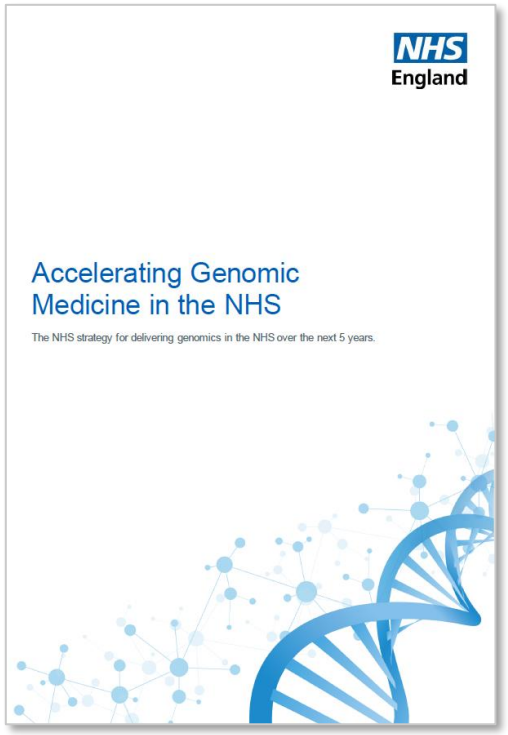
NHS
South West
Genomic Medicine Service

Genomics Update

Rachel Palmer
Pharmacy Lead
SW Genomics Medicine Service Alliance

@SWGenomics / @SWGLH / @NHSgms

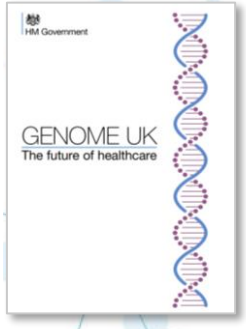
Accelerating Genomic Medicine in the NHS



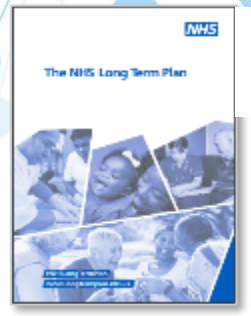
Key themes include:

1. **Embedding genomics across the NHS,** through a world leading innovative service model from primary and community care through to specialist and tertiary care
2. **Delivering equitable genomic testing for improved outcomes in cancer, rare, inherited and common diseases and enabling precision medicine** and reducing adverse drug reactions
3. **Enabling genomics to be at the forefront of the data and digital revolution,** ensuring genomic data can be interpreted and informed by other diagnostic and clinical data;
4. **Evolving the service driven by cutting-edge science, research and innovation** to ensure that patients can benefit from rapid implementation of advances

UK Life Sciences Vision sets 10-year strategy for sector to solve some of the biggest healthcare problems of our generation



Genome UK; the future of healthcare sets out a 10 year vision how we will achieve progress in genomic medicine across Diagnosis & Personalised medicine, Prevention and Research



NHS Long Term Plan genomics commitments

Driving the use of precision treatments and optimising the use of medicines

Gene therapies	• Use cutting-edge technology to deliver tailor-made genetic material into a patient's cells to treat disease
New targeted treatments	• Based on an increased understanding of the genomic basis for disease & diagnosis
Pharmacogenomics	• Guide treatment decisions and dosing using genomic data to predict drug response
Repurposing	• New indications for existing medicines
Predicting	• Drug resistance and pathogen resistance

Pharmacogenomics (PGx)

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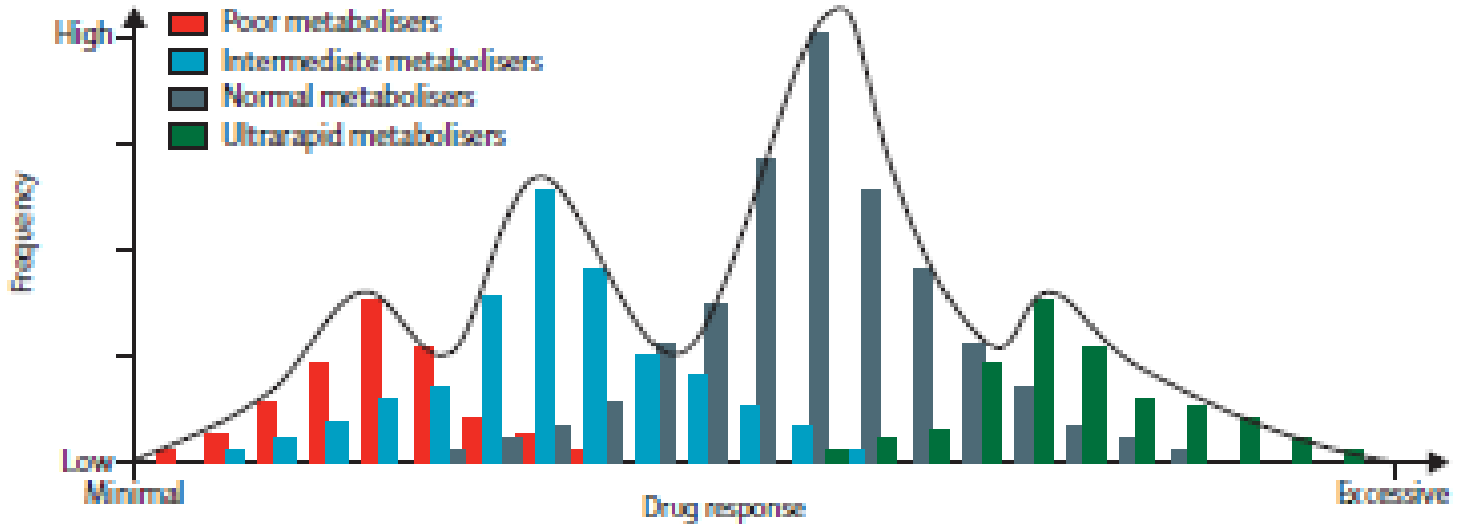
Pharmacogenomic variants affect an individual's response to a drug

