NHS
North West
Genomic Medicine Service Alliance

The potential applications of pharmacogenetics in the health service

Adelphi Genetics Forum
Teachers' Conference 2024

Jessica Keen
Pharmacy Lead
North West GMSA

Overview

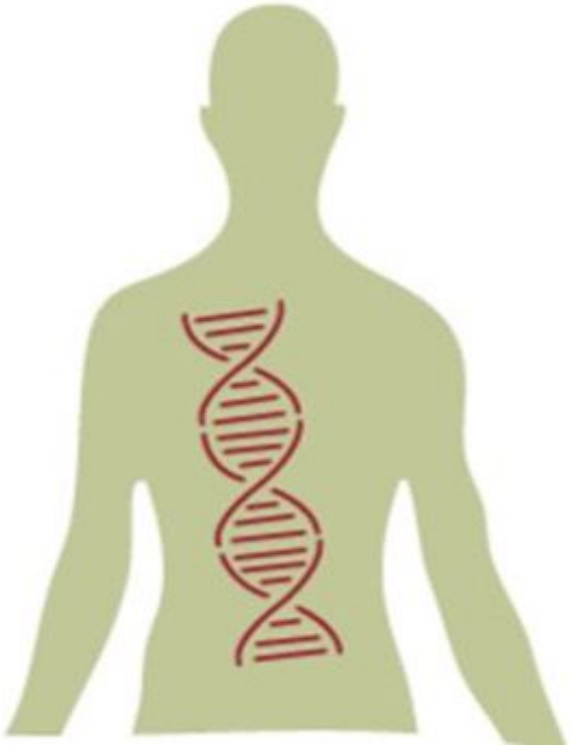
What do we mean by pharmacogenomics

Pharmacogenomics implementation in the NHS – current and future applications

Genomics and Personalised Medicine

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

from a person



from a person's cancer

from an infective organism

Image credit: NHS England Genomics Education Programme

Genomics in 2023

Early 1960s

From late 1990s (*BRCA1/2* and Huntington's Disease)

Approx. 2015 onwards

2019 WGS rollout began

Slide credit NEY GMSA

Why is there variation in drug response between individuals?

- Multiple health conditions
- Genomic variation
- Demographic
- Environment
- Drug-food interactions
- Drug-drug interactions

