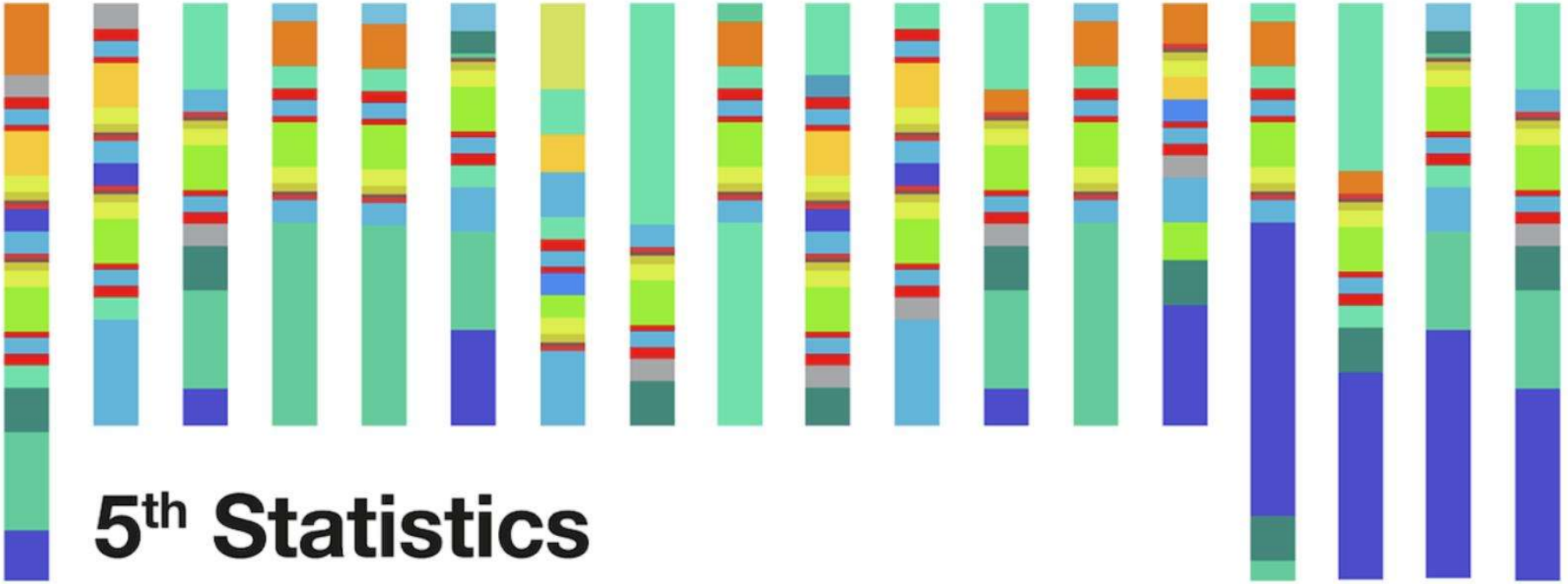


5th Statistics on Health Decision Making:

Personalized Medicine

June 1-2, 2023 | University of Aveiro

Personalised Medicine: towards implementation in healthcare

Maria Luís Cardoso

m.luis.cardoso@insa.min-saúde.pt

Departamento de Promoção da Saúde e Prevenção de Doenças não Transmissíveis

02.06.2023

Personalised medicine is part of the broader concept of **Person-Centered Care**, based on the principle that

(i) each user is unique,

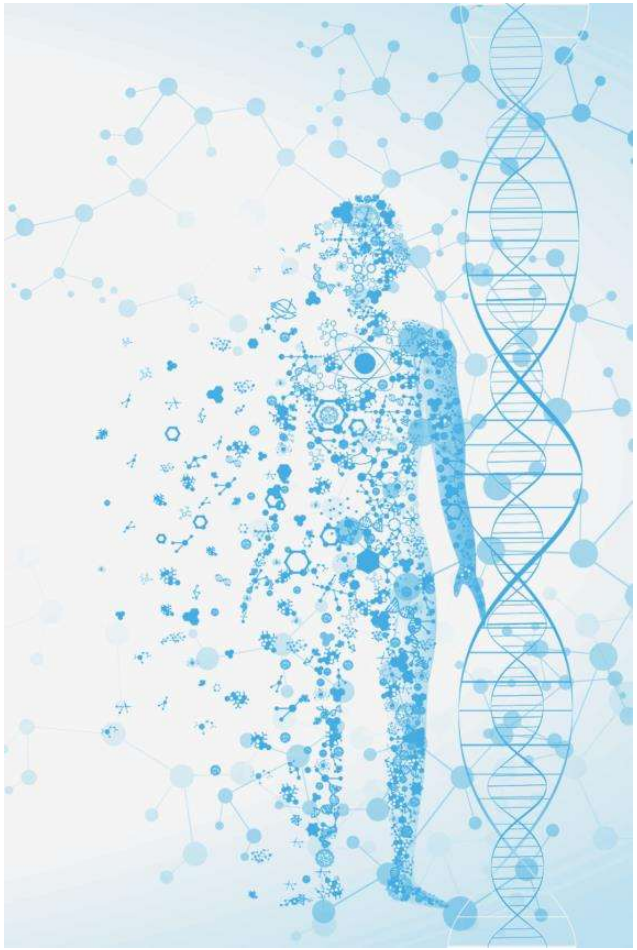
(ii) has individual needs,

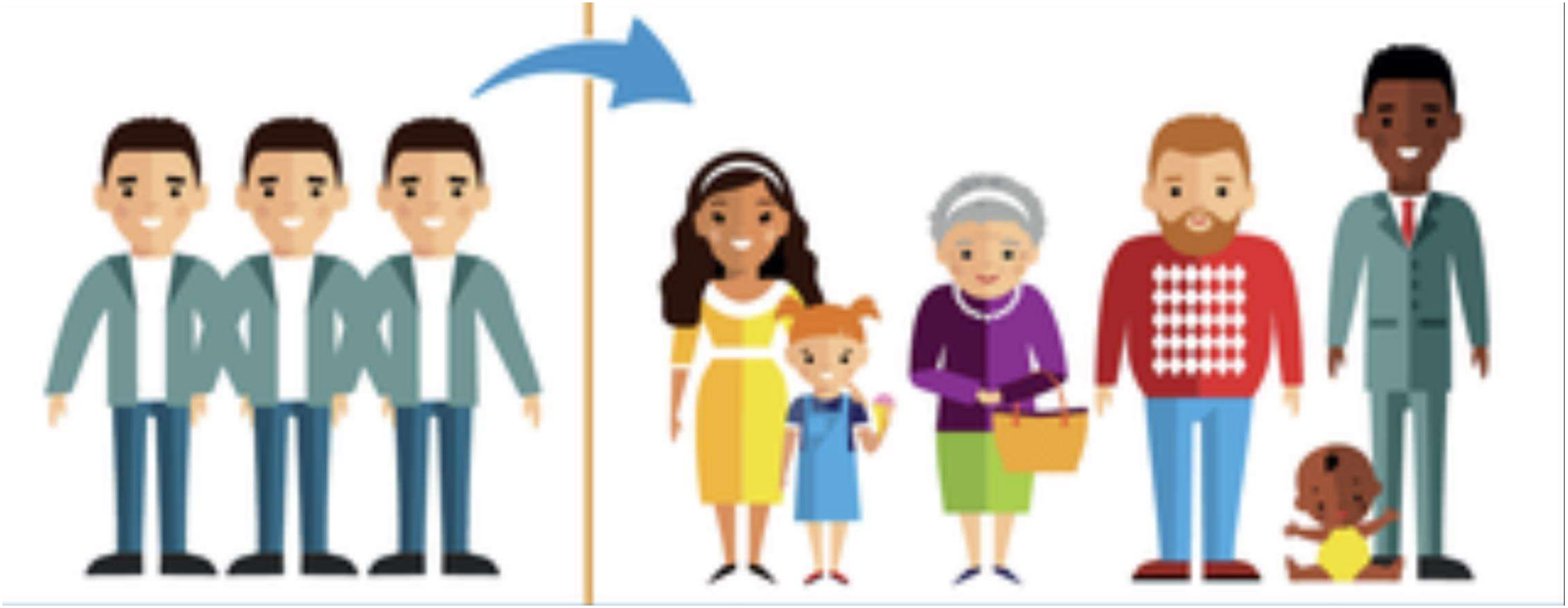
(iii) has to be informed (to give consent) and

(iv) participate in decisions therapies that concerns him.

Personalised medicine refers to a **medical model** using characterisation of individuals' phenotypes and genotypes (e.g. **molecular profiling, medical imaging, lifestyle data**) for tailoring the right **therapeutic strategy** for the right person at the right time, and/or to evaluate the **predisposition to disease** and/or to deliver timely and **targeted prevention**."

European Council Conclusion on personalised medicine for patients (2015/C 421/03).





https://m.facebook.com/genomicsedu/photos/treat-the-person-not-the-disease-this-is-at-the-core-of-genomics-and-its-the-fut/2201513400127492/

PERSONALISED MEDICINE
FOCUSING ON CITIZENS' HEALTH

European Commission

PREVENTION
DIAGNOSIS
TREATMENT

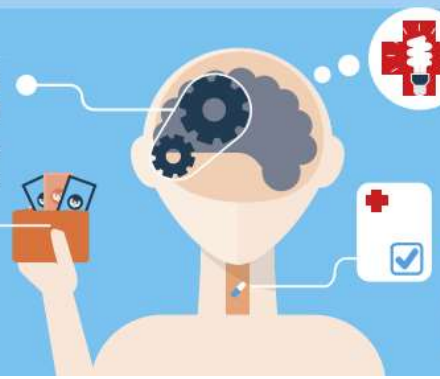
PERSONALISED MEDICINE
tailor-made prevention, diagnosis and treatment
for individuals or groups of individuals

Enabling
HEALTHIER, MORE PRODUCTIVE LIVES

Significant EU investments in research on personalised medicine to

TREAT PATIENTS WITH THE **THERAPIES THAT WORK BEST FOR THEM**
many common medicines are not effective for many patients

CUT HEALTHCARE COSTS
as Europe's population ages and chronic diseases become more prevalent



DRIVE HEALTHCARE INNOVATION
Establish Europe as a global leader in healthcare industry and innovation, and create jobs and economic growth

AVOID ADVERSE REACTIONS TO MEDICINES
6% of acute hospital admissions are due to serious adverse reactions to medicines

Personalised medicine integrates information **from multiple sources** to make HEALTHCARE SMARTER, BETTER AND MORE COST-EFFICIENT.

