MEDICLINIC PRECISE

PHARMACOGENETIC (PGx) TESTING IN CLINICAL PRACTICE

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Mediclinic Precise

ADVERSE EVENTS
THE PATIENT EXPERIENCE

An adverse event is an undesired occurrence that results from taking a medication correctly.

The event can either be a type A reaction or a type B reaction.
Type A reactions: predictable adverse events , dose dependent [mild, moderate, or sever]e (i.e. preventable).

Type B reactions are completely unpredictable, not associated with dose

Any patient who has any untoward effect or outcome observed with medical treatment is experiencing an adverse event. This can include a wide range of symptoms that fall between the parameters of temporary harm to death

https://www.ncbi.nlm.nih.gov/books/NBK558963/

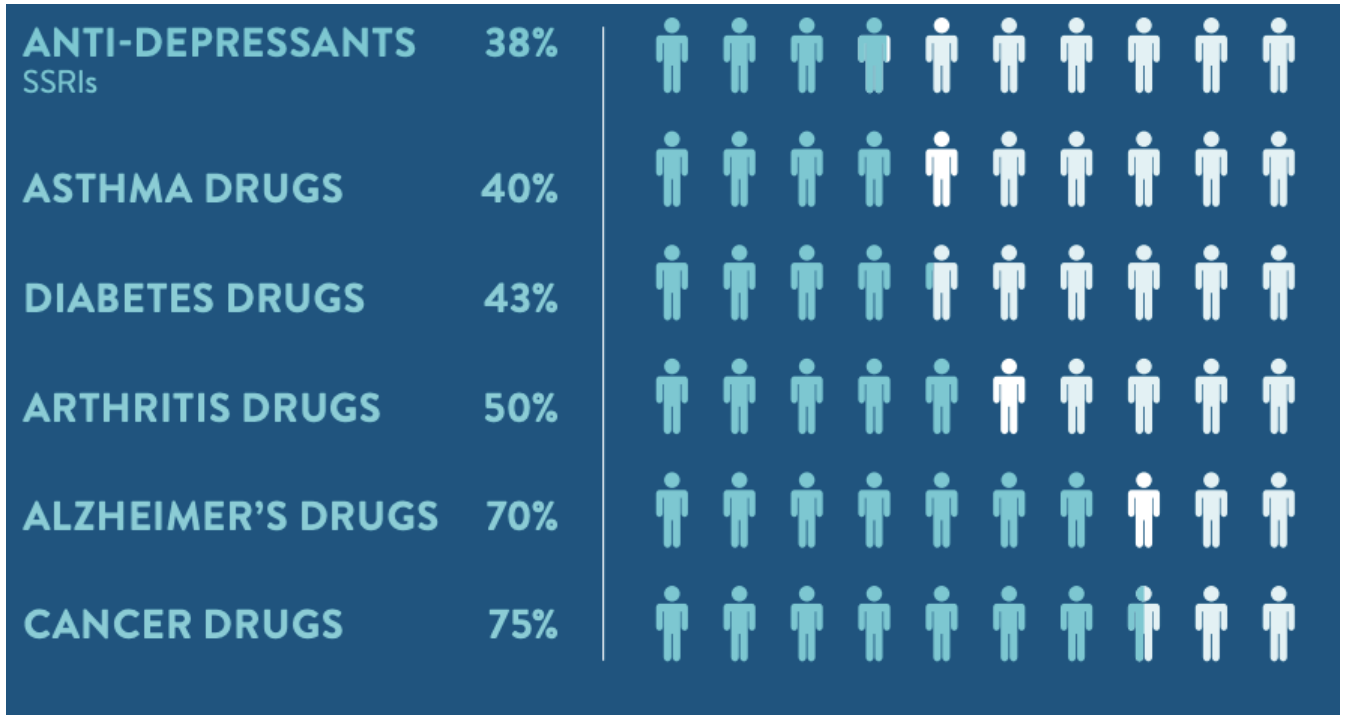
ADVERSE EVENTS
THE PATIENT EXPERIENCE

- In the United States: over 250,000 patients will experience an adverse event.
- Globally: +- 10% of patients experienced at least one adverse event.
- Annual incidence of adverse events of around 10%,
- 50% were found to be preventable.

https://www.ncbi.nlm.nih.gov/books/NBK558963/

VARIATION IN EFFICACY

Percentage of the patient population for which a particular drug in a class is ineffective on average:



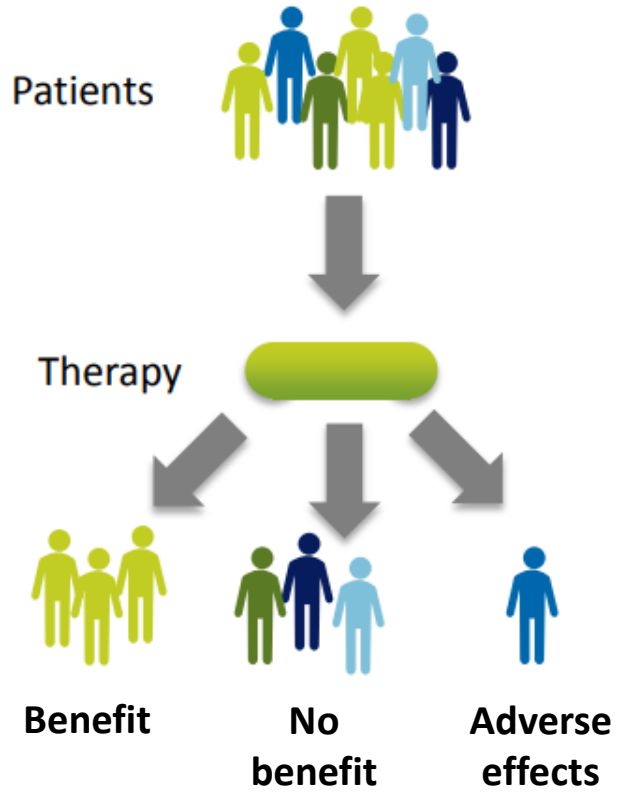
https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pdf

WHY DO SOME MEDICATIONS NOT WORK

Drug-Gene Interactions

A ONE-FOR-ALL APPROACH

Traditional prescribing



Clinical Guidelines

PK/PD

Potential SE profile + DDIs

…some benefit, some do not

https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pdf

A ONE-FOR-ALL APPROACH

Patient visits Doctor

Doctor prescribes medication

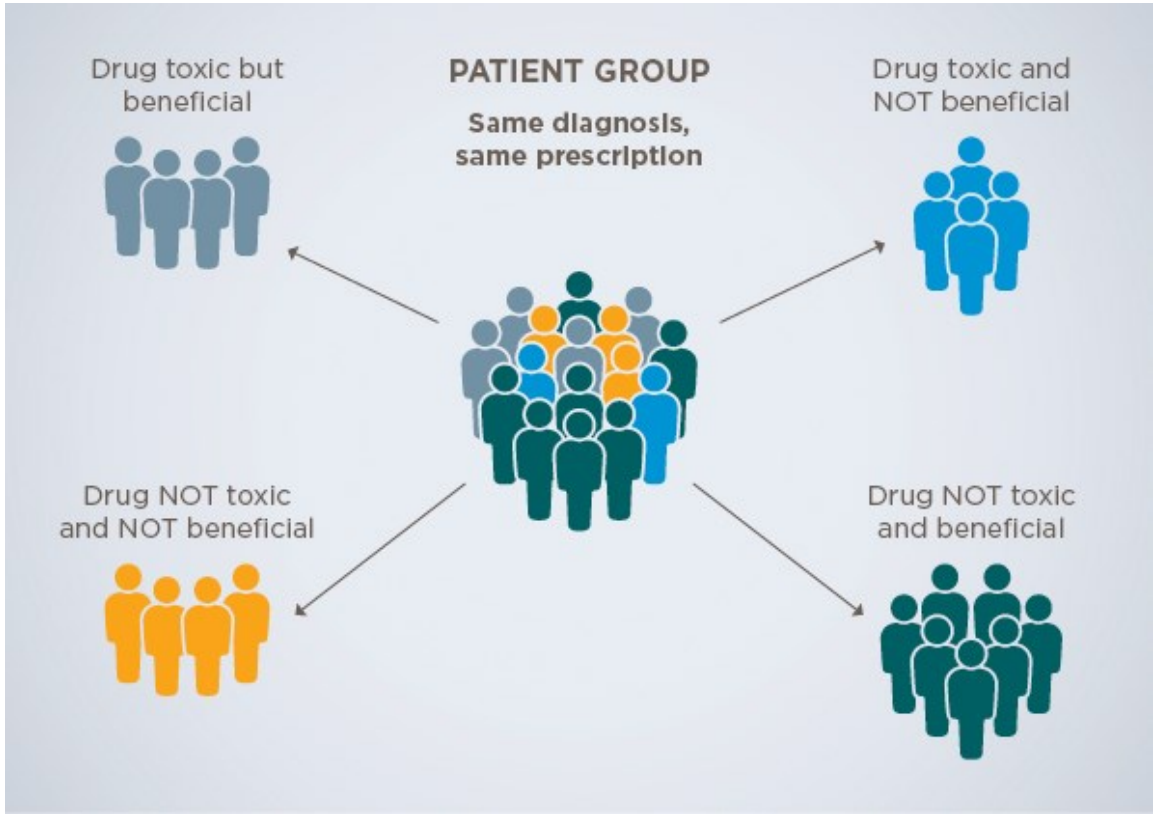
Drug is **effective**, minimal SE

Drug is **ineffective**, or significant SE

Trial and error

INTRODUCTION TO PGx TESTING

Pharmacogenetics is the science of how an individual's unique genetic profile affect the pharmacology of certain medications.



