# Global Leaders in Genomic Medicine 2014

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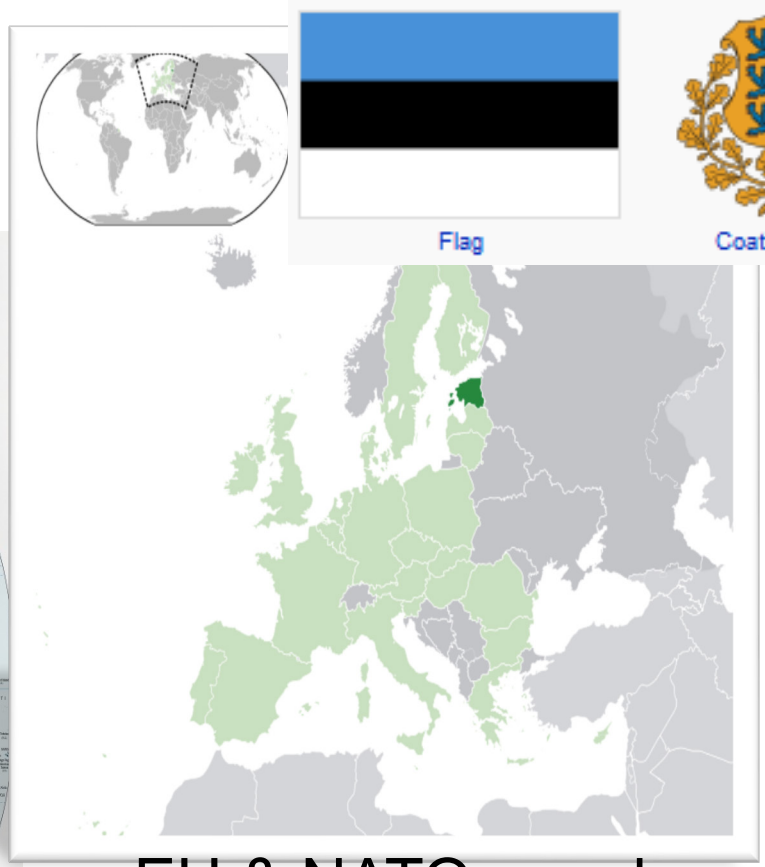
# Republic of Estonia


- Population size: ~1.3 million
- Territory: 45 000 km$^2$

EU & NATO member since 2004

Schengen Treaty since 2007

EUR as our currency since 2011

# Genetic (personalized) medicine

## Medical genetics

- newborn screening
- microarray analysis (InfiniumDx CytoSNP-12 BeadChip)
- exome sequencing

All covered by Estonian Health Care Insurance Fund

## Medical genomics

- biobank
- eHealth
- microarray analysis
- full genome sequencing

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# Estonian Biobank


- Estonian Genome Center, University of Tartu
- A prospective, longitudinal, population-based database with health records and biological materials
- 52,000 participants - 5% of the adult population of Estonia
- Individuals are recruited by GPs, physicians in the hospitals and medical personnel in the EGCUT recruitment offices
- Estonian Human Genes Research Act (HGRA)

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# Estonian Human Genes Research Act

## § 3. Chief processor of Gene Bank

- (1) The chief processor of the Gene Bank is the University of Tartu, whose objectives as the chief processor are to:
- 1) promote the development of genetic research;
- 2) collect information on the health of the Estonian population and genetic information concerning the Estonian population;
- 3) use the results of genetic research to improve public health.

