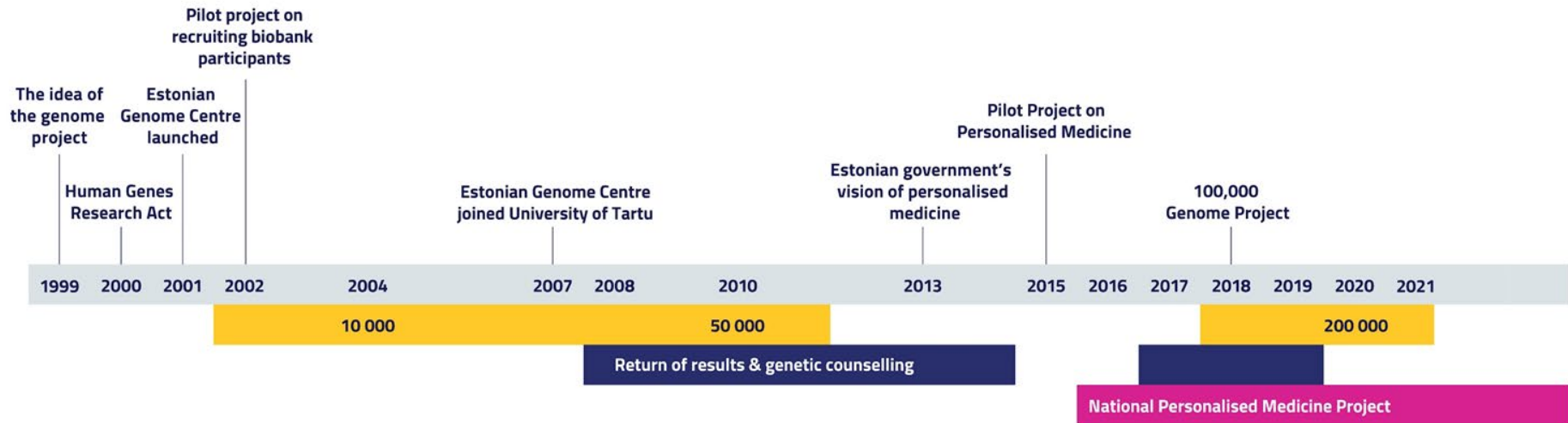




**Will genomics help to
support the long-expected
shift towards prevention?**

Lili Milani
Head of Estonian Genome Centre
Vice Director, Institute of Genomics, University of Tartu





Biobank participants



202 282

biobank participants

- Health records, diet, physical activity, etc.
- DNA, plasma and cell samples

Estonian adult population



20%
biobank
participants

5000+ return of results (RoR)*



*RoR & genetic counselling

202 282 genotyped



3000 sequenced



- Estonian Human Genes Research Act
- Broad informed consent
- Open for research:
Clear access rules

Whole-genome sequencing + genotyping + genotype imputation (+ validation)

1. 3000 whole genomes and 2500 whole exomes sequenced
2. Genotyping of 700K markers (Global Screening Array, Illumina)
3. Imputation and long-range haplotyping
4. Rare mutations and polygenic risk scores for common diseases