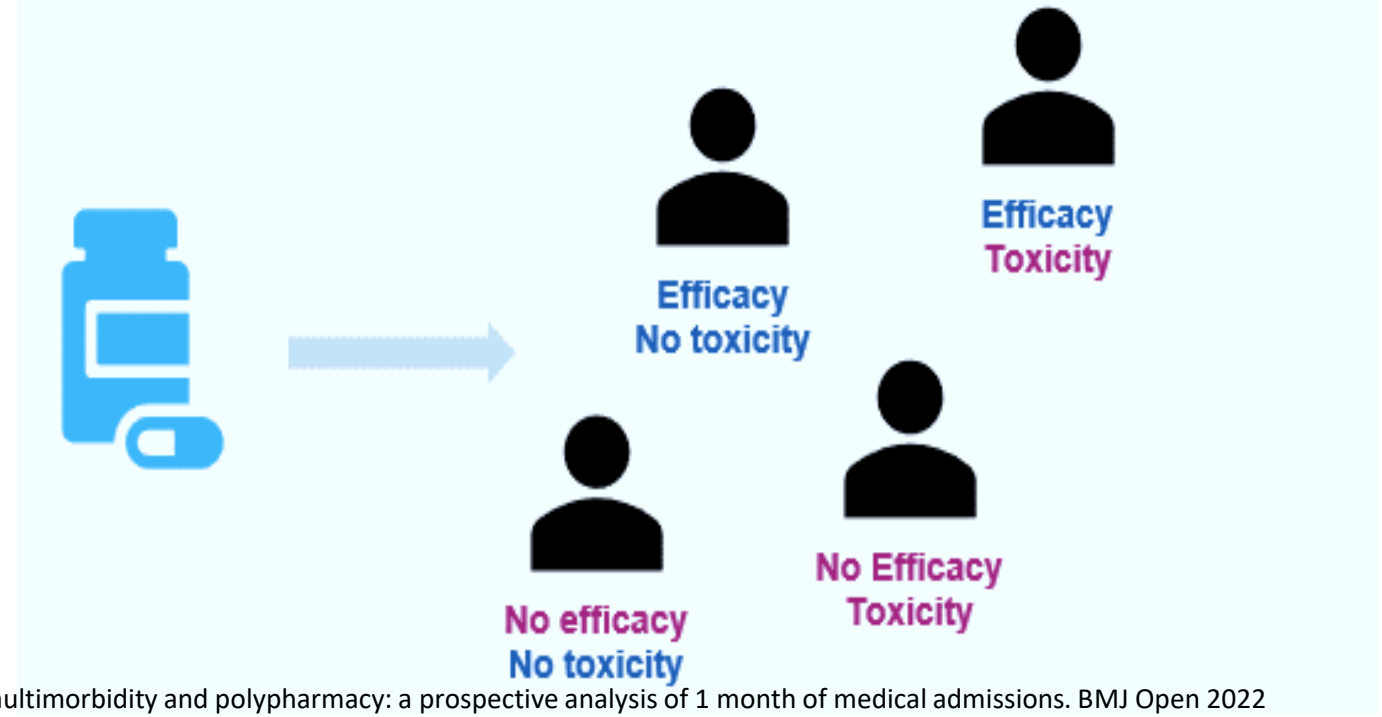
Pharmacology + **Genomics** = **Safe, effective medicines tailored to variations in a person's genes**



Roden et al (2019)

Why is it important?

- >95% of the population carry at least one actionable pharmacogenomic variant.
- Drug interventions effective in only around **30%-50%** of patients
- One in 15 UK hospital admissions is linked to adverse drug reactions, costing the NHS more than £2.21 billion each year.



Ref: Osanlou R, et al. Adverse drug reactions, multimorbidity and polypharmacy: a prospective analysis of 1 month of medical admissions. BMJ Open 2022