CSP CADERNOS DE SAÚDE PÚBLICA
REPORTS IN PUBLIC HEALTH

ARTIC
ARTICL

In-hospital adverse drug events: analysis of trend in Portuguese public hospitals

Eventos adversos a medicamentos durante a internação hospitalar: análise de tendência em hospitais públicos de Portugal

Eventos adversos con medicamentos dentro de hospitales: análisis de tendencia en hospitales públicos portugueses

Mavilde Vitorino [1,2]
Pedro Aguiar [2,3]
Paulo Sousa [2,3]

doi: 10.1590/0102-311X00056519

Abstract

The objectives of this study were to analyze in-hospital adverse drug events (ADEs) in Portuguese public hospitals, and their association with mortality and the duration of hospitalization. We analyzed an administrative database containing the registration of all hospitalizations occurring in Portuguese public hospitals in 2013-2015. ADEs were identified using the codes E850-858.9 and E930-949.9 from ICD-9-CM. We identified all episodes with registration of in-hospital ADE and we compared them with a random sample of an equal number of episodes with no events recorded. A total of 3,041,443 cases were analyzed, 60,521 presented at least one ADE from which 17,213 occurred in hospital context. The most frequent drug classes associated with ADE were the antineoplastics/immunosuppressant drugs, antibiotics and steroids. Patient characteristics associated with a greater occurrence of in-hospital ADEs (all with p < 0.001) were medical admissions (OR = 1.29), the diagnosis – myeloid leukaemia (OR = 18.63), nephrotic syndrome (OR = 15.75), pneumonia (OR = 1.33) –, a higher number of secondary diagnoses (OR = 1.27), and increased duration of hospital stay (OR = 1.06). Hospitalizations with records of in-hospital ADEs presented a significantly higher mortality (9.6% vs. 4.5) and duration of hospitalization (22.6 vs. 6.4 days). ADEs were shown to be directly associated with an increase in the duration of hospital stay of 8.18 days. This study adds some interesting insights related to the most frequent drug classes and patient characteristics that can influence the frequency of ADEs in Portuguese public hospitals and also the burden of injury resulting from them.

https://run.unl.pt/bitstream/10362/101583/1/Vitorino_Cad_Saud_Pub_2020_36_3.pdf

5–11% of patients

experience an adverse drug reaction during hospitalization in the EU

Source: Jordan et al., Adverse Drug Reactions, Power, Harm Reduction, Regulation and the ADRe Profiles. *Pharmacy* 2018:6(102)

60% of adverse drug reactions

are not recognised and are not reported

Source: Jordan et al., Adverse Drug Reactions, Power, Harm Reduction, Regulation and the ADRe Profiles. *Pharmacy* 2018:6(102)

Adverse drug reactions are the

5th leading cause of death

in Europe (197,000/year)

Source: EU pharmacovigilance impact statement 2008. https://www.myereport.eu/doc/200183EC.pdf

GOV.UK

Instituto_Nacional de Saúde Doutor Ricardo Jorge

Press release

MHRA and Genomics England to launch pioneering resource to better understand how genetic makeup influences the safety of medicines

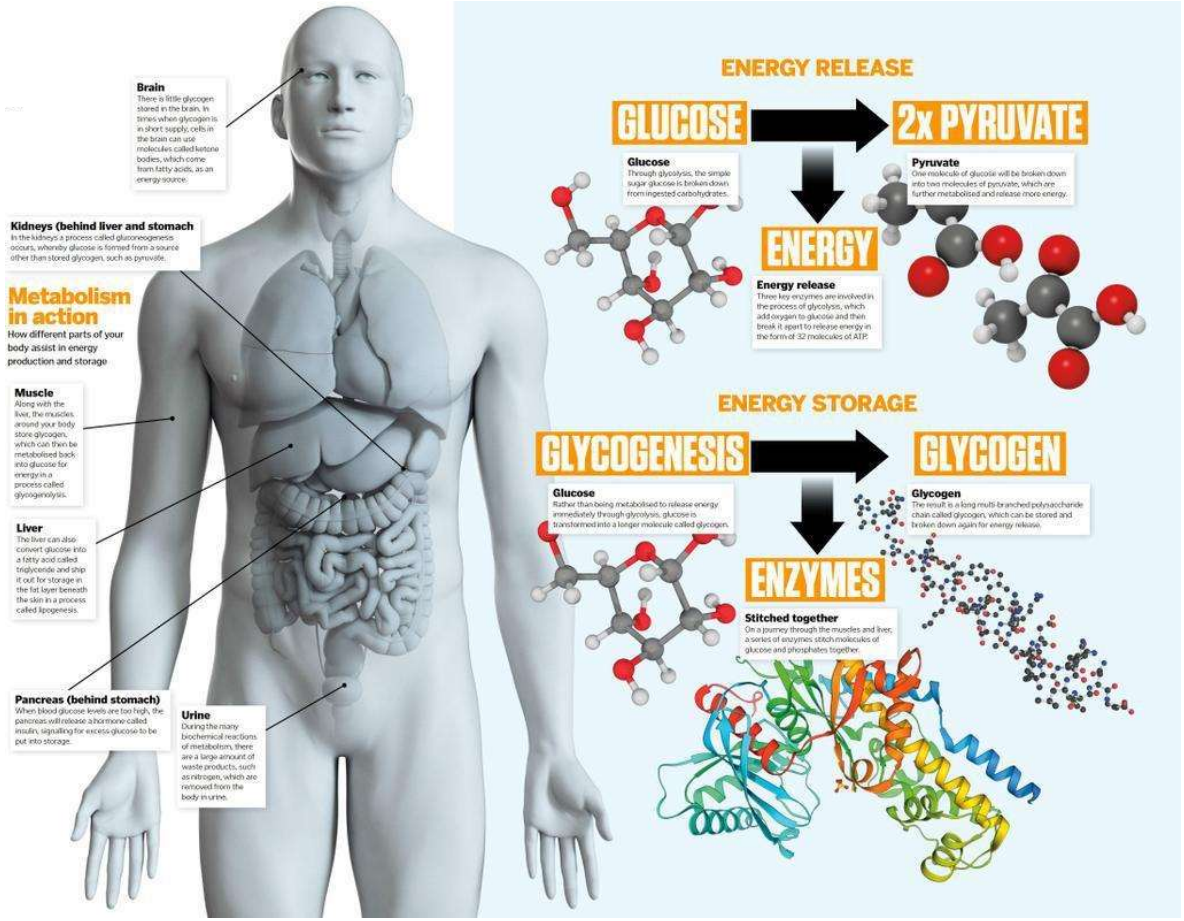
The Medicines and Healthcare products Regulatory Agency (MHRA) has today announced it will be the first drug safety regulator in the world to pilot its own genetic 'biobank', launching 1 June 2023

A brand-new genetic research resource, known as a 'biobank', will be piloted by the Medicines and Healthcare products Regulatory Agency (MHRA) in a joint venture with Genomics England to better understand how a patient's genetic makeup can impact the safety of their medicines.

The Yellow Card biobank, which will contain genetic data and patient samples, will operate alongside the MHRA's Yellow Card reporting site for suspected side effects and adverse incidents involving medicines and medical devices. It forms part of a long-term vision for more personalised medicine approaches, as scientists will use the repository of genetic information in the biobank to determine whether a side effect from a medicine was caused by a specific genetic trait. This will in turn enable doctors to target prescriptions using rapid screening tests, so patients across the UK will receive the safest medication for them, based on their genetic makeup.

Adverse Drug Reactions (ADRs), or side effects, continue to be a significant burden on the NHS and account for one in 16 hospital admissions. Understanding the underlying mechanism of an adverse reaction would support the development of pharmacogenetic testing strategies, such as the screening tests enabled through the information provided by the Yellow Card biobank. These strategies would in turn provide the opportunity to prevent rather than react to adverse drug reactions.

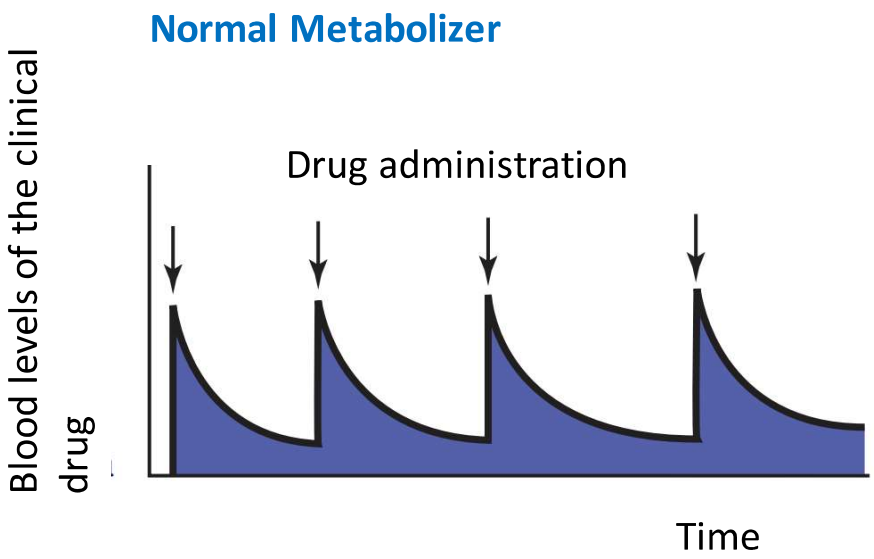
https://yellowcard.mhra.gov.uk/biobank

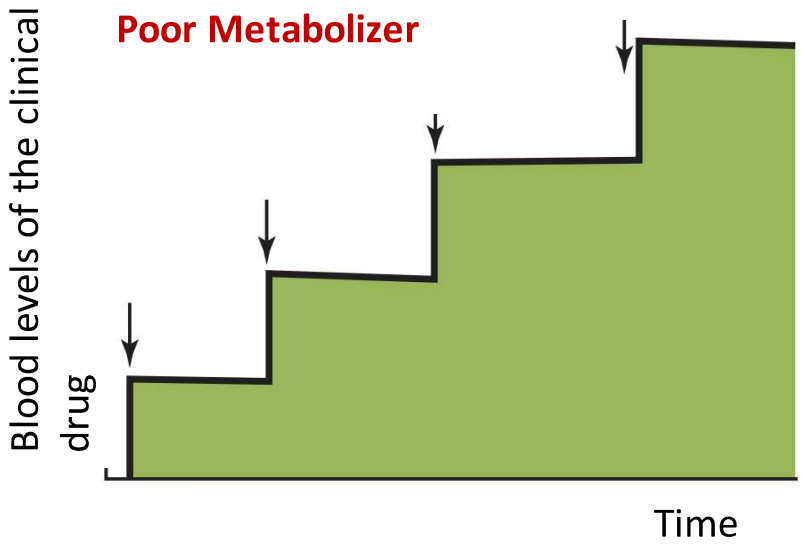


METABOLISM – All the chemical processes that occur within a living organism in order to maintain life.

EXAMPLES
Metabolism of glucose
Metabolism of cholesterol
Metabolism of alchool
Metabolim of drugs
Overdoses

https://gdi.onemilliongenomes.eu/





https://triggered.edina.clockss.org/ServeContent?url=http%3A%2F%2Fmolinterv.aspetjournals.org%2Fcontent%2F3%2F4%2F194.full.pdf

Autopsy Case Reports

Article / Autopsy Case Report

Dihydropyrimidine dehydrogenase deficiency as a cause of fatal 5-Fluorouracil toxicity

Shiraz S. Fidai[a], Aarti E. Sharma[a], Daniel N. Johnson[a], Jeremy P. Segal[a], Ricardo R. Lastra[a]

How to cite: Fidai SS, Sharma AE, Johnson DN, Segal JP, Lastra RR. Dihydropyrimidine Dehydrogenase deficiency as a cause of fatal 5-Fluorouracil toxicity. Autops Case Rep [Internet]. 2018;8(4):e2018049. https://doi.org/10.4322/acr.2018.049

ABSTRACT

5-Fluorouracil (5-FU), in combination with other cytotoxic drugs, is commonly used to treat a variety of cancers. Dihydropyrimidine dehydrogenase (DPD) catalyzes the first catabolic step of the 5-FU degradation pathway, converting 80% of 5-FU to its inactive metabolite. Approximately 0.3% of the population demonstrate complete DPD deficiency, translating to extreme toxicity of 5-FU. Here we present a case of a patient who had a fatal outcome after treatment with 5-FU who was found to have an unknown DPD deficiency discovered at autopsy.