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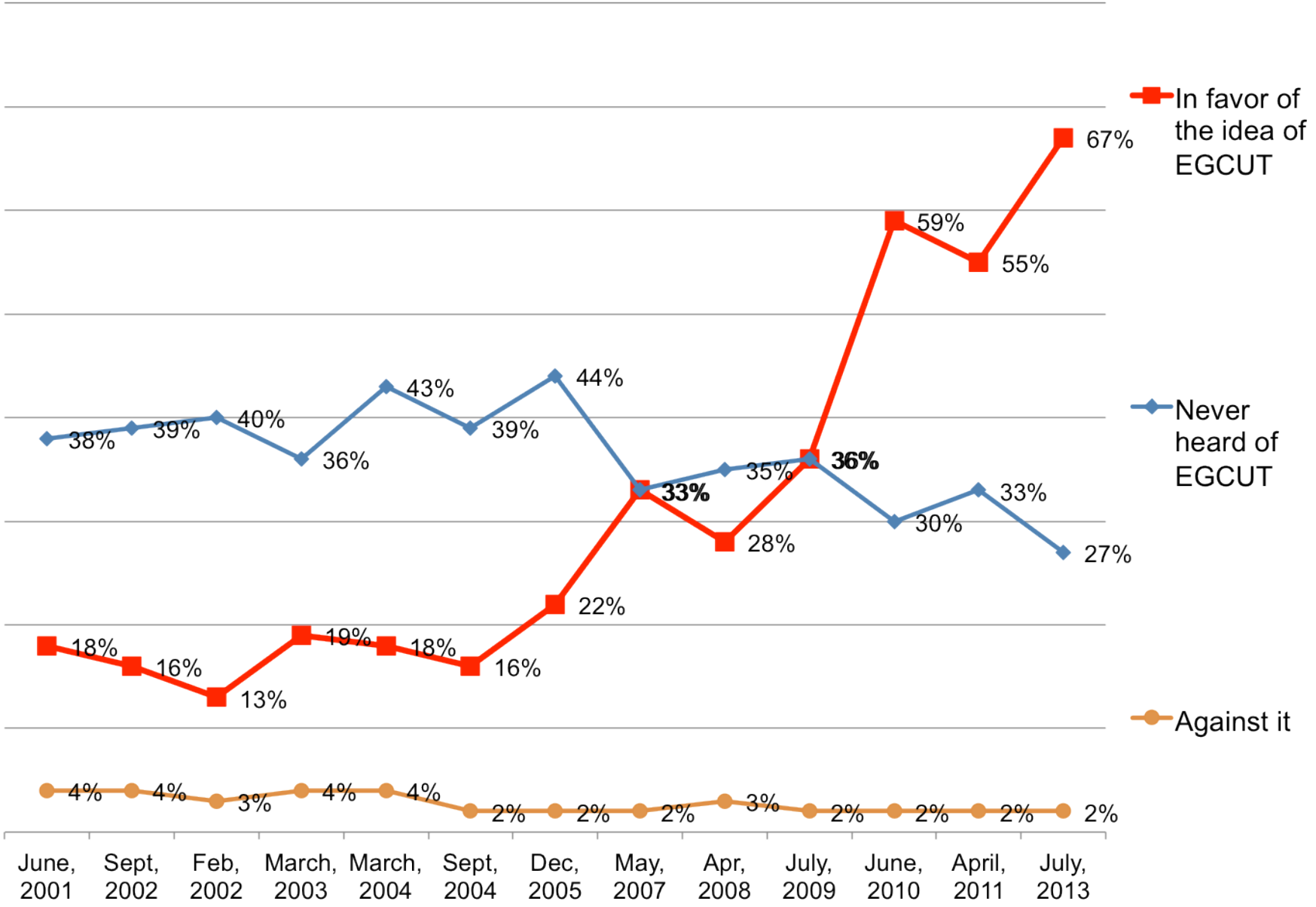
# Public opinion and awareness of the EGCUT 2001-2013



# Genetic map of Europe


Nelis & Esko et al 2009

# Data available for research

- 52,000 participants with health data and DNA, plasma, WBC
  - Continuously being updated through follow-up projects and linking to national health registries
- A broad informed consent form
- Over 1 million biological aliquotes
  - Around 20 000 participants' DNA samples genotyped, 12 000 hve NMR data
  - 120 full genomes plus 100 exomes are have been sequenced
  - 1000 RNA expression arrays
  - Access rules are clear

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# eHealth

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# The Estonian ID card

- The ID card is a **mandatory** ID document for all Estonian residents from the age of 15
- Enables secure digital authentication and signing
- A digital signature has the same legal consequences as a hand-written signature
- Does not have any additional information
  - No bank account, no health information etc.
- Active cards: **1 214 428** (31.12.2013)
  - Estonian Population 1 286 540 (01.01.2013)
  - Estonia has been issuing electronic ID cards from January 1st 2002
  - Also Mobile-ID


