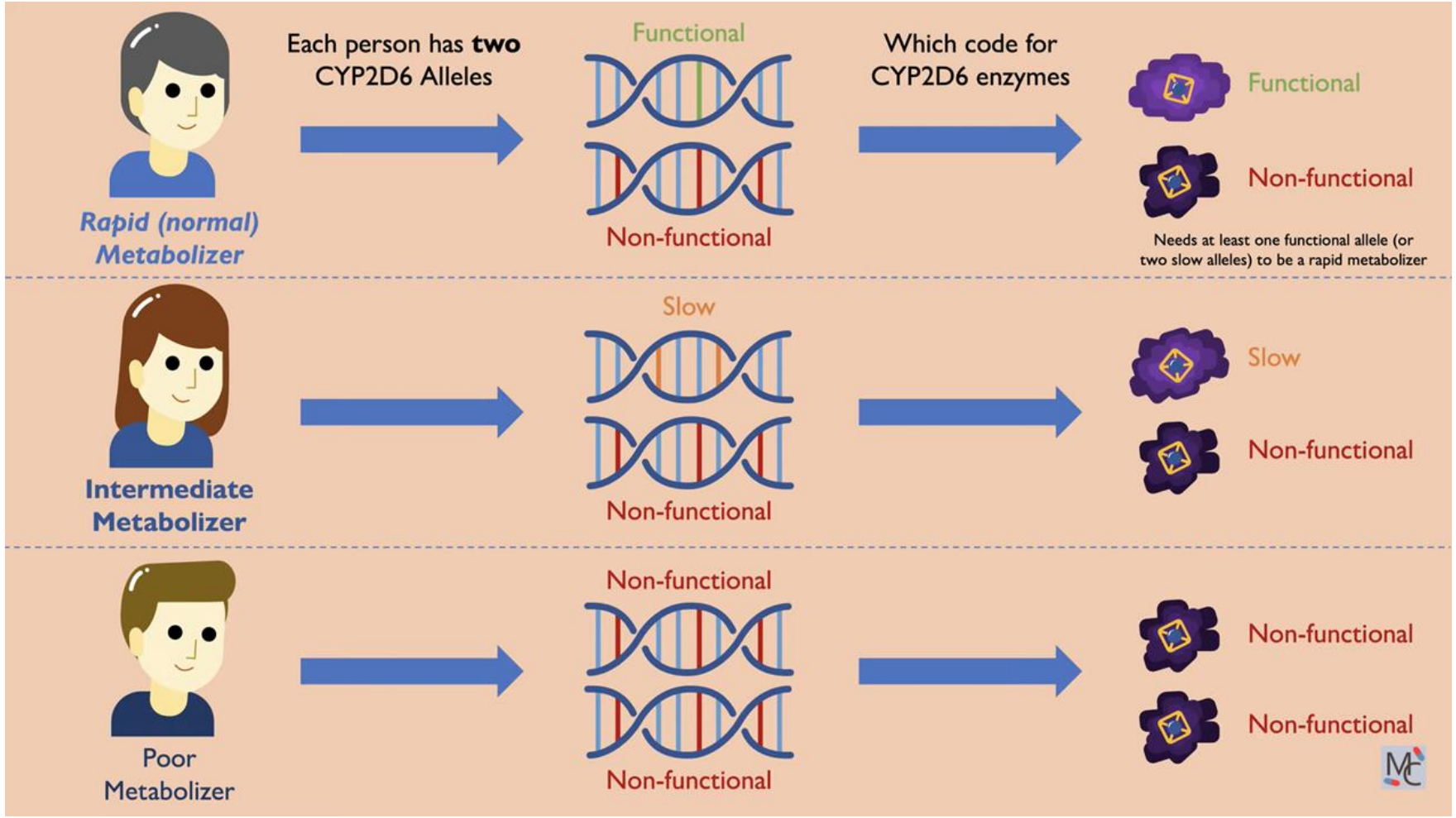
Differences in drug metabolism can affect our response to drugs



Differences in drug metabolism can be caused by variation in our genes….

Slide from Uni of Exeter lecture slides for Pharmacogenomics module

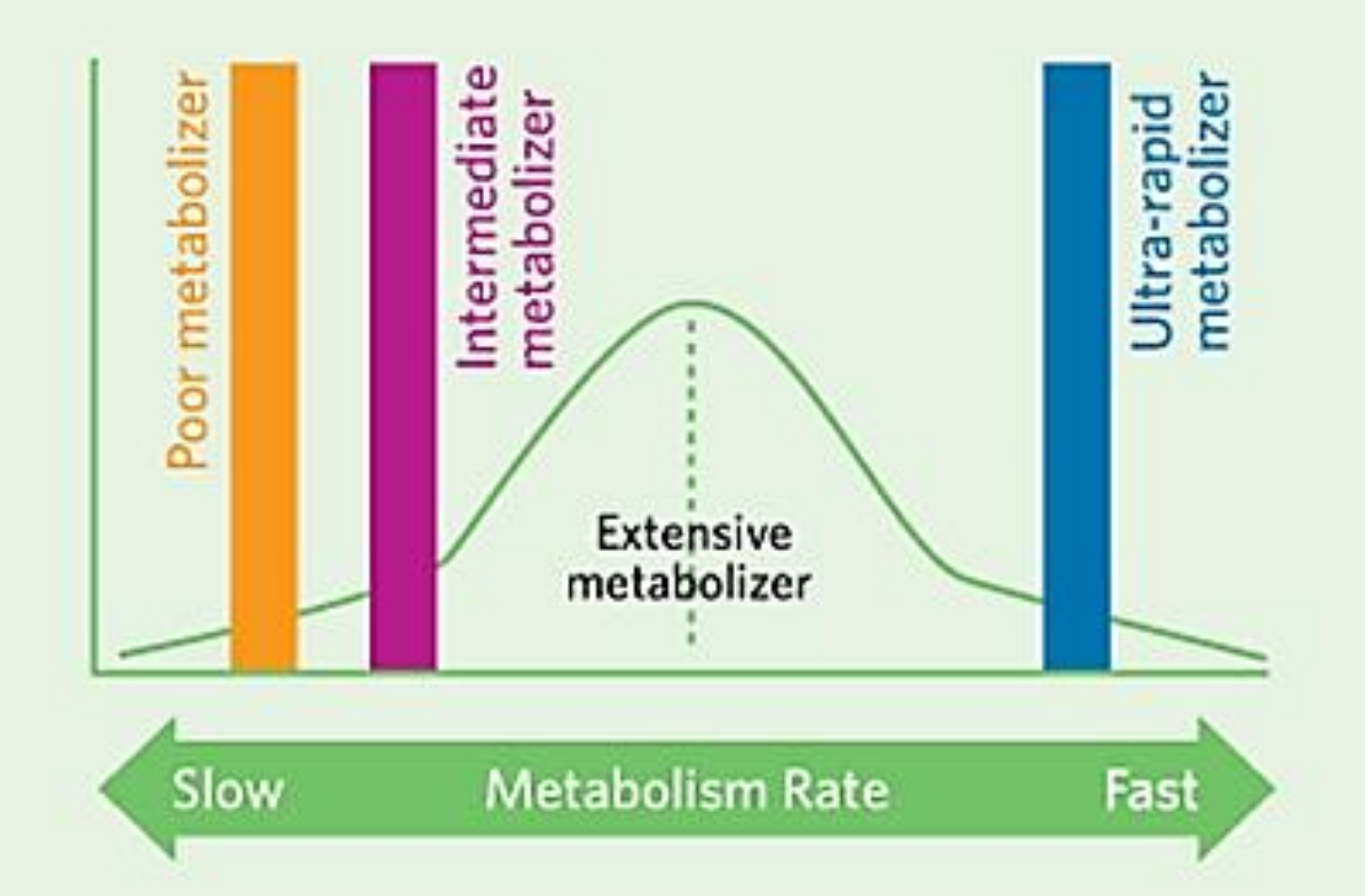
The type of metaboliser you are depends on your genetic code and the corresponding enzyme activity…



https://medicurioblog.wordpress.com/2020/04/06/pharmacogenomics/

Types of metabolisers

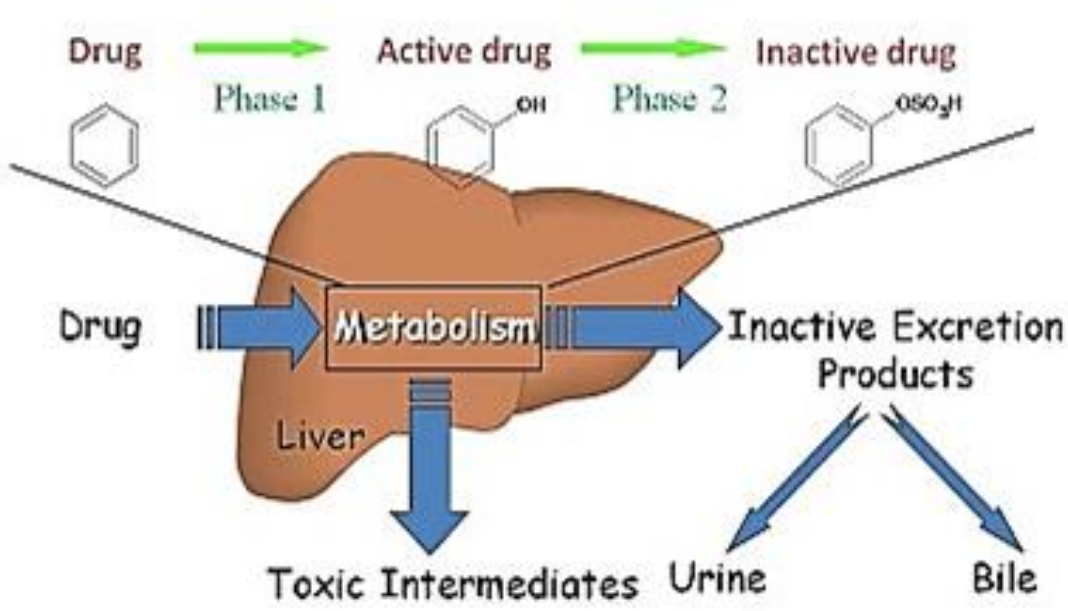
- Poor metaboliser
- Intermediate metaboliser
- Extensive (normal) metaboliser
- Ultra rapid metaboliser