Keywords:
Dihydropyrimidine Dehydrogenase Deficiency; Drug-Related Side Effects and Adverse Reactions; Genetic Testing; Fluorouracil; Pancytopenia

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6360833/pdf/autopsy-08-04e2018049.pdf

Submitted on: July 25th, 2018
Accepted on: September 11th, 2018

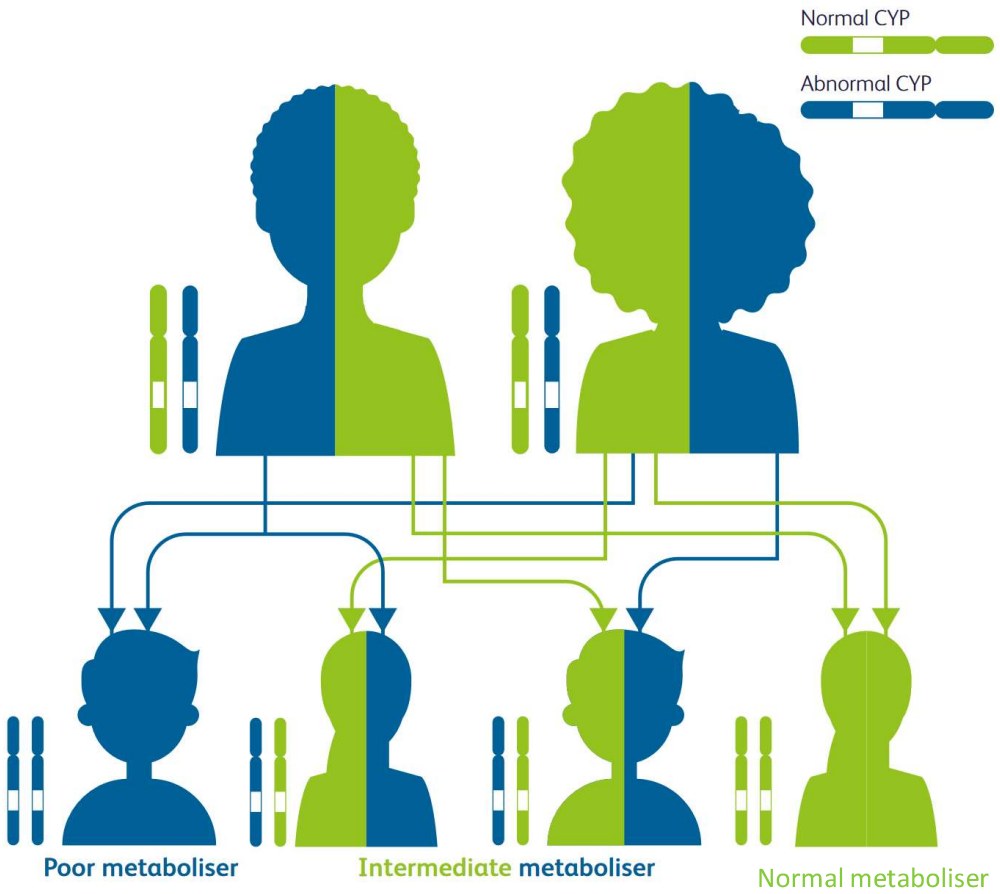
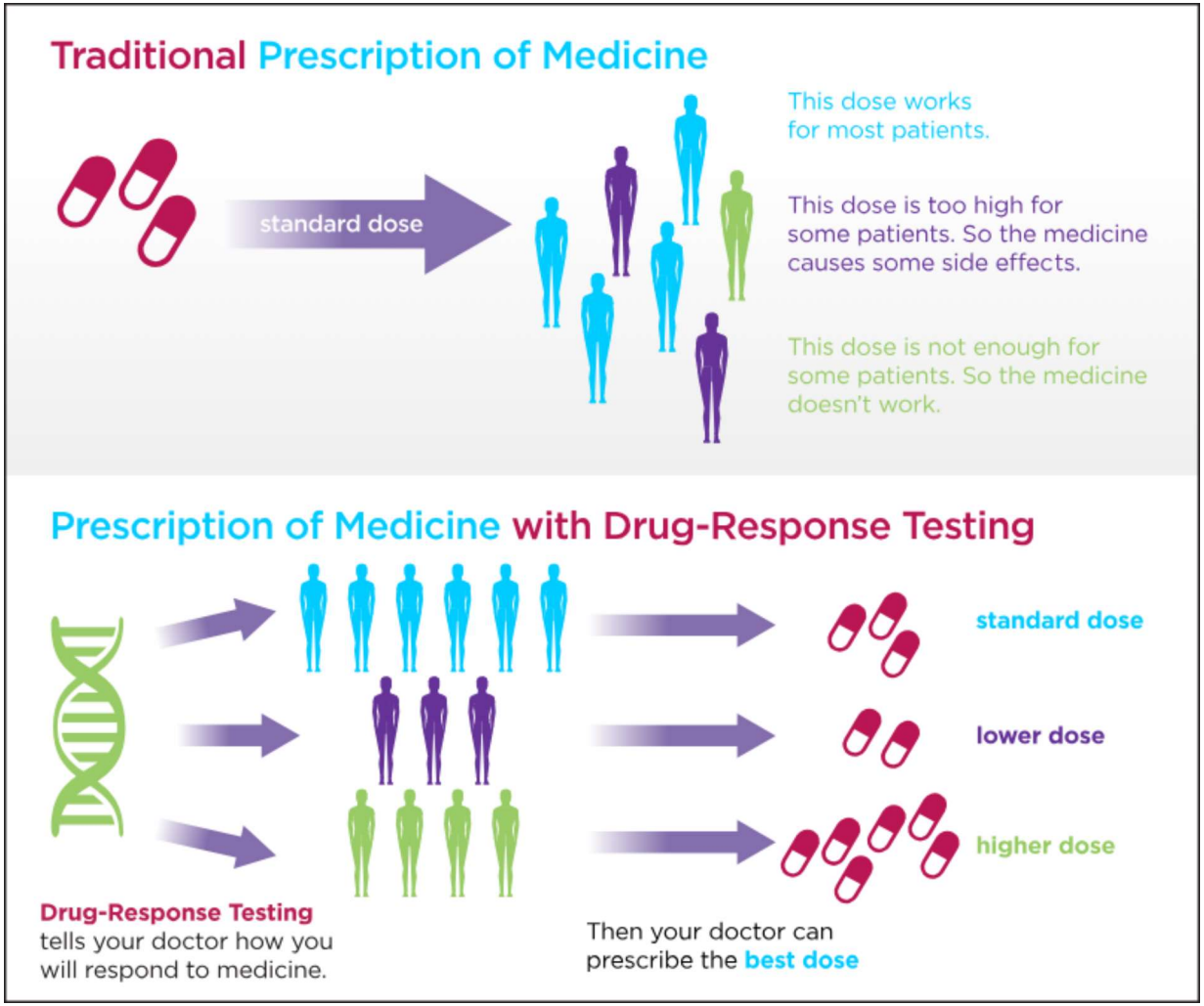


Fig 4. Cytochrome P450 pharmacogenetic variation leading to changes in enzyme activity and thereby metaboliser status

https://www.bps.ac.uk/getmedia/b43a3dca-1bbf-4bff-9379-20bef9349a8c/Personalised-prescribing-full-report.pdf.aspx

https://gdi.onemilliongenomes.eu/

https://www.bps.ac.uk/getmedia/b43a3dca-1bbf-4bff-9379-20bef9349a8c/Personalised-prescribing-full-report.pdf.aspx



https://gdi.onemilliongenomes.eu/

Codeina

Motherisk Update
Current Practice • Pratique courante

Safety of codeine during breastfeeding

Fatal morphine poisoning in the breastfed neonate of a mother prescribed codeine

Parvaz Madadi Gideon Koren, MD, FRCPC James Cairns, MD David Chitayat, MD Andrea Gaedigk, PHD
J. Steven Leeder, PHARMD, PHD Ronni Teitelbaum, MSC Tatyana Karaskov, MD Katarina Aleksa, PHD

ABSTRACT

QUESTION Recently a newborn died from morphine poisoning when his mother used codeine while breastfeeding. Many patients receive codeine for postlabour pain. Is it safe to prescribe codeine for nursing mothers?

ANSWER When a mother is an ultrarapid metabolizer of cytochrome P450 2D6, she produces much more morphine when taking codeine than most people do. In this situation, newborns might be exposed to toxic levels of morphine when breastfeeding. Options to reduce this risk include discontinuing codeine after 2 to 3 days of use and being aware of symptoms of potential opioid toxicity in both mothers and newborns.

VOL 53: JA NUARY • JA NVI ER 2007 Canadian Family Physician • Le Médecin de famille canadien

Science

Experts push for genetic testing to personalise drug prescriptions

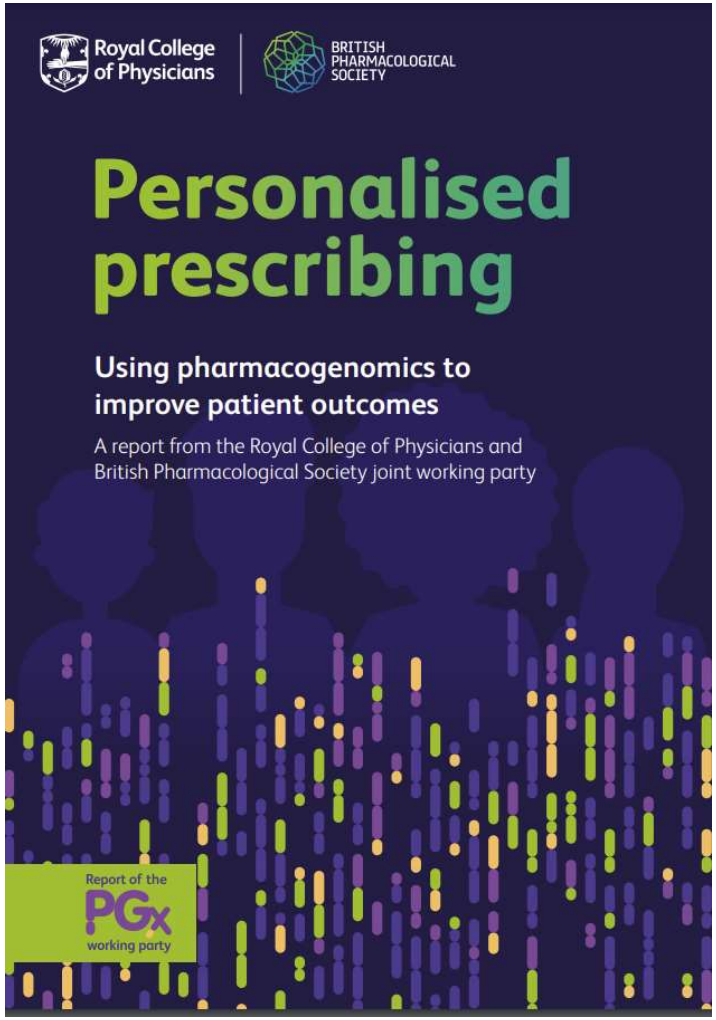
Pharmacogenomic testing could save the NHS money in the long term and reduce the risks of side-effects

