

Tailored to Heal: *The New Era of Individualised Medicine*

Chandanie Wanigatunge

MBBS Hons (NCCMC), MD (Col), FCCP, FRCP Edin, FRCP

Chair Professor of Pharmacology

FMS, USJ





Helen gives '*pharmakon*', an Egyptian drug, with wine to Telemachus, who was sad about the absence of his father, Odysseus. *Pharmakon* was used to ease grief and anger, allowing people to forget their troubles.

- Odyssey by Horner



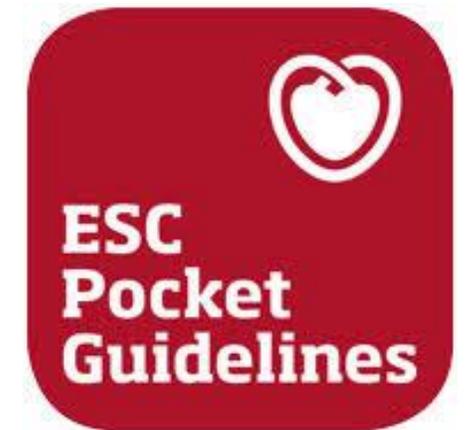
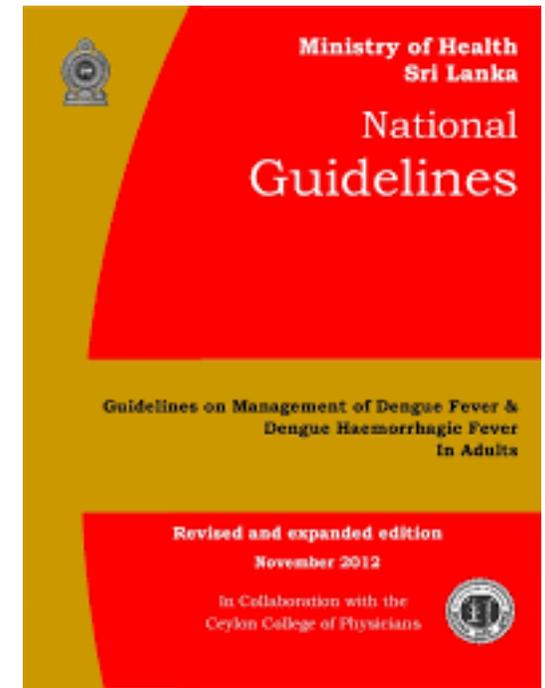
The Doctor (Detail) – Luke Fildes, 1891
Image credits: Wikipedia



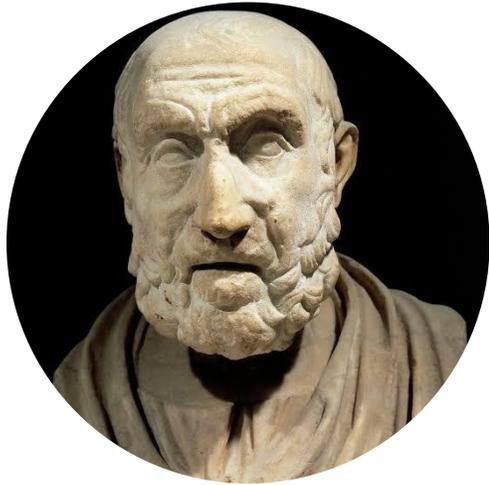
Guidelines

Guidelines provide **evidence-based, standardised** approaches to patient care

- Support clinical decision-making
- Improve patient outcomes
- Enhance quality of care
- Reduce variation in practice

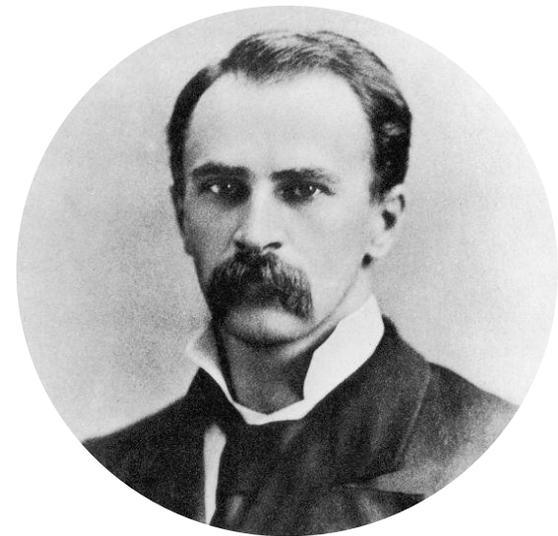


- Mr A and Mr B are patients in their 50s with T2DM, HT, and dyslipidaemia
 - Had similar control, no complications
- Both experienced NSTEMIs
 - Stented
 - prescribed DAT
- 10 days after stent placement
 - Mr B presented with stent thrombosis
 - Mr A remained well



Hippocrates (460-377 BCE)

There is great interindividual variability in the response to a standard dose of most drugs



Sir William Osler, 1849–1919

“..... different [drugs] to different patients, for the sweet ones do not benefit everyone, nor do the astringent ones, nor are all the patients able to drink the same things.”

- Corpus Hippocraticum

“**Variability is the law of life**, and as no two faces are the same, so no two bodies are alike, and no two individuals react alike, and behave alike .”

Efficacy

Safety



“...Drugs out there on the market work, but they don't work in everybody.
> 90% of drugs **work in only 30-50% of patients.**”

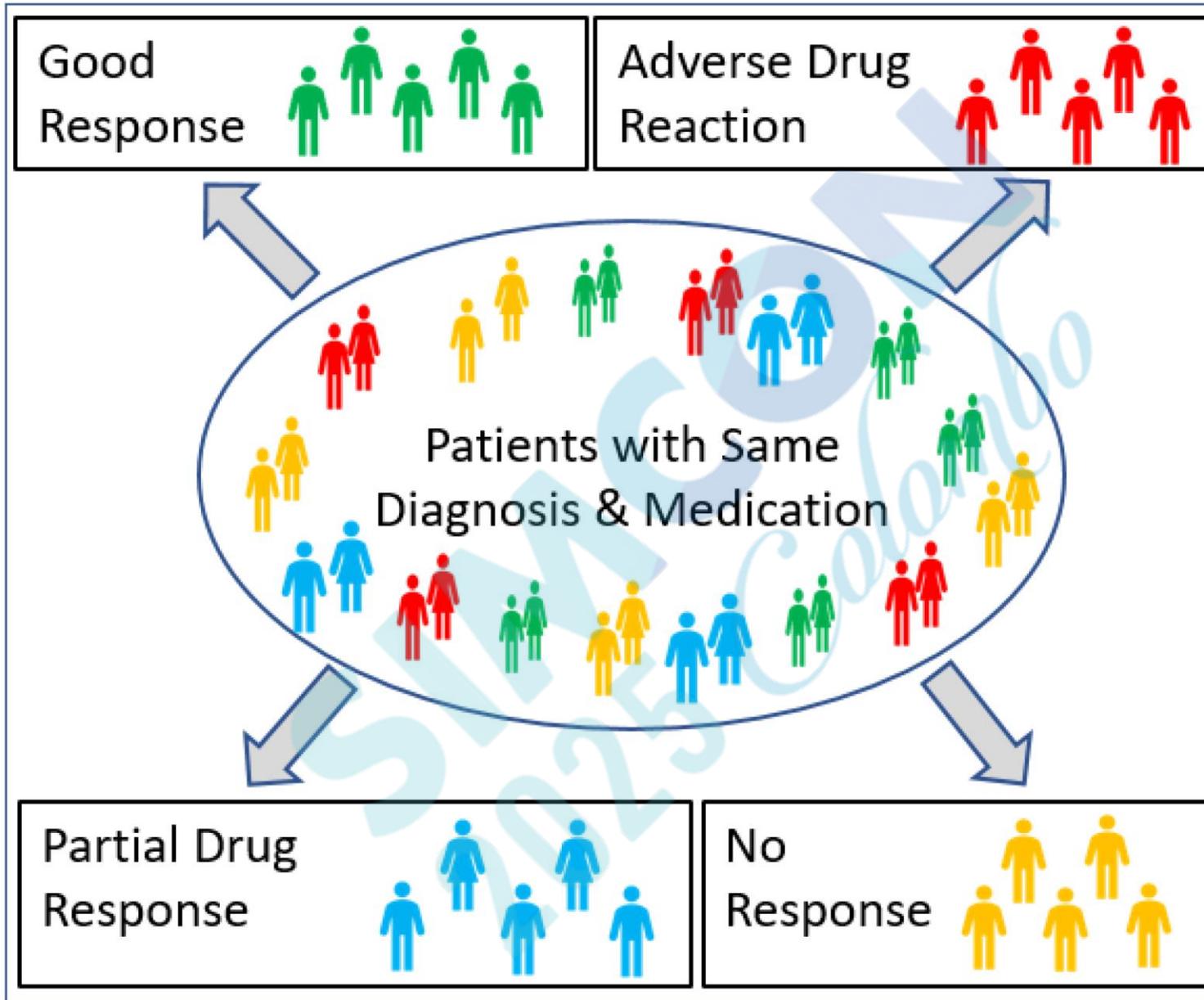
– Dr Allen Roses

Worldwide VP of Genetics at GlaxoSmithKline (GSK)

- “6.5% of all hospital admissions are due to ADRs”
- “Increases to >15% in those with multimorbidity”

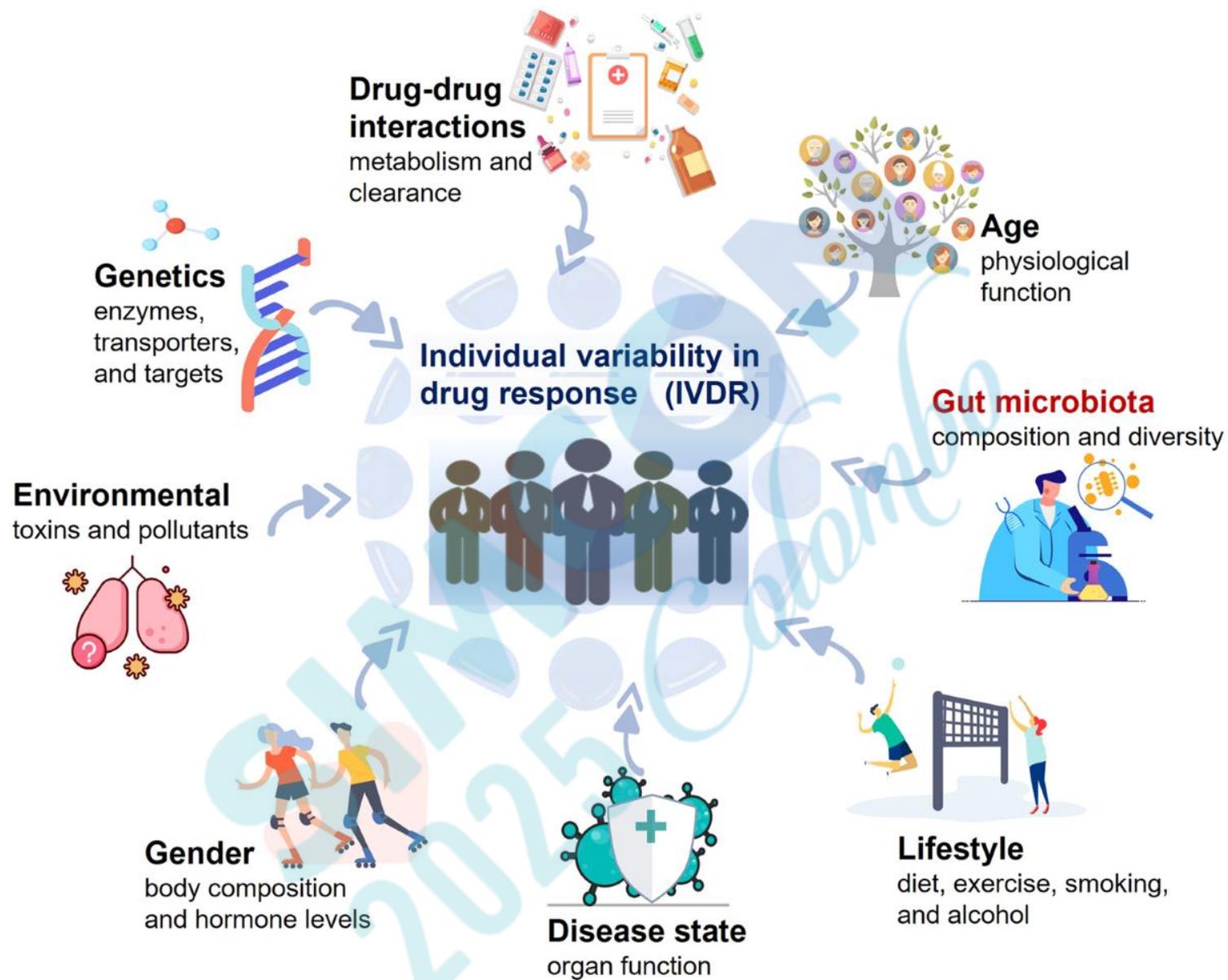
- UK data





Who is which?