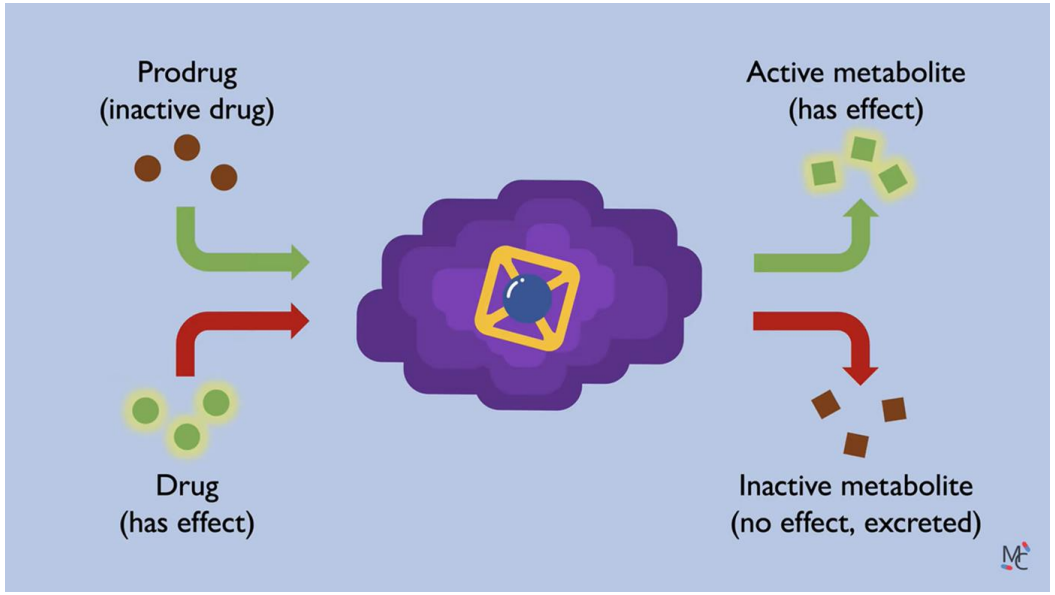


Slide taken from Uni of Exeter lecture slides for Pharmacogenomics module

Types of drugs

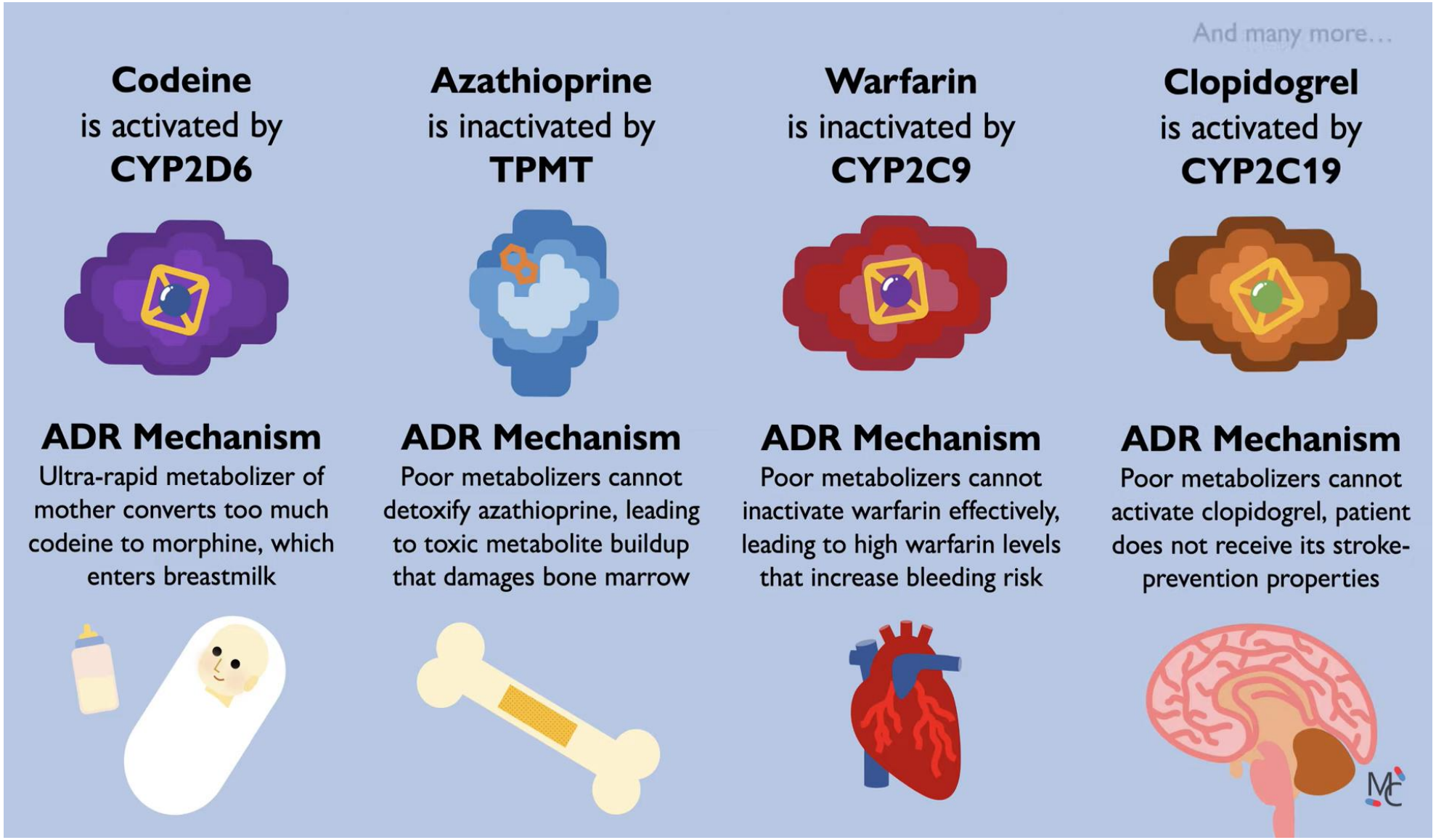
- Prodrugs
  - Codeine
  - Clopidogrel
  - Tamoxifen
- Active drugs
  - Warfarin
  - Omeprazole
  - Phenytoin





https://medicurioblog.wordpress.com/2020/04/06/pharmacogenomics/

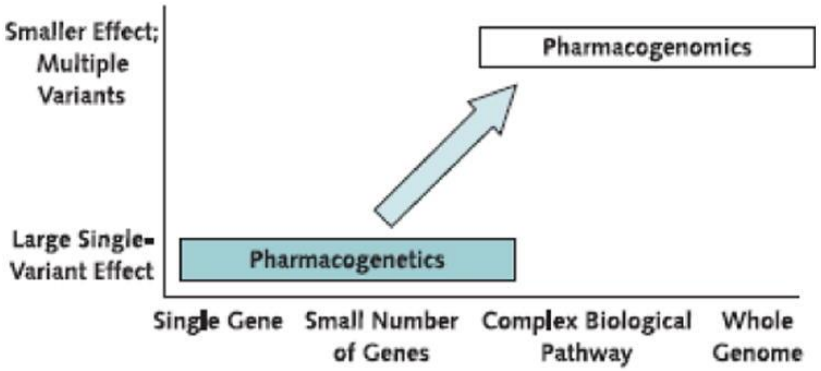
Examples of gene-drug pairs



https://medicurioblog.wordpress.com/2020/04/06/pharmacogenomics/

What is Pharmacogenomics?