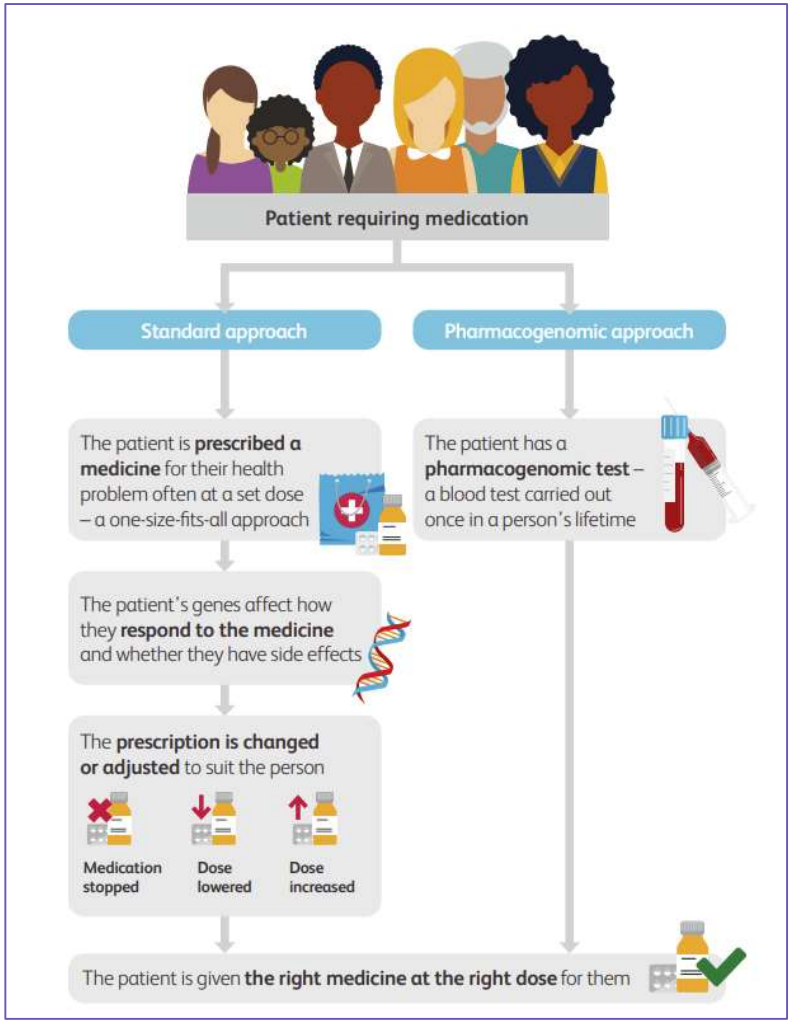
Linda Geddes *Science correspondent*

Tue 29 Mar 2022 00.01 BST

Pharmacogenomic testing would cost about £100 to £150 a person, while adverse drug reactions can cost the NHS up to £2bn a year. Photograph: CMB/Getty Images

Genetic testing to predict how individuals will respond to common medicines should be implemented without delay to reduce the risk of side-effects and ensure that everyone is given the right drug at the right dose, experts have said.


Royal College of Physicians
BRITISH PHARMACOLOGICAL SOCIETY
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


Patient requiring medication
Standard approach
Pharmacogenomic approach
The patient is prescribed a medicine for their health problem often at a set dose – a one-size-fits-all approach
The patient has a pharmacogenomic test – a blood test carried out once in a person's lifetime
The patient's genes affect how they respond to the medicine and whether they have side effects
The prescription is changed or adjusted to suit the person
Medication stopped
Dose lowered
Dose increased
The patient is given the right medicine at the right dose for them

UK's NICE Recommends Genetic Testing for Therapy Selection in Stroke Patients

May 19, 2023 | staff reporter

Save for later

NEW YORK – The UK National Institute for Health and Care Excellence (NICE) said Friday that it recommends genetic testing for patients with ischemic stroke or transient ischemic attack prior to prescribing clopidogrel because the drug is less effective at preventing subsequent strokes in patients with certain genetic variations in the CYP2C19 gene.

In a draft guidance, NICE recommended laboratory-based genetic testing using blood or saliva samples prior to administering the antiplatelet therapy to patients who have had an ischemic stroke or transient ischemic attack. Those with certain variations of the CYP2C19 gene cannot convert the drug to the active form, and testing allows selection of an alternative therapy that will be more effective at preventing blood clots, the organization said.

About 32 percent of UK residents have at least one of the CYP2C19 gene variants, which are more common among people of Asian descent but can occur in people of any ethnicity, NICE said. People with these variants have an estimated 46 percent increased risk of subsequent stroke when taking clopidogrel compared to those without the variants, according to the draft guidance.

Mark Chapman, NICE's interim director of medical technology and digital evaluation, said in a statement that the recommendation will help ensure people receive personalized care.

"Treatment with clopidogrel is effective in preventing further strokes for the majority of people who don't have the gene variant," he said. "But until now doctors have not known who cannot be treated with clopidogrel until after they've had a second stroke or TIA, and that could be too late."


U-PGx | Ubiquitous Pharmacogenomics


WE WANT TO MAKE EFFECTIVE TREATMENT OPTIMIZATION ACCESSIBLE TO EVERY EUROPEAN CITIZEN
TELL ME MORE

U-PGx | Ubiquitous Pharmacogenomics

European Pharmacogenomics Implementation Project

Funded by the

European Union's Horizon 2020 research and innovation programme

??

- €15 million, H2020, 10 EU countries
- Implement pre-emptive PGx testing in a real world clinical setting across 7 EU sites
- Evaluate **patient outcome** and **cost effectiveness** using solid **scientific methodology**
- Start 1 Jan 2016, 5 yr

Overall aim U-PGx:

"Making actionable pharmacogenomic data and effective treatment optimization accessible to every European citizen"

https://www.youtube.com/watch?v=X2KK_FfsrS4&feature=youtu.be

Scan QR code

http://safety-code.org/

genomeweb

PGx Testing Reduces Adverse Drug Events, Multi-Site European Study Finds

Feb 03, 2023 | Jessica Kim Cohen

Premium *Save for later*

NEW YORK – Pharmacogenetic testing to guide treatment with drugs that are influenced by someone's genotype significantly reduces patients' risk of experiencing an adverse drug reaction, according to results from a large-scale European study.

iStock

In about 7,000 patients who all received testing with a PGx panel, researchers compared those who had an actionable genetic variant and received PGx-informed drug treatment against a control group that also had an actionable genetic variant but received standard care. They observed a 30 percent lower risk of having an adverse drug reaction in the former group, according to a paper published in *The Lancet* on Friday. The study, called PREemptive Pharmacogenomics Testing for Preventing Adverse Drug REactions (PREPARE), was conducted by the Ubiquitous Pharmacogenomics (U-PGx) Consortium, a group of 10 academic and government research institutions in Europe that was founded in 2016.

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

Jesse J Swen, Cathelijne H van der Wouden, Lisanne EN Manson*, Heshu Abdullah-Koolmees, Kathrin Blagec, Tanja Blagus, Stefan Böhringer, Anne Cambon-Thomsen, Erika Cecchin, Ka-Chun Cheung, Vera HM Deneer, Mathilde Dupui, Magnus Ingelman-Sundberg, Siv Jonsson, Candace Joefield-Roka, Katja S Just, Mats O Karlsson, Lidija Konta, Rudolf Koopmann, Marjolein Kriek, Thorsten Lehr, Christina Mitropoulou, Emmanuelle Rial-Sebbag, Victoria Rollinson, Rossana Roncato, Matthias Samwald, Elke Schaeffeler, Maria Skokou, Matthias Schwab, Daniela Steinberger, Julia C Stingl, Roman Tremmel, Richard M Turner, Mandy H van Rhenen, Cristina L Dávila Fajardo, Vita Dolžan, George P Patrinos, Munir Pirmohamed, Gere Sunder-Plassmann, Giuseppe Toffoli, Henk-Jan Guchelaar, on behalf of the Ubiquitous Pharmacogenomics Consortium†*

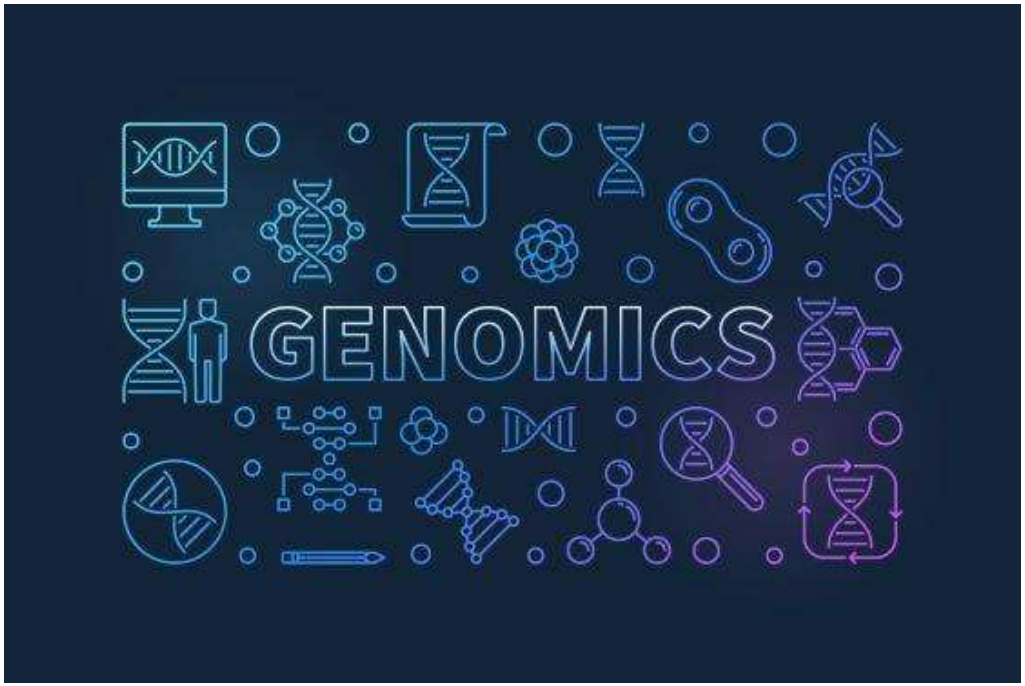
Summary

Background The benefit of pharmacogenetic testing before starting drug therapy has been well documented for several single gene–drug combinations. However, the clinical utility of a pre-emptive genotyping strategy using a pharmacogenetic panel has not been rigorously assessed.

Methods We conducted an open-label, multicentre, controlled, cluster-randomised, crossover implementation study of a 12-gene pharmacogenetic panel in 18 hospitals, nine community health centres, and 28 community pharmacies in seven European countries (Austria, Greece, Italy, the Netherlands, Slovenia, Spain, and the UK). Patients aged 18 years or older receiving a first prescription for a drug clinically recommended in the guidelines of the Dutch Pharmacogenetics Working Group (ie, the index drug) as part of routine care were eligible for inclusion. Exclusion criteria included

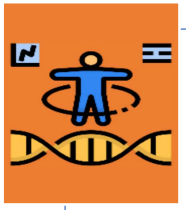
Interpretation Genotype-guided treatment using a 12-gene pharmacogenetic panel significantly reduced the incidence of clinically relevant adverse drug reactions and was feasible across diverse European health-care system organisations and settings. Large-scale implementation could help to make drug therapy increasingly safe.