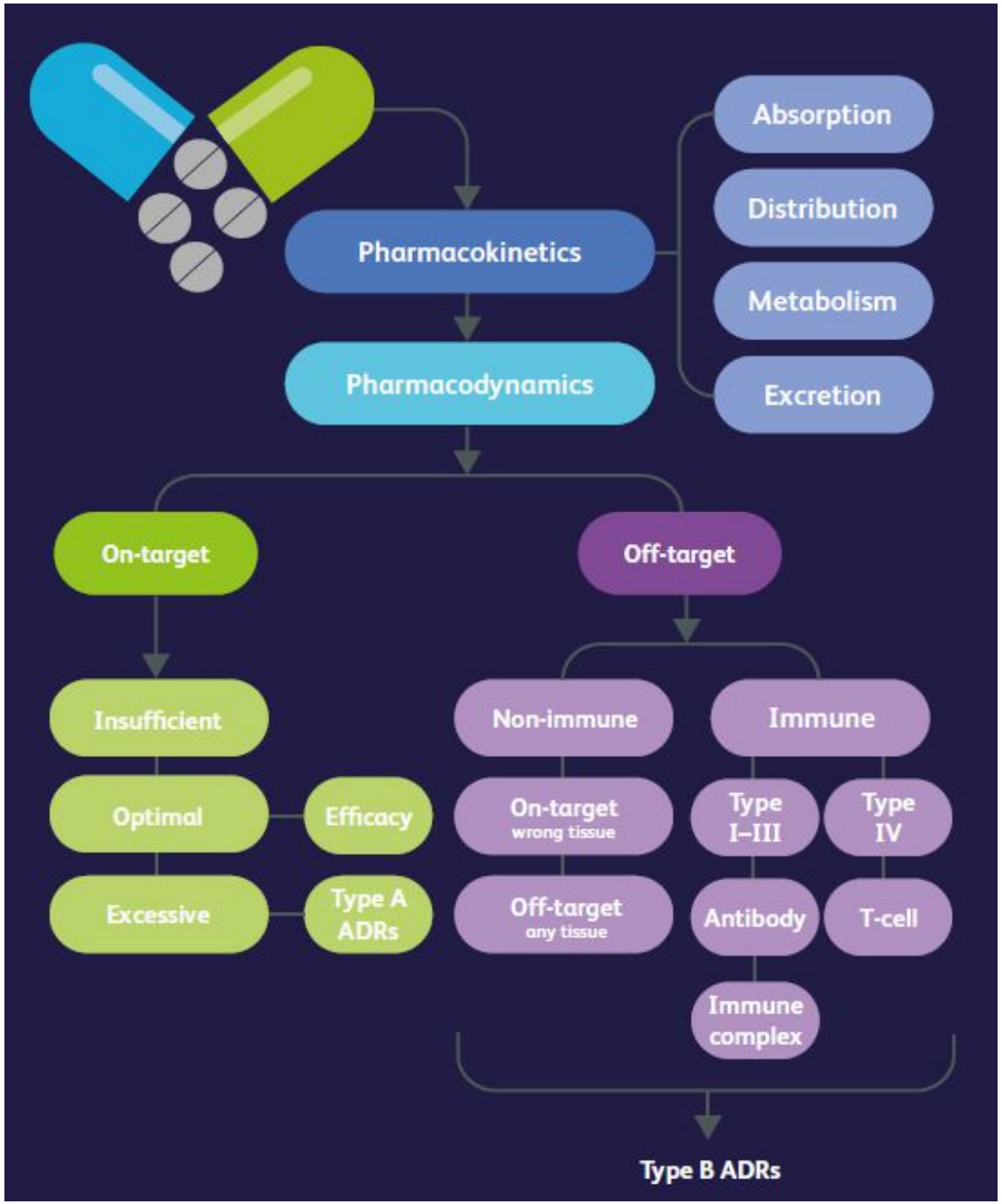
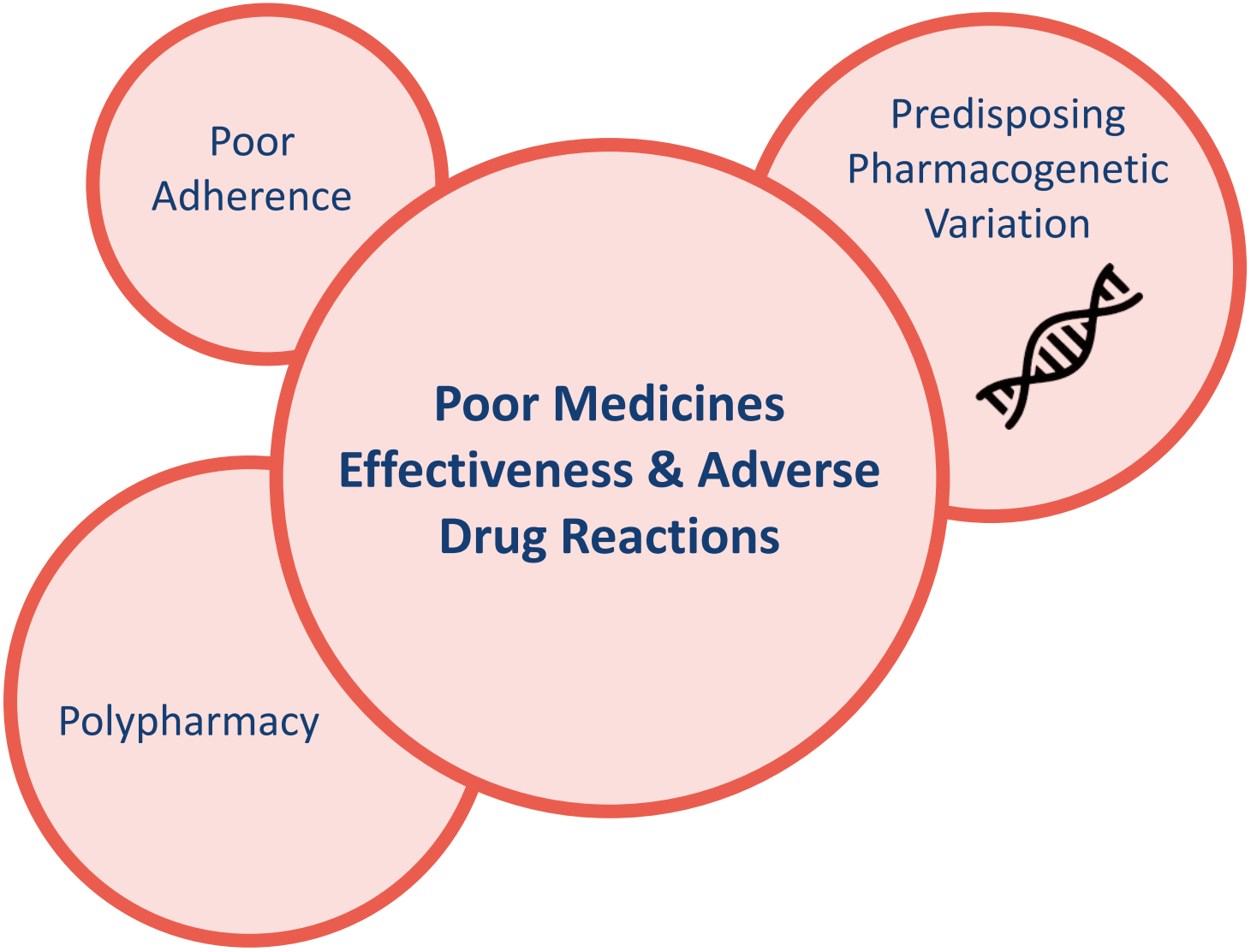
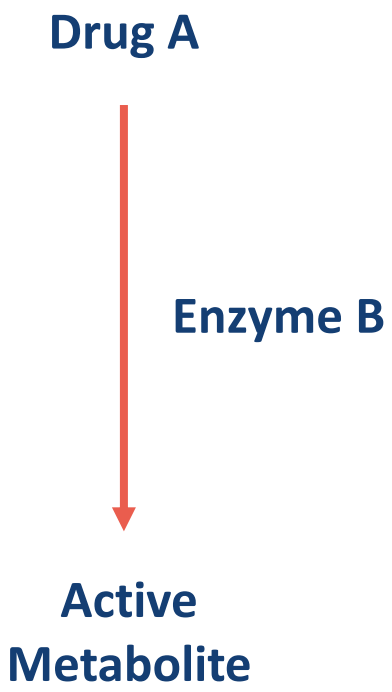


Image credit British Pharmacological Society

Common Genetic Variation is Associated with Poor Medicines Effectiveness and Adverse Drug Reactions