Zhao, Q., Chen, Y., Huang, W. *et al.* Drug-microbiota interactions: an emerging priority for precision medicine. *Sig Transduct Target Ther* **8**, 386 (2023).



- **Precision** - the quality, condition or fact of **being exact and accurate**
 - *Oxford Dictionary of English*

- **Precision medicine**

- Uses **combined knowledge** (i.e. clinical, genetic, genomic, and epigenetic/environmental) **to anticipate** a person's
 - vulnerability
 - prognosis of their disease
 - response to therapy
- Enhance individual's health



In this
presentation....

- Precision medicine
 - Pharmacogenomics
 - Digital human twins
- Dilemmas and challenges in the application of precision medicine

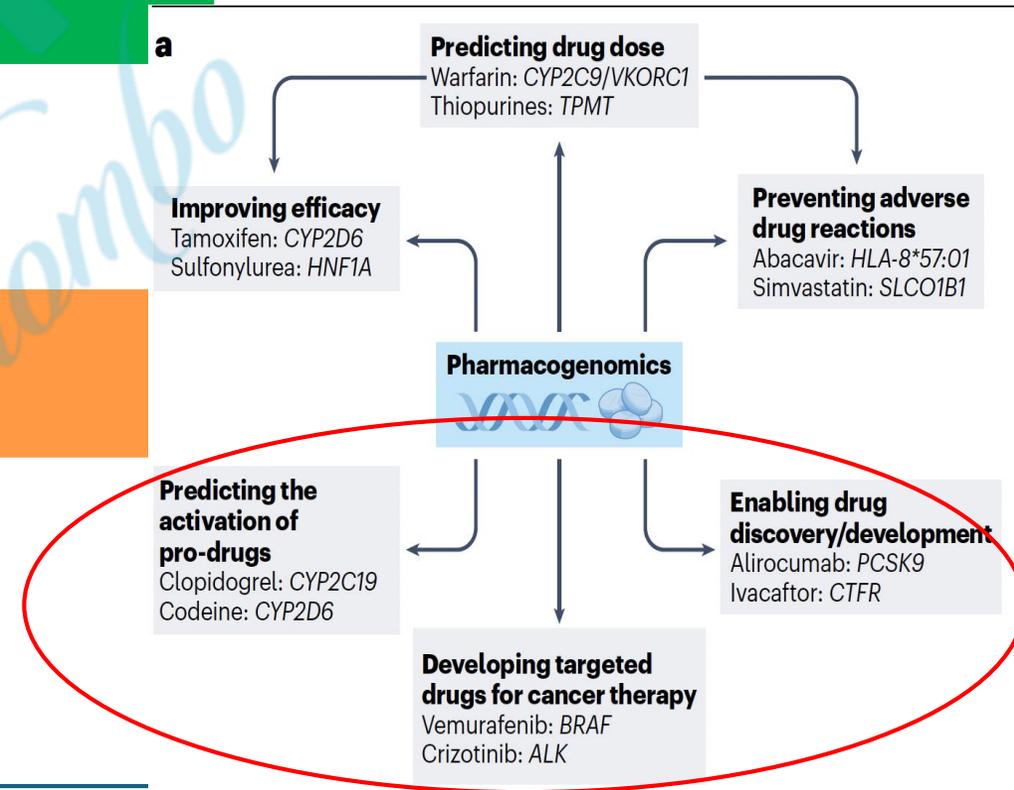
Pharmacogenomics (PGx)

Current definition

Study of how a person's genetic make-up affects their response (efficacy and/or safety) to a drug

Broader definition

Study of genomic technologies to enable the discovery and development of novel drugs, and the optimisation of drug dose and choice in individual patients to maximise efficacy and minimise toxicity



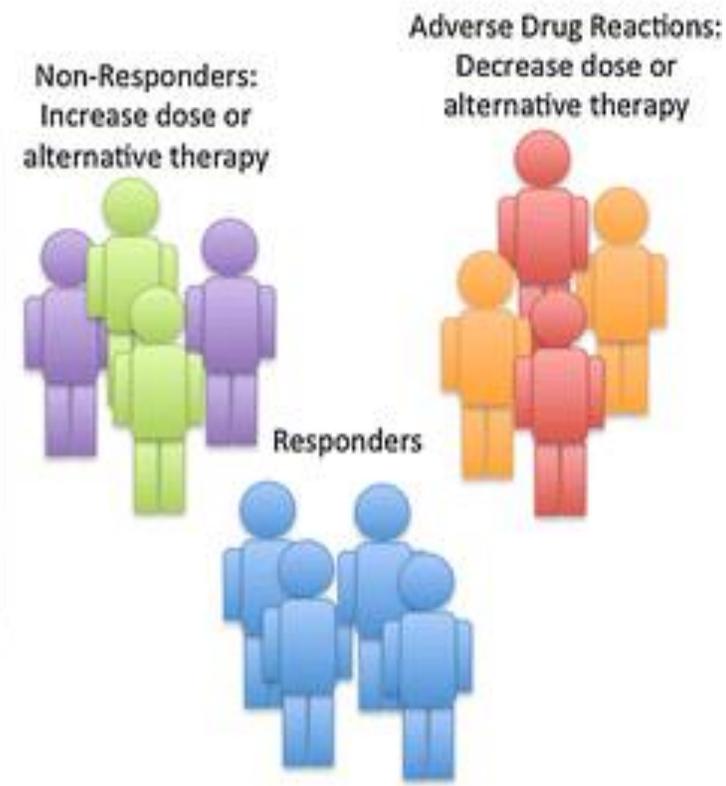
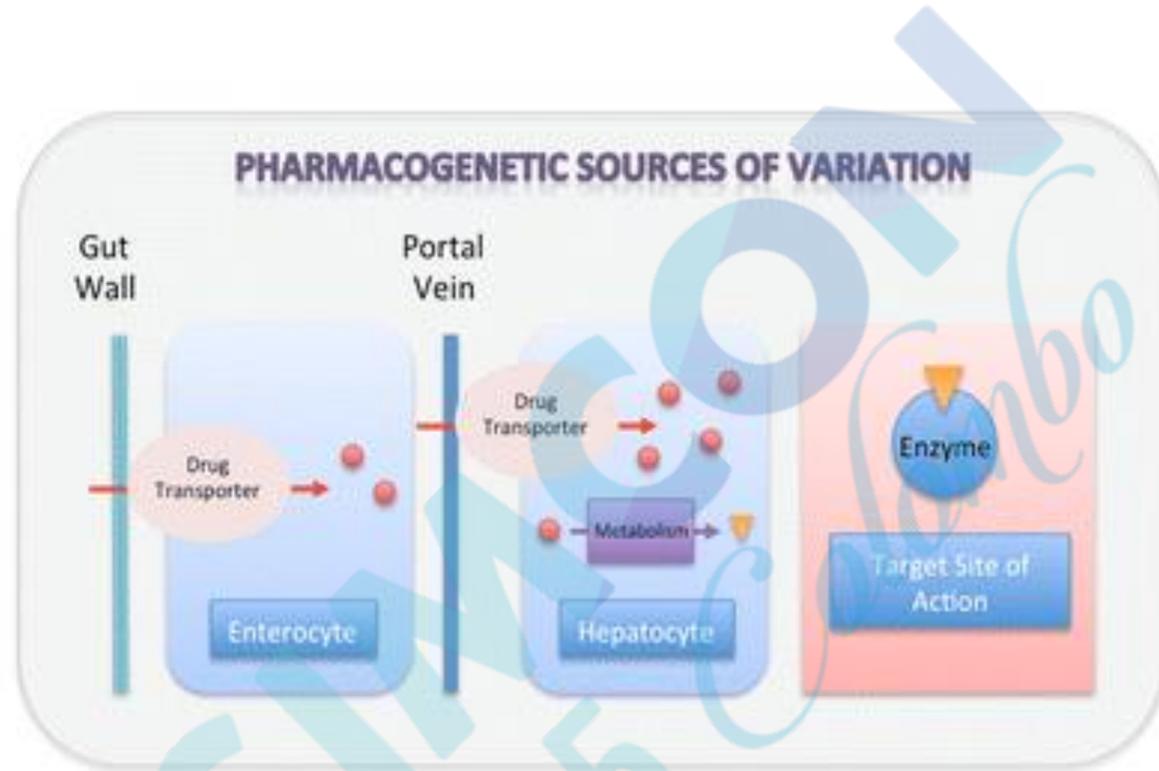
Pirmohamed, M. Pharmacogenomics: current status and future perspectives.
Nat Rev Genet **24**, 350–362 (2023).



Pharmacogenomics

- **Utilise** information about a person's genes, including his nucleotide sequence
- **Seek** to identify **genetic contributors** to human variation in drug efficacy and toxicity
- **Aims** to improve clinical outcomes for the individual by making drugs better and safer



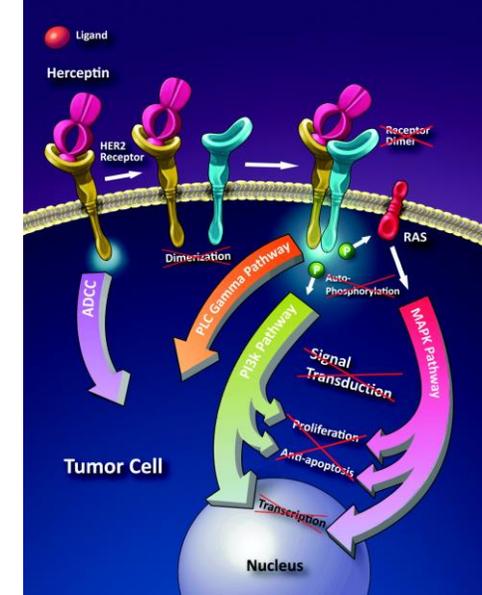


Gong, I.Y., Kim, R.B. Pharmacogenetic Advances in Cardiovascular Medicine: Relevance to Personalized Medicine. *Curr Genet Med Rep* 1, 1–14 (2013).