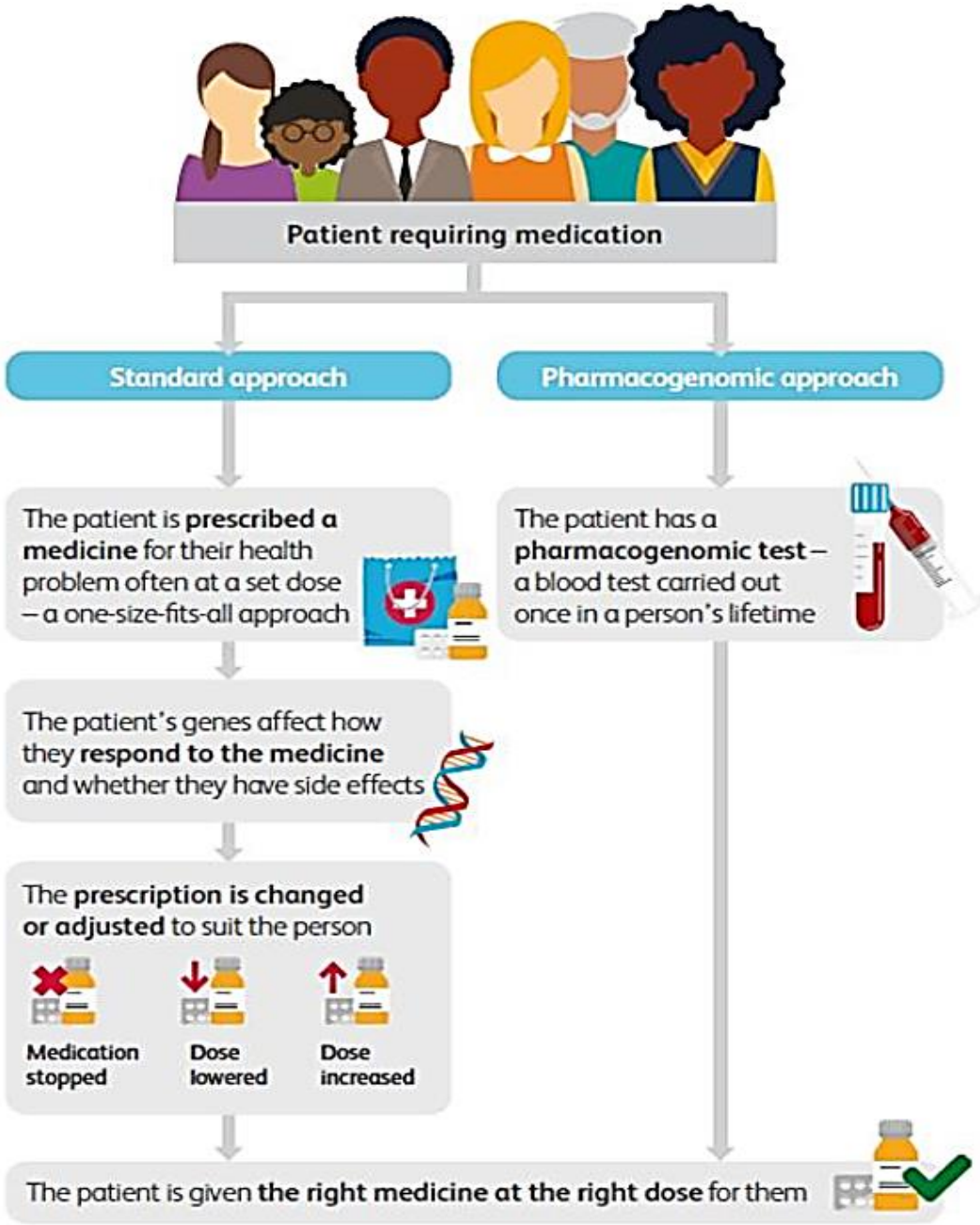
- An example of Personalised medicine
- One aspect of genomics
- Genetic test – single/panel/WGS
- Test result used to guide treatment decisions with consideration for other relevant factors



Roden DM, Altman RB, Benowitz NL, et al. Pharmacogenetics Research Network. Pharmacogenomics: challenges and opportunities. Ann Intern Med. 2006 Nov 21;145(10):749-57.

How PGx impacts patient care

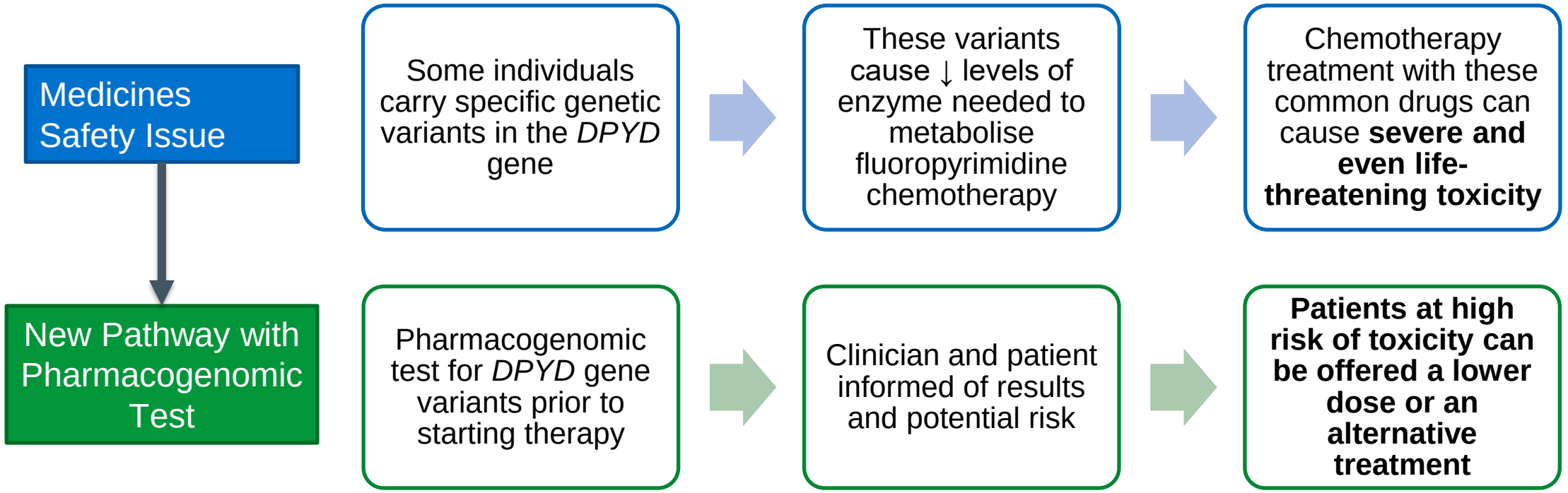
The Pharmacogenomic approach vs standard approach



Ref: BPS ‘ Personalised Prescribing’ document

Pharmacogenomics in Practice: *DPYD* Testing

- *DPYD* pharmacogenomic test offered to all patients prior to starting fluoropyrimidine chemotherapy (5-fluorouracil, capecitabine)



- Anticipated to ↓ severe toxicity (≥ grade 3), ↓ hospitalisation, ↓ deaths, ↓ use of rescue drug

Ref: HEE/GEP slide deck

Pharmacogenomics <u>does not do/is not</u>…

- Sci-fi and only for the future

- Only relevant for specialist healthcare settings
- Doesn’t cover all areas of genomics
- <u>Not</u> the only aspect of genomics where pharmacy can play a significant role

Benefits & Challenges of Pharmacogenomics

Potential Benefits

- Improve patient care and compliance
- Reduce medicine wastage
- Reduced impact on healthcare services
- Improve drug safety
- Test result required once per lifetime
- To ‘personalise’ patient treatment

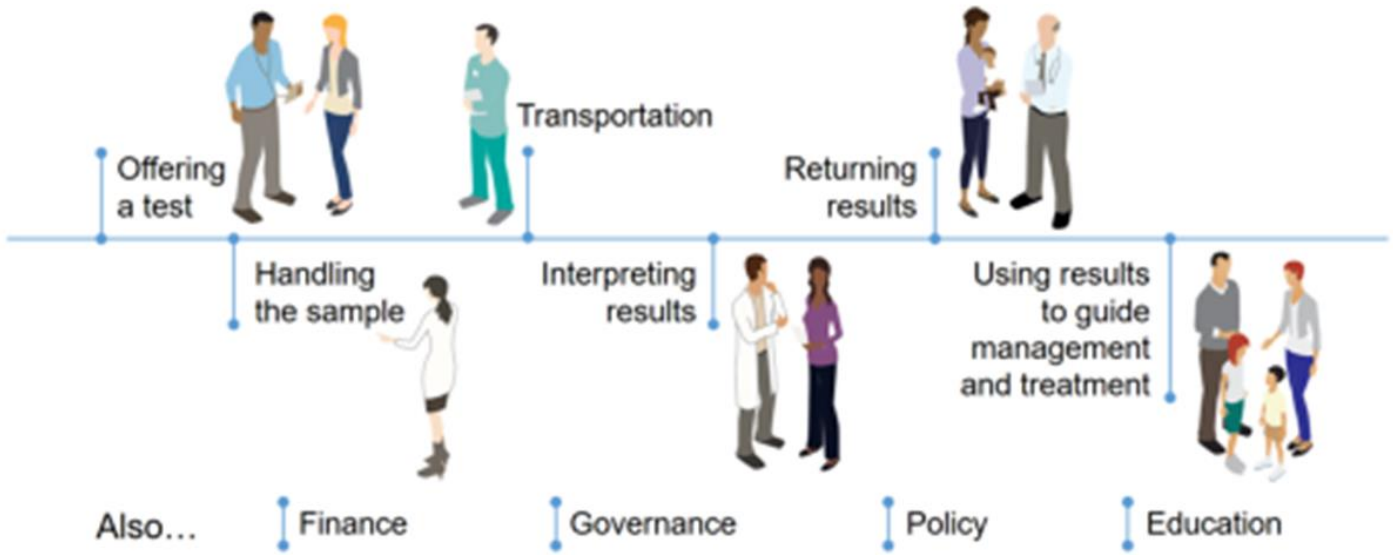
Potential Challenges

- Access to testing
- Data management
- Consent
- Research
- Population diversity
- Up-skilling the workforce
- Education

How does PGx impact you?