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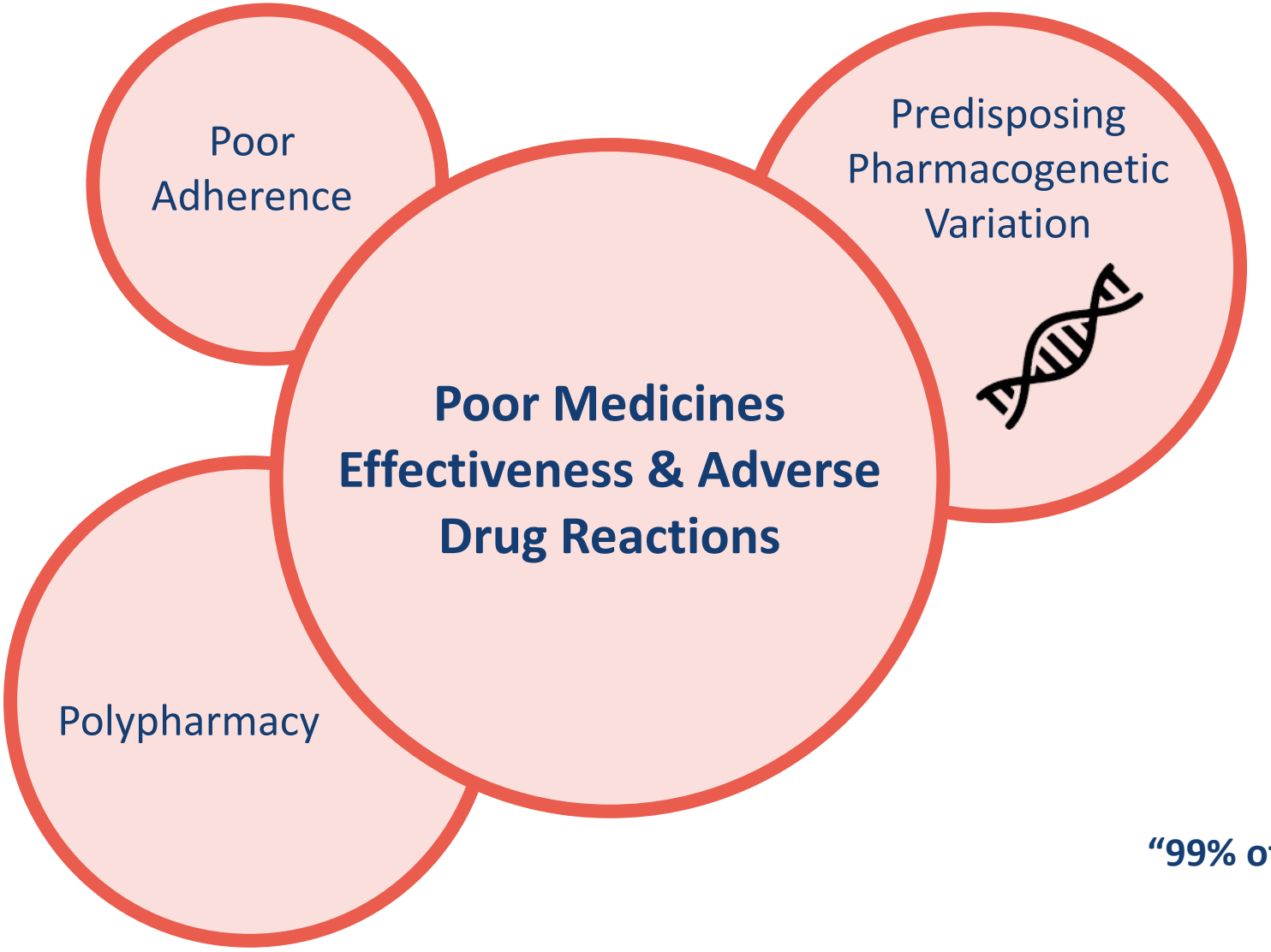
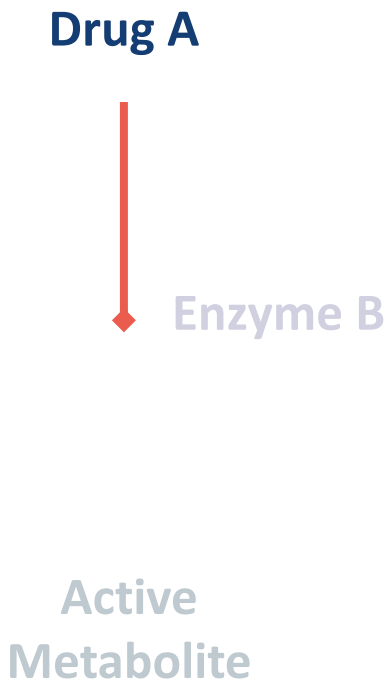




"99% of Individuals Carry Pharmacogenetic Variation"

Why does Pharmacogenomics Matter?

- Medicines effective in 30-60% of patients
- Up to 99% of patients will have a pharmacogenetic variant
- Prescribing is the most common intervention in the NHS, £10.9billion in England in community alone 2023/4
- Approx. 20% of all new prescriptions in UK primary care have an actionable drug-gene interaction#
- Estimated up to 15% of UK hospital admissions related to ADRs at a cost >£2.2billion*