Clinical Guidelines

PK/PD

Potential SE profile + DDIs

PGx Profile

ADDING AN ADDITIONAL TOOL:
PGx TESTING

Patient visits Doctor

Doctor orders PGx test

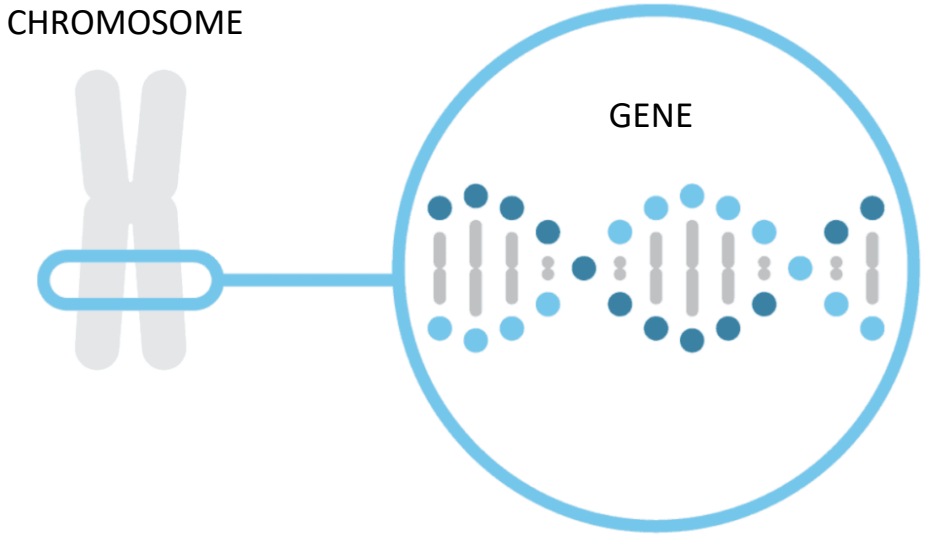
Doctor prescribes *RIGHT* medication, at the *OPTIMAL* dose, for the *INDIVIDUAL*