Slide credit Genomics Education

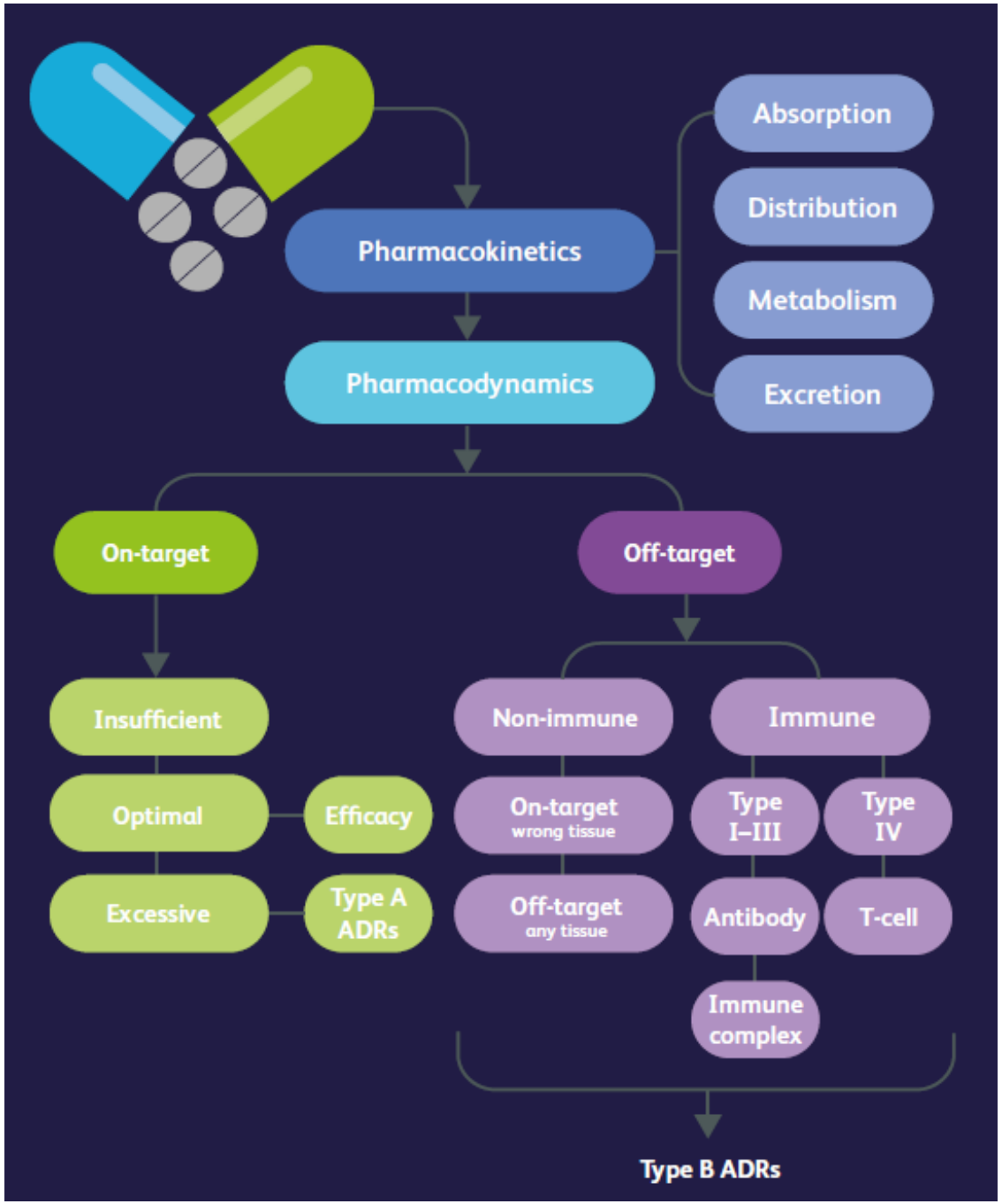


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Image credit British Pharmacological Society

National Genomic Test Directory

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The National Genomic Test Directory is a published list of **nationally commissioned genomic tests** (and associated eligibility criteria). There are three documents:

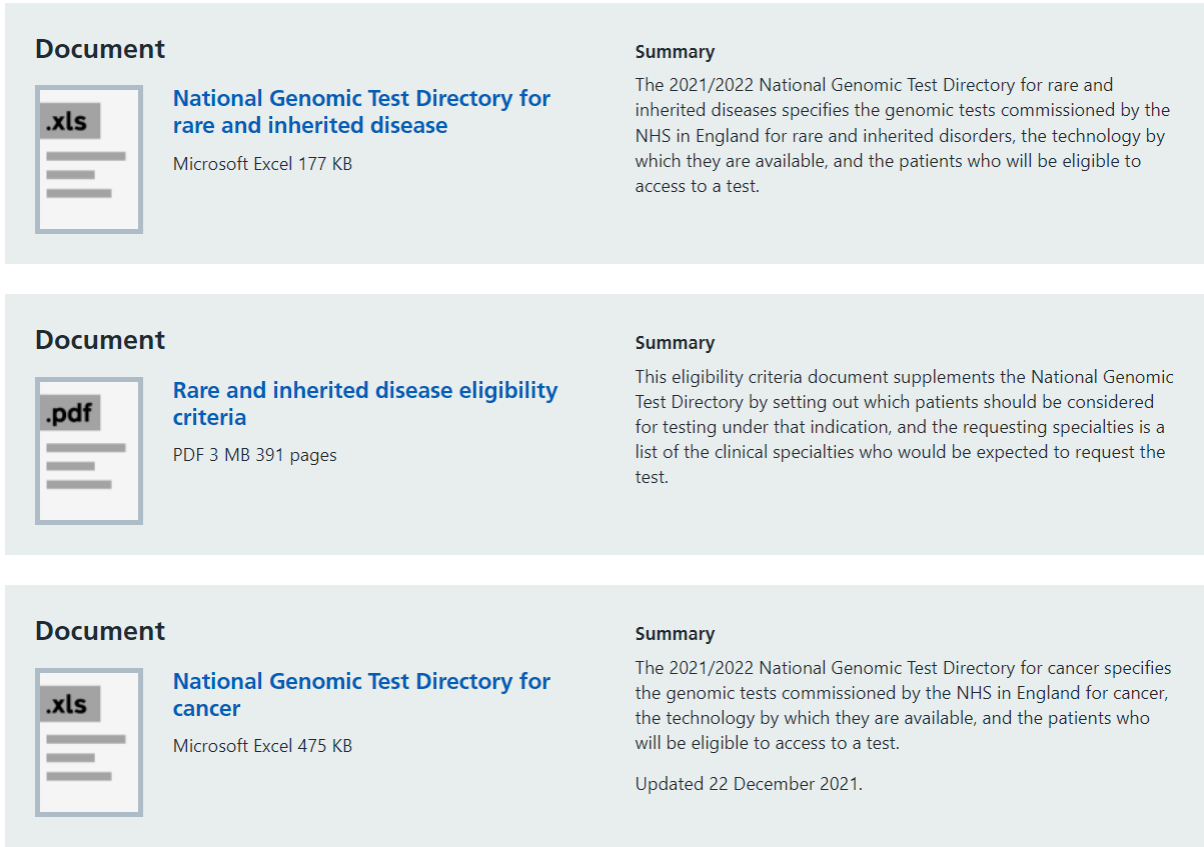
- National Genomic Test Directory for rare and inherited disease (Excel)
- Rare and inherited disease eligibility criteria (PDF)
- National Genomic Test Directory for cancer (Excel)

Pharmacogenomic testing is currently reflected on the Rare Disease and Cancer Test Directories. In the future, this will move towards **one online directory** that encompasses all three specialities.

Aims

- To ensure the directory reflects **latest technological developments and scientific advances**
- To support **fair and equitable access** to genomic testing
- To ensure **best value** is achieved for the NHS
- To improve our understanding of **clinical utility** of genomic tests and the implications of testing on patients and the clinical pathway.