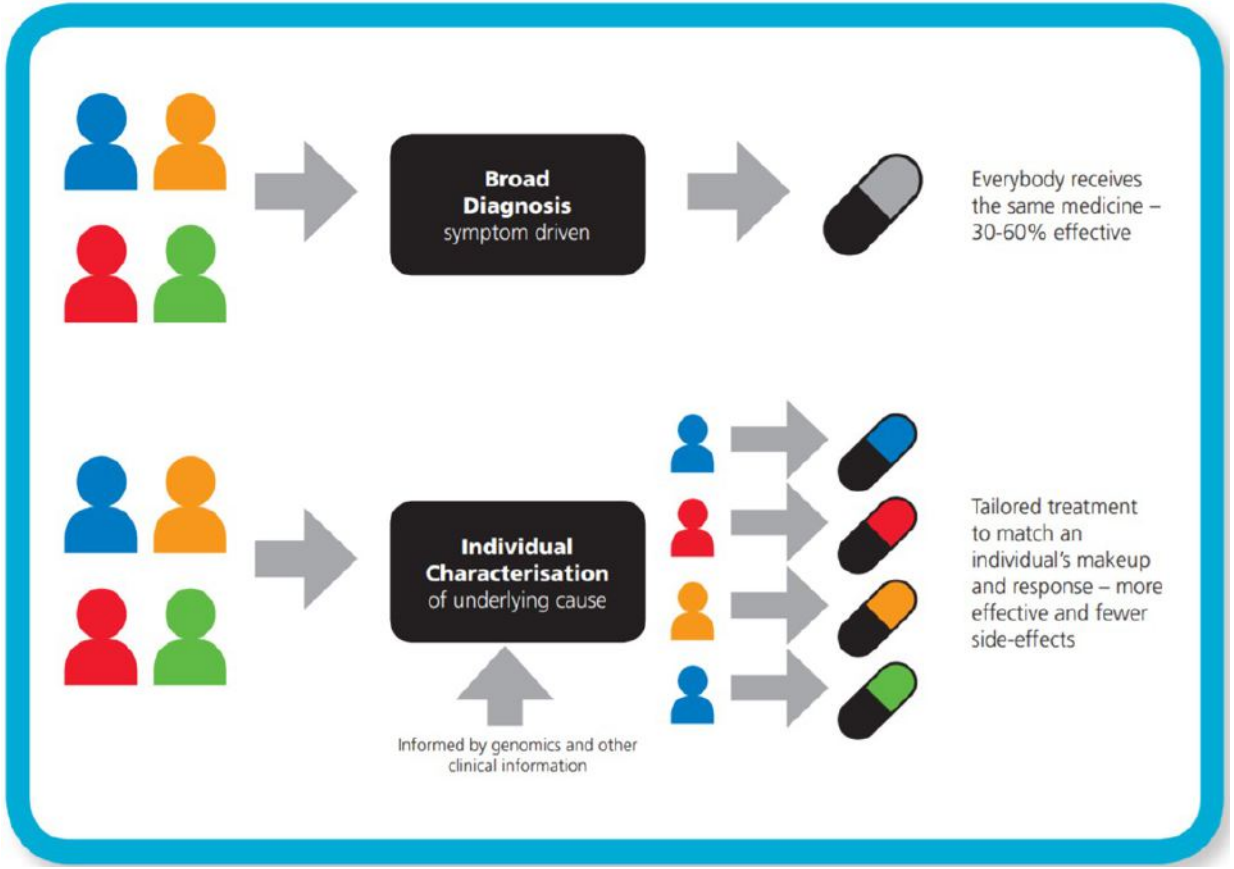
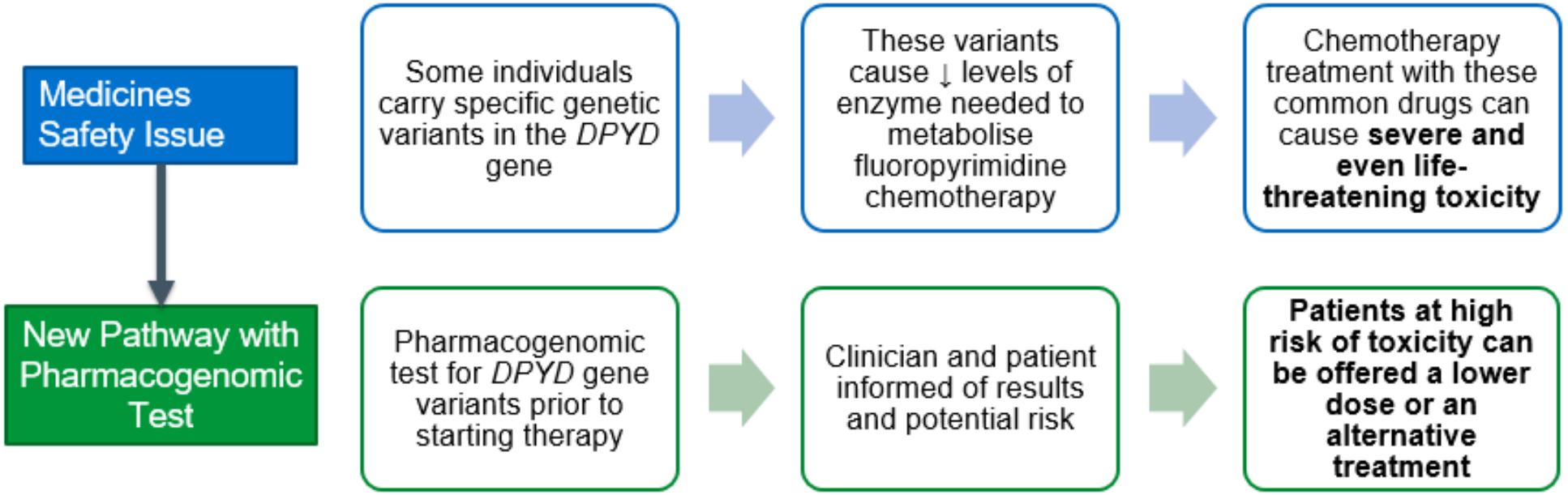