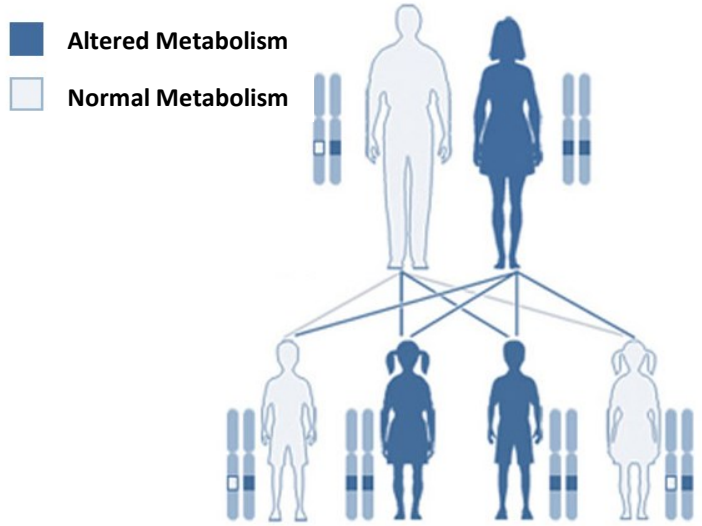
Drug is effective, minimal SE

https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pdf

PGx TESTING BACKGROUND

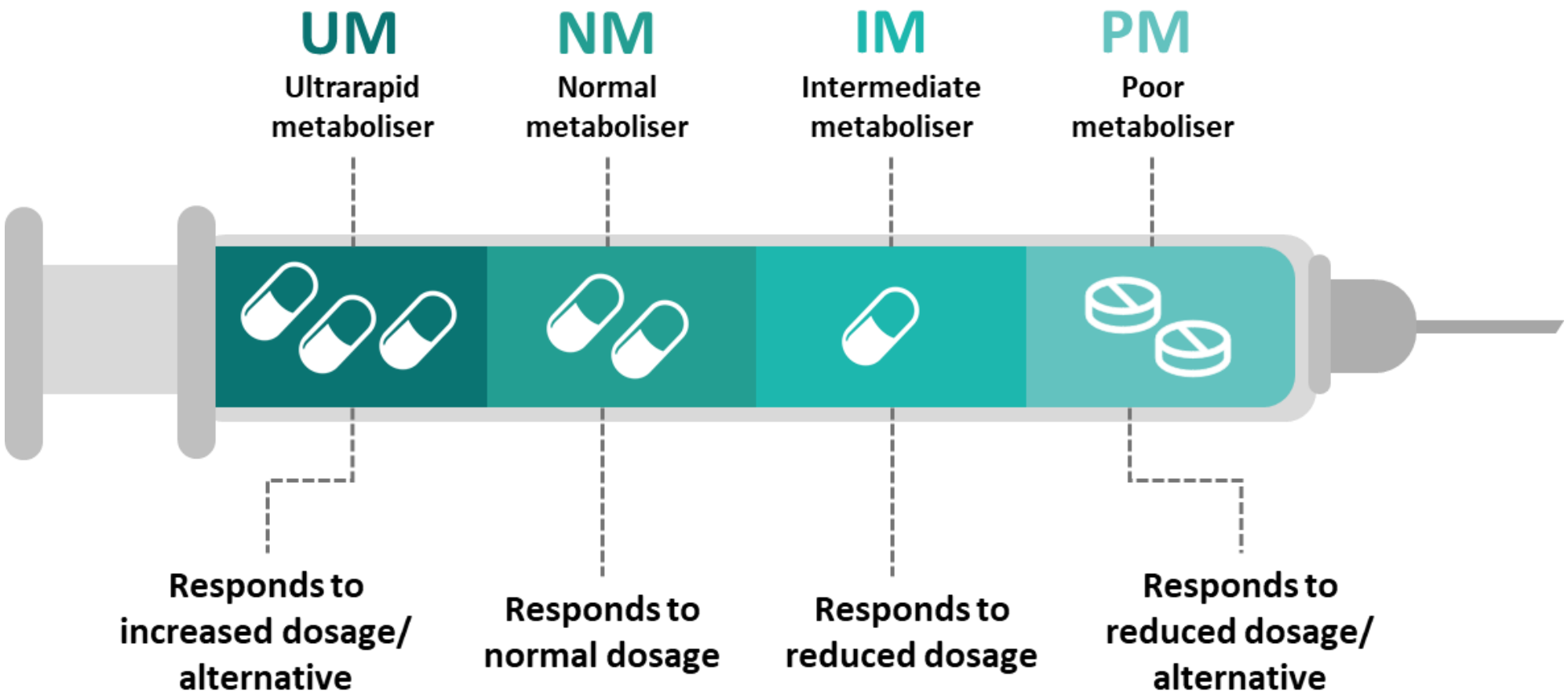
- Genes code for proteins and metabolic pathways
- Responsible for drug metabolism/activation/efficacy
- Inherit one copy of a gene per parent
- E.g. Inherits one/more with decreased function
- Results in altered drug response





https://www.illumina.com/science/education/genomics-101/genes-inherited-diseases.html

VARIATION IN METABOLISM



Malsagova et al., Pharmacogenetic testing: A too for personalised drug therapy optimisation, *Pharmaceutics* (2020)

DRUG-GENE PAIRS

Gene	Drug
DPYD	Fluorouracil, capecitabine, tegafur
CYP2D6	Codeine, tramadol, antidepressants
CYP2C19	Clopidogrel, antidepressants
CYP2C9	Warfarin, phenytoin
HLA-A & HLA-B	Carbamazepine, allopurinol, abacavir
MT-RNR1	Aminoglycoside antibiotics