Application process for new tests detailed in published policy document alongside application forms and supplementary guidance: https://www.england.nhs.uk/genomics/the-national-genomic-test-directory/



https://www.england.nhs.uk/publication/national-genomic-test-directories/

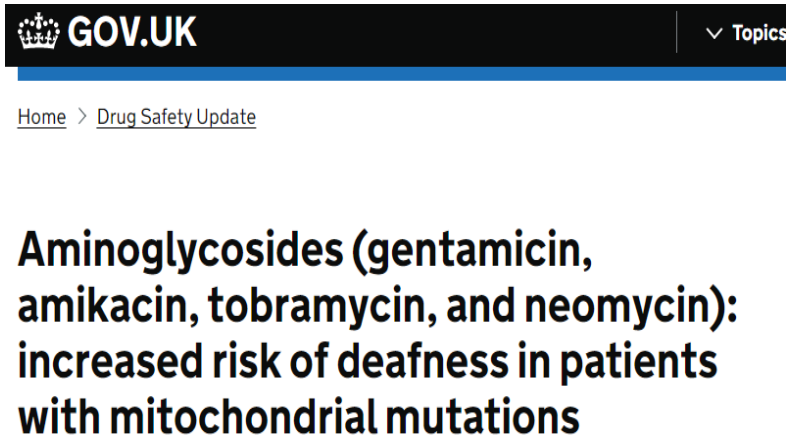
Nationally Commissioned Pharmacogenomic Tests (Test Directory)

- ***DPYD* for fluoropyrimidines**

- ***TPMT/NUDT15* in ALL**

- ***MT-RNR1*; Aminoglycoside induced hearing loss**

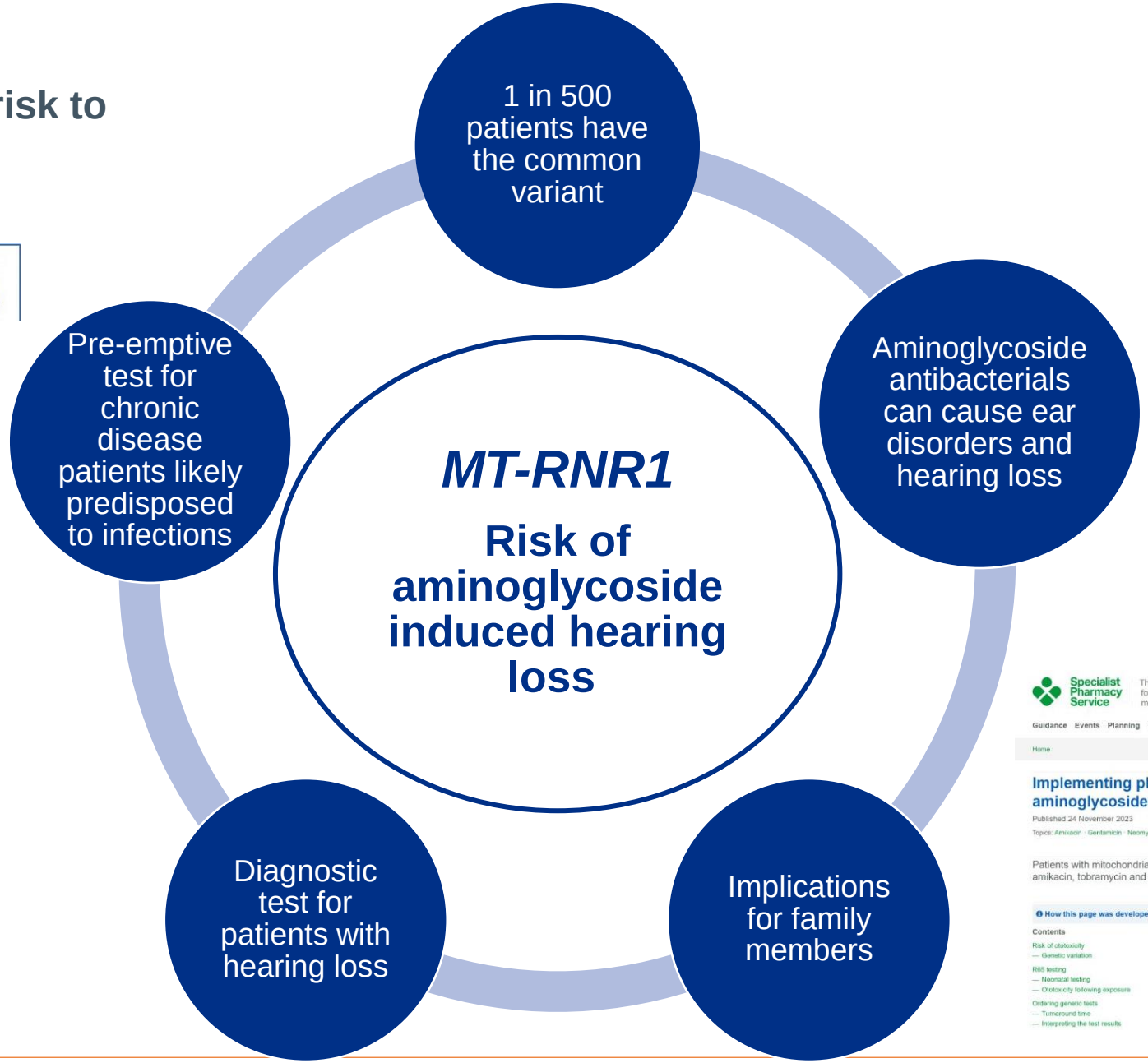
- ***individuals with a predisposition to gram negative infections*** *for example due to known respiratory disease such as bronchiectasis, cystic fibrosis or due to structural or voiding genitourinary tract disorders*
  OR
- ***individuals with hearing loss who have been exposed to aminoglycosides***