Familial hypercholesterolemia

Frequency >1:200

LDLR, APOB, PCSK9



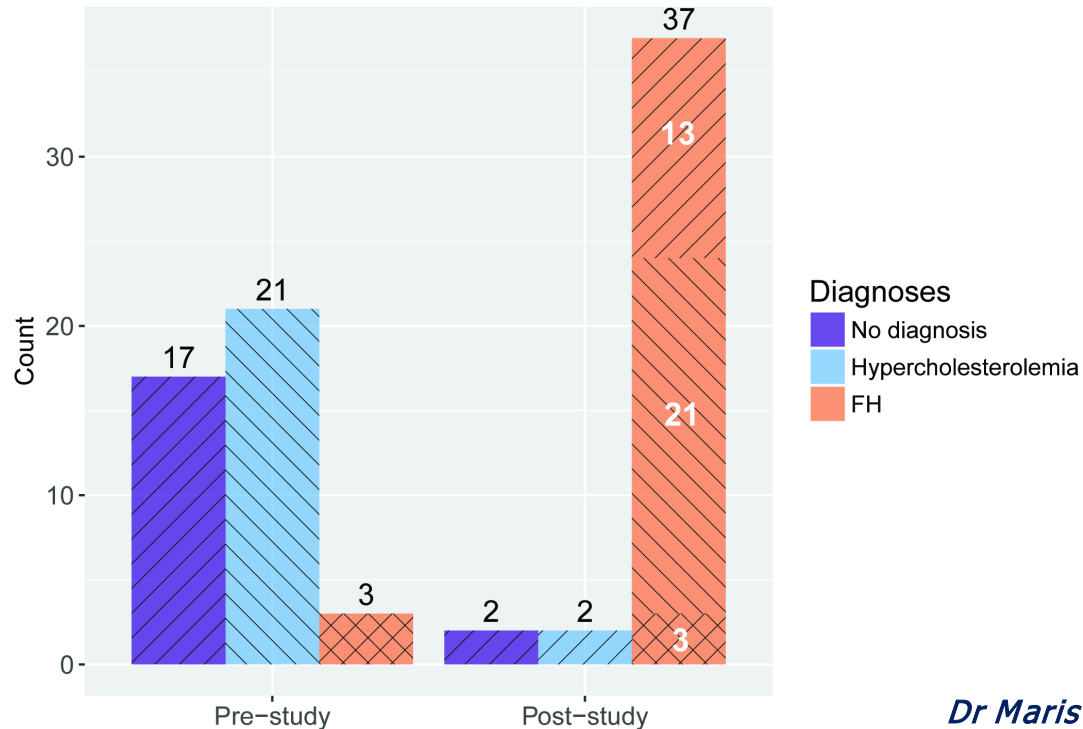
Familial breast cancer

Frequency >1:200

BRCA1, BRCA2

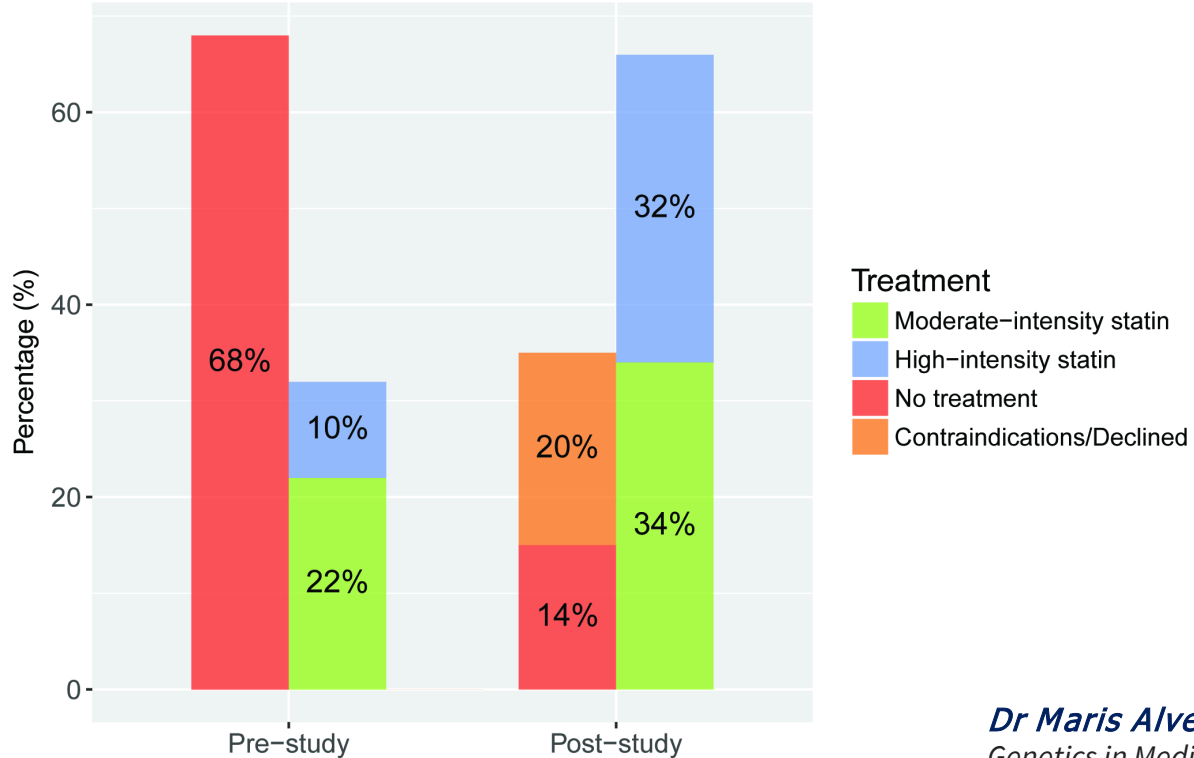
Diagnosed?