Image credit: NHSE

*Osanlou BMJ Open, 2022
Youssef et al. 2021

Example: DPYD

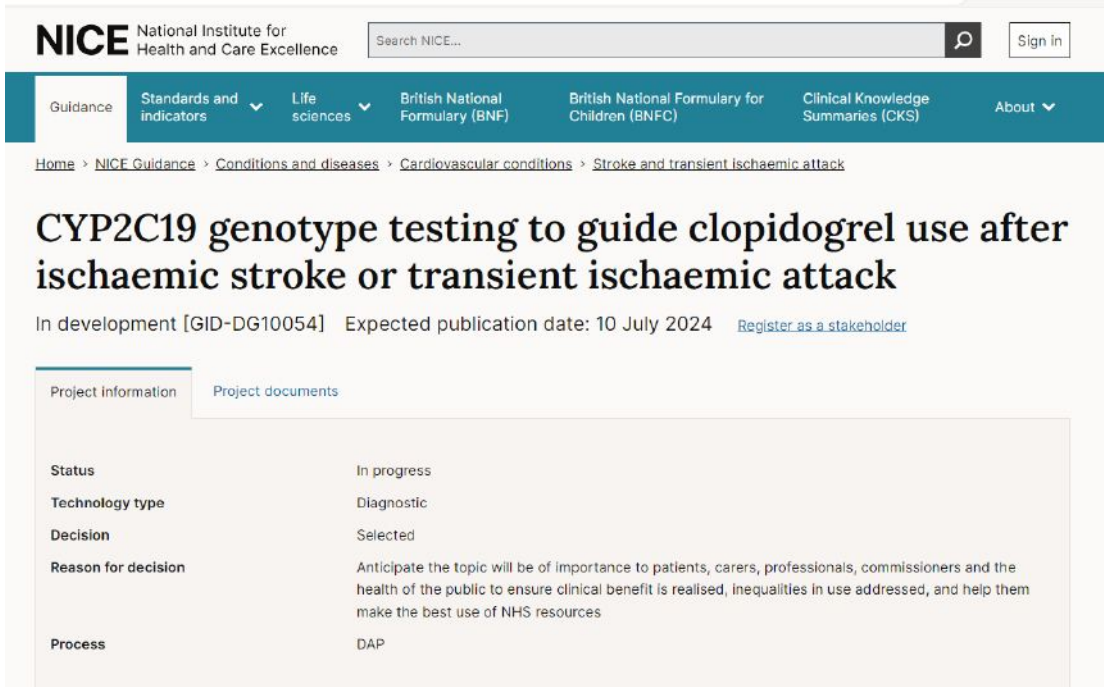
- DPYD pharmacogenomic test offered to all patients prior to starting fluoropyrimidine chemotherapy (5-fluorouracil, capecitabine)



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

Not just avoiding ADRs: Clopidogrel and CYP2C19

- CYP2C19 enzyme responsible for metabolism of many commonly used medicines
- Coded for by *CYP2C19*
- Approx 60% of people may have altered metabolism due to genetic variation (% variable by ethnicity)
- CPIC: CYP2C19 genotype = variability in clopidogrel response
- Increased risk of cardiovascular events in loss of function carriers - NB – different recommendations based on clinical indication



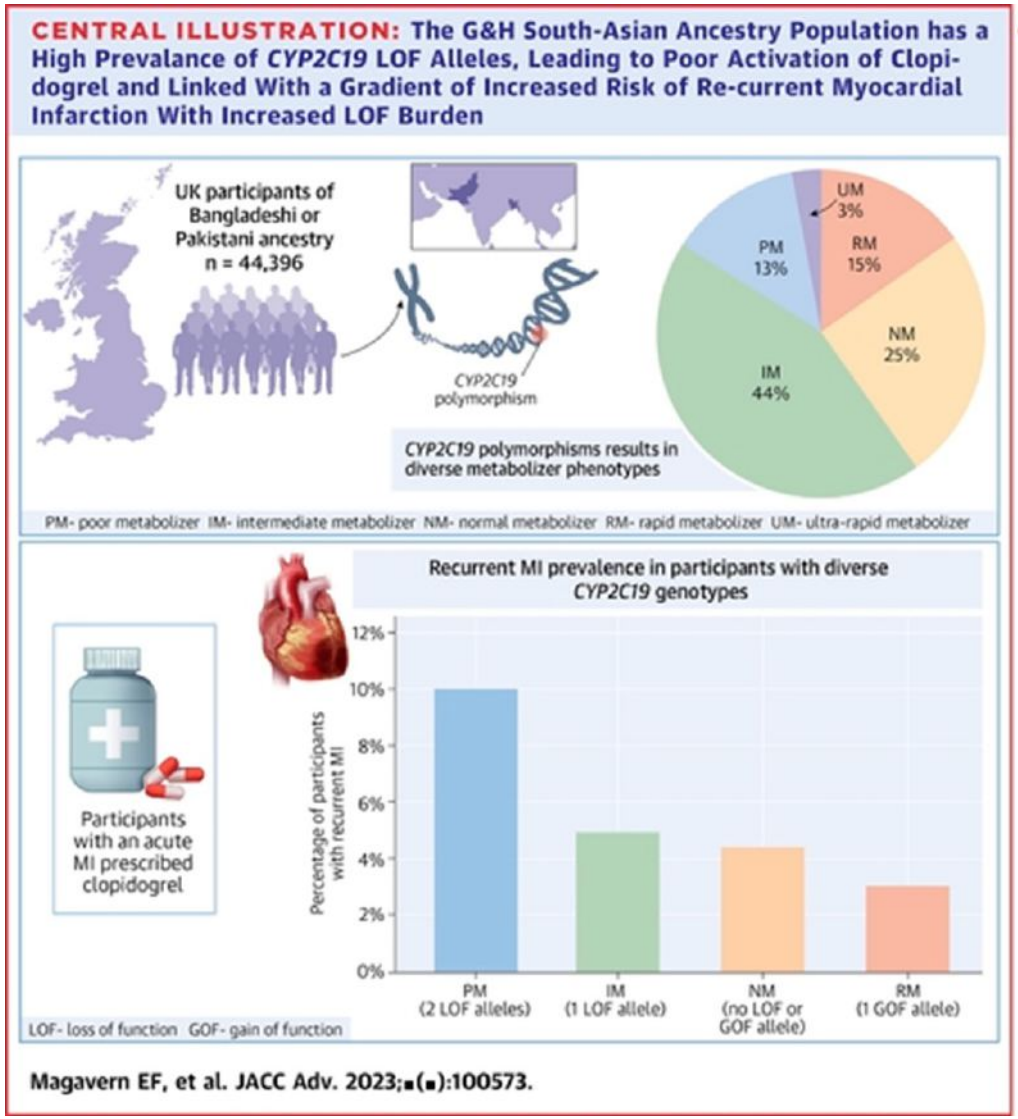
CPIC Guideline for Clopidogrel and CYP2C19 – Jan 2022 update:

https://cpicpgx.org/guidelines/guideline-for-clopidogrel-and-cyp2c19/

PGx & Health Inequalities

Stroke is linked to socioeconomic status and ethnicity

- Stroke risk is twice as high in the most deprived groups compared to least deprived
- Strokes happen more often in people who are from Black African, Black Caribbean, or South Asian family backgrounds
- Clopidogrel resistance (*CYP2C19* LOF alleles) present disproportionally across different ethnic groups
- LOF carriers have 46% increased risk of recurrent stroke when taking clopidogrel



Pharmacogenomics in practice

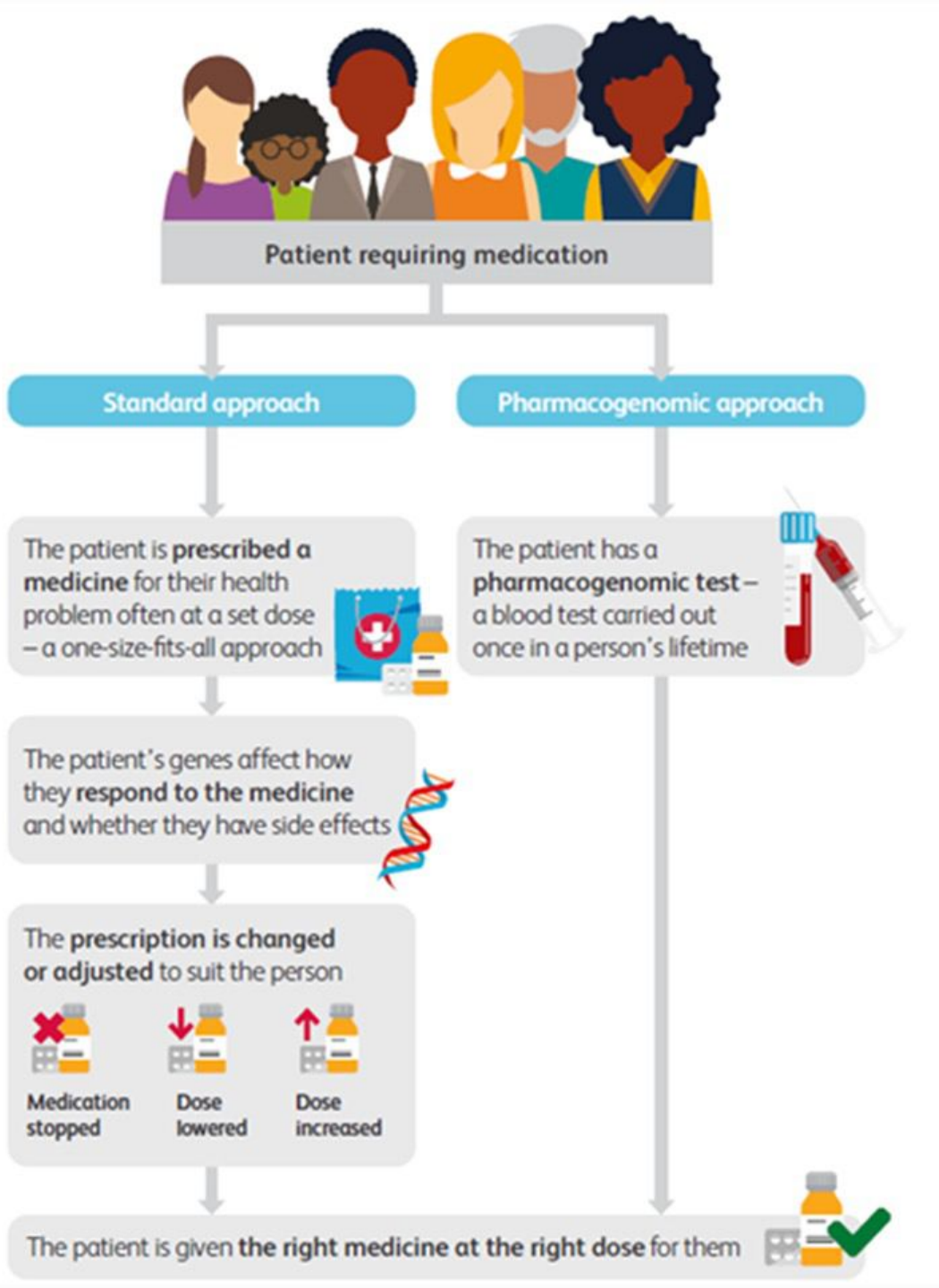
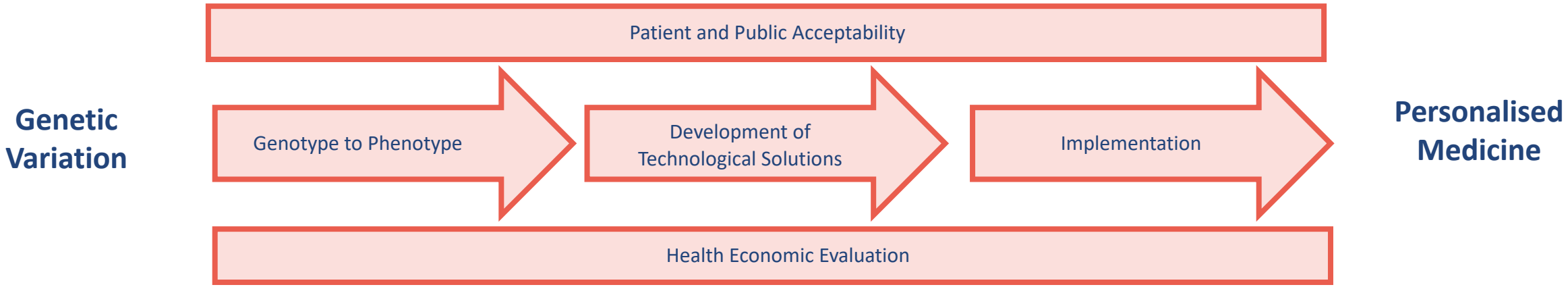