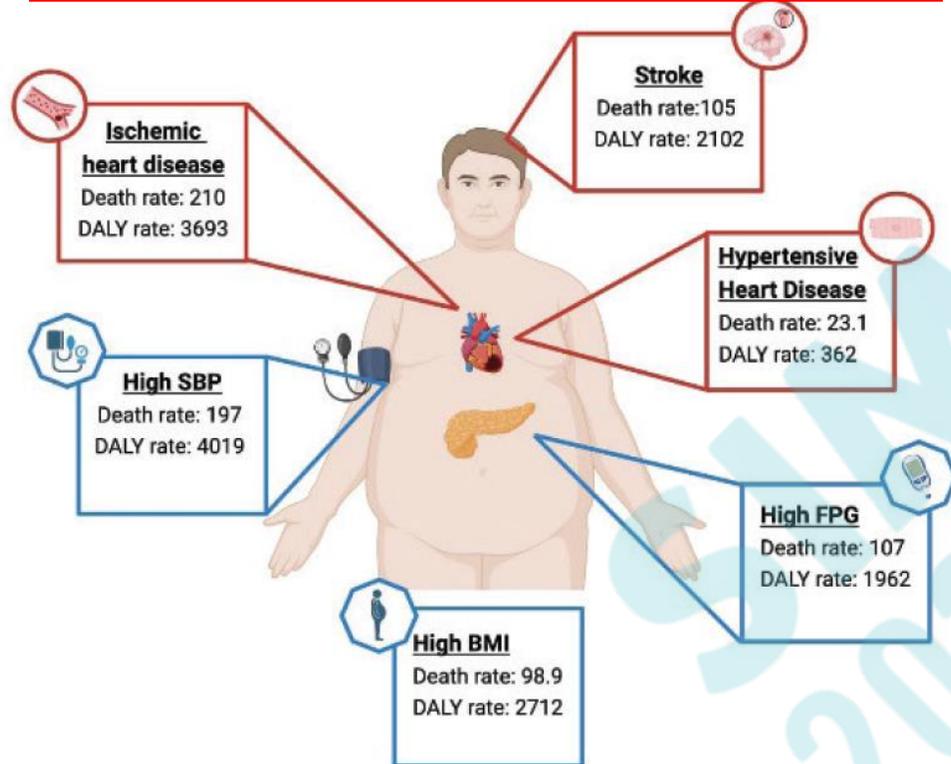


PGx – practical application

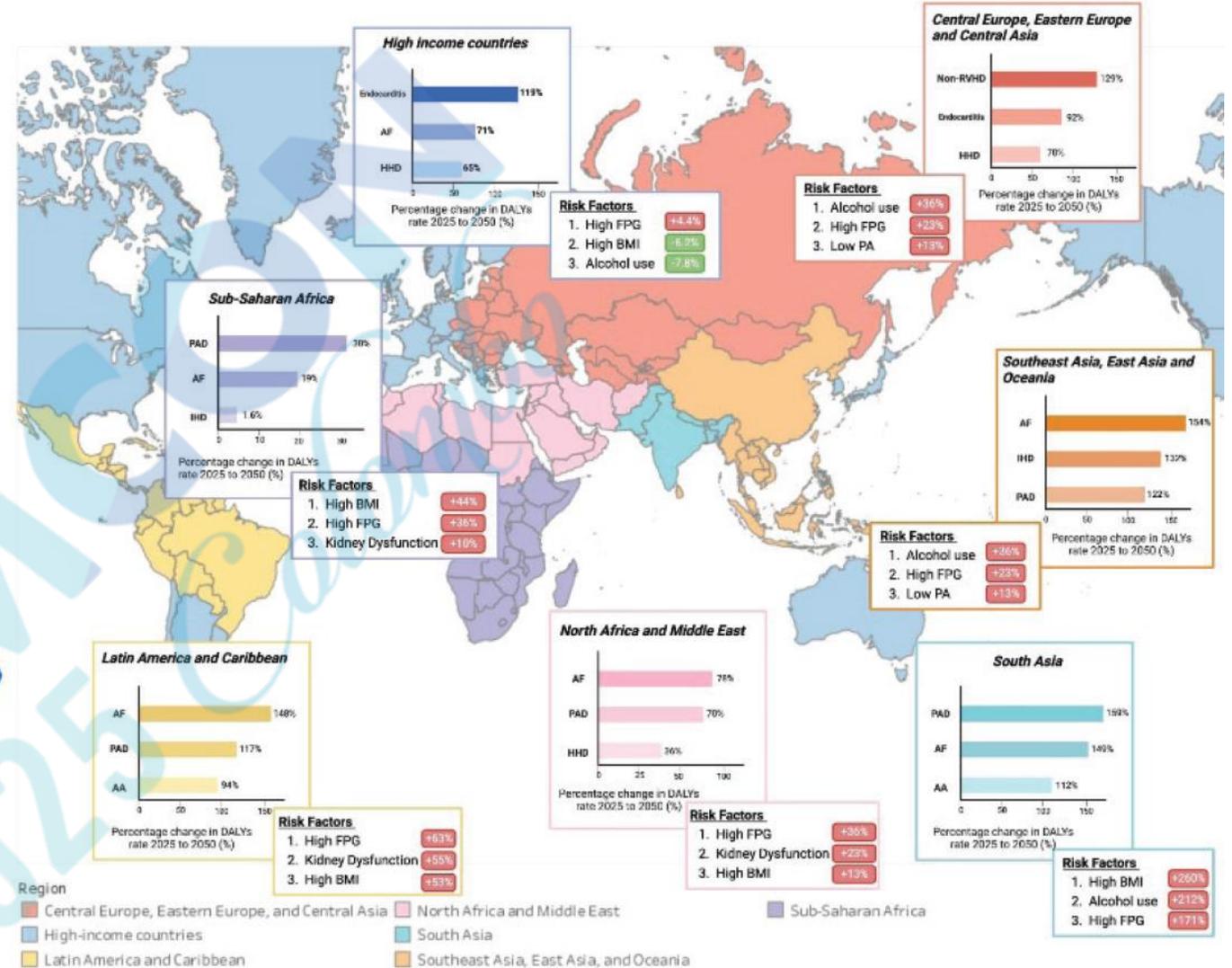
- HER 2 gene predicts the response to *trastuzumab* (*Herceptin*[®]) in women with breast cancer
- Use of trastuzumab (anti-oestrogen therapy) in patients whose tumours were HER2-positive
 - improves disease-free and overall survival
 - avoid unnecessary toxicity



Global Burden of Cardiovascular Diseases: Projections to 2050



*All rates are presented in per 100,000 population

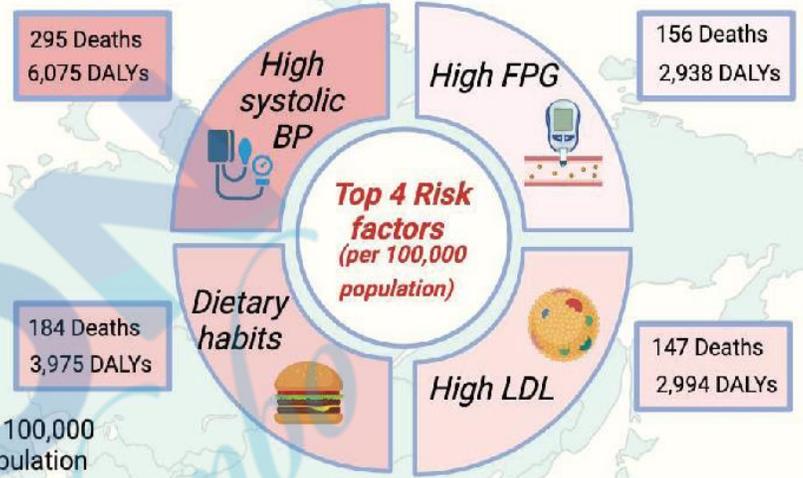
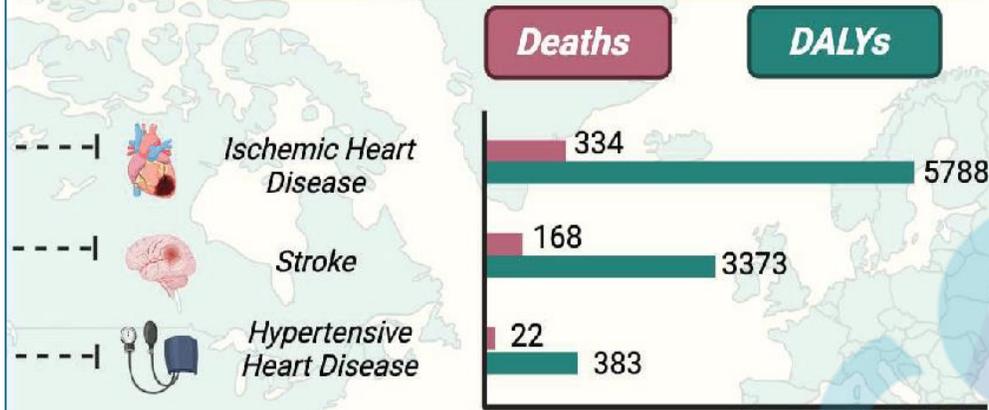


*AA - aortic aneurysm; AF - atrial fibrillation and flutter; DALYs - disability adjusted life years; HHD - hypertensive heart disease; IHD - ischemic heart disease; Non-RVHD - non-rheumatic valvular heart disease; SBP - systolic blood pressure; PA - physical activity

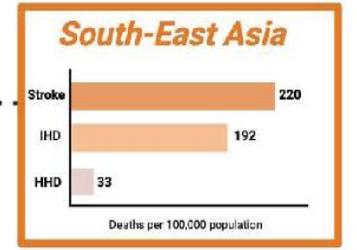
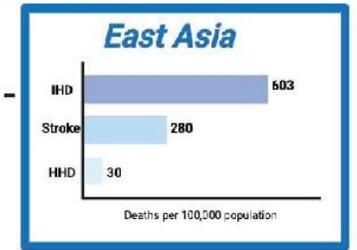
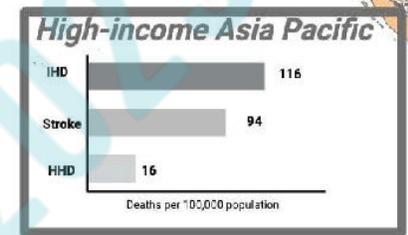
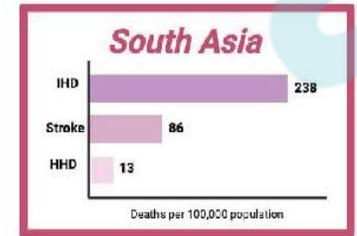
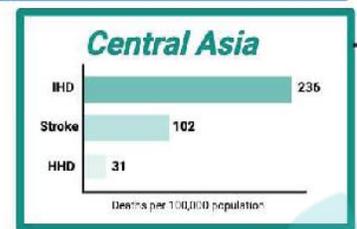


Projected Burden of Cardiovascular Diseases in Asia: 2025 to 2050

In Asia in 2050, top 3 causes of cardiovascular ...