Funding European Union Horizon 2020.

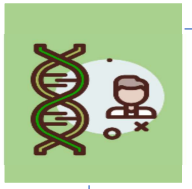


- Last few decades > huge advancementsin genetics > development + application of innovative technologies.
- These discoveries > understanding of genetic information > molecular mechanisms of many hereditary diseases.
- Advances genetic diagnostics + genetic testing > impact (+++) healthcare > more efficient and accurate testing methods.
- Genetics → genomics > strong impact on healthcare systems (all over the world) > the **genomic medicine.**
- **Genomics medicine is part of Personalised Medicine**

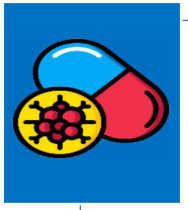
Benefits of genomic medicine



Accurate diagnosis, reducing the time, number of medical appointments, exams and the "diagnostic odyssey."

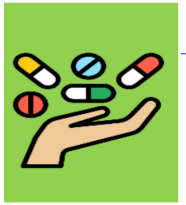


Evaluation of genetic risk profile for the development of chronic diseases (PRS) > Enabling Prevention



The knowledge of patient genome + genetic profile of the tumor, enables more precise cancer treatment.

Matching clinical trials with appropriate patients (Identification of patients who can benefit the most with the participation)



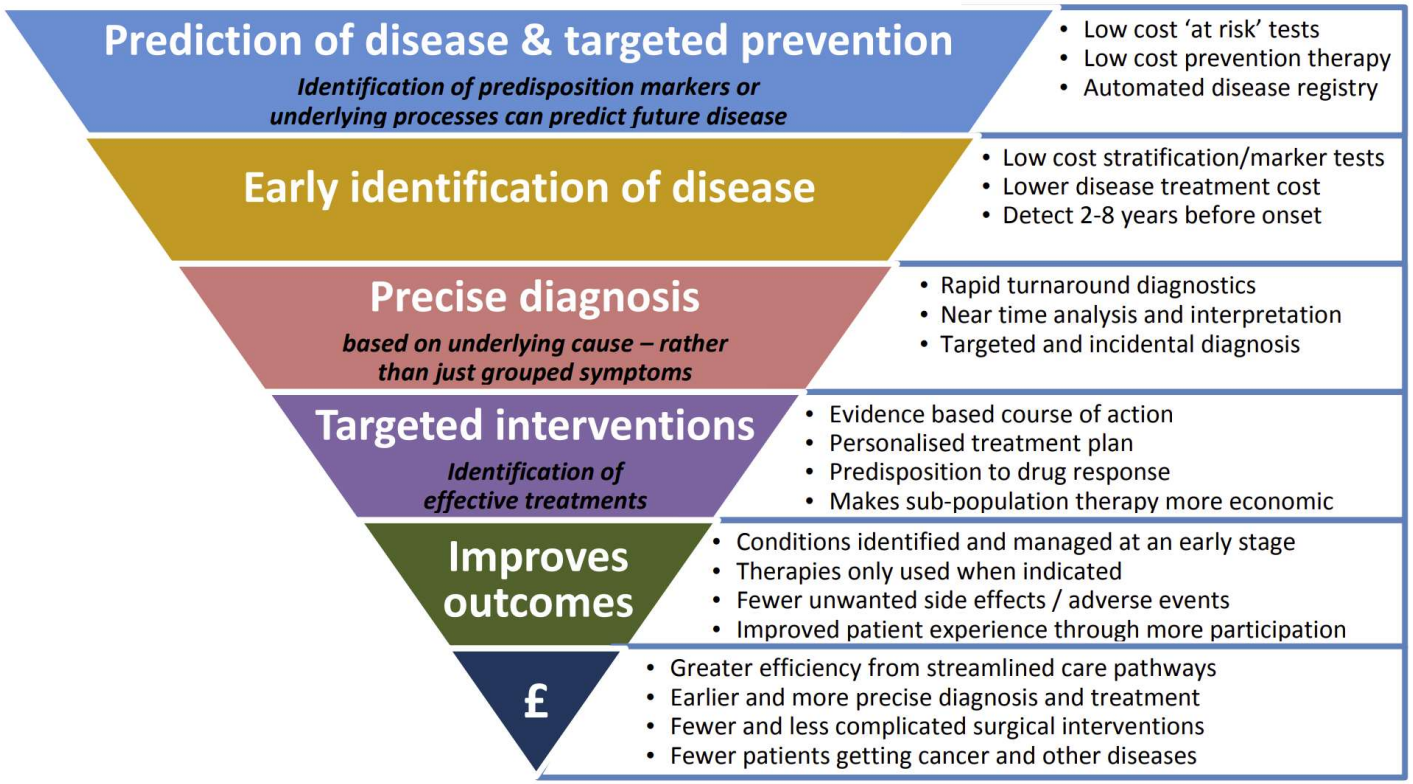
Pharmacogenomics: The right drug at the right dose for the right patient ↑ effectiveness, ↓ ADRs.

Improve equity - appropriate treatments for people of different ethnicities

Nowadays Genomics, is already making possible to predict, diagnose, and treat diseases more precisely and personally than ever.

https://www.england.nhs.uk/wp-content/uploads/2015/09/item5-board-29-09-15.pdf

Personalised Medicine – improving outcomes



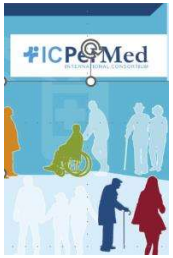
What is going on in EU and Portugal?

PT_MedGen
Estratégia Nacional para a Medicina Genómica

Stepping stones for the implementation of a Genomic Medicine Strategy in Portugal DG-REFORM

Genome of Portugal

2016 2018 2020 2021 2022 2023



+1MG

B1MG

European Genomic Data Infrastructure

Genome of Europe

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

can.heal

ICPerMed
INTERNATIONAL CONSORTIUM

ICPerMed | Activities | Services | Internal

Since **2016**, ICPerMed is a consortium that brings together European, regional and international partners, representing (i) ministries, (ii) funding agencies and the (iii) European Commission (EC).

ICPerMed support:

- PM science base through a **coordinated research approach**.
- **Research to investigate the benefits** of PM to citizens and healthcare systems.
- **Pave the way for PM approaches for citizens**.

HORIZON-HLTH-2023-CARE-08-01

European Partnership on Personalised Medicine

Type d'action : HORIZON Programme Cofund Actions
Nombre d'étapes : Single stage
Date d'ouverture : 12 janvier 2023
Date de clôture : 13 avril 2023 17:00

Détail du topic

Budget : €100 000 000

Call : Partnerships in Health (2023)
Call Identifier : HORIZON-HLTH-2023-CARE-08

PT_MedGen
Estratégia Nacional para a Medicina Genómica

Stepping stones for the implementation of a Genomic Medicine Strategy in Portugal DG-REFORM

Genome of Portugal

2016 | 2018 | 2020 | 2021 | 2022 | 2023

#ICPerMed

+1MG

B1MG

European Genomic Data Infrastructure

Genome of Europe

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

can.heal

Declaration of Cooperation
"Towards access to at least 1 million sequenced genomes in the EU by 2022"

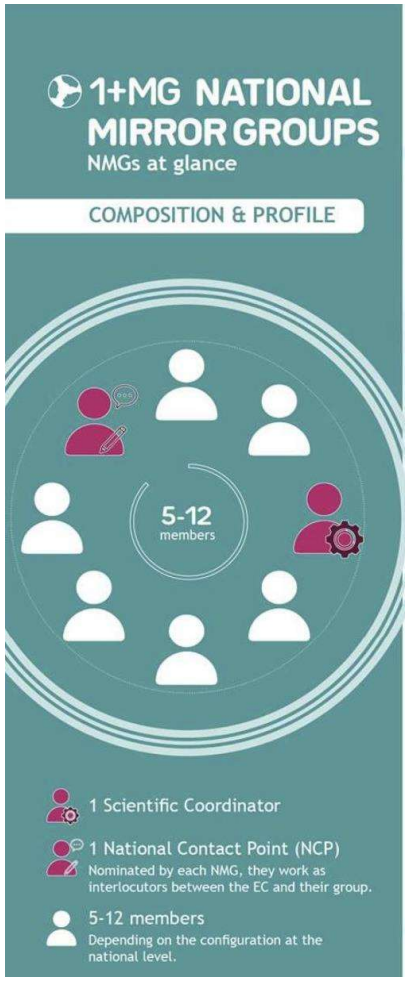
The Declaration was signed by the Portuguese Ministry of Health (2018) - Adalberto Campos Fernandes

1+MG Working Groups

1. **Organisation and governance** - Coordination
2. **ELSI aspects**
3. **Clinical data**
4. **Quality**
5. **Infrastructures**
6. **Health economics**
7. **Industry involvement**
8. **Rare Diseases**
9. **Cancer**
10. **Common complex diseases**
11. **Infectious diseases (COVID 19)**

Technical Working Groups

Use cases Working Groups



The 1+MG National Mirror Groups (NMGs) feed their national experience into the 1+ Million Genomes Initiative.

Summary of the roadmap document adopted
on 4 February 2020
by the signatories of the Declaration

Towards access to at least 1 million sequenced genomes in the EU by 2022

Engage

Governance, cooperation, and collaboration

- Governance model, national "mirror groups"
- Terms and conditions for distributed access
- Guidelines on good genomic practice
- Funding, communication

2021

Translate

Infrastructure, guidelines, and pilots

- Distributed, authorised and secure access
- Legal guidelines for cross-border use
- Technical specifications, interoperability
- Secure infrastructure and tools

2022

Drive

Sharing, scaling, and sustaining

- Coordinated data governance
- Plan for scale-up of the infrastructure
- Economic evaluation
- Roadmap for longer-term sustainability

LOUISE

IMPROVING CANCER TREATMENT

BREAST CANCER

Louise has a long family history of breast cancer. One day, she heard on TV that mutations in the BReast CAncer genes *BRCA1* and *BRCA2* increase the risk of breast cancer by up to 80%. Although it turned out that she doesn't have mutations in these genes, her risk of developing the condition is still high due to her family history.

CANCER SCREENING

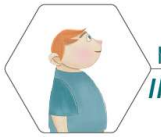
In order to detect early potential breast cancer, she started breast cancer screening at age 35, much earlier than the usual recommended routine screening. A few years later, Louise indeed developed breast cancer. To determine the most suitable type of treatment, she underwent a genomic test assessing the utility of chemotherapy versus other treatments in her case.

TREATMENT

Test results showed that Louise would not benefit much from chemotherapy, so doctors opted for a more effective personalised treatment, which also prevented her from experiencing the unpleasant side effects of chemotherapy.

CHEMO

Developments in the sequencing of cancer genomes are rapidly improving insights and predictive power of genomic tests on risk, prognosis and treatment of cancer. The 1+MG network will greatly increase the availability of this knowledge to oncologists, improving the choices for patients and the reducing over-treatment.



MARTIN

IMPROVING PROGNOSIS FOR RARE DISEASES

MICROCEPHALY

In 2015 Martin was born in Dublin, Ireland. Doctors recorded an abnormally small head and face, as well as a slow development rate. Genome sequencing identified many possible candidates for the genes that were causing his slow development. However, a precise diagnosis would be needed to start treatment.