- Opportunity to:
  - Increase job satisfaction
  - Raise the profile of pharmacy within healthcare to benefit patient care
  - Influence at the point of prescribing personalised medicines
  - Develop new treatment/clinical pathways
  - Work within a wider MDT to ensure personalised approach

Personalised Medicine Pathway



Slide courtesy of HEE Genomics Education programme

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www.genomicseducation.hee.nhs.uk

Acknowledgements/References

- Dr Vikki Moye – Module Lead for Pharmacogenomics module within MSc Genomic Medicine, Exeter University
- HEE/GEP slide deck

- BPS/RCP - Personalised Prescribing document https://www.bps.ac.uk/getmedia/b43a3dca-1bbf-4bff-9379-20bef9349a8c/Personalised-prescribing-full-report.pdf.aspx
- Roden DM, Altman RB, Benowitz NL, et al. Pharmacogenetics Research Network. Pharmacogenomics: challenges and opportunities. Ann Intern Med. 2006 Nov 21;145(10):749-57.
- https://medicurioblog.wordpress.com/2020/04/06/pharmacogenomics/

A practical approach on the implementation of PGx

Fleur van Gelder

July 2022

Leiden, the Netherlands

Short introduction

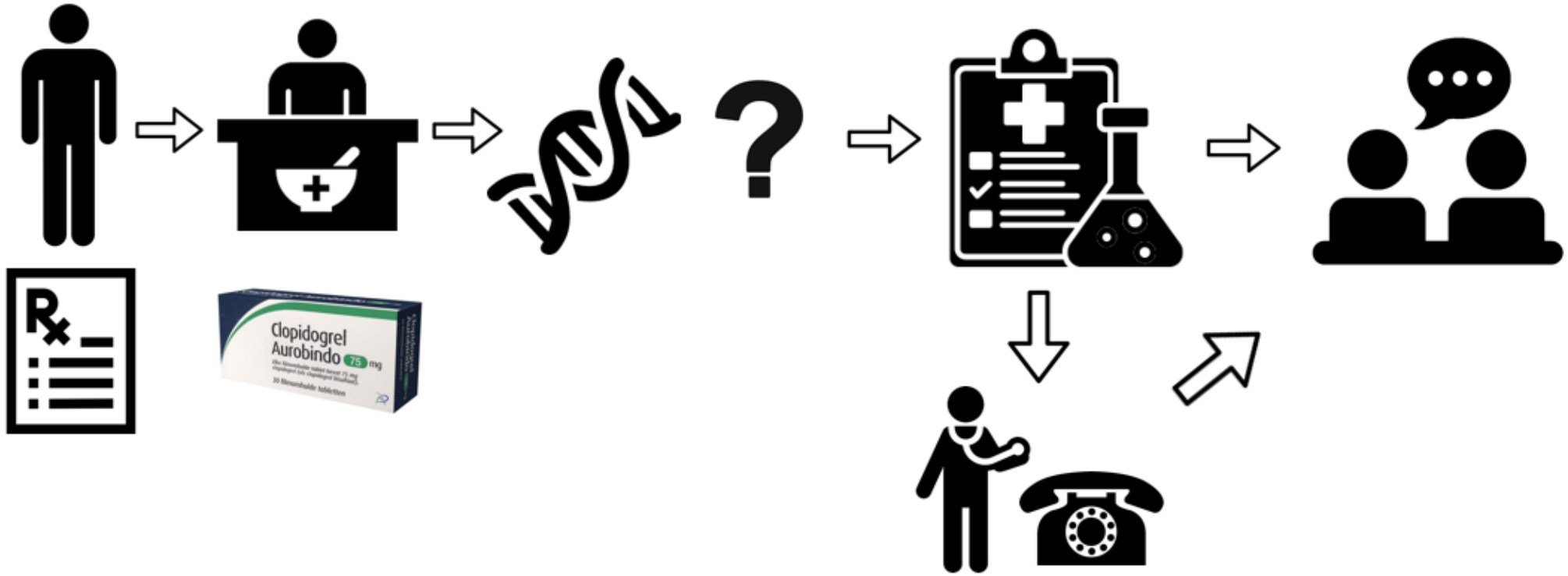
- 6 years Bachelors & Masters degree
  - Groningen

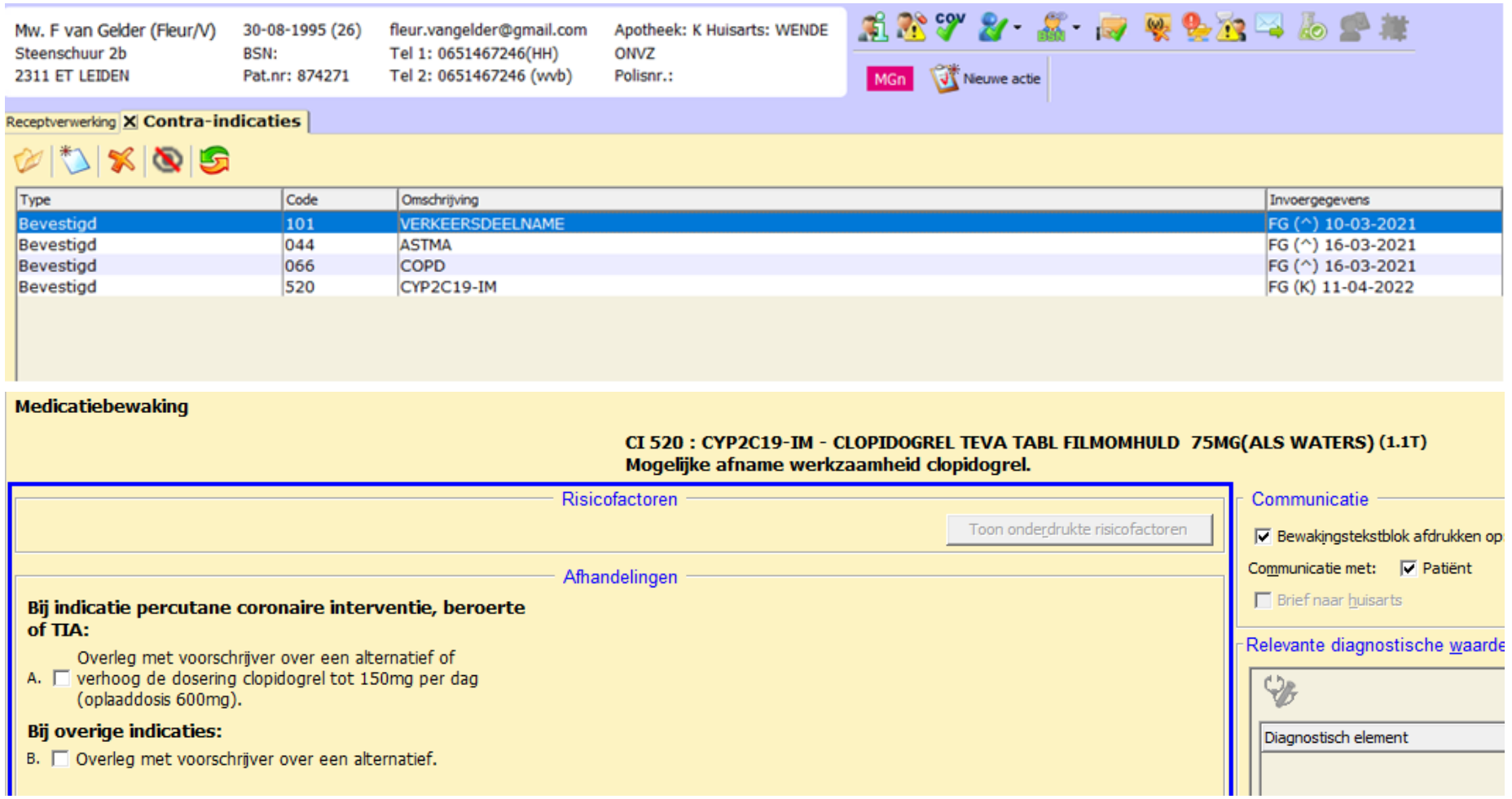
- Additional training to community pharmacist; another 2 years
  - Utrecht

How we started

- PREPARE study: Preventing Adverse Drug Reactions
  - Dr. Jesse J. Swen, Leiden University Medical Center
- CYP2C19 study
  - Switch from Brilique to clopidogrel by PGx

Patient’s journey





Administrative actions

CYP2C19 IM

Apothekertekst

Het risico op ernstige cardio- en cerebrovasculaire incidenten is verhoogd bij een dotterbehandeling of stentplaatsing (percutane coronaire interventie) en bij patiënten met een beroerte of TIA, doordat de genvariatie de activering van clopidogrel vermindert. Bij andere patiënten zijn geen negatieve klinische gevolgen gevonden.

- PERCUTANE CORONAIRE INTERVENTIE, BEROERTE of TIA:
  - kies een alternatief of verdubbel de dosering tot 150 mg/dag (oplaaddosis 600 mg)
    Prasugrel, ticagrelor en acetylsalicylzuur/dipyridamol worden niet of in mindere mate door CYP2C19 gemetaboliseerd.
- OVERIGE indicaties:
  - geen actie nodig

Balietekst

Het risico op ernstige klinische gevolgen is verhoogd bij een dotterbehandeling en/of stentplaatsing (percutane coronaire interventie) en bij patiënten met een beroerte of TIA, doordat de genvariatie de activering van clopidogrel vermindert. Bij andere patiënten zijn geen negatieve klinische gevolgen gevonden.