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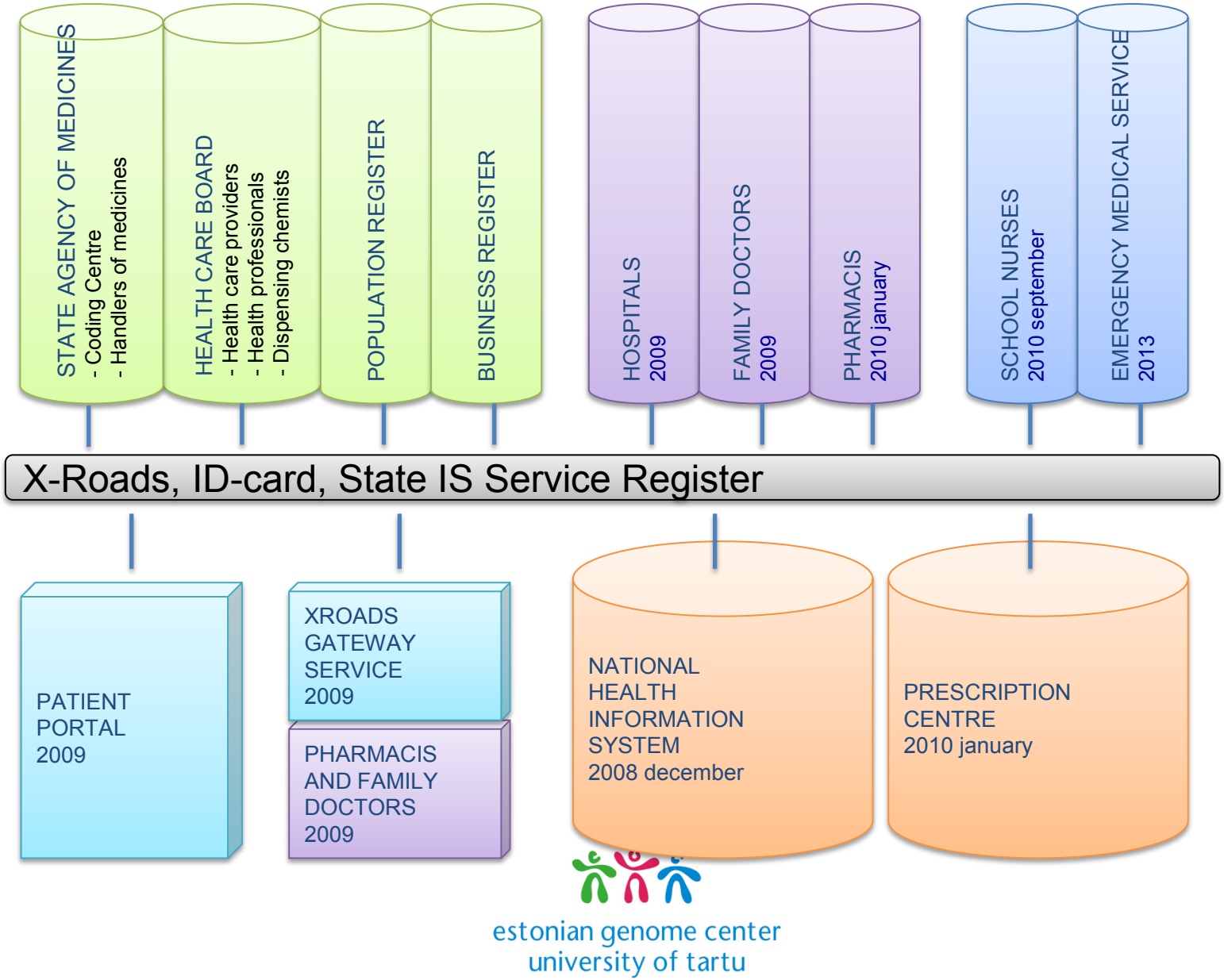
# Architectural “Big picture”