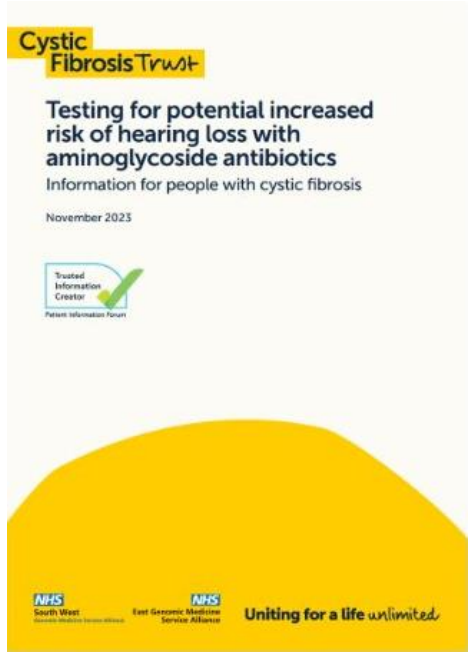


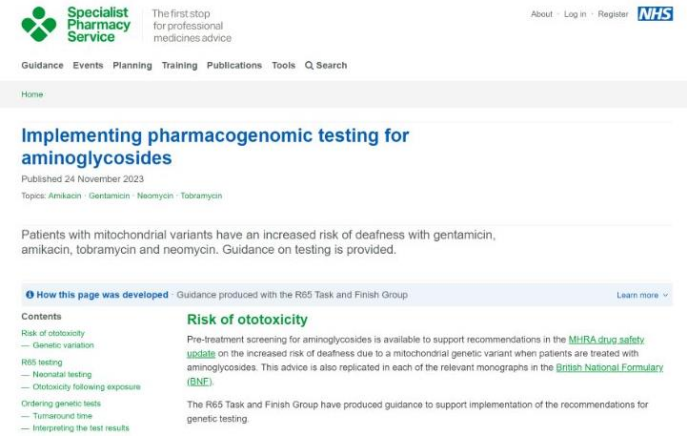
Slide credit SE GMSA

Aminoglycoside exposure posing risk to hearing

Drug Safety Update MHRA







Pharmacogenomics: *Aminoglycosides*

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2 April 2022

NHS Develops World-First Bedside Genetic Test To Prevent Babies Going Deaf

Slide credit SW GMSA

NICE TA913 Mavacamten for obstructive hypertrophic cardiomyopathy

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Camzyos 2.5 mg hard capsules ▼

Patients should be genotyped for Cytochrome P450 (CYP) 2C19 (CYP2C19) in order to determine appropriate mavacamten dose. Patients with CYP2C19 poor metabolizer phenotype may have increased mavacamten exposures (up to 3 times) that can lead to increased risk of systolic dysfunction

Clopidogrel and *CYP2C19* genotyping

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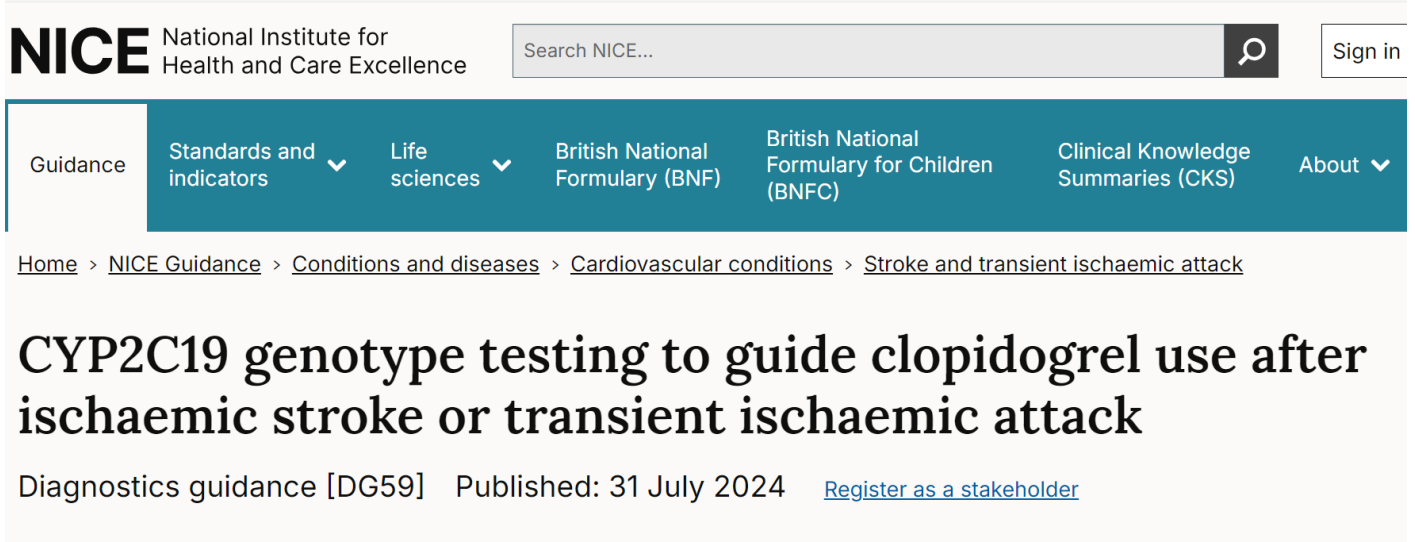

- NICE give positive opinion for genotyping & advise to use;
  - Laboratory-based testing as first choice
  - Genedrive PoC device if lab-based testing unavailable

- Considerable logistical challenge recognised by NICE
- NICE working with NHSE to deliver a **national pilot** of testing, to inform future implementation of this guidance.
- Genedrive PoC device also being piloted via DEVOTE programme Research & Innovation (cmft.nhs.uk)

CYP2C19 genotyping for clopidogrel stroke/TIA

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Lab based testing

- Accredited genomic laboratory
- Highly skilled, experienced staff
- Likely centrally funded
- Turnaround ??
- *Potential* to screen wide range of variants

Point of care test

- Requirement for staff training
- Quality control/assurance
- Funding unclear - ? Local
- Turnaround 1-2hrs
- Limited range of genetic variants

Recording, storage and re-use of CYP2C19 results

North West Genomic Laboratory Hub (Liverpool Site)
Manchester Centre for Genomic Medicine
Liverpool Women's Hospital, Crown Street, Liverpool, L8 7SS
Scientific Operational Director: Dr E. Howard
https://mft.nhs.uk/nwglh/ dna.liverpool@nhs.net Tel +44(0) 151 702 4228

NHS North West
NHS Genomic Laboratory Hub

Referred by:
<TOPERSON>
<TOJOBTITLE>
<TOADDRESS>

SAMPLE TYPE: <SAMPLETYPE>
COLLECTED DATE: <COLLECTIONDATE>
RECEIVED DATE: <RECEIPTDATE>
ACTIVATED DATE: <ACTIVATIONDATE>
REPORT DATE: <CURRENTDATE>

Copies to: <COPYTOADDRESS> (ref: <EXTERNALID>)

PATIENT NAME: <PATIENTFIRSTNAME> <PATIENTSURNAME>
YOUR REF: <HOSPITALNO>/<EXTERNALID>
SEX: <GENDER>

DATE OF BIRTH: <DATEOFBIRTH>
NHS No: <NHSNUMBER>
OUR REF: <FOLDERNO>

GENOMICS LABORATORY REPORT: PHARMACOGENOMICS – *CYP2C19* VARIANTS

Reason for testing: *CYP2C19* genotyping to guide mavacamten dosing.