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- OVERIGE indicaties:
  - geen actie nodig

Voorschrijvertekst

Upscaling the service

Until now:
- CYP2C19
- CYP2D6/CYP2C9/SCLO1B1/VKORC1 by experiencing adverse effects

Starting clopidogrel
- Everybody using clopidogrel needs to be tested

Providing education

Clear work instructions

Patient experience

"The test is very easy to do. I've understood that I am the chosen one for a double dosage. I agreed."

"This was all very clear. The liver didn't process the medication very well. Of course I need it because of my head. I did not get enough medication to prevent a second cerebral infarction from occuring."

Practical tips for implementation

1. Educate the GPs and your colleagues
2. Start by a project or study
3. Which hospitals perform the tests?
    1. What material do they prefer (saliva/blood)?
    2. How do they want it delivered?
    3. How do you receive the results?
4. A collective database with information
5. Make a practical guide, inform patients!

Thank you for your attention

Genomics Education Programme

NHS
Health Education England

The Genomics Education Programme

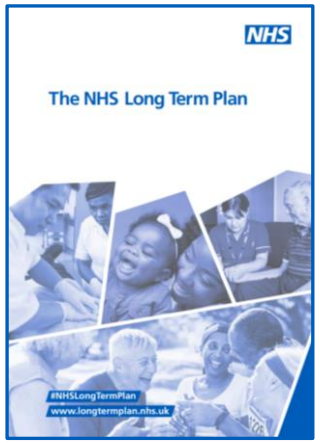


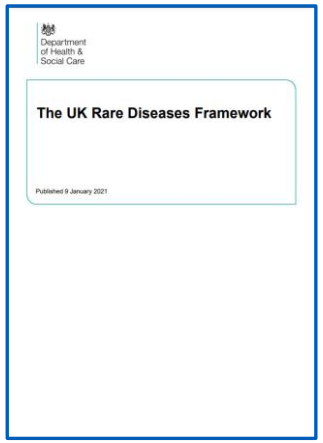

Professor Kate Tatton-Brown,

Clinical Director and head of the Genomics Education Programme

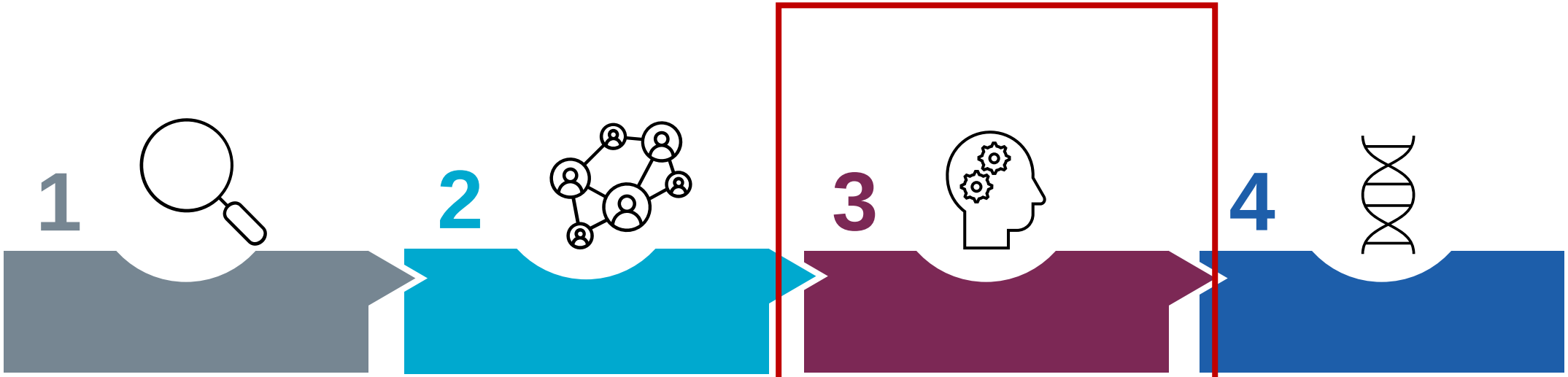
The imperative

To upskill at scale and pace the multi-professional, multi-specialty and multi-regional 1.3 million healthcare workers to adopt and utilise genomic medicine for the diagnosis and management of patients





The aims



Identify NHS workforce needs

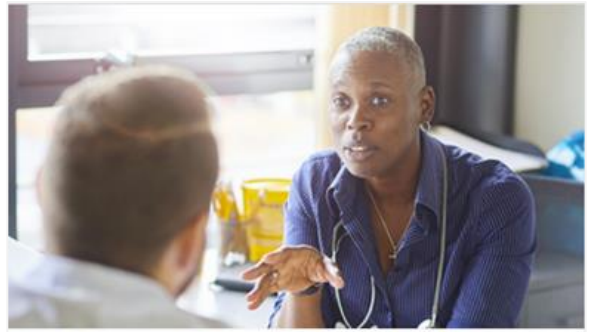
…and build and join networks across the country

…to help educate and develop the NHS workforce

….and increase awareness of genomics across healthcare

GeNotes

- Online ‘just in time’ educational tool – accessed at the point of need
- Provides educational information to support clinicians to make the right genomic decisions
- Aligned to the National Genomic Test Directory
- Two tiers of content:
  - Tier 1: In the Clinic
  - Tier 2: Knowledge Hub



In the Clinic

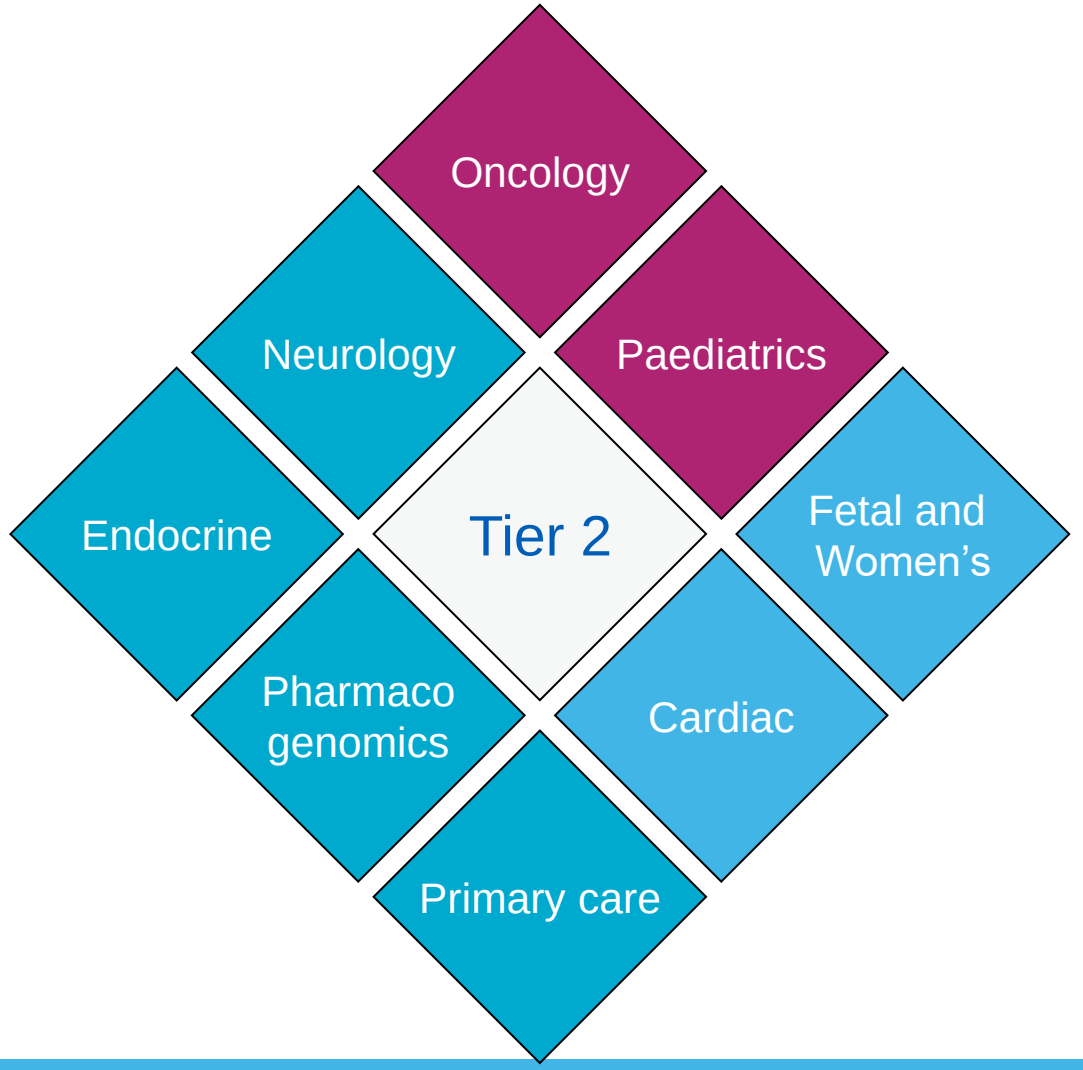
Focused on the point of patient care, these short scenarios look at when to consider genomic testing and what you need to do

Knowledge Hub

From autosomes to X-linked inheritance, this encyclopaedia of resources will support your understanding of genomics in medicine