4776 genomes ➤ 41 mut (LDLR, APOB, PCSK9) ➤ 3 diagnosed



Treatment?

33% pre-study ➔ **66-86% post-study**



Familial breast cancer (1:200): Recall by genotype



22 BRCA1/2 mutation carriers



17 with family history of breast cancer



1 referred to medical geneticist

(2 diagnosed with BrCa and 2 diagnosed with PrCa)

Conclusions of FH & BRCA studies

Unawareness of the familial background of the diseases

Low pre-established treatment adherence

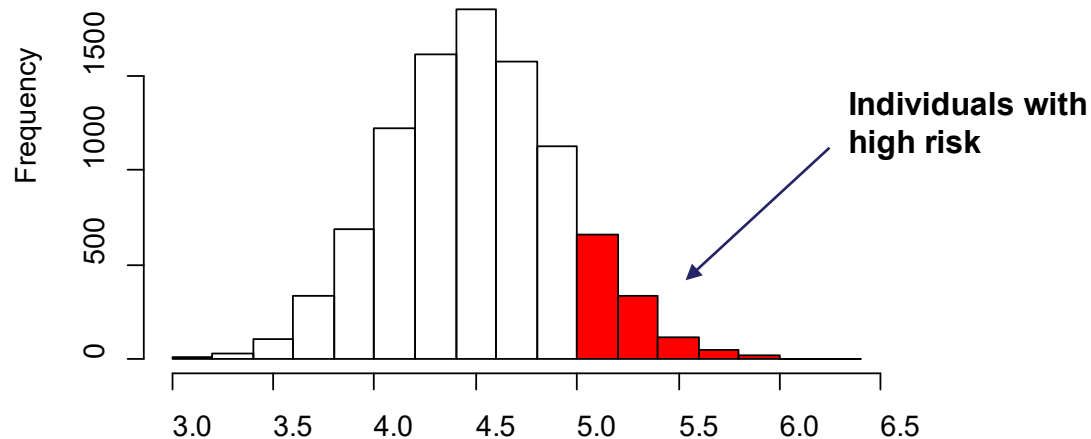
Cardiologists & oncologists acknowledge the value of genetics-first approaches