RESULT SUMMARY: *CYP2C19* (*2/*2) [**CYP2C19 Poor Metaboliser**]

Result and Interpretation: This patient has been tested for the three most frequent *CYP2C19* variants affecting cytochrome p450 2c19 enzyme activity: The loss-of-function c.681G>A (*CYP2C19*2*) and c.636G>A (*CYP2C19*3*) variants, and the c.-806C>T (*CYP2C19*17*) gain-of-function variant.

<PATIENTFIRSTNAME> <PATIENTSURNAME> was found to be homozygous for the c.681G>A (*CYP2C19*2*) variant. <HESHE> is therefore predicted to be a poor metaboliser of mavacamten.

These results can be used to guide dosing of mavacamten. Prescribers should refer to the UK summary of product characteristics (SPC) for dosing and monitoring guidance.

Please note that an individual's CYP2C19 metaboliser status can influence the effectiveness or safety of multiple medicines. For contemporaneous pharmacogenetic recommendations please visit www.cpicpgx.org/guidelines and discuss any prescribing queries with your local pharmacist.

This result can be stored in the patient's Electronic Health Record as SNOMED-CT code **738786005 Finding: Cytochrome P450 family 2 subfamily C member 19 poor metabolizer.**

CYP2C19 genotyping & clopidogrel

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Previous stroke/TIA?

Other indications?

?Private testing uptake

Reuse of CYP2C19 results for new/existing prescriptions

Antiplatelet choice

Integration into system wide stroke pathway – oversight and governance

Pharmacogenomics guidance

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Commonly used:

- **CPIC** https://cpicpgx.org/
- **DPWG** https://www.knmp.nl/dossiers/farmacogenetica

Product license

- **SmPC**
- **FDA**

Databases

- DDRx - DNA-Driven Rx (pharmgkb.org)
- PharmGKB - https://www.pharmgkb.org/
- PharmVar - https://www.pharmvar.org/

UK resources / guidance

- DPYD - https://www.uksactboard.org/publications
- TPMT and NUDT15 - https://www.bopa.org.uk/resources
- Pharmacogenomics Ge-notes - https://www.genomicseducation.hee.nhs.uk/genotes/
- National Genomic Test Directory - NHS England » National genomic test directory
- **UKCPA PGx handbook in development!**

Slide credit NT GMSA

Information sources – SPCs; 4.2 Posology & administration

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Citalopram

Reduce initial dose for ‘known’ CYP2C19 PM

Carbamazepine

Screen Han Chinese and Thai patients for HLA-B*1502 whenever possible

Metoprolol

PM [CYP2D6] may require lower than normal doses

Amitriptyline

Consider 50% dose reduction for known CYP2C19 or CYP2D6 PM

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Respiratory metagenomics

Am J Respir Crit Care Med. 2024 Jan 15; 209(2): 164–174.
Published online 2023 Nov 8. doi: 10.1164/rccm.202305-0901OC
PMCID: PMC108064
PMID: 379381

Routine Metagenomics Service for ICU Patients with Respiratory Infection

Themoula Cha
Mark Tan, [1] To
Duncan L. A. V
Simon Golden
Penelope R. C
+

Severe presentation of infectious disease NHS genomic network of excellence

This NHS Genomic Network of Excellence will bring together experts to transform the understanding and management of patients with life threatening infectious disease, through the application of novel genomic technologies in pathogen detection and host immunity profiling.

The Network of Excellence will focus on pathogen sequencing and host immunity profiling in patients with acute illnesses in healthcare settings. This can accelerate personalised treatments for vulnerable patients.

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Respiratory metagenomics network of excellence

- Metagenomics = study of all genetic material from sample
- Rapid pathogen identification
  - Earlier targeted anti-infectives
- Potential for identifying antimicrobial resistance
- Host immunity profiling
- Pilot at several UK centres

PROGRESS Pharmacogenomics Pilot Project

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- Aims to deliver the **evidence,** including **health economics,** to make national commissioning **decisions about implementing pharmacogenomics in the NHS**
- Pharmacogenomic gene panel testing if 'trigger drug' prescribed **in primary care;**
  - TCAs
  - SSRIs
  - Statins
  - PPIs
- Develop a system to **translate results to prescribing advice**
- To be expanded to at least one **SW PCN** in 2024
- Project updates at https://www.nw-gmsa.nhs.uk/about-us/our-regional-and-national-projects/our-2022-2023-projects