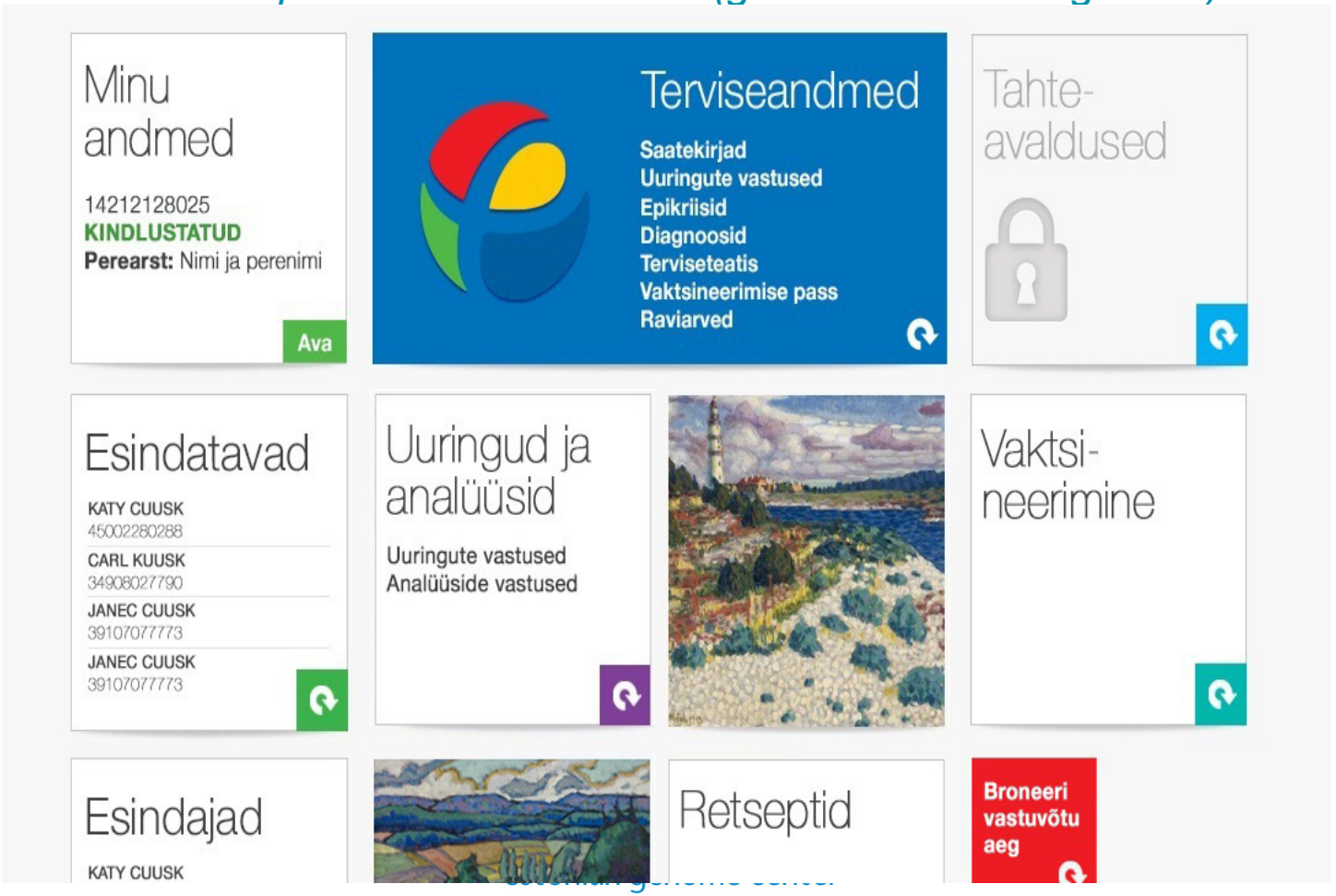
# Tools and enablers of information exchange

- One universal national identification code
  - Registries and databases use same code to uniquely identify persons
- National PKI infrastructure
- The Estonian ID card
  - Smartcard with two digital certificates
  - Also Mobile-ID – safe digital ID with mobile phone
- National Data Exchange Layer X-Road
- Obligatory national data security framework
- High public acceptance and trust
  - No public incidents or misuses (10 years)