Common complex diseases & Polygenic risk scores

Polygenic risk scores for common diseases

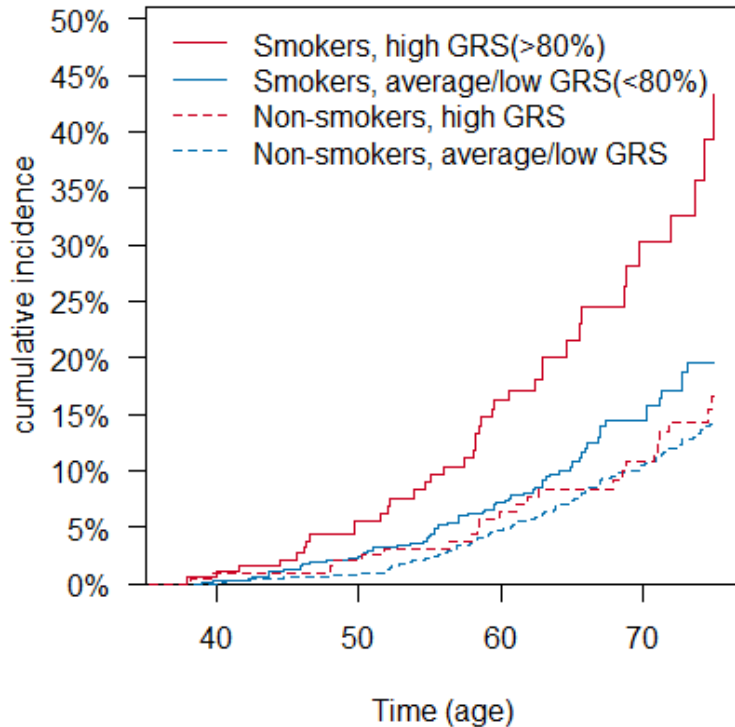
- Effect of each single variant is small
- Variants and effect sizes can be summed into **risk scores**

Distribution of polygenic risk score for Cardiovascular disease



Incident Myocardial Infarction: analysis of 246 incident cases among men

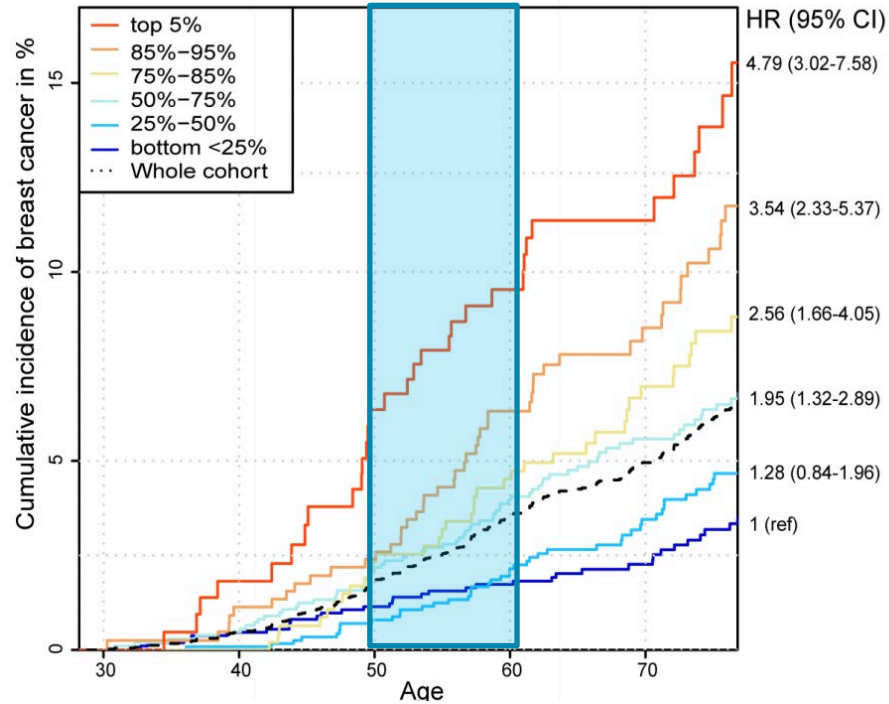
MI incidence in men by GRS category
(n=8345, age 30-75)



HR=2.2, $p=7.6 \times 10^{-5}$ (compared to lower GRS)
40 cases (n=204)