Top causes of deaths by region



*BP- blood pressure; DALYs; disability-adjusted life years; HHD- hypertensive heart disease; IHD -ischemic heart disease; LDL - Low-density lipoprotein



Clopidogrel

- Marked interpatient variation in responsiveness
- 21% - non-responders: at risk for CVD (MI & strokes) and stent thrombosis after PCI

Statins

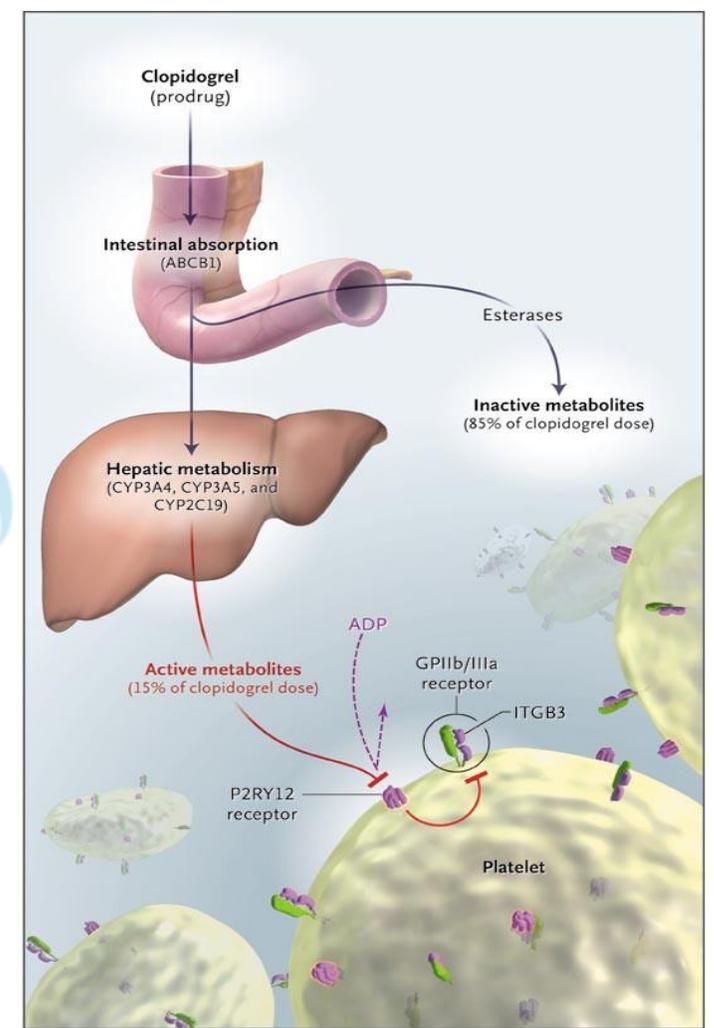
- Substantial interindividual variability in PK and PD
- Some patients
 - fail to attain sufficient cholesterol reduction and prevention of cardiovascular events
 - At a higher risk of ADRs – e.g. myopathy

Warfarin

- Marked interindividual variations
- Narrow therapeutic range

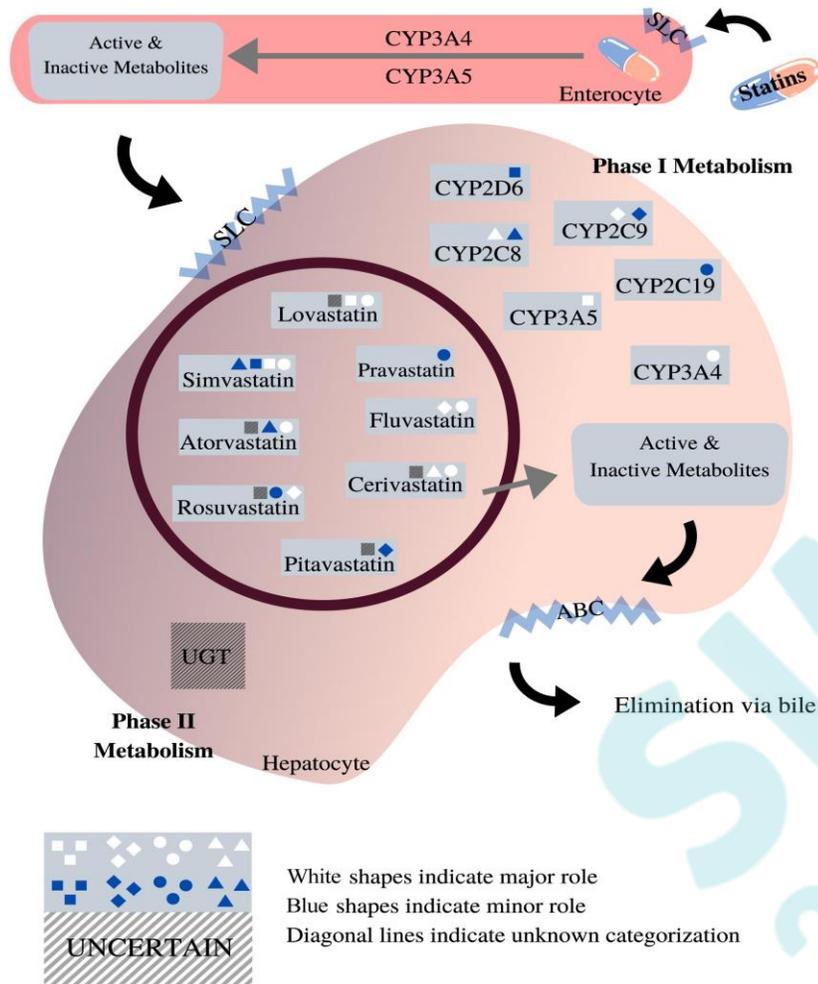
Clopidogrel

- Clopidogrel is a prodrug
 - Activation catalysed by several **CYP isozymes**
- CYP2C19*2 (rs4244285) and CYP2C19*3 (rs4986893) - loss-of-function SNPs - result in
 - lower platelet inhibition
 - increased risk of major cardiovascular events particularly stent thrombosis in PCI patients
- **CYP2C19 is thought to represent only a portion of the observed variation in antiplatelet response**



Simon T, Verstyuyt C, Mary-Krause M, et al. Genetic determinants of response to clopidogrel and cardiovascular events. *N Engl J Med* 2009;360:363-375

Statins

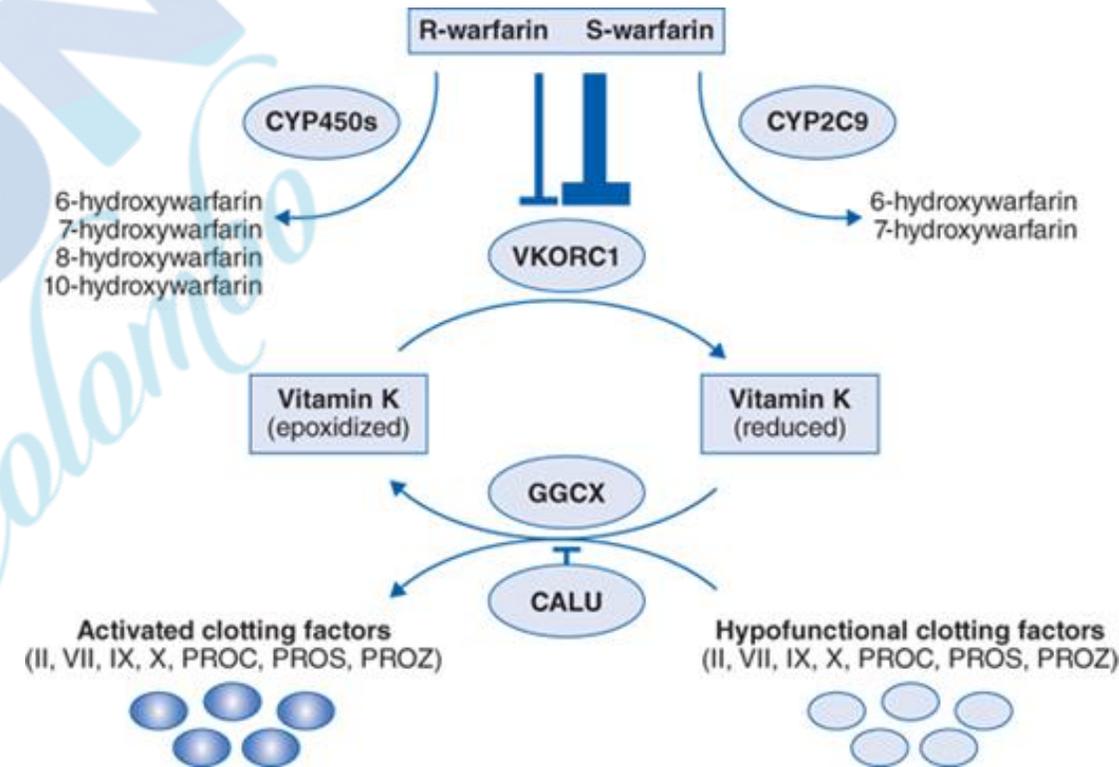


- Different CYP enzymes metabolise different statins
 - Variants can affect LDL lowering effect
- Statin-induced myopathy (SIM)
 - Prevalence – 7 – 30%
 - **Dose dependent**
 - Higher risk of SIM with a polymorphism in the SLCO1B1 gene

Kee PS, Chin PKL, Kennedy MA, Maggo SDS. Pharmacogenetics of Statin-Induced Myotoxicity. Front Genet. 2020 Oct 16;11:575678.

Warfarin

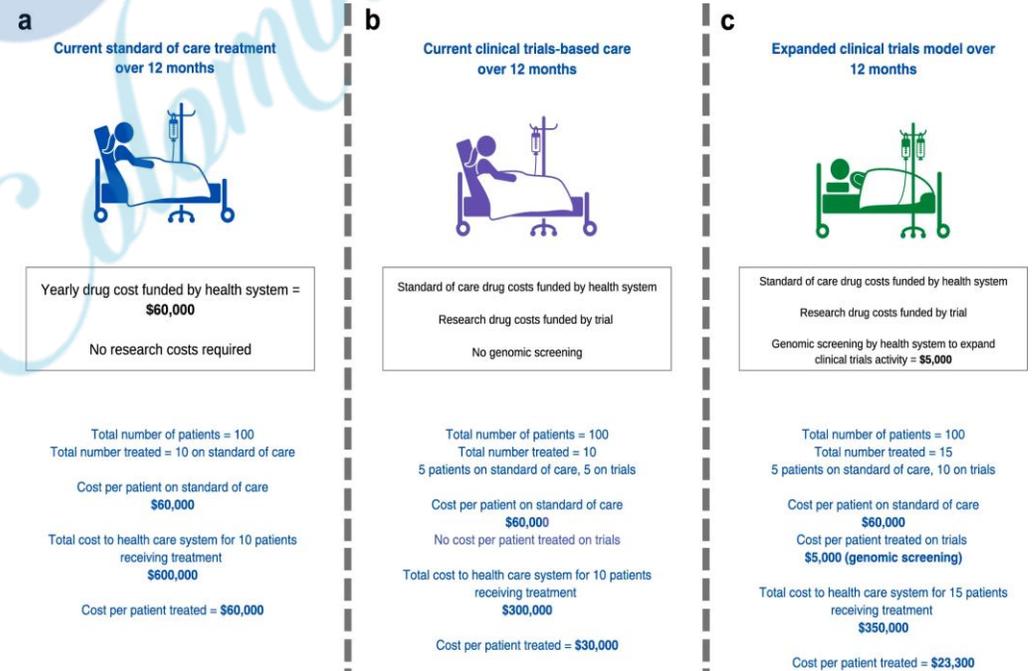
- 2 isomers – S & R
 - S more potent
- SNPs of CYP2C9 reduce metabolism of S warfarin
 - reduces requirement by 36 -72%
- VKORC1
 - Determines how a person responds to warfarin
 - Genetic variations determine the dosage



- Pharmacogenomic data

- can be used to guide the choice of medicine and dose
- increase the likelihood that each person receives the most effective medicine for them, at the best dose, **the first time they are treated**

- Can be economical



Lu, C.Y., Terry, V. & Thomas, D.M. Precision medicine: affording the successes of science. *npj Precis. Onc.* 7, 3 (2023)



Personalised prescribing

Using pharmacogenomics to
improve patient outcomes

A report from the Royal College of Physicians and
British Pharmacological Society joint working party

Report of the
PGx
working party

Box 1

Recommendations for the implementation of pharmacogenomics in clinical practice⁷⁵

- Clinical implementation of pharmacogenomics should occur in all health-care settings and should focus on drugs that have actionable information. One model might be to start with a small number of drug-gene pairs and gradually increase to a comprehensive service.
- Appropriate funding is needed for implementing a pharmacogenomic clinical service; active efforts should be made from the beginning to ensure that the service does not exacerbate health inequalities.
- The pharmacogenomic service should be adaptable — that is, able to modify and refine the available tests based on new evidence.
- A comprehensive education and training package that is relevant to all involved health-care professionals should accompany the implementation of a pharmacogenomic service.
- Support is needed for clinicians, including clinical decision support systems, to minimize errors and maximize cost efficiency.
- The pharmacogenomic service should undergo continuous audit and evaluation, leading to the development of a learning health system that maximizes patient benefits.
- A pharmacogenomic service should be accompanied by funding for research — not only biomedical research, but also research into ethical, legal and social issues.
- Clear lines of communication should be established with health-care managers, patient representative bodies, the public and the media.