EUROPEAN PLATFORM ON RARE DISEASES REGISTRATION

Launching a query through an EU federated platform that facilitates matching of cases with similar phenotypic and genotypic profiles allowed his doctors to find a second case in Spain with similar symptoms. Comparison of the sequencing results of the Irish and Spanish patients highlighted one mutation both had in common, which pointed to a defect that could be counteracted by supplying a specific metabolite.

Matching of cases with similar phenotypic and genotypic characteristics through an EU federated platform facilitates reaching an accurate diagnosis and treatment for rare disease patients with different backgrounds in separate countries. In this case this worked not only for Martin's condition but also for the Spanish patient.

JUSTYNA

PREVENTING COMMON AND COMPLEX DISEASES

POLYGENIC RISK SCORE

Justyna heard about the ongoing biobanking project in her country in the media, so she read more about the genetic risks of certain diseases.

Her healthcare provider recommended a genomic analysis to estimate her Polygenic Risk Score (PRS), a test for most common diseases which was just introduced as a new clinical trial in the university hospital.

CORONARY ARTERY DISEASE

This genomic analysis showed that she has a PRS in the top 5% for Coronary Heart Disease (CAD). Drugs such as statins and other preventive measures lower the cholesterol levels in the blood and reduce the CAD risk, so her doctor suggested to initiate statin treatment and make some lifestyle changes.

PREVENTION

Now Justyna has to take statins. The genomic analysis also showed that one specific statin could increase her risk of muscle inflammation and should be avoided.
Justyna is now more aware of how to prevent CAD and make adjustments in her lifestyle, as well as receive the right treatment and regular check-ups, if needed.

Europe is currently developing PRS tests for early identification of risks factors for common diseases. The 1+MG project will yield genome sequences for many European citizens, in combination with phenotypic information, all collected with informed consent in biobanks across Europe. This will further the implementation of PRS testing in regular health care and will boost the availability of cheap prevention throughout Europe and elsewhere.

PABLO & PEDRO

TACKLING HIGH SENSITIVITIES TO INFECTIOUS DISEASES

COVID-19

Pablo (27 years old) develops severe COVID-19 symptoms. Shortly after, his brother Pedro (30 years old) is also tested positive. Both need to be treated in intensive care. The two brothers do not belong to any of the known risk groups, but their close family relationship suggests a genetic risk factor.

INFLUENCES

GENETIC

Genetic profiling of the brothers is undertaken and compared to other disease cohorts and population biobank resources. It turns out that Pablo and Pedro are carriers of a rare genetic mutation in TLR7 (Toll-Like Receptor 7). This gene on the X chromosome regulates the interferon level as a defensive response to viruses. Based on this finding, Pablo and Pedro receive a specific treatment to restore the natural capacity of their immune system to fight the virus.

DATABANK *NETWORK*

Imagine we would have the EU federated genomic data network of 1+MG in place offering European clinicians the possibility to receive alerts when they encounter patients with similar characteristics. Patients' increased susceptibility to life-threatening conditions caused by an infectious disease such as COVID-19 could be rapidly discovered and the necessary treatment adapted and personalised.

The 1+ Million Genomes initiative has the potential to improve disease prevention, allow for more personalised treatments and support groundbreaking research.

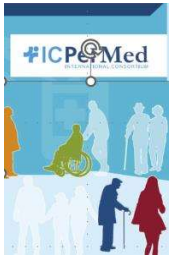
- The **1+MG Initiative**, a collaboration involving 25 EU countries, the UK, and Norway, aims to facilitate **secure access to genomic and associated clinical data throughout Europe** while ensuring privacy protection.
- The **primary goal** is to enhance **the investigation** of diseases and **using genetic data in healthcare settings**.
- This collaborative project **aims** to improve the EU's **competitiveness** in the fast-evolving field of **PM,** which seeks to **deliver predictive**, **preventive**, and **participatory** healthcare.
- It is assumed that EU-wide **cooperation** is **crucial** for the **1+MG** initiative **success**.

PT_MedGen
Estratégia Nacional para a Medicina Genómica

Stepping stones for the implementation of a Genomic Medicine Strategy in Portugal DG-REFORM

Genome of Portugal

2016 2018 2020 2021 2022 2023



+1MG

B1MG

European Genomic Data Infrastructure

Genome of Europe

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

can.heal

The B1MG project provides coordination and support to the 1+MG.

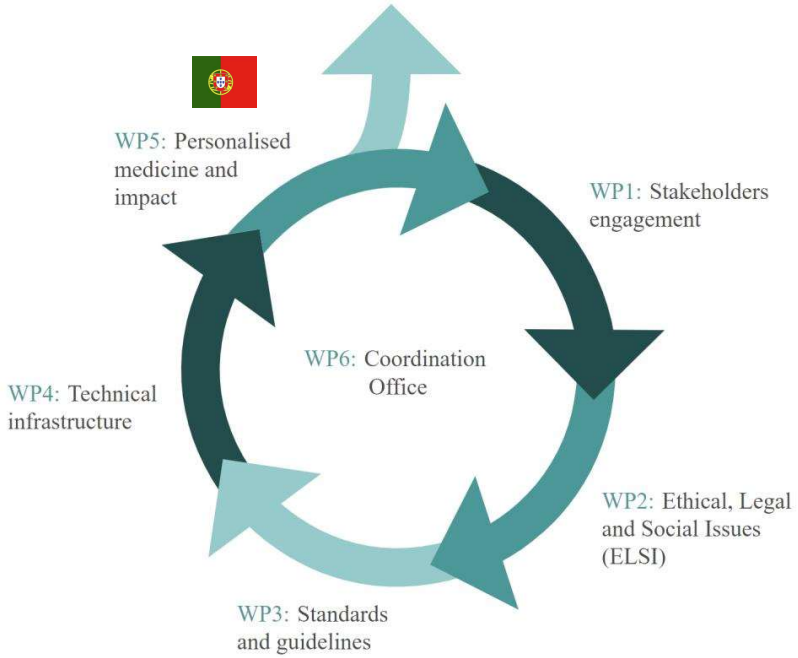
To work with European stakeholders to **define the requirements** **for cross-border access to genomics** and **PM data**.

To **translate requirements** for

- data quality,
- standards,
- technical infrastructure,
- Ethical,
- Legal,
- and Social Implications (ELSI)

into **technical specifications** and **implementation guidelines** that capture European best practice.

To drive **adoption and support** for long-term operations **by providing guidance on phased development** and a methodology for economic evaluation.



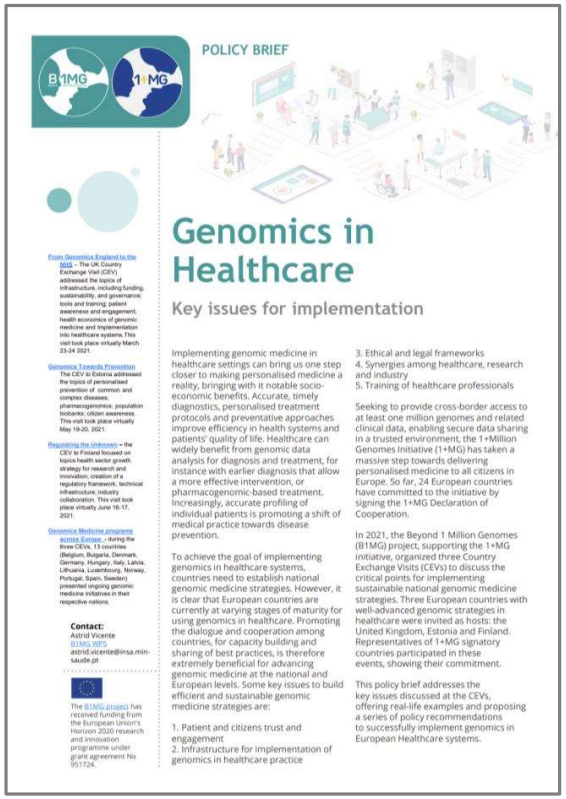
Duration

3Y (june 2020 – October 2023)

Funding

€ 4M, from EU Horizon 2020 Research and Innovation Programme

WP 5 - Delivering Personalised Medicine cross-borders: Implementation in healthcare systems and societal impact



POLICY BRIEF

Genomics in Healthcare

Key issues for implementation

Implementing genomic medicine in healthcare settings can bring us one step closer to making personalised medicine a reality, bringing with it notable socio-economic benefits. Accurate, timely diagnostics, personalised treatment protocols and preventative approaches improve efficiency in health systems and patients' quality of life. Healthcare can widely benefit from genomic data analysis for diagnosis and treatment, for instance with earlier diagnosis that allow a more effective intervention, or pharmacogenomic-based treatment. Increasingly, accurate profiling of individual patients is promoting a shift of medical practice towards disease prevention.

To achieve the goal of implementing genomics in healthcare systems, countries need to establish national genomic medicine strategies. However, it is clear that European countries are currently at varying stages of maturity for using genomics in healthcare. Promoting the dialogue and cooperation among countries, for capacity building and sharing of best practices, is therefore extremely beneficial for advancing genomic medicine at the national and European levels. Some key issues to build efficient and sustainable genomic medicine strategies are:

1. Patient and citizens trust and engagement
2. Infrastructure for implementation of genomics in healthcare practice
3. Ethical and legal frameworks
4. Synergies among healthcare, research and industry
5. Training of healthcare professionals

Seeking to provide cross-border access to at least one million genomes and related clinical data, enabling secure data sharing in a trusted environment, the 1+Million Genomes Initiative (1+MG) has taken a massive step towards delivering personalised medicine to all citizens in Europe. So far, 24 European countries have committed to the initiative by signing the 1+MG Declaration of Cooperation.

In 2021, the Beyond 1 Million Genomes (B1MG) project, supporting the 1+MG initiative, organized three Country Exchange Visits (CEVs) to discuss the critical points for implementing sustainable national genomic medicine strategies. Three European countries with well-advanced genomic strategies in healthcare were invited as hosts: the United Kingdom, Estonia and Finland. Representatives of 1+MG signatory countries participated in these events, showing their commitment.

This policy brief addresses the key issues discussed at the CEVs, offering real-life examples and proposing a series of policy recommendations to successfully implement genomics in European Healthcare systems.

From Genomics England to the NHS – The UK Country Exchange Visit (CEV) addressed the topics of infrastructure, including funding, sustainability, and governance; tools and training; patient awareness and engagement; health economics of genomic medicine and implementation into healthcare systems. This visit took place virtually March 23-24 2021.