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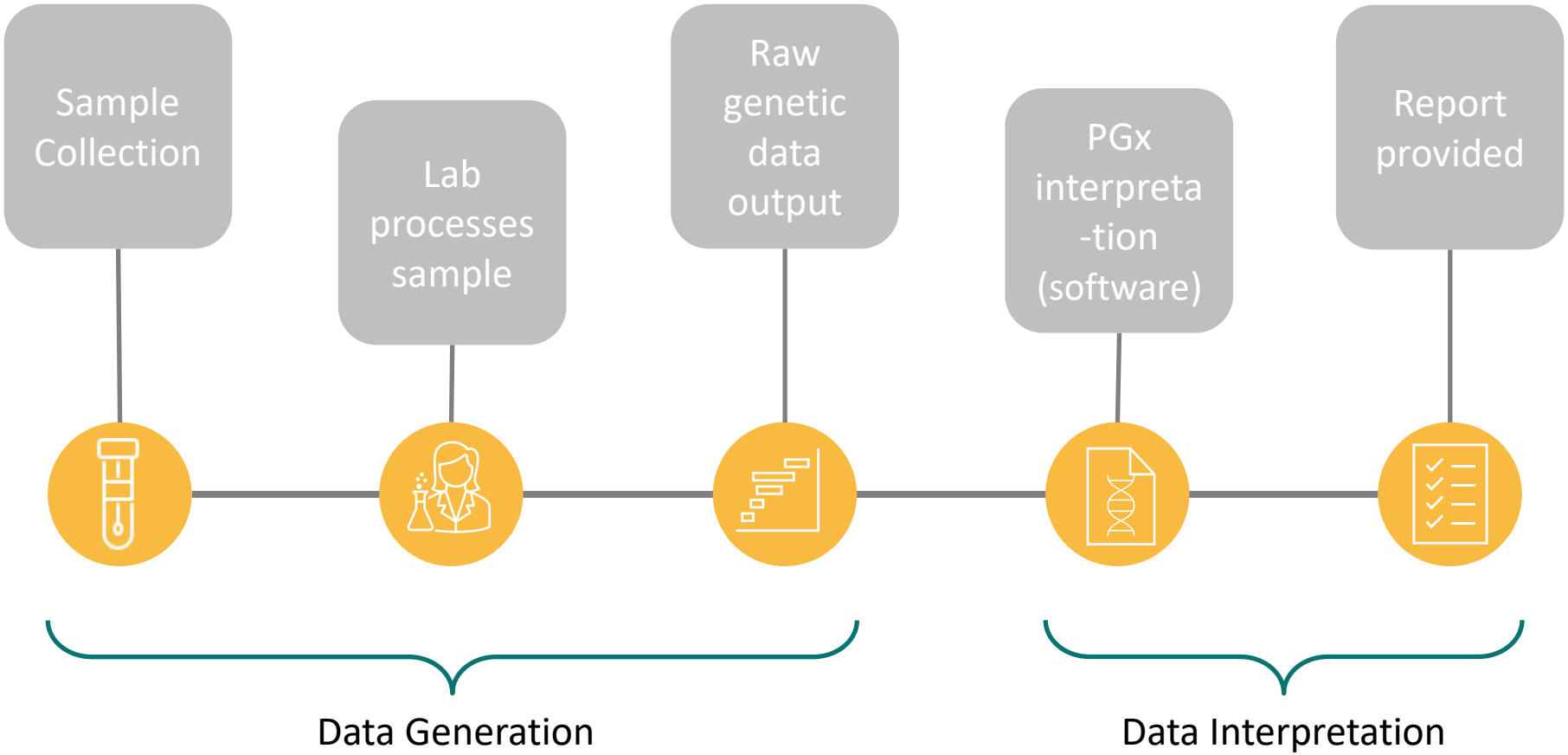
CPIC® Clinical Pharmacogenetics Implementation Consortium

Genetic Results (PM/IM/NM/UM) → PGx dosing guidelines

https://www.illumina.com/science/education/genomics-101/genes-inherited-diseases.html

TESTING WORKFLOW



IN PRACTICE…

PAIN
codeine

- Acute severe pain after injury
- PM = minimal relief
- Alternative medication

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IN PRACTICE…

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Cardiac disease
metoprolol

- Hypertension
- UM = treatment failure
- Give max target dose;
- 2.5x standard dose OR alternative medication

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IN PRACTICE…

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- Acute severe pain after injury
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Cholesterol
Statins (simvastatin)

- Middle aged male
- Myopathy after new medication
- Decreased function gene
- Give alternative (pravastatin)

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Depression
TCAs (amitriptyline)

- Patient struggling with MH
- Complaints and poor adherence
- PM = increased [plasma]
- Avoid OR give 50% lower dose AND do TDM