Examples of 'Informative' PGx Data in Drug Labels

CYP2D6 Poor metabolizers have higher than expected plasma concentrations of tricyclic antidepressants (TCAs) when given usual doses

Reduce the starting dose of Beleodaq to 750 mg/m² in patients known to be homozygous for the UGT1A1*28 allele to minimize dose limiting toxicities

Genetic variants of the TPMT gene may contribute to cisplatin-induced ototoxicity; although this association has not been consistent across populations and study designs

LIPITOR reduces LDL-C in some patients with homozygous familial hypercholesterolemia (a genetic disease)

Table of Pharmacogenetic Associations

Precision Medicine

Table of Pharmacogenetic Associations

[FDA Recognition of Public Human Genetic Variant Databases](#)

Pharmacogenetic tests, along with other information about patients and their disease or condition, can play an important role in drug therapy. When a health care provider is considering prescribing a drug, knowledge of a patient's genotype may be used to aid in determining a therapeutic strategy, determining an appropriate dosage, or assessing the likelihood of benefit or toxicity.

On this page:

- [About the Table](#)
- [Section 1: Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations](#)
- [Section 2: Pharmacogenetic Associations for which the Data Indicate a Potential Impact on Safety or Response](#)
- [Section 3: Pharmacogenetic Associations for which the Data Demonstrate a Potential Impact on Pharmacokinetic Properties Only](#)
- [Updates to the Table](#)
- [Additional Resources](#)

Content current as of:
10/26/2022

Regulated Product(s)
Medical Devices

Feedback

The fact that the FDA has included a particular gene-drug interaction in the table does not necessarily mean the FDA advocates using a pharmacogenetic test before prescribing the corresponding medication, unless the test is a companion diagnostic. Tests that are essential for the safe and effective use of a therapeutic product, including those that identify patients for which the drug is contraindicated, are companion diagnostics.





Search CPIC Website

What is CPIC?

The [Clinical Pharmacogenetics Implementation Consortium \(CPIC®\)](#) is an international consortium of individual volunteers and a small dedicated staff who are interested in facilitating use of pharmacogenetic tests for patient care.

One barrier to implementation of pharmacogenetic testing in the clinic is the difficulty in translating genetic laboratory test results into actionable prescribing decisions for affected drugs.

CPIC's goal is to address this barrier to clinical implementation of pharmacogenetic tests by creating, curating, and posting freely available, peer-reviewed, evidence-based, updatable, and detailed gene/drug clinical practice guidelines (click [here](#) for all CPIC publications). CPIC guidelines follow standardized formats, include systematic grading of evidence and clinical recommendations, use [standardized terminology](#), are peer-reviewed, and are published in a leading journal (in partnership with

Guidelines

CPIC guidelines are designed to help clinicians understand HOW available genetic test results should be used to optimize drug therapy, rather than WHETHER tests should be ordered. A key assumption underlying the CPIC guidelines is that clinical high-throughput and pre-emptive (pre-prescription) genotyping will become more widespread, and that clinicians will be faced with having patients' genotypes available even if they have not explicitly ordered a test with a specific drug in mind. CPIC's guidelines, processes and projects have been endorsed by several professional societies – [read more](#).

Each CPIC guideline adheres to a standard format, and includes a standard system for [grading levels of evidence linking genotypes to phenotypes](#), how to assign phenotypes to clinical genotypes, prescribing recommendations based on genotype/phenotype, and a standard system for assigning [strength to each prescribing recommendation](#). The SOP for guideline creation has been published in Current Drug Metabolism: [Incorporation of Pharmacogenomics into Routine Clinical Practice: The Pharmacogenetics Implementation Consortium \(CPIC\) Guideline Development Process](#). The [CPIC authorship guidelines](#) contain more details on minimizing and managing conflicts of interest.

[View CPIC's process for prioritizing CPIC guidelines](#)

Search:

Guidelines	Drugs	Genes
CFTR and Ivacaftor	ivacaftor	CFTR
CYP2B6 and efavirenz	efavirenz	CYP2B6
CYP2B6 and methadone	methadone	CYP2B6

CYP2C9 CPIC guidelines

Search: warfarin

Guidelines

Drugs

Genes

[CYP2C9, VKORC1, CYP4F2 and Warfarin](#)

warfarin

[CYP2C9](#)
[CYP4F2](#)
[VKORC1](#)

Showing 1 to 1 of 1 entries (filtered from 29 total entries)

[CPIC guideline for NSAIDs based on CYP2C9 genotype](#)

[CPIC guideline for phenytoin based on CYP2C9 and HLA-B genotype](#)

[CPIC guideline for warfarin based on CYP2C9, VKORC1 and CYP4F2 genotype](#)

For gene-specific information tables (i.e. CYP2C9 allele definition, allele functionality, diplotype-phenotype and frequency tables) see [guideline pages](#) or [PharmGKB](#).





AHA SCIENTIFIC STATEMENTS

CYP2C19 Genetic Testing for Oral P2Y12 Inhibitor Therapy: A Scientific Statement From the American Heart Association

Naveen L. Pereira, MD, FAHA, Chair, Sharon Cresci, MD, FAHA, Vice Chair, Dominick J. Angiolillo, MD, PhD, Wayne Batchelor, MD, MHS, Quinn Capers IV, MD, Larisa H. Cavallari, PharmD, Dana Leifer, MD, FAHA, Jasmine A. Luzum, PharmD, PhD, FAHA, Dan M. Roden, MD, FAHA, Konstantinos Stellos, MD, FAHA, Stephanie L. Turrisse, PhD, RN, FAHA, and Sony Tuteja, PharmD, MS, FAHA on behalf of the American Heart Association Professional/Public Education and Publications Committee of the Council on Genomic and Precision Medicine; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Peripheral Vascular Disease; and Stroke Council

Abstract: There is significant variability in the efficacy and safety of oral P2Y12 inhibitors, which are used to prevent ischemic outcomes in common diseases such as coronary and peripheral arterial disease and stroke. Clopidogrel, a prodrug, is the most used oral P2Y12 inhibitor and is activated primarily after being metabolized by a highly polymorphic hepatic cytochrome CYP2C19 enzyme. Loss-of-function genetic variants in *CYP2C19* are common, can result in decreased active metabolite levels and increased on-treatment platelet aggregation, and are associated with increased ischemic events on clopidogrel therapy. Such patients can be identified by *CYP2C19* genetic testing and can be treated with alternative therapy. Conversely, universal use of potent oral P2Y12 inhibitors such as ticagrelor or prasugrel, which are not dependent on CYP2C19 for activation, has been recommended but can result in increased bleeding. Recent clinical trials and meta-analyses have demonstrated that a precision medicine approach in which loss-of-function carriers are prescribed ticagrelor or prasugrel and noncarriers are prescribed clopidogrel results in reducing ischemic events

without increasing bleeding risk. The evidence to date supports *CYP2C19* genetic testing before oral P2Y12 inhibitors are prescribed in patients with acute coronary syndromes or percutaneous coronary intervention. Clinical implementation of such genetic testing will depend on among multiple factors: rapid availability of results or adoption of the concept of performing preemptive genetic testing, provision of easy-to-understand results with therapeutic recommendations, and seamless integration in the electronic health record.

Key Words: AHA Scientific Statements ■ genetic testing ■ platelet inhibitors

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Home > NICE Guidance > Conditions and diseases > Cardiovascular conditions > Stroke and transient ischaemic attack

CYP2C19 genotype testing to guide clopidogrel use after ischaemic stroke or transient ischaemic attack

Diagnostics guidance | DG59 | Published: 31 July 2024

[Register as a stakeholder](#)

[Download guidance \(PDF\)](#)

[Overview](#)

1 Recommendations

[2 The diagnostic tests](#)

[3 Committee discussion](#)

[4 Implementation](#)

[5 Diagnostics advisory committee members and NICE project team](#)

Recommendations

- 1 Use CYP2C19 genotype testing to assess if clopidogrel is a suitable antiplatelet drug for people who have just had an ischaemic stroke or a transient ischaemic attack (TIA).
- 1.2 When offering CYP2C19 genotype testing:
 - take into account that the prevalence of different CYP2C19 genotypes may vary between ethnic groups
 - explain to the person having the test the possible implications of the results and give support and information.

Laboratory-based testing

- 1.3 Use laboratory-based testing for CYP2C19 genotype testing.

Point-of-care testing

- 1.4 Use the Genedrive CYP2C19 ID Kit point-of-care test for CYP2C19 genotype testing when laboratory-based testing is not available.
- 1.5 Use the Genomadix Cube point-of-care test when laboratory-based testing and the Genedrive CYP2C19 ID Kit point-of-care test are not available.
- 1.6 CYP2C19 point-of-care genotype testing is recommended only if quality-assurance processes and arrangements are in place.

This guidance does not replace existing guidance on antiplatelet therapy when genotype testing is not available, or when results from testing have not been received. Starting antiplatelet treatment should not be delayed while waiting for test results.





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SRI LANKA
(Incorporated by Act of Parliament No. 22 of 1984)

IOBSL RESEARCH STORIES



Sri Lankan ethnic disparities are not reflected in their genetic signatures, scientists say

<http://www.iobsl.org/>

N=838 unrelated individuals representing 4 major ethnic groups

Perera, N., Galhena, G., & Ranawaka, G. (2021). X-chromosomal STR based genetic polymorphisms and demographic history of Sri Lankan ethnicities and their relationship with global populations. *Scientific reports*, 11(1), 1-12.

Sri Lankan data

28 Original article

OPEN

Genetic diversity of variants involved in drug response and metabolism in Sri Lankan populations: implications for clinical implementation of pharmacogenomics

Sze Ling Chan^a, Nilakshi Samaranyake^g, Colin J.D. Rossⁱ, Meng Tiak Toh^a, Bruce Carletonⁱ, Michael R. Hayden^{a,j}, Yik Ying Teo^{b,c,d,e}, Vajira H.W. Dissanayake^h and Liam R. Brunham^{a,f,k}

Pharmacogenetics and Genomics, 2015. 26:28–39

“substantial differentiation between Sri Lankan and European populations for important pharmacogenomic variants related to warfarin (VKORC1 rs9923231) and clopidogrel (CYP2C19 rs4986893) response.”

Original Article

Genetic variants in the cytochrome P450 2D6 gene in the Sri Lankan population

T. D. Praveen Tharanga, C. M. V. Jinadasa¹, M. F. Risama¹, Priyadarshani Galappaththy, R. L. Jayakody, Vajira H. W. Dissanayake¹

Departments of Pharmacology and ¹Human Genetics Unit, Faculty of Medicine, University of Colombo, Colombo 00800, Sri Lanka

Indian Journal of Human Genetics October-December 2013

CYP2D6 *3, *4 and *10 variants

- associated with reduced or loss of CYP2D6 enzyme function
- found in our population in significant frequencies
- CYP2D6*4, reported to be a Caucasian variant was also found in all three ethnic groups.
- A high percentage of Sri Lankans carry enzyme inactivation alleles of the CYP2D6 gene

“This warrants prescription of smaller doses of drugs metabolized through CYP2D6 enzymes when such drugs are prescribed.”