No significant GRS effect seen among
non-smoking men

PRS for breast cancer

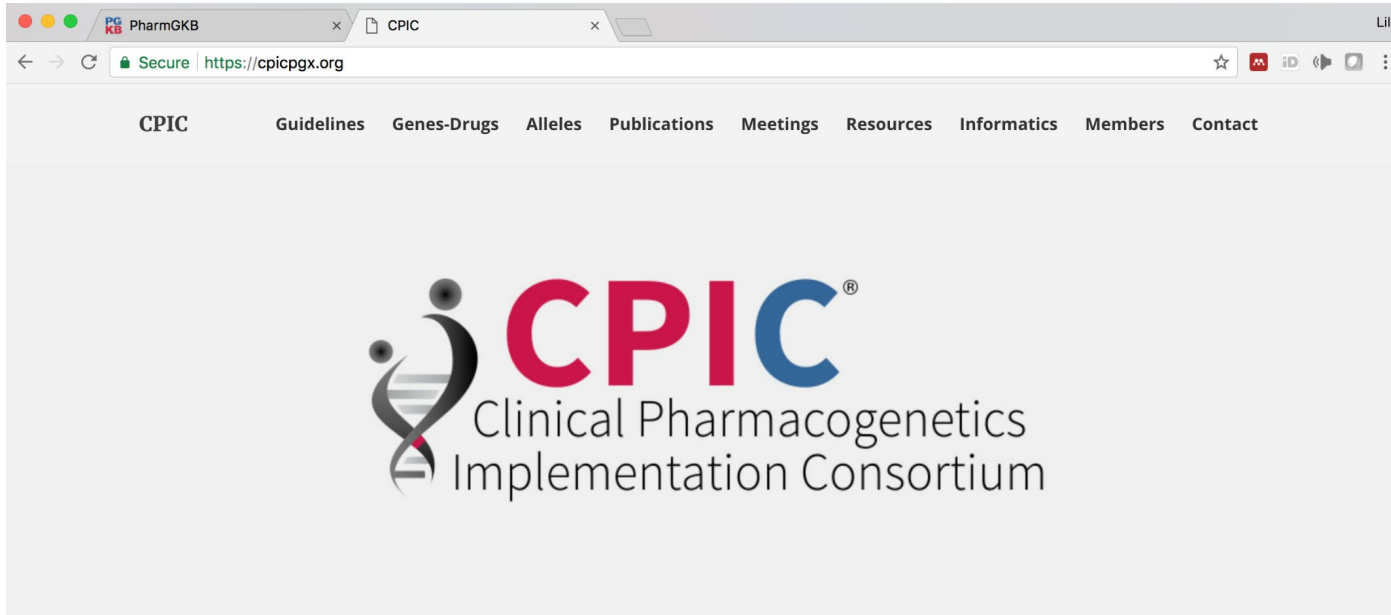


Top 5% highest genetic risk score = 20% of cardiovascular deaths

Targeted disease prevention

Pharmacogenetics

>98% of individuals carry mutations that affect drug response













What is CPIC?

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



Pharmacogenetics report

Geen	Genotüüp	Hinnang	Soovitus	Mõjutatud ravimi toimeained
CYP2C19	*2/*2	Aeglane ravimi lagundamine		Estsitalopraam, Tsitalopraam, Klopidoogrel, Sertraliin, Vorikonasool, Esomeprasool, Lansoprasool, Pantoprasool, Omeprasool, Klomipramiin, Amitriptüliin
CYP2C9	*1/*1	Tavapärane ravimi lagundamine		Fenütoiin
CYP2C9; VKORC1	*1/*1; rs9923231 (AA)	Tavapärasest madalam doosisoovitus		Varfariin
CYP3A5	*3/*3	Aeglane ravimi lagundamine, Tavapärane muster		Takroliimus
DPYD	*1/*5	Tavapärane ravimi lagundamine		Kapetsitabiin, Fluorouratsiil
IFNL3	rs12979860 (CC)	Tavapärane ravimi toime		Alfa-2b-peginterferoon, ribaviirin
SLCO1B1	rs4149056 (TT)	Tavapärane müopaatia risk		Simvastatiin
TPMT	*1S/*1	Tavapärane ravimi lagundamine		Tioguaaniin, Merkaptopuriin, Asatiopriin

 - Tarvitada tavapäraselt.  - Tarvitada ettevaatusega, võib vajada doosi muutmist.  - Tarvitada väga ettevaatlikult, oht kõrvaltoimeteks.