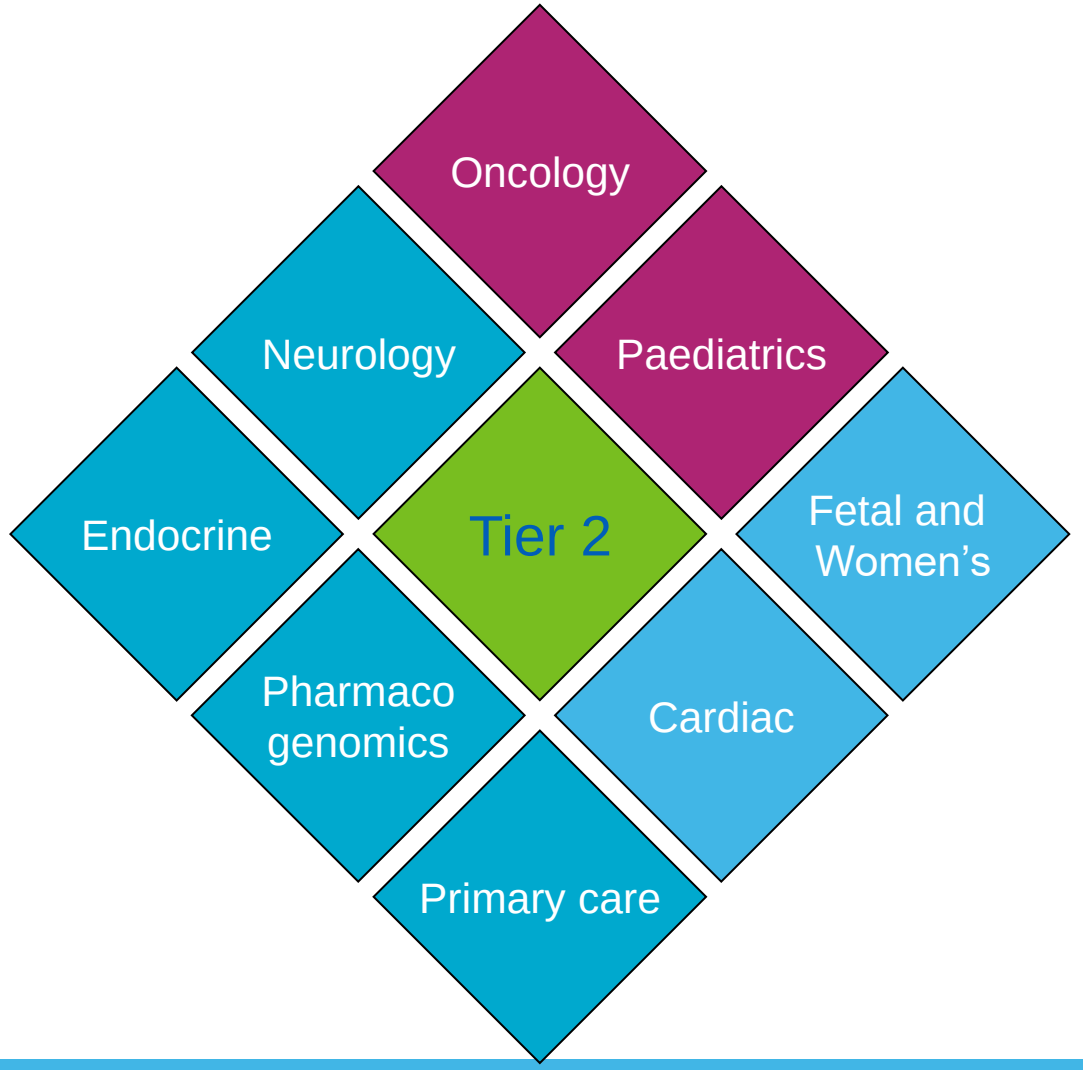
GeNotes "in the clinic"

- Tier 1
- Nine working groups
- Discovery, alpha, private beta phase testing complete
- Oncology public beta phase launched: 15th June
- Others to follow in late Summer/Autumn



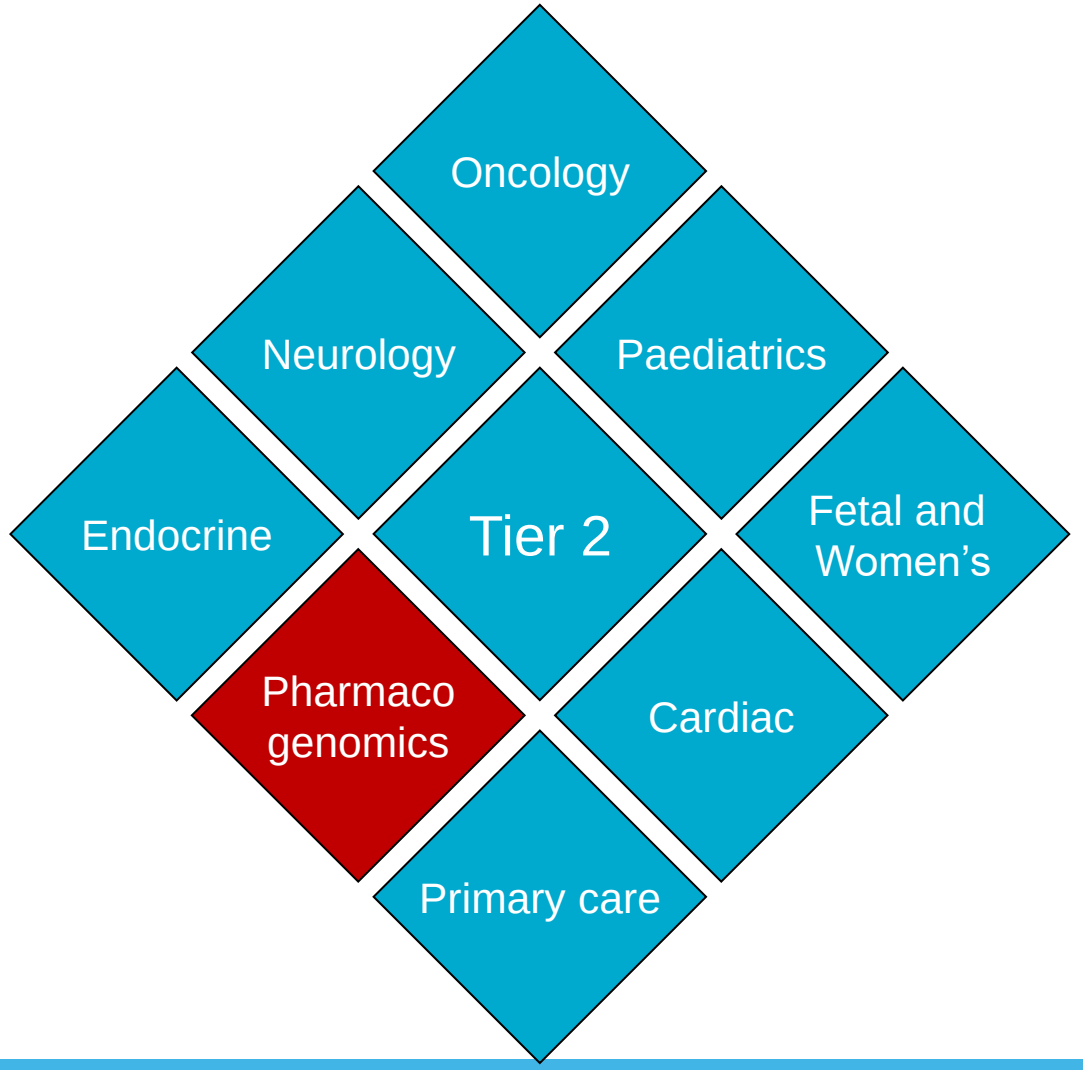
GeNotes "learning hub"

- Tier 2
- Can be used proactively to assemble:
  - Bespoke learning journeys
  - Packages aligned to training requirements
  - Specific learning opportunities ie fundamentals principles