Sri Lankan data

Research Article
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Pharmacogenomics

Diversity of pharmacogenomic variants affecting warfarin metabolism in Sri Lankans

Priyanga Ranasinghe*¹, Nirmala Sirisena², Vidarsha Senadeera², Gayani Anandagoda² & Vajira HW Dissanayake²

¹Department of Pharmacology, Faculty of Medicine, University of Colombo, Colombo 8, Sri Lanka
²Department of Anatomy, Genetics and Biomedical Informatics, Faculty of Medicine, University of Colombo, Colombo 8, Sri Lanka
*Author for correspondence: priyanga@pharm.cmb.ac.lk



Pharmacogenomics (2022) 23(17), 917–923

- The distribution of CYP2C9, VKORC1 and CYP4F2 genes in the Sri Lankan population is **different from that observed in other populations**.
 - *The CYP2C9*2 variant - significantly less frequent but CYP2C9*3 variant - significantly more frequent*
 - *SNVs in the VKORC1 and CYP4F2 more frequent*

- *N= 400*

Pharmacogenomics

Taylor & Francis
Taylor & Francis Group

Pharmacogenomics

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/ipgs20

CYP2C19 and CES1 gene variants affecting clopidogrel metabolism in a South Asian population from Sri Lanka

Priyanga Ranasinghe, Pulasthi B. Gunarathna, Hajanthy Jeyapragasam, Nirmala Sirisena, D.P. Bhagya Hendalage & Vajira H. W. Dissanayake



Pharmacogenomics 2024, 25(16–18), 657–660

- MAFs of variants CYP2C19 rs12769205 (A>G) and CYP2C19 rs4244285 (G>A) were almost 42%
 - **significantly higher compared to Europeans.**
- It can be **postulated** that a significant proportion of the Sri Lankan population is **likely poor responders to clopidogrel therapy**
- *N= 690*



Sri Lankan data

Research Article
For reprint orders, please contact: reprints@futuremedicine.com

Pharmacogenomics

Pharmacogenomic variants affecting efficacy and toxicity of statins in a south Asian population from Sri Lanka

Priyanga Ranasinghe^{*1,2}, Nirmala Sirisena³, Jeremy N Ariadurai³, Thuwaragesh Vishnukanthan³, Sathsarani Thilakarathne³, Gayani Anandagoda³ & Vajira HW Dissanayake³



Pharmacogenomics (2023) 24(15), 809–819

SLCO1B1*5, **CYP2C9*2**, CYP2C9*3 - responsible for SIM

- Present in our population
- Distribution differs to that seen in European (and other) populations
- **CYP2C9*2 > in SL population**
 - > likely to have a favourable response to lower doses
 - < risk of SIM
- N= 346

Sri Lankan data

- Alleles that affect pharmacodynamics of commonly prescribed medicines for CVD are **present** in our population
- They **differ** from those seen in Caucasian populations
 - Clinical guidelines are typically based on clinical data derived from European and other Western populations
 - *These guidelines are also adopted by countries like Sri Lanka when deriving recommendations for the local population*
- Limitations – small sample (from data stored in the data banks)
 - not representative of the population

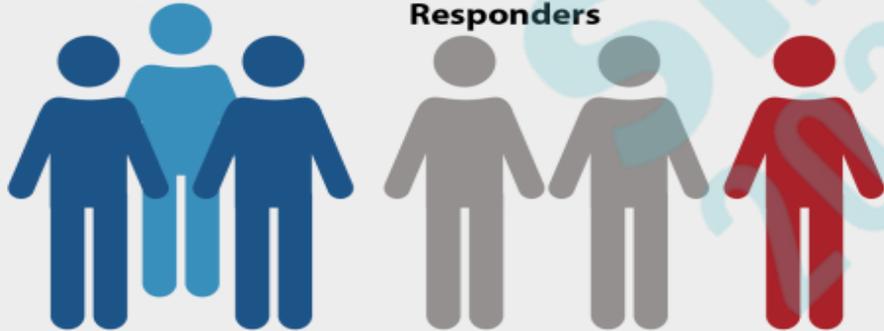
Standard Approach to Prescribing Medication



Standard Responders

Non Responders

Adverse Responders



Favorable

Unfavorable

Precision Medicine Approach

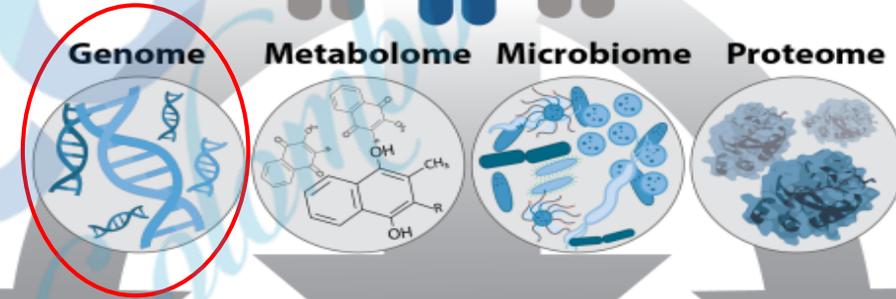


Genome

Metabolome

Microbiome

Proteome



Standard Dose



Higher Dose



Alternative Drug

Favorable

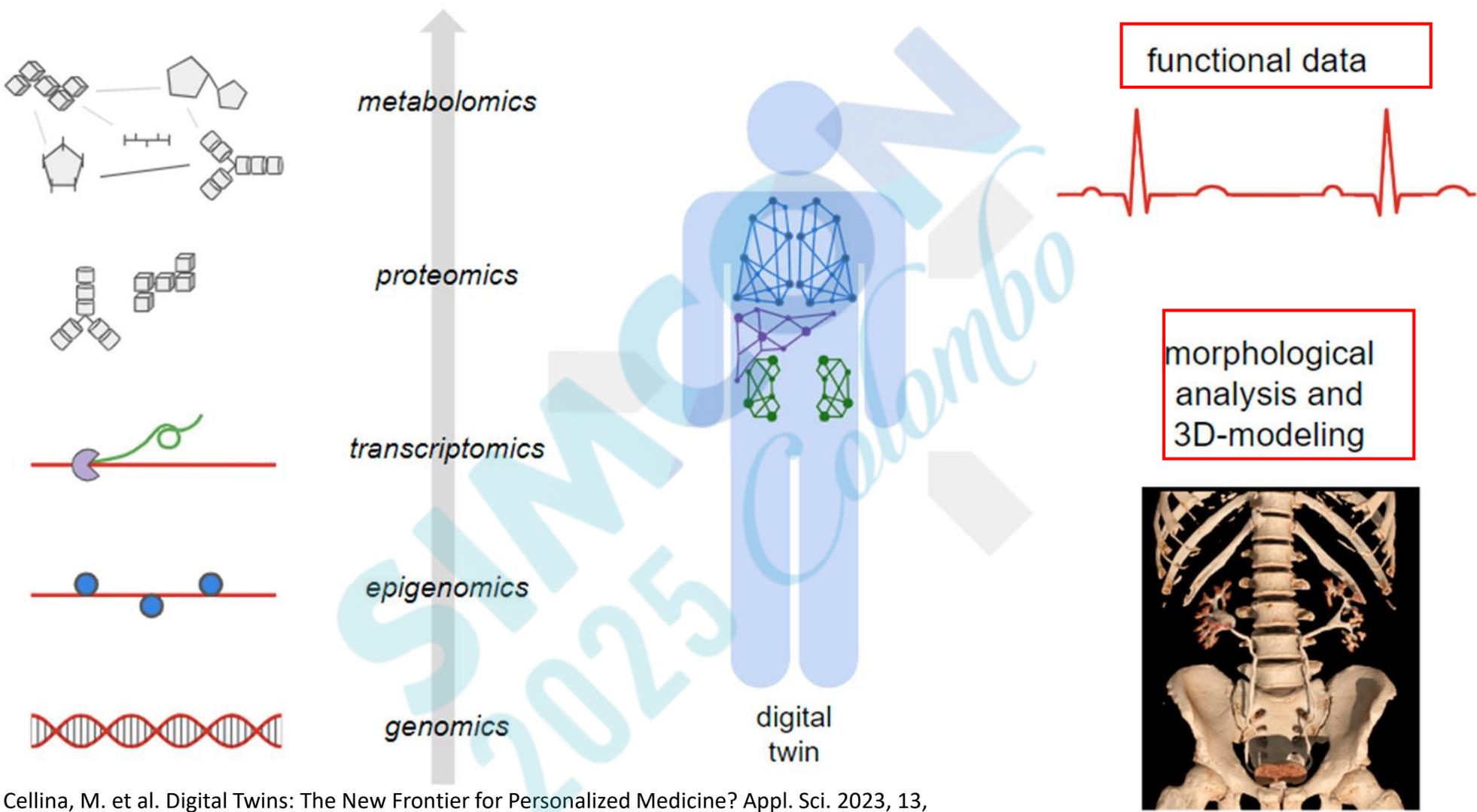
Unfavorable



Digital human twins (DHTs): “me who is not me”



Multi-omics

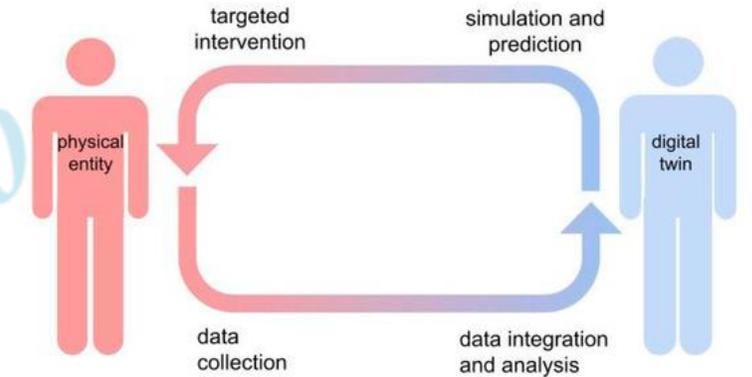


Cellina, M. et al. Digital Twins: The New Frontier for Personalized Medicine? Appl. Sci. 2023, 13, 7940.



DHTs in Medicine

- DHT - A virtual doppelganger
 - will have all the physical and biological characteristics of the person– tissues, organs, systems etc
 - allows for in silico simulations of several real-world scenarios
- Can be updated real-time with new data
 - can monitor the patient's condition and adjust their treatment plan accordingly
- Unlike humans/human brain – can assimilate and process limitless amounts of data



Cellina, M. et al. Digital Twins: The New Frontier for Personalized Medicine? Appl. Sci. 2023, 13, 7940.

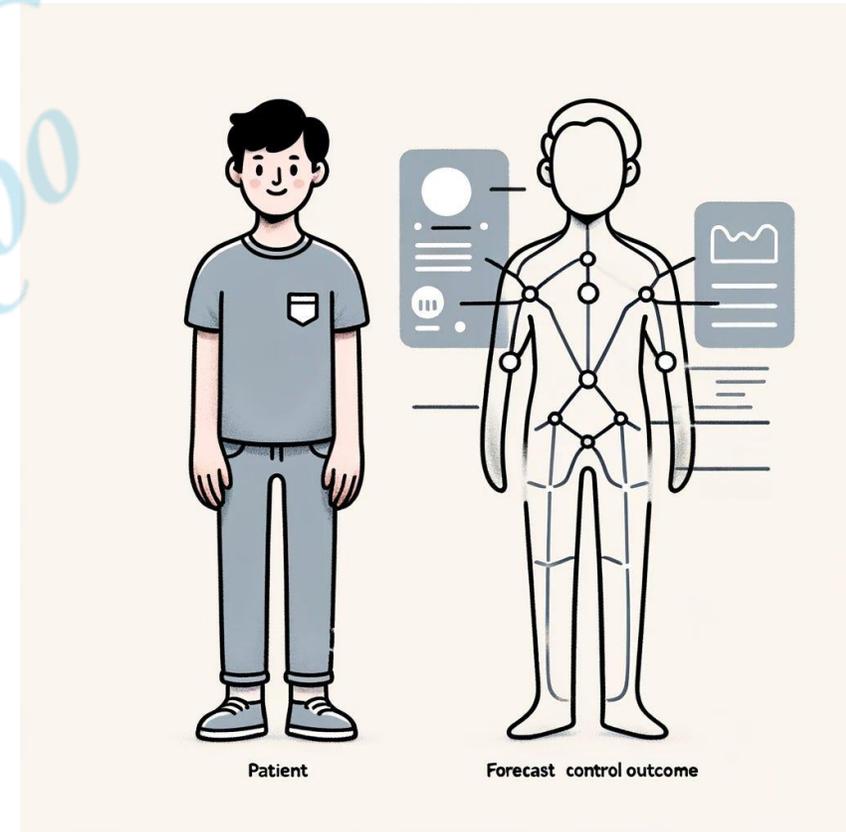
Medical Training and Education

- To learn and practice procedures without risk to actual patients
- **Not** an effective model to learn the **human touch**