Translation into digital prescription recommendations in the clinic

Ravim Meditsiineseade

Sr	Number	Kinnitatud	Annuleeritud
	2077528207	19.07.2021 11:50	
	3077528207	19.07.2021 11:50	

PATSIENT Koostamise kuupäev: 19.07.2021 EG Sertraliin - CYP2C19 aeglase lagundaja

Eesnimi:
Perekonn:
Isikukood: Ravilugu nr. 40

Volitusliik: avalik privaatne volitatud
Retsepti liik: R N
Kehtivus päevades: 180 Kordsus: 1 2 3

Diagnoos: I11.9 Südamekahjustusega

Ravimpreparaat: ATC: C09BX01 **Perindoprilum+Amlodipinum+Indapamidum**
Nimetus:
Ravimvorm: tablett
Hulk pakendis: 30TK



mitte asendada,

Annustamine detailselt
Ühekordne annus: 1 tablett
Annustuskordi ajaühikus: 1 x päevas
Ravikuuri tüüp: Pidev Kestvus päevades:

Sivi koostatud retsepte... Sivi Retseptikeskuse retsepte...

Valjakirjutatud ühikute koguarv 60 TK Orig. arv 2

Lisainfo/selgitus: Müügiloa taotlus... Tüüpil...
hommikul

 Euroopa Liit
Euroopa
Regionaalarengu Fond
 Eesti
tuleviku heaks

Apt. Inf. koostoime... Kinnita retsept Soodustus Ravimileht... Printi Ravimi koostoimed Kõik koostoimed Sule

Marko Arrak, Dr Sulev

Reisberg

Coming soon: Estonian biobank portal

The mockup shows a user interface for the Estonian biobank portal. At the top left is the logo for Eesti Geenivaramu. The main content is divided into four sections, each with a large icon and a number:

- Teadusartiklit** (27): kus sinu andmeid kasutatud on. [vaata lähemalt >](#)
- Uuringut** (3): kus sul on võimalik osaleda. [vaata lähemalt >](#)
- Minu geeniinfo** (50%): Uuri, millist infot teadlased sinu geenidest leidsid. [vaata lähemalt >](#)
- Pikaajaline tervis** (75%): Kuidas on seotud geenid ja tervis? Mida ma ise teha saan? [vaata lähemalt >](#)
- Vaatan sisse geenilaborisse** (100%): Uuri, kuidas geeniteadlased igapäevaselt teadust loovad. [vaata lähemalt >](#)
- Mis on geenid** (0%): Tutvume lähemalt, mis geenid üldse on ja mida nad teevad? [vaata lähemalt >](#)

At the top right of the interface are two circular icons: a gear for settings and a refresh symbol.

Andres Metspalu, Tõnu Esko, Krista Fischer, Reedik Mägi, Maris Alver, Kristi Krebs, Kristi Läll, Mart Kals, Tom Haller, Liis Leitsalu, Neeme Tõnisson, Marili Palover, Maarja Lepamets, Anu Reigo, Kelli Lehto, Tuuli Jürgenson, Helene Alavere, Ene Mölder, Kristjan Metsalu, Kairit Mikkell, Mari-Liis Tammesoo, Steven Smit, and many more.



STACC

Software Technology and
Applications Competence Center



Prof. Jaak Vilo, Hedi Peterson, Sulev Reisberg, Sven Laur, Dage Särg, jt.



BioMed@STACC: the health data mining team

▼ 18 people



- Alexander Tkachenko
- Anne-Liis Tanav
- Dage Särg
- Gea Pajula
- Harry-Anton
- Karl-Oskar Masing
- Marek Oja
- Margus Jäger
- marje johanson
- Markus Lippus
- Mihkel Manguse
- monika soosaar
- Raul Sirel
- Robert Roosalu
- Sulev Reisberg
- Sven Laur
- Tormi Reinson
- Uku R



REPUBLIC OF ESTONIA
MINISTRY OF SOCIAL AFFAIRS

Kalle Killar, Anneli Laansoo,
Silja Elunurm, Raili Sillart, jt.



Tervise Arengu Instituut
National Institute for Health Development

Prof Toomas Veidebaum, Annika Veimer,
Piret Kuhlbars, Pille Kink, Helen Lepa, jt.



Eesti
Haigekassa

Liis Kruus