The PROGRESS Programme: Implementing Pharmacogenetics in the NHS

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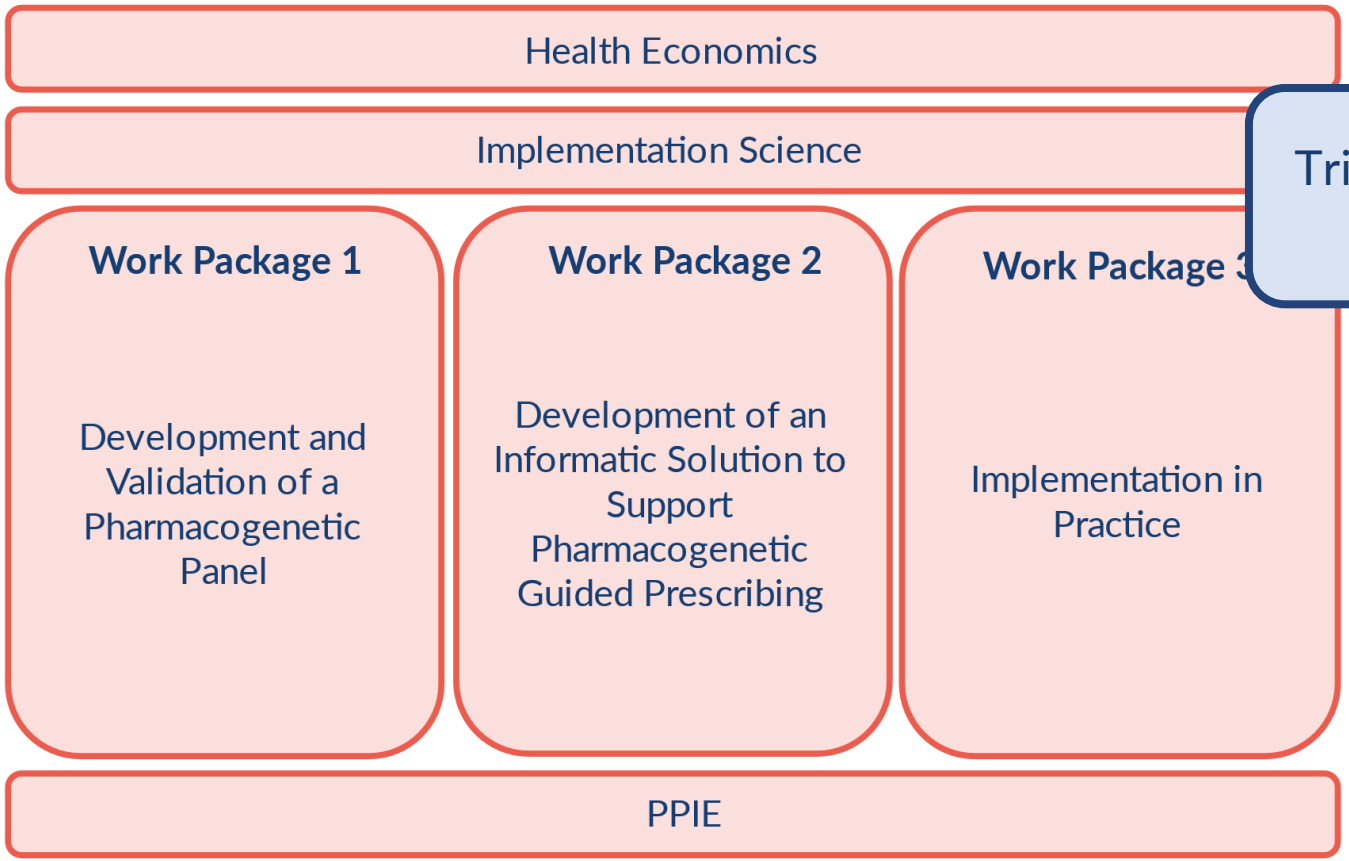

Trigger: Prescription of a new medicine (Antidepressant, Statin, PPI)

The PROGRESS Study will open for recruitment in June 2023 in the North West of England before expansion to other regions in January 2024

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BJCP British Journal of Clinical Pharmacology

ORIGINAL ARTICLE | Open Access

Public preferences for pharmacogenetic testing in the NHS: Embedding a discrete choice experiment within service design to better meet user needs

John H. McDermott, Videha Sharma, William G. Newman, Paul Wilson, Katherine Payne, Stuart Wright

First published: 14 April 2024 | https://doi.org/10.1111/bcp.16058

Public preferences for pharmacogenomic testing (McDermott et al, 2024)

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Survey responses from 1993 members of the public;

- Preferences for;
  - Pharmacogenomic testing vs standard care
  - Non-invasive testing vs blood sample
  - Data to be shared between healthcare organisations to guide future prescribing
  - Regional vs national data sharing
  - Respondents wanted to have access to their data (online portal preferred)
- Big variability on predicted uptake (51 to >99%), depending on design of service

MHRA Biobank

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- Collaboration between MHRA & Genomics England
- Two areas of focus;
  - Allopurinol & SJS/TENs
  - DOACs and major bleeding
- Role for pharmacy in completing yellow card reports to allow patient referral

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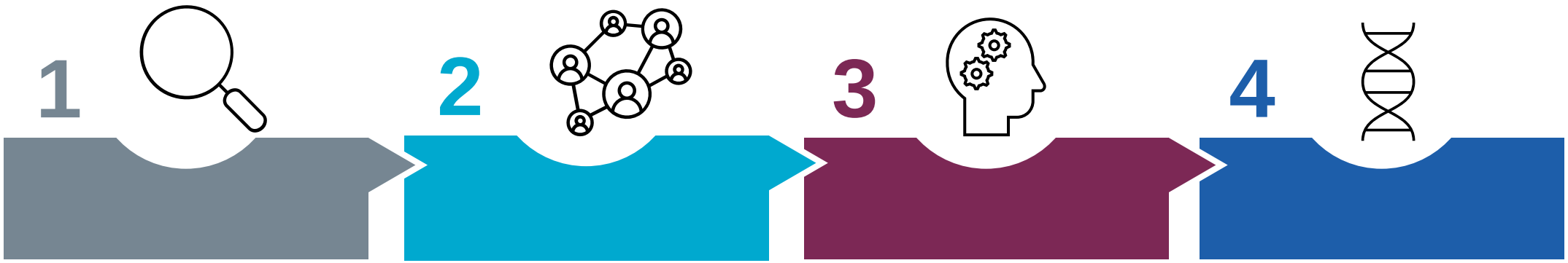
Pharmacy genomics workforce strategic framework

- Published Jan 2024, with 3 year timeframe
  - Present
  - 1-3 years
  - Ongoing
- Suggested tools/resources
- ‘What will success look like’
- Multi-disciplinary education and training
- Appendix of case studies

NHS England » Pharmacy genomics workforce, education and training strategic framework

Pharmacy genomics workforce strategic framework objectives



1. Increase awareness across pharmacy practice
2. Build and join networks across the country
3. Identify pharmacy genomics workforce needs
4. Help educate and develop the pharmacy workforce

Challenges identified by strategic framework

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Differing genomics needs across sectors/specialities

Lack of recognition of relevance to role

Case study availability

Mentor/supervisor availability

Defined roles/responsibilities

What next?