Image credit: Royal College of Physicians and British Pharmacological Society

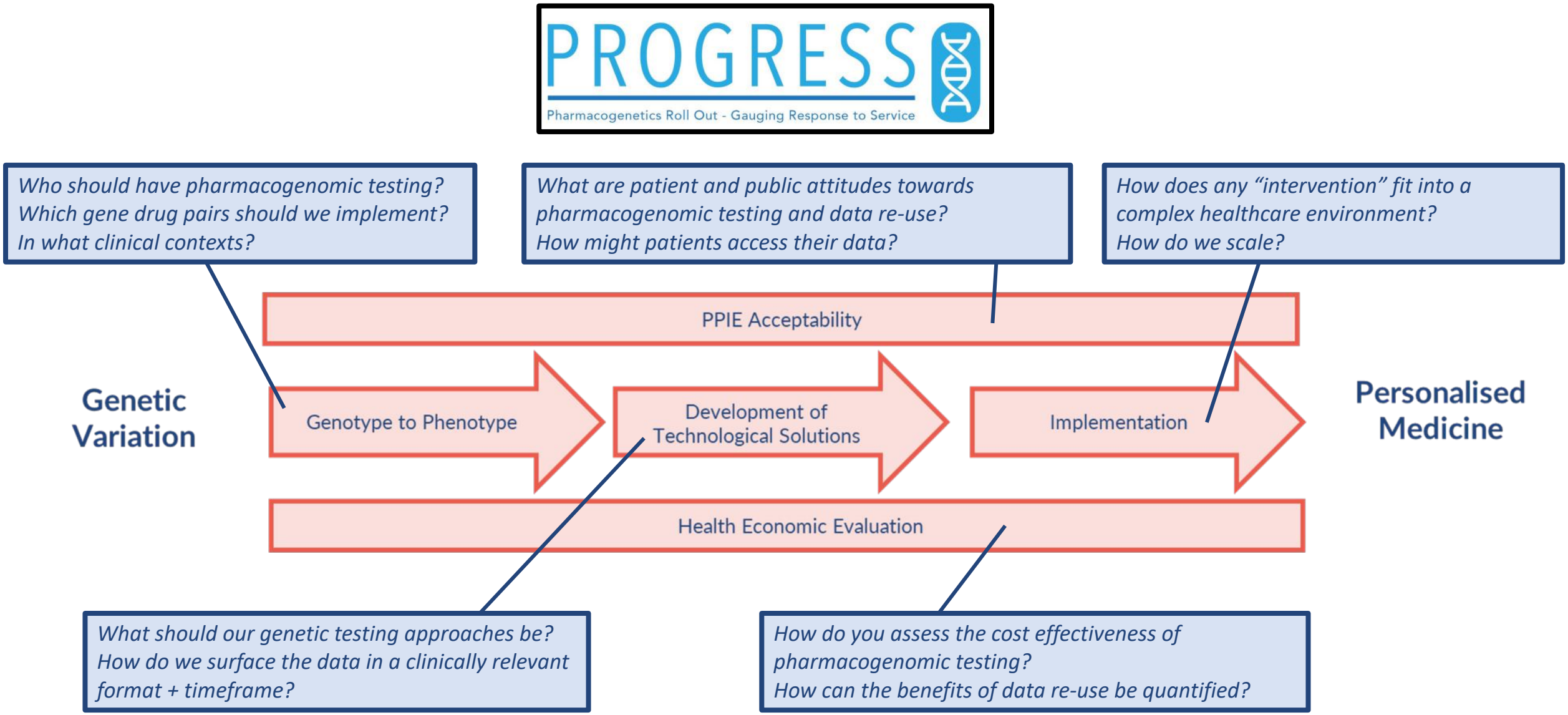
The NHS England PROGRESS Programme

PROGRESS

Pharmacogenetics Roll Out - Gauging Response to Service



The NHS England PROGRESS Programme



Implementation – The PROGRESS Study

PROGRESS
Pharmacogenetics Roll Out - Gauging Response to Service

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

Undertaken via Research Ethics

PGx Guided Prescribing

Greater Manchester

Liverpool

Blackpool

June 2023 June 2024

Phase 1

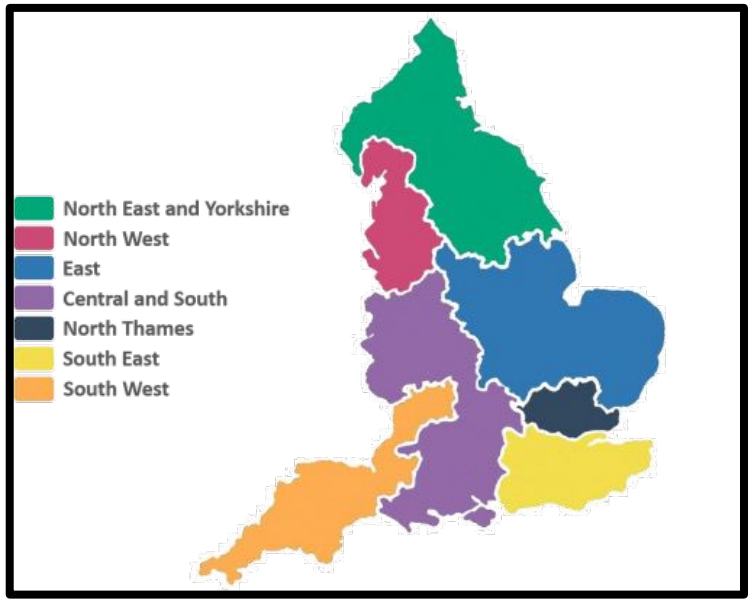
Phase 1 Outcomes: Process Outcomes, Prescribing Modification, Frequency of Clinically Relevant PGx Variation

Phase 1

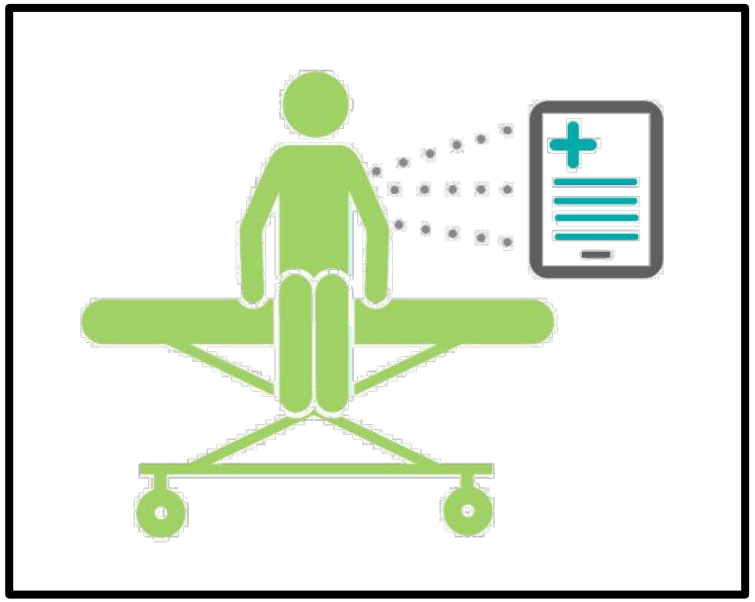
Phase 2

National Clinical Roll Out

Expand recruitment geography



Optimised recruitment & consent process



Integrate with other EHR Providers

Epic

system|one

Why Pharmacy?

"Since pharmacogenomics results are clinically inconsequential
unless considered in the context of drug therapy…
having pharmacists... coordinate this new and expanding type of clinical service would be a logical use of their medication expertise"

Dunnenberger H, Biszewski M, Bell G, Sereika A, May H, Johnson S, Hulick P, Khandekar J. Implementation of a multidisciplinary pharmacogenomics clinic in a community health system. American Journal of Health-System Pharmacy. 2016;73(23):1956-1966.

PALOH (Pharmacogenetics to Avoid Loss Of Hearing) study

- Investigated point-of-care testing for m.1555A>G in neonates
- Able to deliver test result in ~ 25 mins
- 3/751 babies variant identified and offered alternative antibiotic