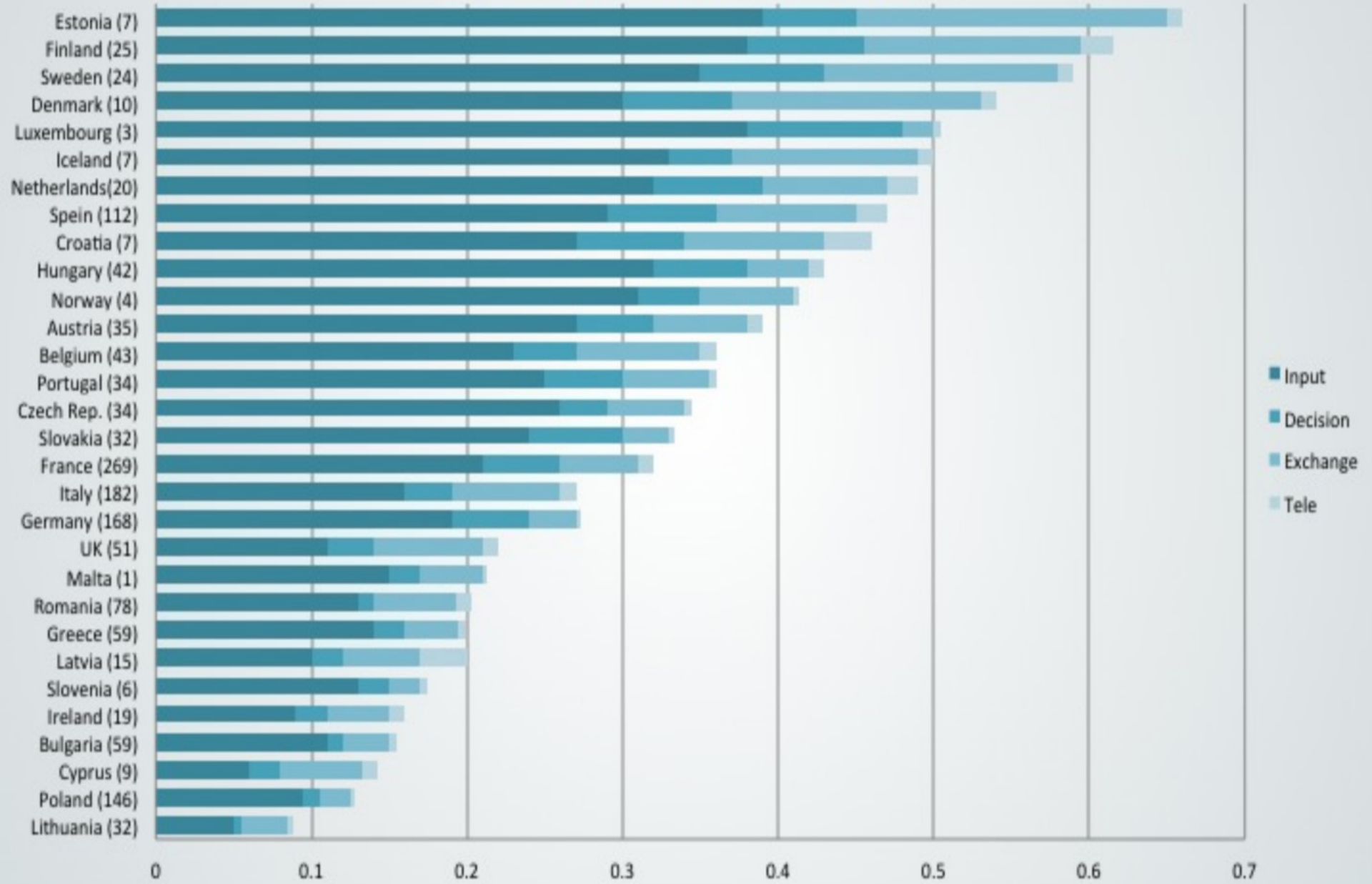
# National Patient Portal

*Documents total – **10.8 mio***

***1.1 mio** persons medical data (growth 20% during 2012)*



Benchmarking Information and Communication Technologies in Health Systems
Joint EC- OECD WORKSHOP Brussels, April 18-19, 2013