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National

- NHSE National pharmacy genomics education & training working group
  - Oversee implementation
  - Communication strategy
  - Support competency/career frameworks
  - Educational resources
    - ‘just in time’ vs ‘just in case’

SW Region

- SW implementation plan
- Review by SW Pharmacy Genomics Steering Group
  - Engagement with community pharmacy –case studies
  - Use of social media
  - Inclusion into organisational priorities
  - Best use of SW pharmacy networks
  - Educational resources/incentives

Genomics education and training resources

View full range of National Genomics Education Programme resources

From… …to

- ‘Bite-sized’ learning (1 min+)
- Genomics 101 courses (30mins)
- Online courses and expert webinars
- GeNotes: Genomic notes for clinicians
- Master’s in genomic medicine framework

GE Notes

NHS South West Genomic Medicine Service

Drumroll please... We are delighted to launch #GeNotes - our flagship new resource developed in collaboration with expert clinicians across the NHS. genomicseducation.hee.nhs.uk/genotes/
But what is GeNotes...? 1/4

NHS Health Education England

Genomics educational resources

NHS South West Genomic Medicine Service

Genomic Medicine Indicative Curriculum IETP

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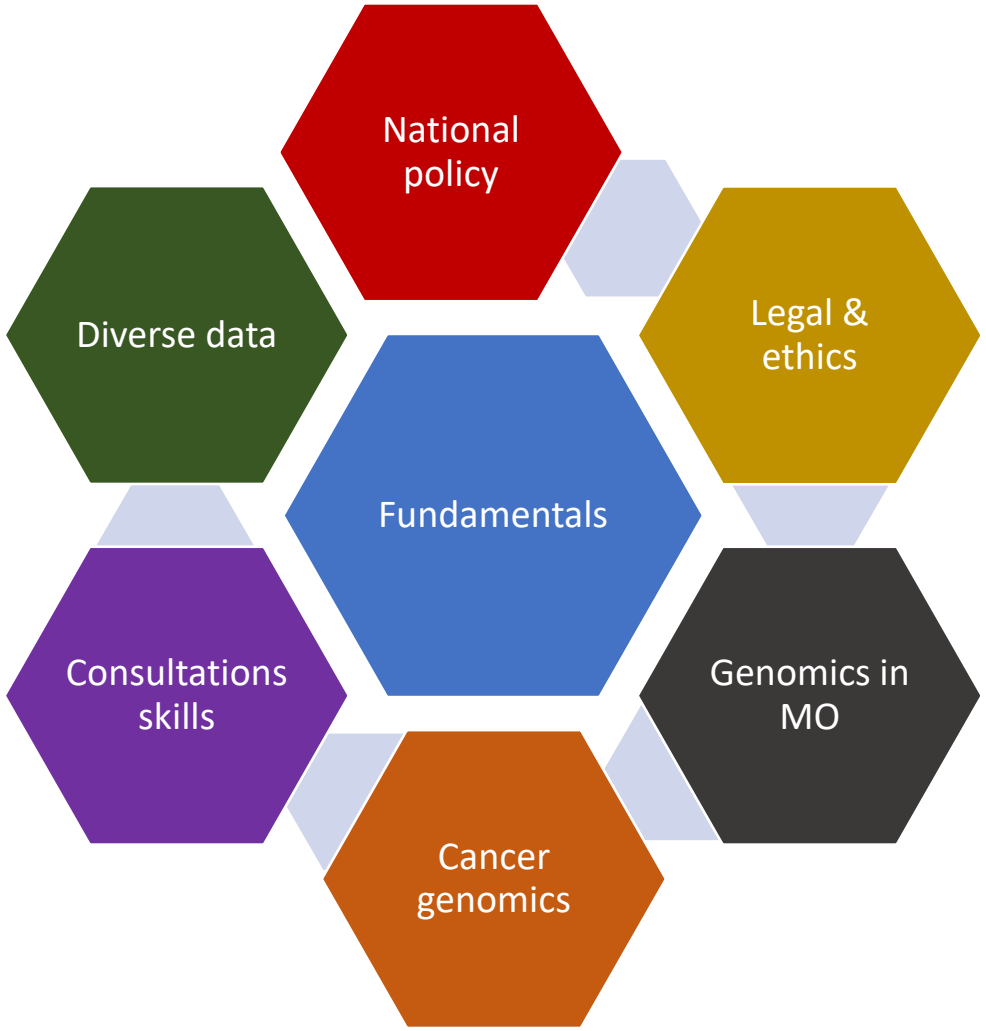
- Resources relevant for the **entire** workforce
- Linked to IETP learning outcomes & RPS Prescribing competencies



North Thames Pharmacogenetics podcasts

South West Genomic Medicine Service

Series 4 Episode 5 - The Future of Pharmacogenetics: Enhancing Patient Care Throu…

Thursday Sep 26, 2024

Welcome to Genomics Now, a podcast series where you can learn how genomics is developing in England's NHS. This podcast series is recorded in 2024 and is part of the North Thames Genomic Medicine Service's educational toolkit.…

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Series 4 Episode 4 - Implementing Pharmacogenetics: What's needed in Mental Healt…

Thursday Sep 26, 2024

Welcome to Genomics Now, a podcast series where you can learn how genomics is developing in England's NHS. This podcast series is recorded in 2024 and is part of the North Thames Genomic Medicine Services Educational Toolkit.…

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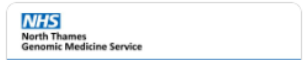

Series 4 Episode 3 - Advancing Pharmacogenetic Testing: Role of Research and Clini…

Feedback

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We want to hear from you!

https://www.surveymonkey.com/r/ZGMHFS2