In clinical trials and research

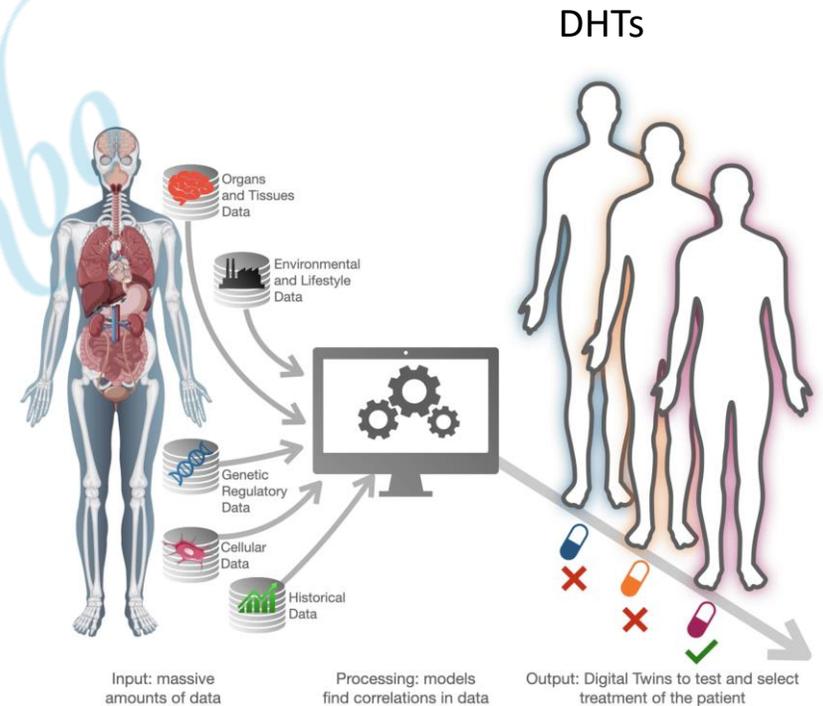
- As 'research participants'
 - Can simulate the effects of new treatments or drugs on the digital twin
- Safer
 - Phase 1 – avoid use of healthy volunteers/ patients with cancers
- Could bridge the gap in treatment response between clinical trials and real-world clinical practice



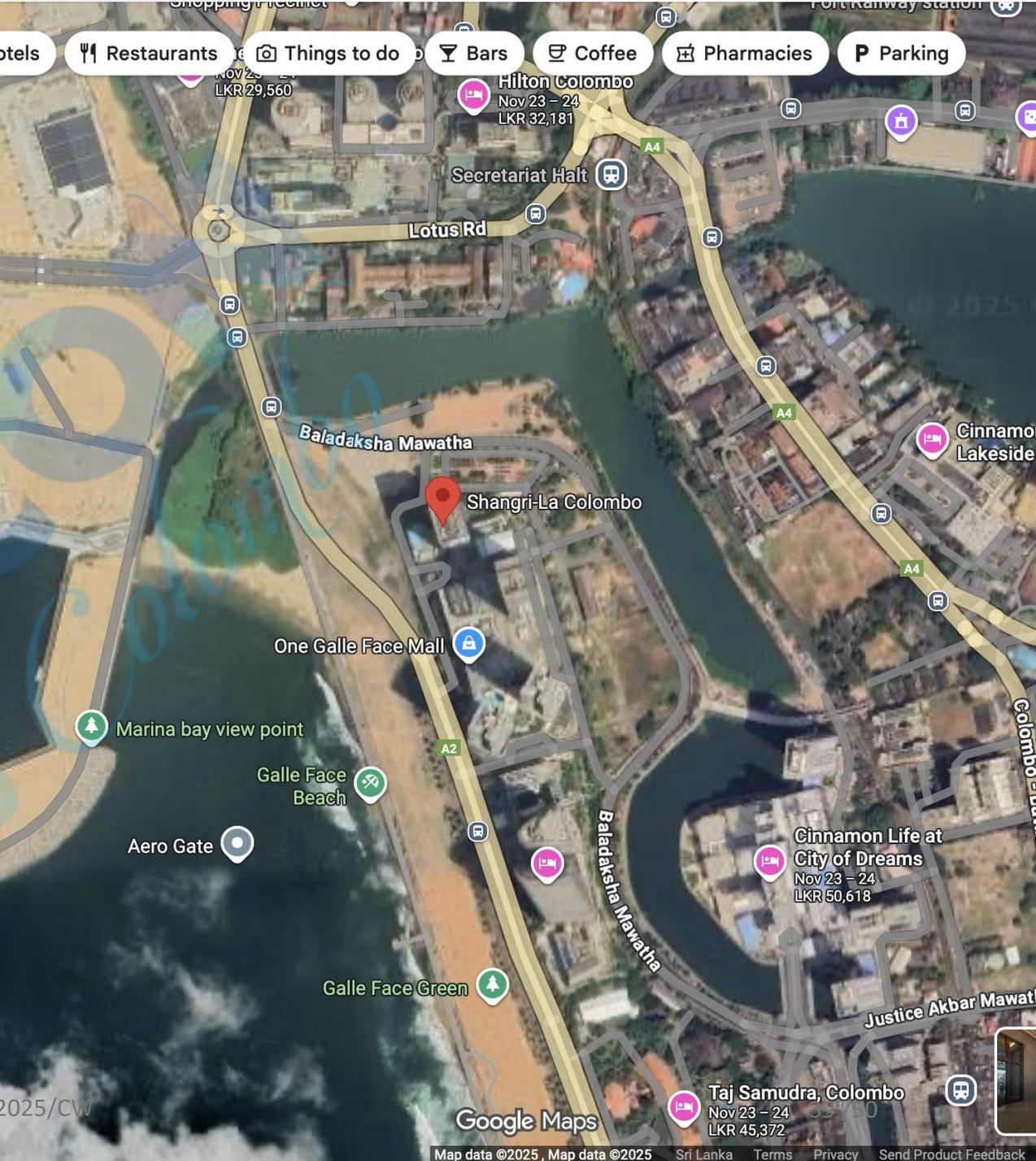
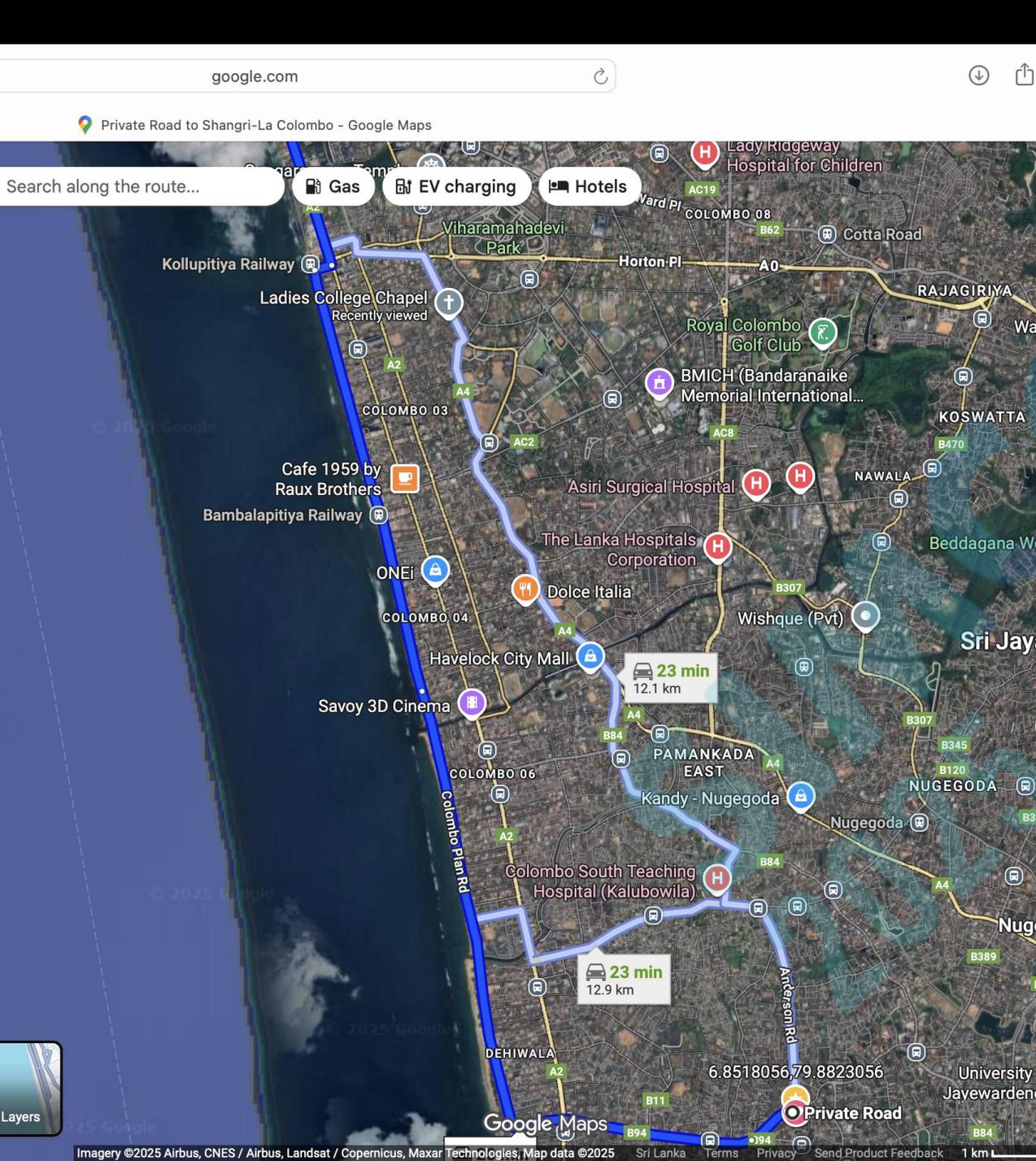
Personalised medicine

- **Predict** how a particular drug/ management plan will affect the individual patient
 - Could try multiple therapies before the actual
- Predictive analysis
 - Forecast health risks
 - Detect early signs of disease
 - Simulate different scenarios to predict the outcome
- Can be effective when discussing management options with patients

Timely interventions



De Domenico, M., Allegri, L., Caldarelli, G. *et al.* Challenges and opportunities for digital twins in precision medicine from a complex systems perspective. *npj Digit. Med.* **8**, 37 (2025)



Challenges and limitations

Digital Human Twins

Massive amounts of data from different people needed

- Issues with data privacy, confidentiality, security
- Issues with informed consent

Wide variation in available data

- Must be high quality, accurate, and complete
- Need for standardisation and proper integration

Digital Human Twins

A model based of past and present data

- Data may not be accurate
- Medical records – incomplete in many instances

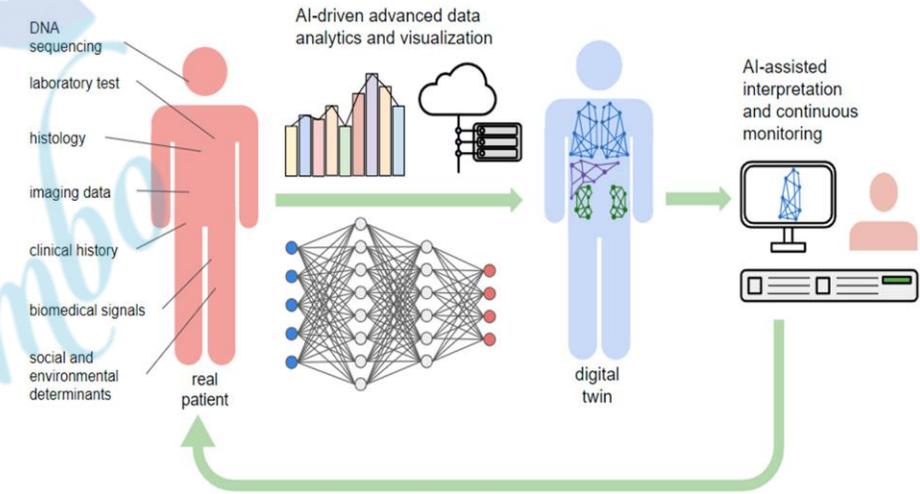
Expensive

- Fairness – access to technology
- Need for highly skilled and specialised personnel
 - More likely to gravitate to resource-rich countries

Digital Human Twins

Liability

- Inaccurate prediction or wrong diagnoses
 - Who is responsible and accountable for the decisions?