eHealth availability and use Indicator 2012: by country

# Do we have enough information to start?

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# Polygenic risk scores

- Genome-wide association studies (GWAS) have discovered a large number of genetic variants that are associated with common complex diseases.
- The effect of each individual marker (SNP) is in most cases not strong enough to justify their use in clinical practice
- Combining several markers across the genome leads to polygenic risk scores that already explain a large proportion of heritability of the trait and are a promising tool to aid personalized disease prediction

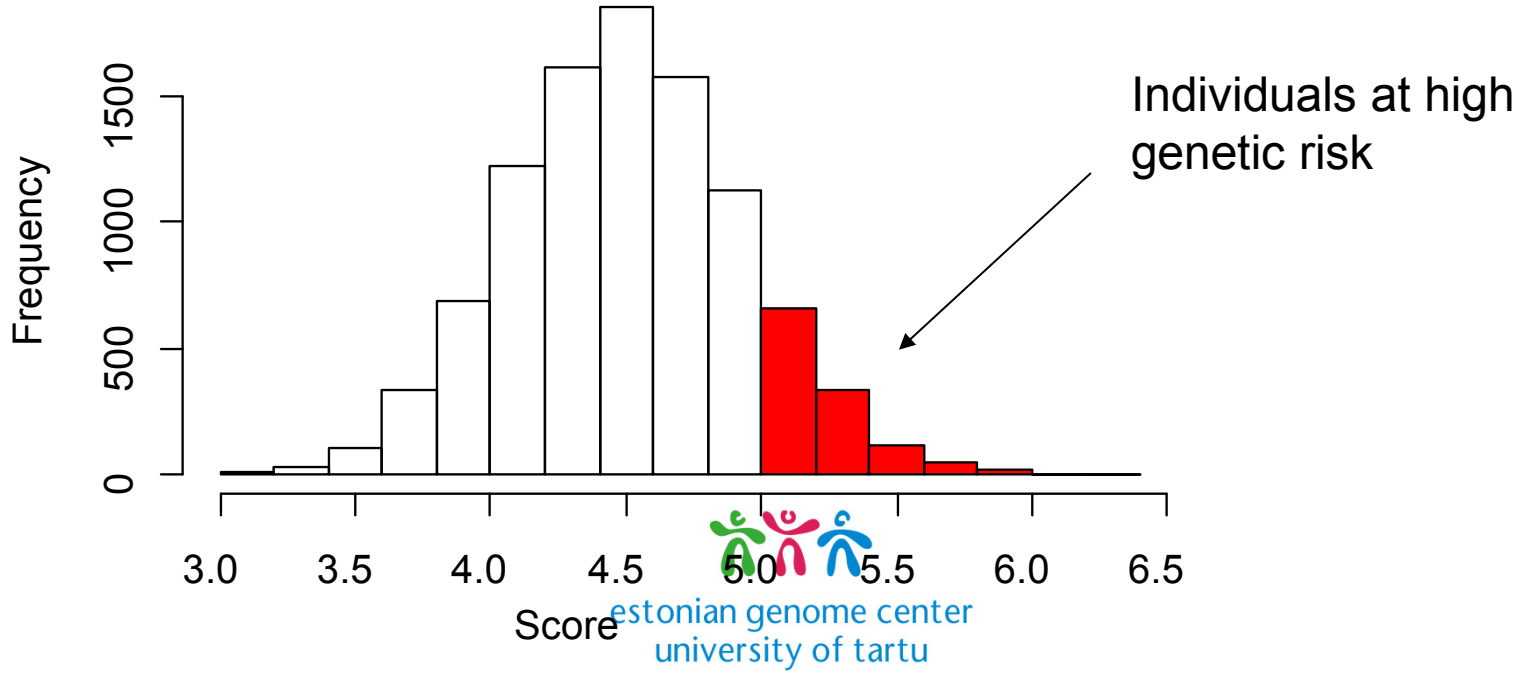
# Polygenic risk scores

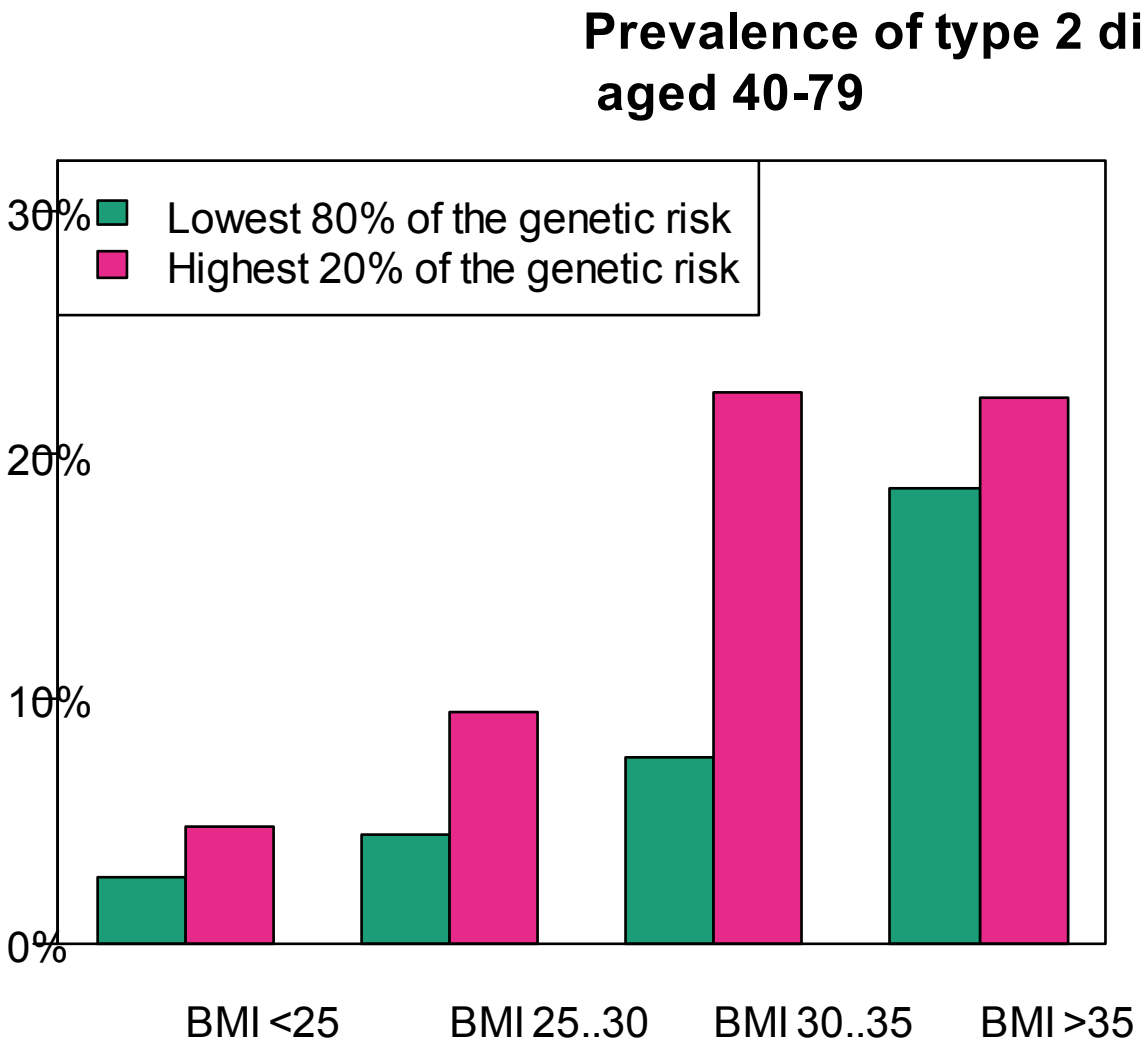
Calculated as $S = \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_k X_k$,

$X_2, \ldots, X_k$ - allele dosages for k independent markers (SNP-s), typically the ones with strongest effect