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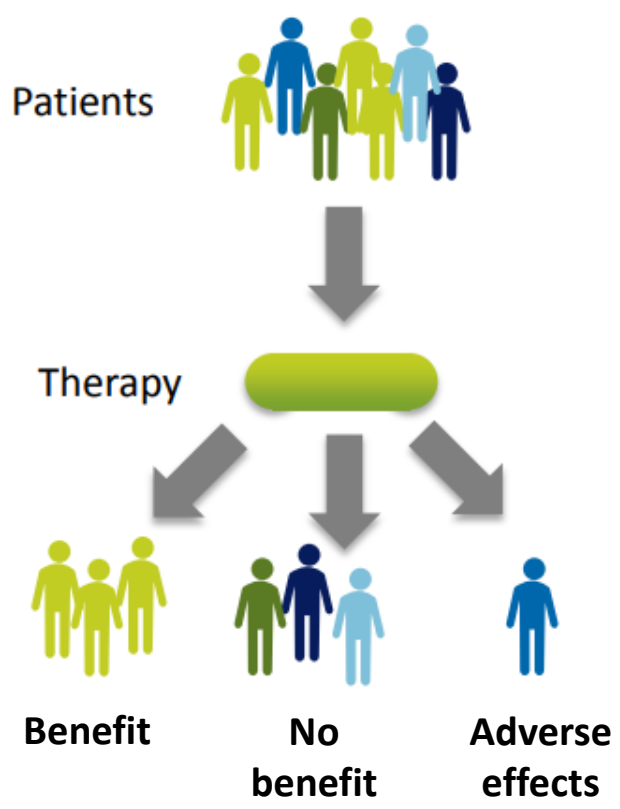
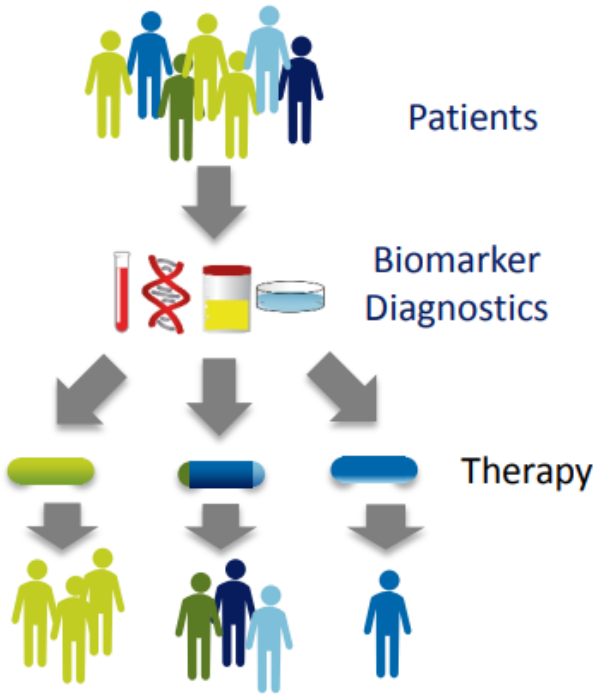
A NEW TREATMENT PARADIGM

Traditional prescribing



Informed prescribing



Each patient benefits from individualized treatment

https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The_PM_Report.pdf

BENEFITS OF PGx TESTING

Personalised Therapy

- Informed prescribing by HCP
- Therapy is tailored to individual patient
- Based on their unique generic makeup

Optimising Regimens

- Ensure maximum efficacy
- Minimal side effects
- Find medications that work for them

Reduce ADR

- Not everyone responds the same
- Limit potential side effects and improve compliance
- Avoid serious ADRs
- Suggest alternatives

BACKGROUND
Evidence for PGx utility

THE LANCET

A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study

PREPARE study published in 02/2023

- Open label, cross-over
- Multicentered
- Cluster randomized implementation
- 6944 participants

Found actionable result in 22% participants

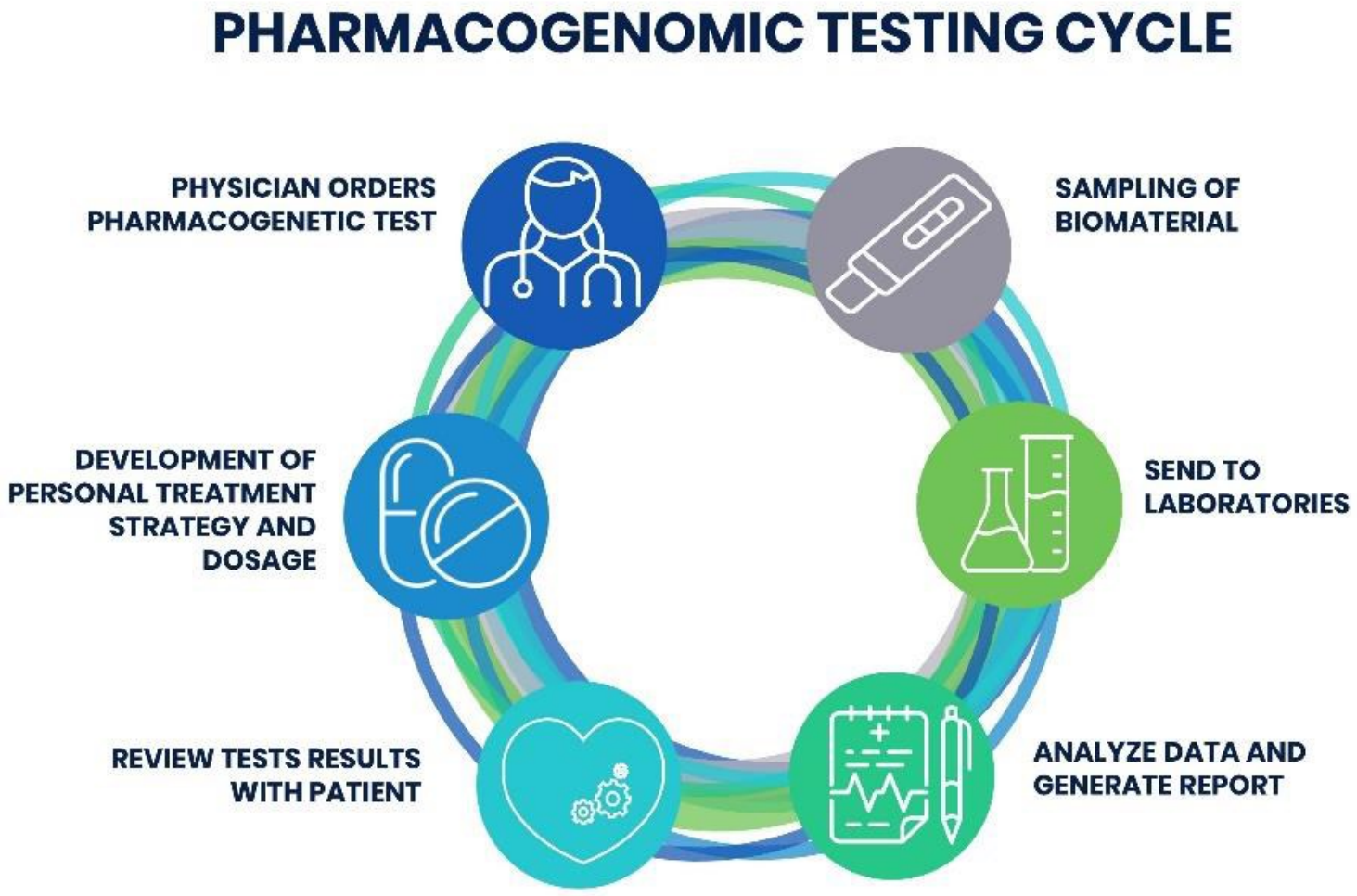
Significantly reduced incidence of ADR risk by ~30%