- NICE Early Value Assessment (EVA) March 2023

Mc Dermott et al. *JAMA Pediatr.* 2022;176(5):486-492

Presumed Consent: Discuss

- 60 minute window for antibiotics – limited time for consent
- Presumed consent
- Delay antibiotics to allow informed consent
- Don’t test – risk hearing loss
- Switch antibiotic – antimicrobial resistance
- Maternal inheritance – family impact

Pharmacogenomics and mental health

Challenges:

- Antipsychotics & antidepressants can vary in therapeutic efficacy & clinical outcome
- Many potential adverse effects, can be disabling/severe
- Non-adherence ⇨ can be >50%, often driven by above factors

Current research & evidence to support PGx testing in psychiatry:

- higher response rates/symptom remission, greater adherence to treatment

PGx plays a significant role in PK of these drugs mainly via CYP metabolism ⇨ genetic variation in ***CYP2D6, CYP2C19*** most relevant for psychotropic drugs

Evidence-based guidelines (CPIC) are available to provide prescribing recommendations based on genotype

- SSRIs, TCAs, Atomoxetine, Anti-epileptics (phenytoin, carbamazepine)

The Opportunity: Personalising Healthcare Through PGx

Results Available

Presentation

Prescription

Presentation

Prescription

Presentation

Prescription

Lifelong Patient-held data?

Pre-emptive Panel Testing

Age 24
Requires antidepressant
PGx helps select option with least side effects

Age 47
Back pain
PGx helps selection of painkiller

Age 68
Acute Coronary Syndrome
Pgx avoids risk of ineffective antiplatelet and future cardiac events

Thank you

Email: Jessica.keen@mft.nhs.uk

@JessicaKPharma1

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