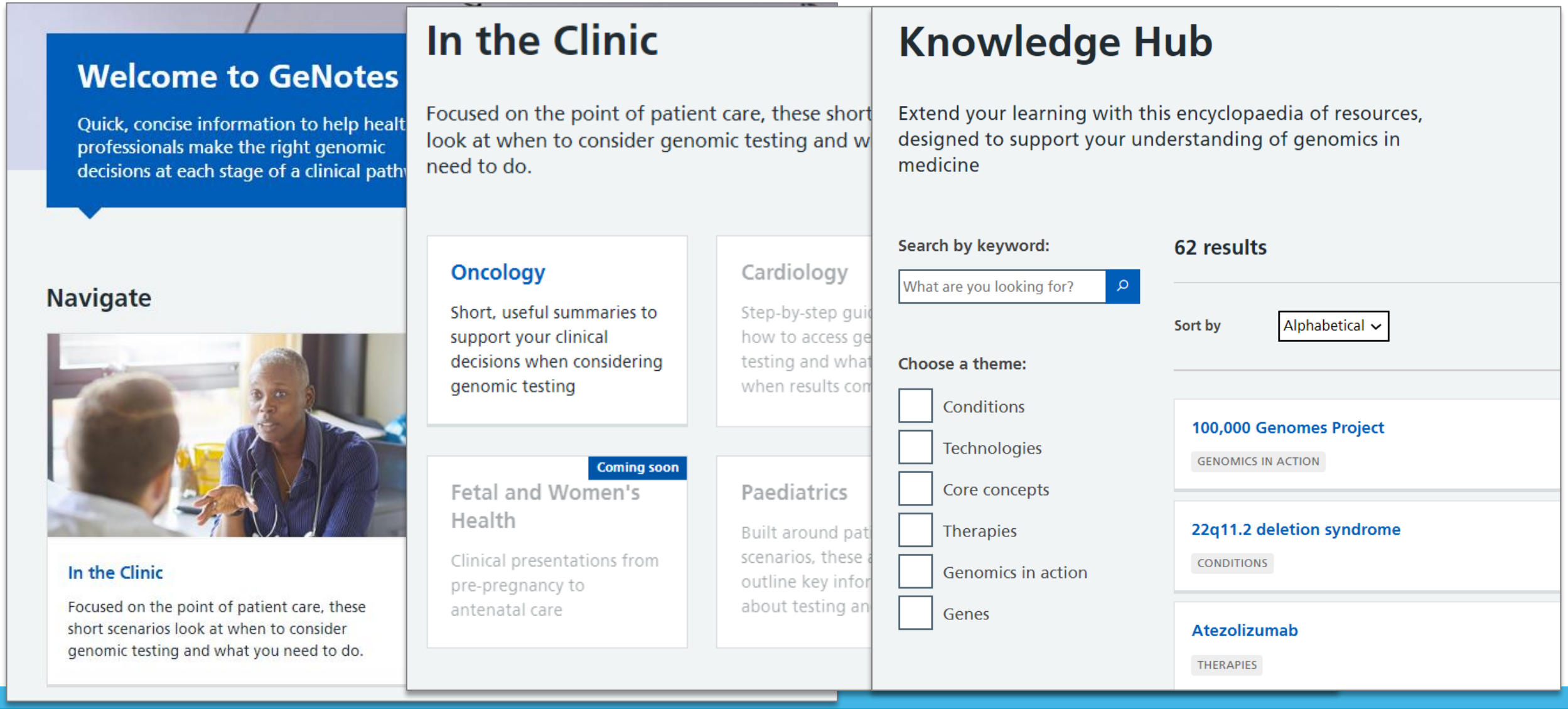


GeNotes Pharmacogenomics

- Working group chaired by Pr Bill Newman and John McDermott
- Multi-professional
- Developing:
  - Tier 1 resources
  - Tier 2 resources
  - Links into other specialty tier 1s



https://www.genomicseducation.hee.nhs.uk/genotes/



@genomicsedu #GenomicsConversation

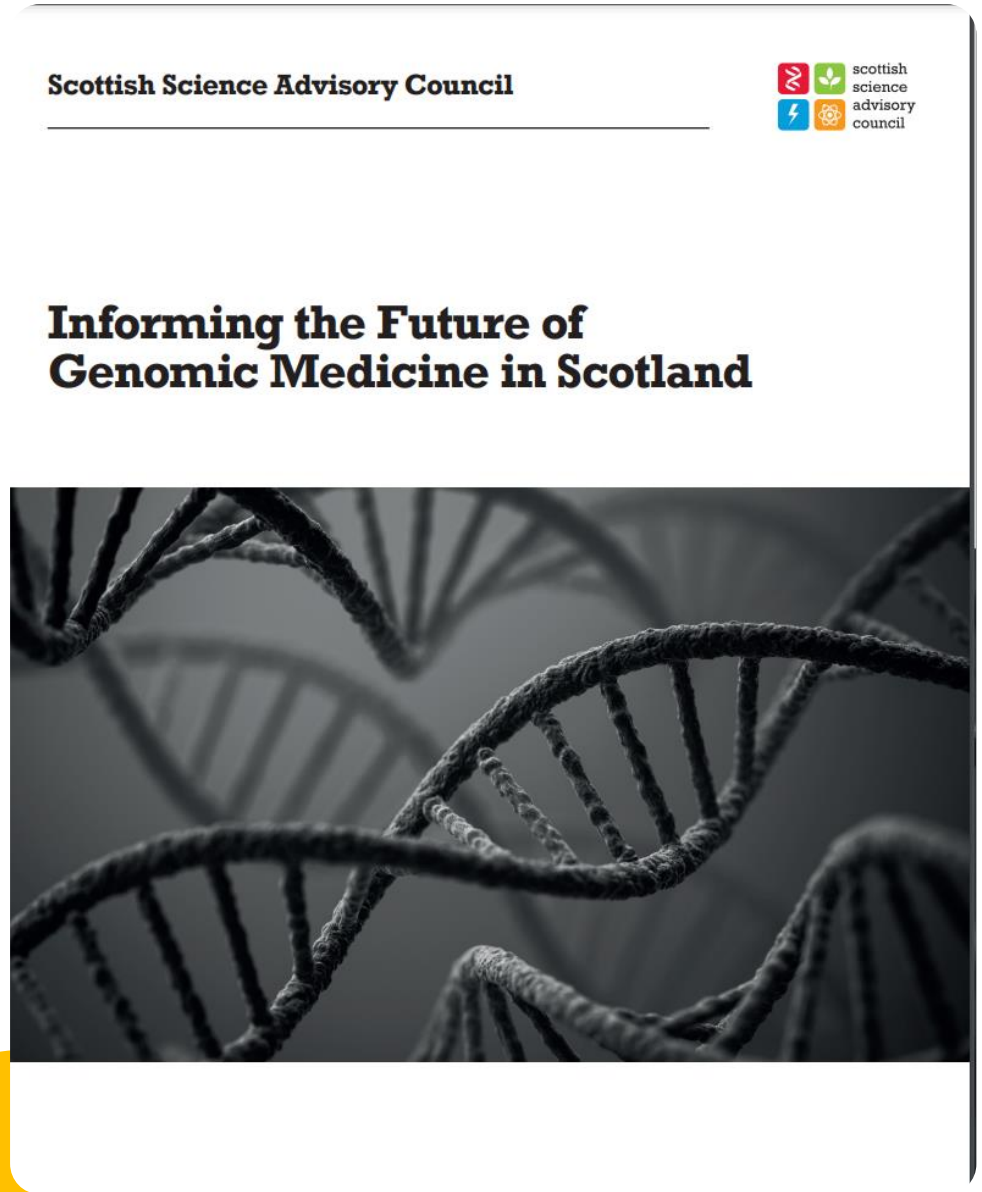
GeNotes Summary

- “Just in time” resource designed for the whole of the NHS workforce;
- Includes an extended learning component;
- Pharmacogenomics working group is shoring up resource for when testing is available;
- Also ensuring relevant signposting into other specialties.

Pharmacogenomics in Scotland so far…

Prof Zosia Miedzybrodzka

Lead Clinician, NHS Scotland Genomics network



SSAC report

- Recommended pharmacogenetics as an important workstream for development
  - Pharmacogenetics consortium established – now subsumed into new network

Pharmacogenomics tests in Scotland

- m. 15558G aminoglycoside ototoxicity
  - All cystic fibrosis patients
  - Otherwise on demand, fast TAT
- DPYD for fluoropyrimides (5FU, capecitabine, tegafur)
  - 5-10% ADR associated with DPD deficiency associated with 5 polymorphisms
  - Each Scottish teaching hospital genomics lab
    - Fast TAT- no transport from centres
    - Specific test for polymorphisms of known function- low cost test & semi-automated reporting
    - Dose reduction or avoid drugs
    - Highly cost-effective- NHSG no admissions with dihydropyramide toxicity since service started
- Not yet substantively funded

“DPYD testing was associated with lower costs and led to better outcomes”

- “Test cost of £38,565 offset by treatment cost savings (£19,292) and inpatient resource savings (£246,983)
- For every 1,000 patients tested prospectively for a DPYD variant, up to 24 serious (grade ≥3) adverse events could be avoided.
- Reduction in the number of HDU/ICU admissions / stays.
- Estimated NHSScotland resource savings £90,000 - £227,000 by implementing a testing strategy.”

- https://shtg.scot/our-advice/pre-treatment-dpyd-genetic-testing-for-patients-who-are-prescribed-chemotherapy-involving-fluoropyrimidines/

Dundee local pilots

- CYP2C19 assay prior to clopidrogel prescription- reduces stroke risk due to ineffective treatment
- TPMT – thiopurinol toxicity
  - Long considered a risk
  - TPMT enzyme assay sporadically in use
  - Test for 3 common variants by Taqman low cost and efficient
- All: Occ. Questions about direct to consumer testing

Acknowledgements

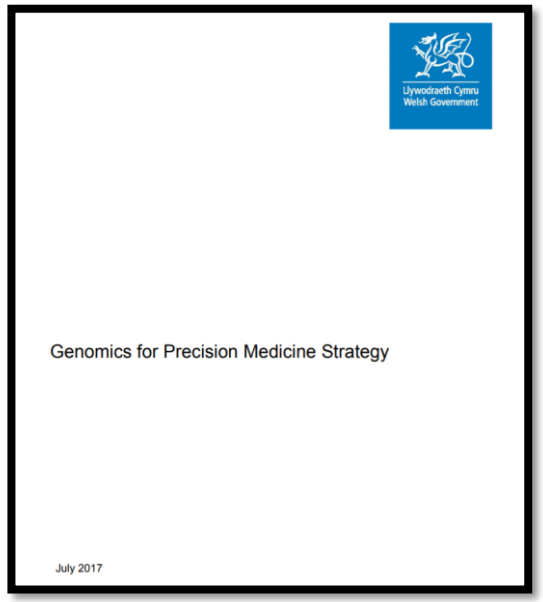
- David Baty, Karina O’Rourke, HIS SHTG
- NHS Scotland Pharmacogenomics consortium

AWMGS

Pharmacogenetics in Wales

Alex Murray, Clinical Director, All Wales Medical Genomics Service

Genomics for Precision Medicine Strategy 2017



- ***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

> *"Working together to harness the potential of genomics to improve the health, wellbeing and prosperity of the people of Wales"*