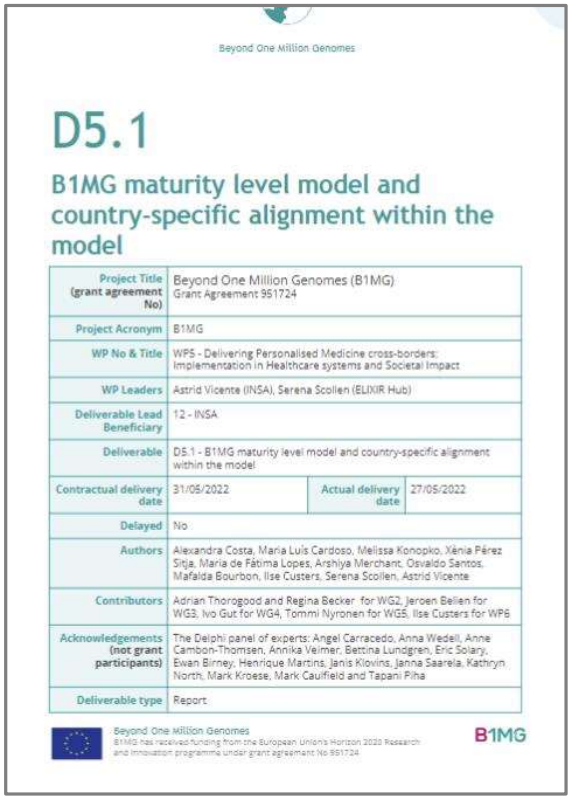
Genomics Towards Prevention The CEV to Estonia addressed the topics of personalised prevention of common and complex diseases; pharmacogenomics; population biobanks; citizen awareness. This visit took place virtually May 19-20, 2021.

Regulating the Unknown – the CEV to Finland focused on topics health sector growth strategy for research and innovation; creation of a regulatory framework, technical infrastructure; industry collaboration. This visit took place virtually June 16-17, 2021.

Genomics Medicine programs across Europe - during the three CEVs, 13 countries (Belgium, Bulgaria, Denmark, Germany, Hungary, Italy, Latvia, Lithuania, Luxembourg, Norway, Portugal, Spain, Sweden) presented ongoing genomic medicine initiatives in their respective nations.

Contact:
Astrid Vicente
B1MG WP5
astrid.vicente@insa.min-saude.pt

The B1MG project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 951724.



Beyond One Million Genomes

D5.1

B1MG maturity level model and country-specific alignment within the model

Project Title (grant agreement No)	Beyond One Million Genomes (B1MG) Grant Agreement: 951724		
Project Acronym	B1MG		
WP No & Title	WP5 - Delivering Personalised Medicine cross-borders: Implementation in Healthcare systems and Societal Impact		
WP Leaders	Astrid Vicente (INSA), Serena Scollen (ELIXIR Hub)		
Deliverable Lead Beneficiary	12 - INSA		
Deliverable	D5.1 - B1MG maturity level model and country-specific alignment within the model		
Contractual delivery date	31/05/2022	**Actual delivery date**	27/05/2022
Delayed	No		
Authors	Alexandra Costa, Maria Luís Cardoso, Melissa Konopko, Xènia Pérez Sitja, Maria de Fátima Lopes, Arshiya Merchant, Osvaldo Santos, Mafalda Bourbon, Ilse Custers, Serena Scollen, Astrid Vicente		
Contributors	Adrian Thorogood and Regina Becker for WG2, Jeroen Belien for WG3, Ivo Gut for WG4, Tommi Nyronen for WG5, Ilse Custers for WP6		
Acknowledgements (not grant participants)	The Delphi panel of experts: Angel Carracedo, Anna Wedell, Anne Cambon-Thomsen, Annika Veimer, Bettina Lundgren, Eric Solary, Ewan Birney, Henrique Martins, Janis Klovins, Janna Saarela, Kathryn North, Mark Kroese, Mark Caulfield and Tapani Piha		
Deliverable type	Report		

Beyond One Million Genomes
B1MG has received funding from the European Union's Horizon 2020 Research and Innovation programme under grant agreement No 951724

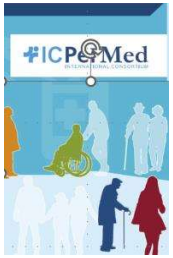
B1MG

PT_MedGen
Estratégia Nacional para a Medicina Genómica

Stepping stones for the implementation of a Genomic Medicine Strategy in Portugal DG-REFORM

Genome of Portugal

2016 2018 2020 2021 2022 2023



+1MG

B1MG

European Genomic Data Infrastructure

Genome of Europe

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

can.heal

European Genomic Data Infrastructure

Instituto_Nacional de Saúde Doutor Ricardo Jorge

The **Genomic Data Infrastructure (GDI)** project is enabling access to genomic and related phenotypic and clinical data across Europe. It is doing this by establishing a federated, sustainable and secure infrastructure to access the data. It builds on the outputs of the Beyond 1 Million Genomes (B1MG) project and is realising the ambition of the 1+Million Genomes (1+MG) initiative.

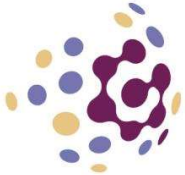
https://gdi.onemilliongenomes.eu/

The vision

In 2018, the 1+Million Genomes (1+MG) initiative was launched to create a European data infrastructure for genomic data. This would implement common national rules enabling federated data access. Twenty four European countries have signed the declaration. The goal of the initiative is **to enable secure access to genomic and the corresponding clinical data across Europe for better research, personalised healthcare and health policy making**.

Designing and testing

In 2020, the Beyond 1 Million Genomes (B1MG) project began. The project is developing guidelines on how to implement the 1+MG initiative. Amongst its outputs are blueprints and recommendations for building a federated network of genomic data (the 1+MG Trust Framework). It is also producing tools to help countries self assess their readiness to implement genomics into healthcare systems.



Scaling up and sustaining

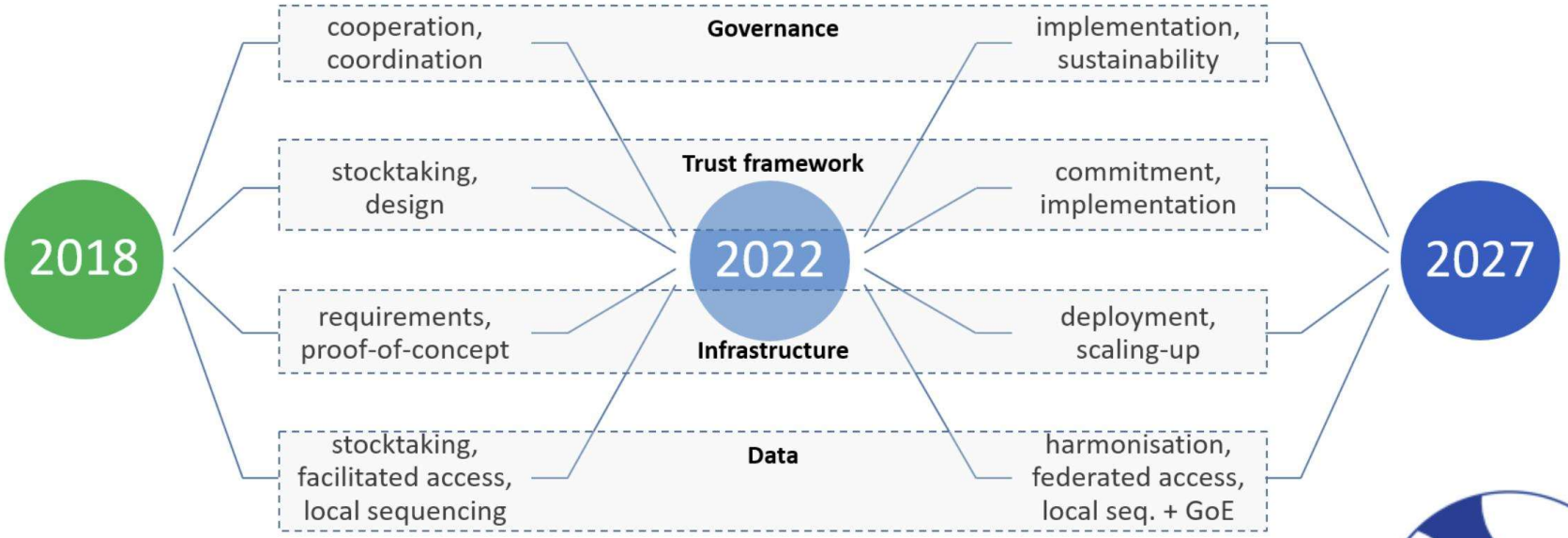
In 2022, the GDI project began. This €40M project is building on the preparatory work of 1+MG working groups, the B1MG project and investments of EU countries. It is **creating and deploying the technical capacity for accessing genomic data**. In this way, it will implement the vision of the 1+MG initiative.

B1MG

design & testing phase

European Genomic Data Infrastructure

scale-up & sustainability phase



1+MG

1+MG

"PROPHET – a PeRsOnalized Prevention roadmap for the future HEalThcare" will develop a **Strategic Research and Innovation Agenda (SRIA)** for Personalized Prevention, in order to support the implementation of innovative, sustainable and effective personalized programmes to prevent common chronic diseases. Technological biomedical advances (including omics data and digital tools) make risk stratification at the individual level possible. PROPHET will be centred around stakeholder engagement and the SRIA co-creation process.

The consortium consists of 18 beneficiaries and 2 affiliated entities across 12 EU Countries, and a large number of stakeholders already engaged from different Target Groups.

The overall objective of PROPHET is co-create with stakeholders a Personalized Prevention Roadmap for the future healthcare, in order to support the definition and implementation of innovative, sustainable and high-quality personalized strategies that are effective in preventing chronic diseases.

PT_MedGen
Estratégia Nacional para a Medicina Genómica

Stepping stones for the implementation of a Genomic Medicine Strategy in Portugal DG-REFORM

Genome of Portugal

2016 2018 2020 2021 2022 2023

#ICPerMed

+1MG

B1MG

European Genomic Data Infrastructure

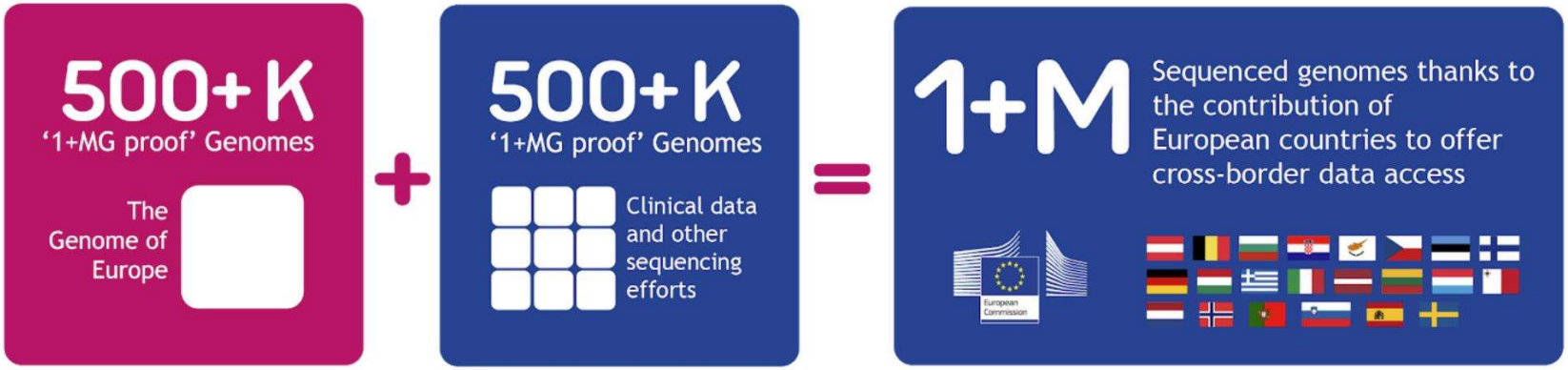
Genome of Europe

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

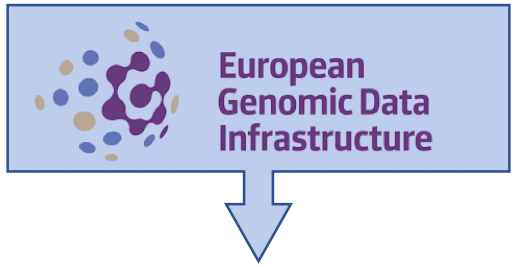
can.heal

Strategy to obtain +1MG

- **1+MG** targets both clinical data derived from **patients** and data collected from the **general citizen population**.
- The **Genome of Europe** (GoE) Project that will contribute at least **500.000 genomes** to the 1+MG ambitions.
- The goal of GoE is to build a **collective reference genome cohort of European citizens**, selected (on a national basis) to mirror the genetic composition of the European population.
- The Genome of Europe is a **multi-country project strategy**
- All c**ountries** participating in GoE **build their own national reference collection** of personal genomic datasets.