12-Gene PGx panel to prevent adverse drug reactions

7 European countries (Austria, Greece, Italy, the Netherlands, Slovenia, Spain, and the UK)

Large-scale implementation could help to make drug therapy increasingly safe.

PRECISION PRESCRIBING
PATIENT JOURNEY



PRECISION PRESCRIBING
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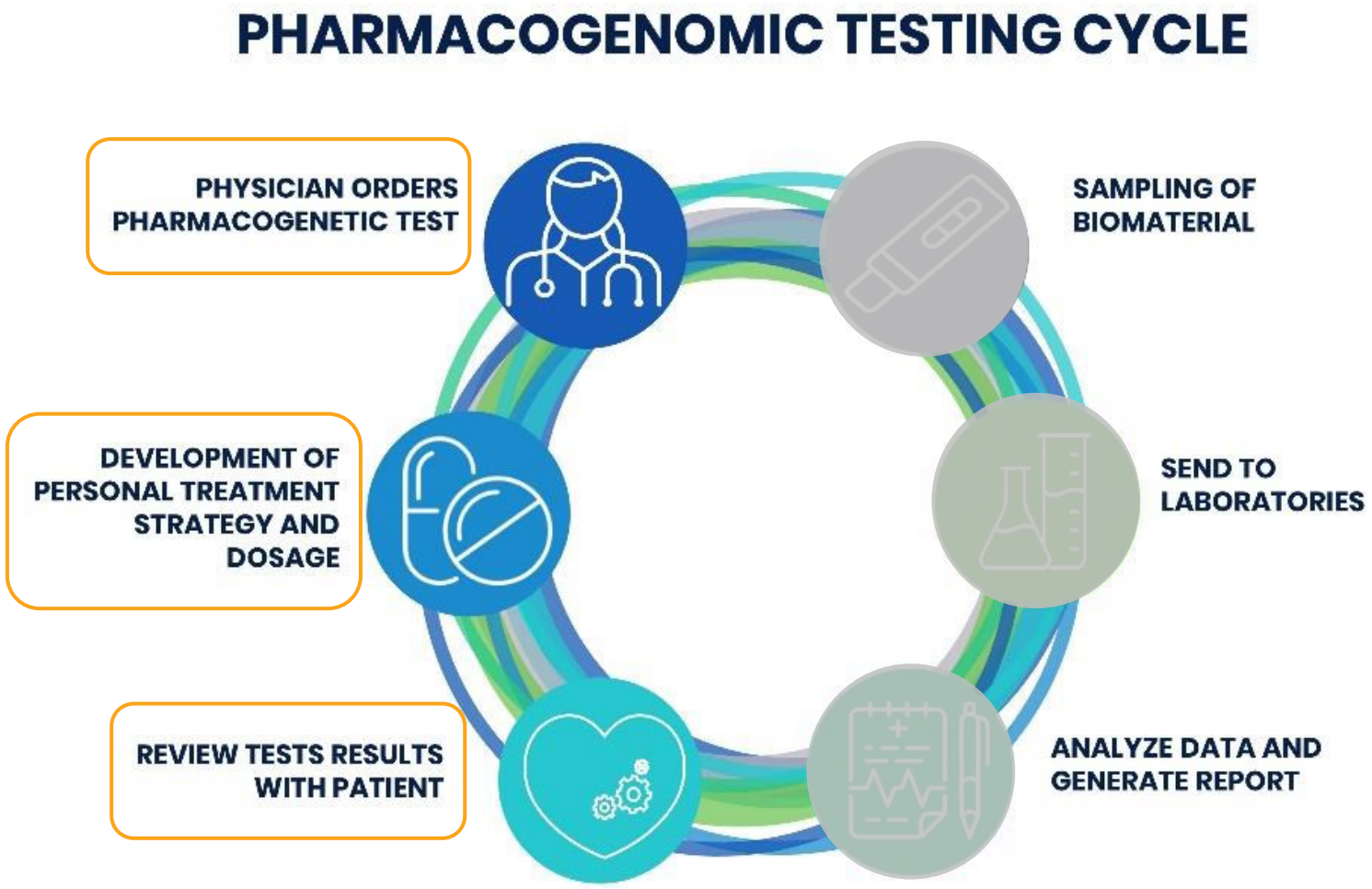