Cellina, M. et al. Digital Twins: The New Frontier for Personalized Medicine? Appl. Sci. 2023, 13, 7940.

Pharmacogenomics

Pharmacogenomic testing - restricted to few centres

Expensive

- Need Electronic Health Records systems, biotechnology resources
- Evidence of clinical utility - not easy to obtain
- Cost-effectiveness - not known for many
- High-cost medicines (cancer drugs) + cost of testing

Equality – not readily available for everyone

Pharmacogenomics

'Genetic exceptionalism'

- Less acceptance by clinicians and regulators of the need for dose modification based on genetic variants
- Variations in recommendations

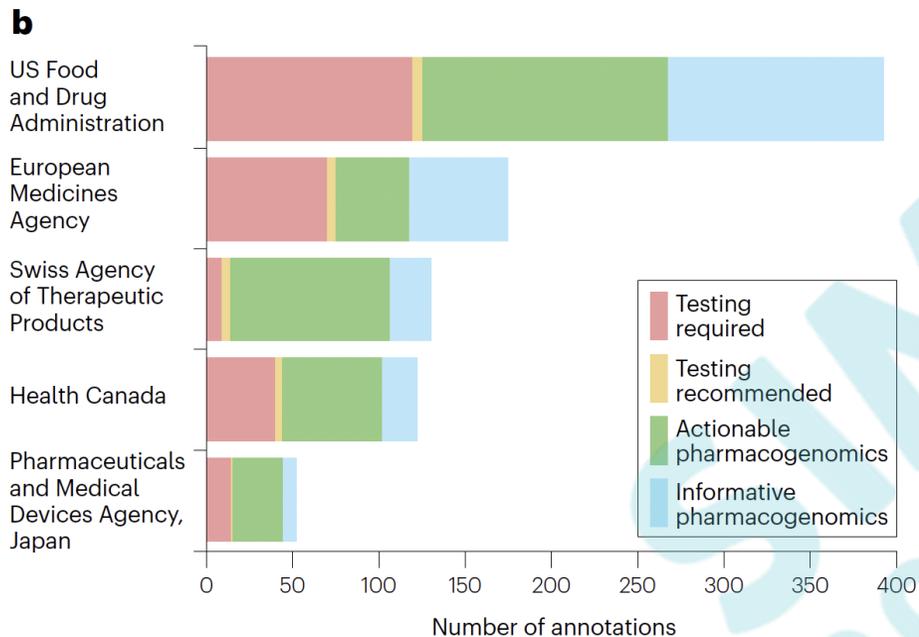
Ethical issue – what should be done if a variant is detected

- Should the choice of medicines be based on the **presence** of a variant
- Possibility of discrimination of individuals – e.g. insurance

What genetic variants should we in Sri Lanka test for

PGx – drug labelling and recommendations

Pharmacogenomic information contained in drug labels from different regulatory agencies

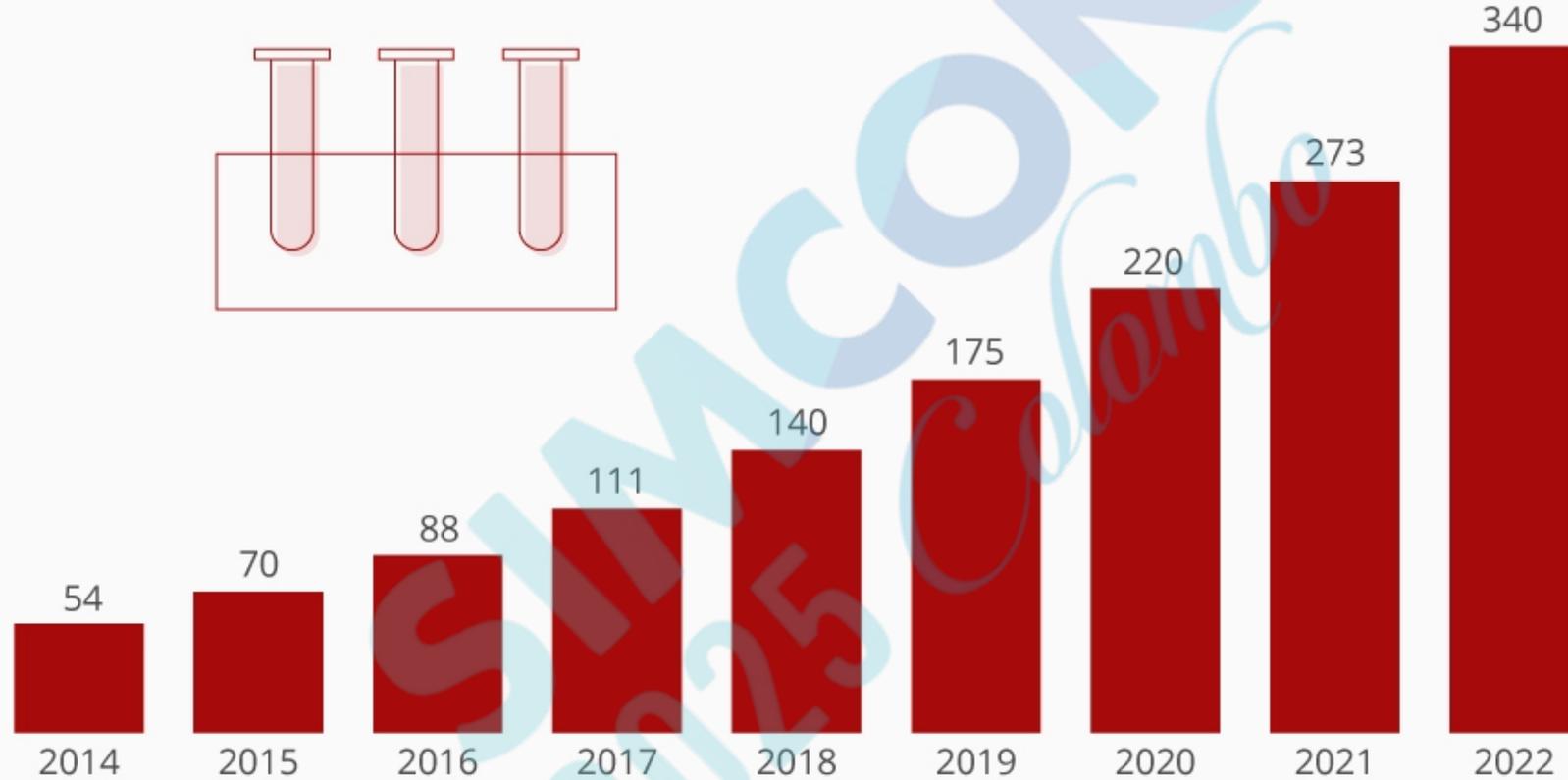


- Vary between different agencies
- ‘Testing recommended/ required’ – must be done
- ‘Actionable pharmacogenomics’
 - Label provides information on drug genetic interaction
 - Does not require/recommend testing
- “Informative pharmacogenomics”
 - a drug–gene interaction has been ruled out, OR
 - is not clinically significant, OR
 - for which the label appears on the FDA biomarker list but does not fit into the above categories

Pirmohamed, M. Pharmacogenomics: current status and future perspectives. *Nat Rev Genet* **24**, 350–362 (2023).

Consumer Genetic Testing Grows in Popularity

Size of the global direct-to-consumer genetic testing market (in million U.S. dollars)



CC BY ND
@StatistaCharts

Includes forecasts

Sources: Credence Research, Statista

statista

In conclusion

Precision medicine is Rapidly evolving, Personalised and Promising

- DHTs are more for the future
- **PGx is already here and here to stay**
 - customises prevention, diagnosis, and treatment **based on individual characteristics**
- Enormous potential to improve patient care

Physicians need to be trained to harness its full potential
BUT should be aware of its limitations

FDA APPROVED
FIRST TRIPLE FIXED-DOSE COMBINATION FOR HYPERTENSION



WIDAPLIK®

WHAT MAKES WIDAPLIK® GROUNDBREAKING?

- Telmisartan (ARB)
- Amlodipine (CCB)
- Indapamide (thiazide-like diuretic)

MECHANISM OF ACTION

- Telmisartan blocks angiotensin II receptors to reduce vasoconstriction and fluid retention
- Amlodipine relaxes arterial smooth muscle to improve circulation
- Indapamide helps excrete sodium and water to reduce blood volume
- Together, they act synergistically for better BP control

DOSING OPTIONS

- 10/1.25/0.625 mg
- 20/2.5/1.25 mg
- 40/5/2.5 mg

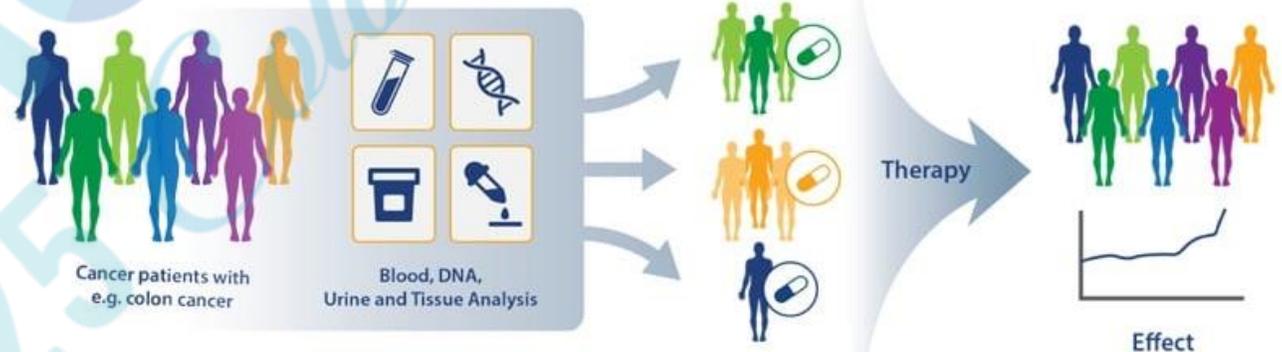
SAFETY

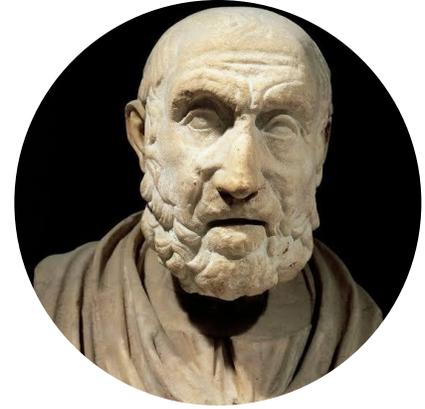
- Generally well tolerated
- Most common AE symptomatic hypotension

APPROVED BY FDA IN JUNE 2025



Future Medicine
More Personalized Diagnostics





Hippocrates
(460-377 BCE)

"It is far more important to know **what person the disease has**
than what disease the person has"



The Doctor – Luke Fildes, 1891
Image credits: Wikipedia