DPYD testing

Pilot project Velindre Cancer Centre: Jan – May 2020

Aim: Well-governed DPYD testing process

- Standardised, robust process
- 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

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

Home | About bowel cancer | How we can help | Research | Campaig

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

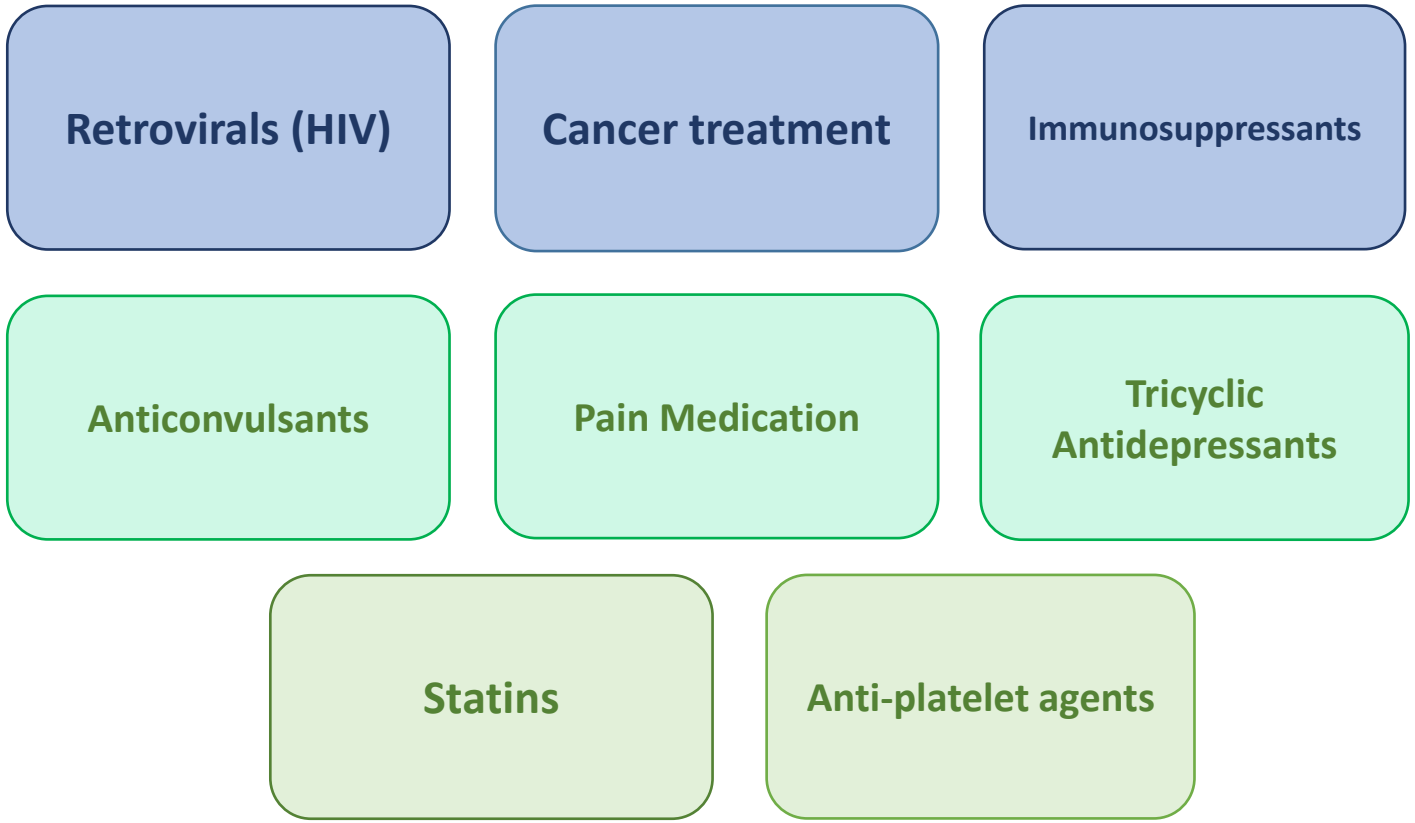
Wednesday 7 October 2020

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.

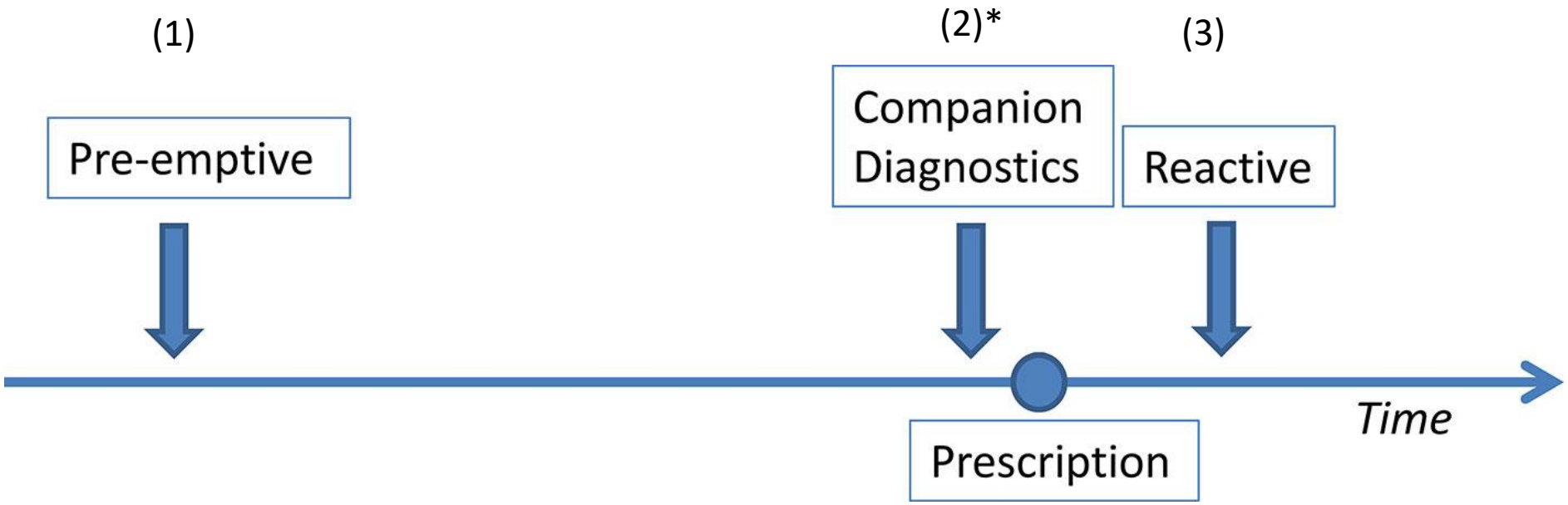
Where next…

What to test: gene panel instead of single genes?



~793,843 prescriptions in primary care (Estimate from 2019 data, Youssef *et al*, 2020)

When to test….



*Includes POCT

National Pharmacogenomics Group (NPGG)

Terms of Reference (Draft v0.3): February 2022

Official Title:	All Wales Pharmacogenomics Group (AWPGG)
Purpose & Aim:	The AWPGG aims to ensure that there is a multidisciplinary, coordinated national approach with defined clinical input to the development and introduction of pharmacogenetic services within Wales.
Remit:	The remit of AWPGG is to: • to ensure delivery of a national, standardised and coordinated pharmacogenetic testing approach in NHS Wales, ensuring appropriate patients can access testing in a timely, consistent and equitable manner • provide service users with rapid access to pharmacogenetic tests in line with Medicines and Healthcare Products Regulatory Agency (MHRA) advice, National Institute for Health and Care Excellence (NICE) technical appraisals, All Wales Medicines Strategy Group (AWMSG) appraisal reports, the Welsh Government Genomics for Precision Medicine strategy and future iterations • standardise genetic reporting pathways for receipt of results by prescribers from the All Wales Medical Genomics Service (AWMGS) until IT systems are in place to enable results to be uploaded directly onto the Welsh Clinical Portal • implement a horizon-scanning approach to predict and commission future requirements for an NHS pharmacogenetic service • disseminate timely information to clinical teams within health boards as new drug/gene pairs are introduced across healthcare pathways (Chief Pharmacists, Medicines Information Pharmacists, Medical Directors/Assistant Medical Directors, Drug and Therapeutics Groups) • highlight service needs to decision makers as appropriate (Welsh Government, Chief Pharmaceutical Officer for Wales, AWMSG, Genomics Partnership Wales Programme Board and
Group reports to:	• to the AWMSG and the Genomics Partnership Wales Programme Board

Chairperson: Prof Dyfrig Hughes

Pharmacogenomics Education

- Genomic Medicine MSc module (Pharmacogenomics & Stratified Healthcare)
  - Currently delivered as part of MSc by Swansea University
  - Undergoing re-procurement in Wales – a more modular approach
    - Each module will be awarded independently to one HEI in Wales
    - Requirement for online delivery to ensure equity of access to all HCPs across Wales
    - 'Marketing' an important consideration – need to reach as many as possible

- Close liaison with HEIW to identify and address training needs of pharmacy workforce
- Working with HEE GEP on GeNotes to avoid duplication and ensure HCPs from Wales can access 'local' information about PGx testing

AWMGS

Thank you

Diolch!

ROYAL PHARMACEUTICAL SOCIETY

NEXT SESSION

Demystifying Pharmacogenomics webinar series

Date for your diary: September 2022

https://www.rpharms.com/resources/webinars