IDEAL CANDIDATES

- Acute and Chronic Pain
- Hypertension and dyslipidaemia
- Depression and anxiety
- Gastrointestinal issues
- Polypharmacy

CHALLENGES MOVING INTO PRACTICE

- Lack of time (both primary HCP and other healthcare staff)
- Replacing ‘prescriber autonomy’
- Medical aid coverage/co-payment/out of pocket
- Relevance of biomarkers to African and mixed populations

INTRODUCING
MEDICLINIC PRECISE

Mediclinic Precise is a bundle of
DNA based diagnostic and clinical interpretation services
offering a new approach to healthcare, based on an individual's genetic profile
to customise their wellness, disease prevention and health management plan

Personalised medical solutions

MEET THE TEAM

Dr Lindsay Petersen
General Manager

Dr Lizahn Haasbroek
Product Manager (PGx)

Paidamoyo Kachambwa
Senior Bioinformatician

Hennie La Grange
Logistics Manager

Lizahn Van Neel
Data Capturer

Independent Health Professionals

Dr Liani Smit
Clinical Geneticist

Dr Chris Maske
Clinical Pathologist

Noelene Kinsley
Genetic Counsellor

MEDICLINIC PRECISE PGx TEST

- Value-add and differentiation
- Accessible through HCP
- Pre- and post-test support
- Reporting on actionable test results
- Summarised results

MEDICLINIC PRECISE PGx TEST
SUMMARY LETTER AND CONSULTATION

1. Your current treatment

Patient-reported medical conditions:

Hypertension, high blood pressure

Patient-reported medications:

Medication	Dosage	Date Started	Side Effects	Still Take
LOSARTAN	50 mg	Aug 2022		Yes
OMEPRAZOLE	20 mg			No

Patient-reported supplements:

Multivitamin, Chromium Picolinate

Considerations for current therapy:

No further recommendation for current therapy.

Patient has a **normal metaboliser status** for the enzyme(s) involved in these drug pathways. i.e. **normal** response and metabolism expected.

MEDICLINIC PRECISE PGx TEST
SUMMARY LETTER AND CONSULTATION

Pharmacogenetic implication for cardiovascular disease:

Biomarker	Function	Summary
CYP2D6	Ultrarapid metabolizer	**Increased metabolism** of **metoprolol**, suggest **alternative drug** (e.g. bisoprolol) or titrate dose to a maximum of 250% of the normal dose and monitor clinical response. **Possible decreased response** to anti-arrhythmic drugs including **mexiletine**, **flecainide** and **propafenone** and **timolol**; **consider** use of an **alternate** anti-arrhythmic drug (**sotalol, disopyramide, amiodarone**) or monitor treatment efficacy.
CYP3A5	Intermediate metabolizer	CYP3A5 intermediate metabolizers have an **increased clearance** of **cilostazol**, which can result in lower clinical response at usual doses. Suggest increased monitoring for possible decreased efficacy.
CYP2C19	Normal metabolizer	**Normal response** to **clopidogrel** is anticipated.

MEDICLINIC PRECISE PGx TEST
ACCESS AND MORE INFORMATION

Mediclinic Precise offers a number of channels to patients and Medical Practitioners to obtain detailed test information as well as guidance on the most appropriate tests for the patient's condition.

Visit our website www.mediclinic.co.za/precise for more information

Email pgx.info@mediclinic.co.za for one-on-one engagements

THANK YOU