What are the Signatories of +1MG Initiative trying to achieve?



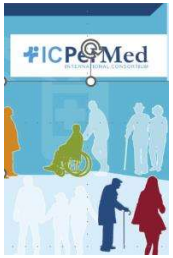
1. Ensuring that appropriate **technical infrastructure** is available **across the EU**, allowing for **secure, federated access to genomic data**;
2. Making sure that **ethical** and **legal** implications of **genomics** are clear and taken into account;
3. Ensuring that the **general public** and **policy makers** in Member States and signatory countries are **well informed about genomics**, in order to ensure its **uptake by healthcare systems** and integration into **personalised healthcare**.
4. The 1+MG initiative will give a **boost to digital innovation of healthcare** and help prepare countries to create a **European Health Data Space.**

PT_MedGen
Estratégia Nacional para a Medicina Genómica

Stepping stones for the implementation of a Genomic Medicine Strategy in Portugal DG-REFORM

Genome of Portugal

2016 2018 2020 2021 2022 2023



+1MG

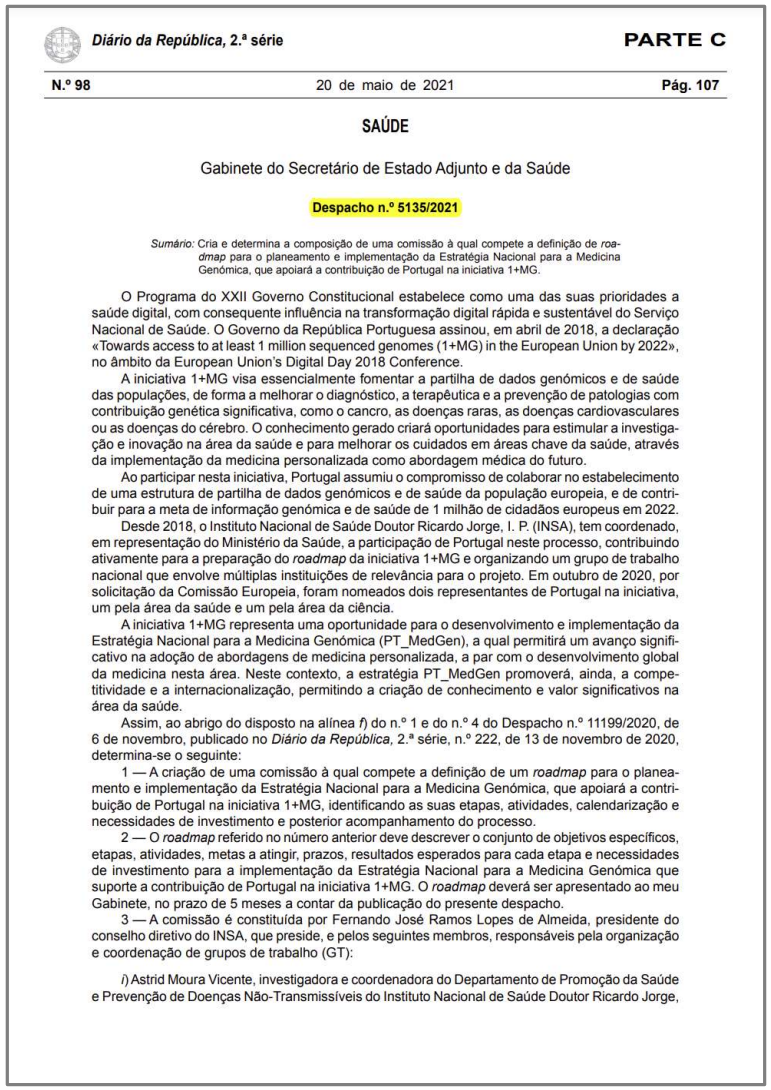
B1MG

European Genomic Data Infrastructure

Genome of Europe

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

can.heal



Diário da República, 2.ª série — PARTE C

N.º 98 — 20 de maio de 2021 — Pág. 107

SAÚDE

Gabinete do Secretário de Estado Adjunto e da Saúde

Despacho n.º 5135/2021

Sumário: Cria e determina a composição de uma comissão à qual compete a definição de *roadmap* para o planeamento e implementação da Estratégia Nacional para a Medicina Genómica, que apoiará a contribuição de Portugal na iniciativa 1+MG.

O Programa do XXII Governo Constitucional estabelece como uma das suas prioridades a saúde digital, com consequente influência na transformação digital rápida e sustentável do Serviço Nacional de Saúde. O Governo da República Portuguesa assinou, em abril de 2018, a declaração «Towards access to at least 1 million sequenced genomes (1+MG) in the European Union by 2022», no âmbito da European Union's Digital Day 2018 Conference.

A iniciativa 1+MG visa essencialmente fomentar a partilha de dados genómicos e de saúde das populações, de forma a melhorar o diagnóstico, a terapêutica e a prevenção de patologias com contribuição genética significativa, como o cancro, as doenças raras, as doenças cardiovasculares ou as doenças do cérebro. O conhecimento gerado criará oportunidades para estimular a investigação e inovação na área da saúde e para melhorar os cuidados em áreas chave da saúde, através da implementação da medicina personalizada como abordagem médica do futuro.

Ao participar nesta iniciativa, Portugal assumiu o compromisso de colaborar no estabelecimento de uma estrutura de partilha de dados genómicos e de saúde da população europeia, e de contribuir para a meta de informação genómica e de saúde de 1 milhão de cidadãos europeus em 2022.

Desde 2018, o Instituto Nacional de Saúde Doutor Ricardo Jorge, I. P. (INSA), tem coordenado, em representação do Ministério da Saúde, a participação de Portugal neste processo, contribuindo ativamente para a preparação do *roadmap* da iniciativa 1+MG e organizando um grupo de trabalho nacional que envolve múltiplas instituições de relevância para o projeto. Em outubro de 2020, por solicitação da Comissão Europeia, foram nomeados dois representantes de Portugal na iniciativa, um pela área da saúde e um pela área da ciência.

A iniciativa 1+MG representa uma oportunidade para o desenvolvimento e implementação da Estratégia Nacional para a Medicina Genómica (PT_MedGen), a qual permitirá um avanço significativo na adoção de abordagens de medicina personalizada, a par com o desenvolvimento global da medicina nesta área. Neste contexto, a estratégia PT_MedGen promoverá, ainda, a competitividade e a internacionalização, permitindo a criação de conhecimento e valor significativos na área da saúde.

Assim, ao abrigo do disposto na alínea *f*) do n.º 1 e do n.º 4 do Despacho n.º 11199/2020, de 6 de novembro, publicado no *Diário da República*, 2.ª série, n.º 222, de 13 de novembro de 2020, determina-se o seguinte:

1 — A criação de uma comissão à qual compete a definição de um *roadmap* para o planeamento e implementação da Estratégia Nacional para a Medicina Genómica, que apoiará a contribuição de Portugal na iniciativa 1+MG, identificando as suas etapas, atividades, calendarização e necessidades de investimento e posterior acompanhamento do processo.

2 — O *roadmap* referido no número anterior deve descrever o conjunto de objetivos específicos, etapas, atividades, metas a atingir, prazos, resultados esperados para cada etapa e necessidades de investimento para a implementação da Estratégia Nacional para a Medicina Genómica que suporte a contribuição de Portugal na iniciativa 1+MG. O *roadmap* deverá ser apresentado ao meu Gabinete, no prazo de 5 meses a contar da publicação do presente despacho.

3 — A comissão é constituída por Fernando José Ramos Lopes de Almeida, presidente do conselho diretivo do INSA, que preside, e pelos seguintes membros, responsáveis pela organização e coordenação de grupos de trabalho (GT):

i) Astrid Moura Vicente, investigadora e coordenadora do Departamento de Promoção da Saúde e Prevenção de Doenças Não-Transmissíveis do Instituto Nacional de Saúde Doutor Ricardo Jorge,

- In 2021, our government created the multidisciplinay **Commission PT-MedGen** (experts in the field of genomics and related areas) to **define the roadmap** for planning the implementation of the **Portuguese National Strategy for Genomics Medicine,** that will support **Portuguese contribution** to the **1+MG initiative.**
- This roadmap describes the
  - **objectives**,
  - **stages,**
  - **activities,**
  - **goals to achieve,**
  - **deadlines**,
  - **expected results** for each stage and
  - **needs of investment** for the implementation of the National Strategy for Genomic Medicine

PT_MedGen
Estratégia Nacional para a Medicina Genómica

PT_MedGen

Estratégia Nacional para a Medicina Genómica

Instituto_Nacional de Saúde Doutor Ricardo Jorge

Estratégia Nacional para a Medicina Genómica

PT_MedGen

Desafios e prioridades

Instituto_Nacional de Saúde Doutor Ricardo Jorge

AICIB

Março, 2022

TÉCNICO LISBOA · BioData.pt · GenomePT · Health Cluster Portugal · U.PORTO · 3S · UNIVERSIDADE DE COIMBRA · SPMS

Projeto Genoma de Portugal

Fevereiro 2023

Instituto_Nacional de Saúde Doutor Ricardo Jorge

AICIB

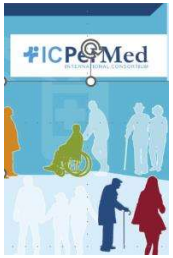
TÉCNICO LISBOA · BioData.pt · GenomePT · Health Cluster Portugal · U.PORTO · 3S · UNIVERSIDADE DE COIMBRA · SPMS

PT_MedGen
Estratégia Nacional para a Medicina Genómica

Stepping stones for the implementation of a Genomic Medicine Strategy in Portugal DG-REFORM

Genome of Portugal

2016 2018 2020 2021 2022 2023



+1MG

B1MG

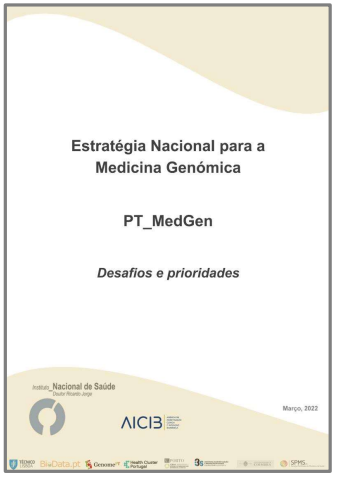
European Genomic Data Infrastructure

Genome of Europe

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

can.heal

Stepping stones for the implementation of a Genomic Medicine Strategy in Portugal
DG-REFORM




INSTITUTO NACIONAL
DE SAÚDE DOUTOR
RICARDO JORGE