$\beta_1, \beta_2, \ldots, \beta_k$ – effect estimates (logistic regression parameters, ln OR) from a GWAS meta-analysis

**Polygenic risk score for type II diabetes: histogram of the score in 7462 individuals (Estonian Biobank)**



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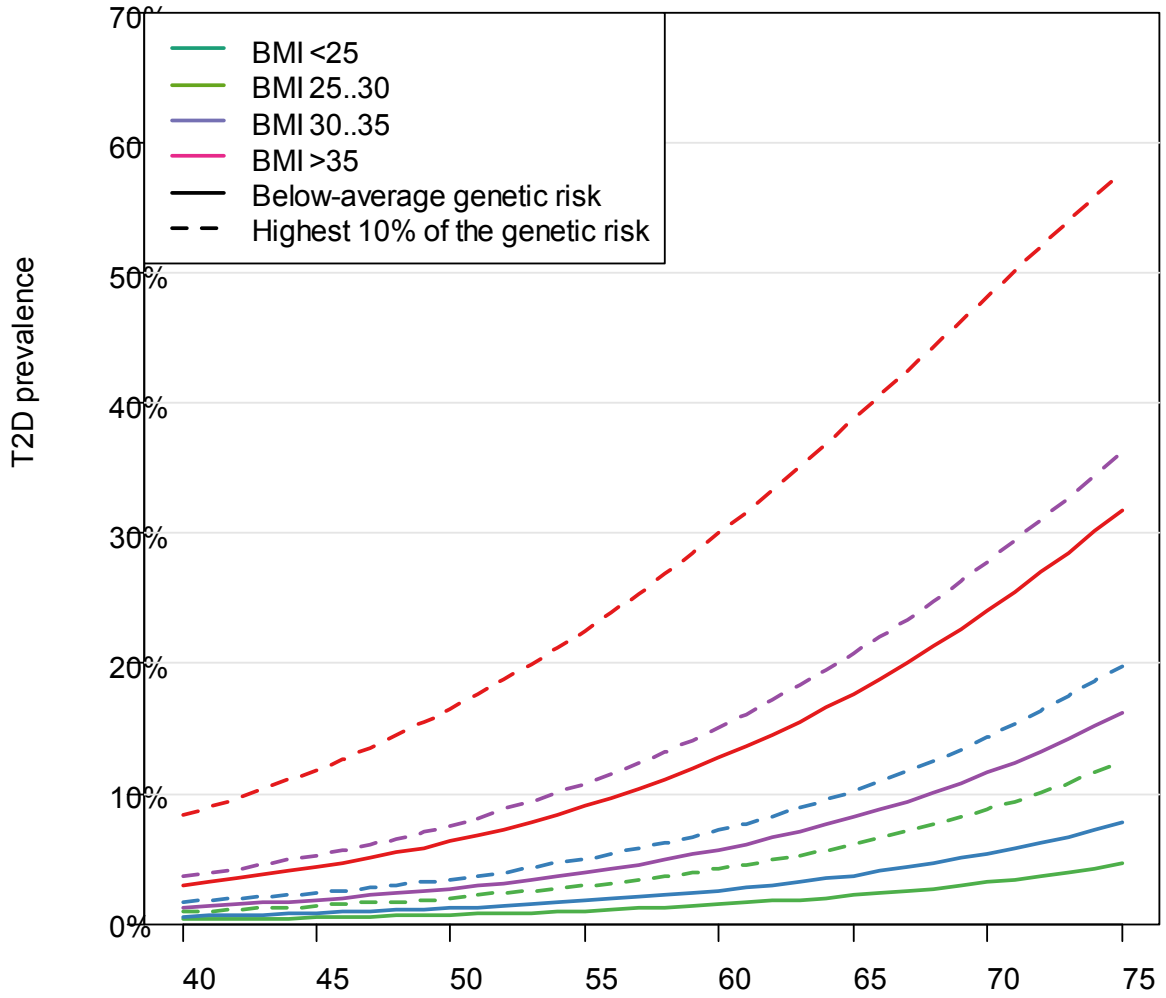
# Model-based predictions of T2D risk

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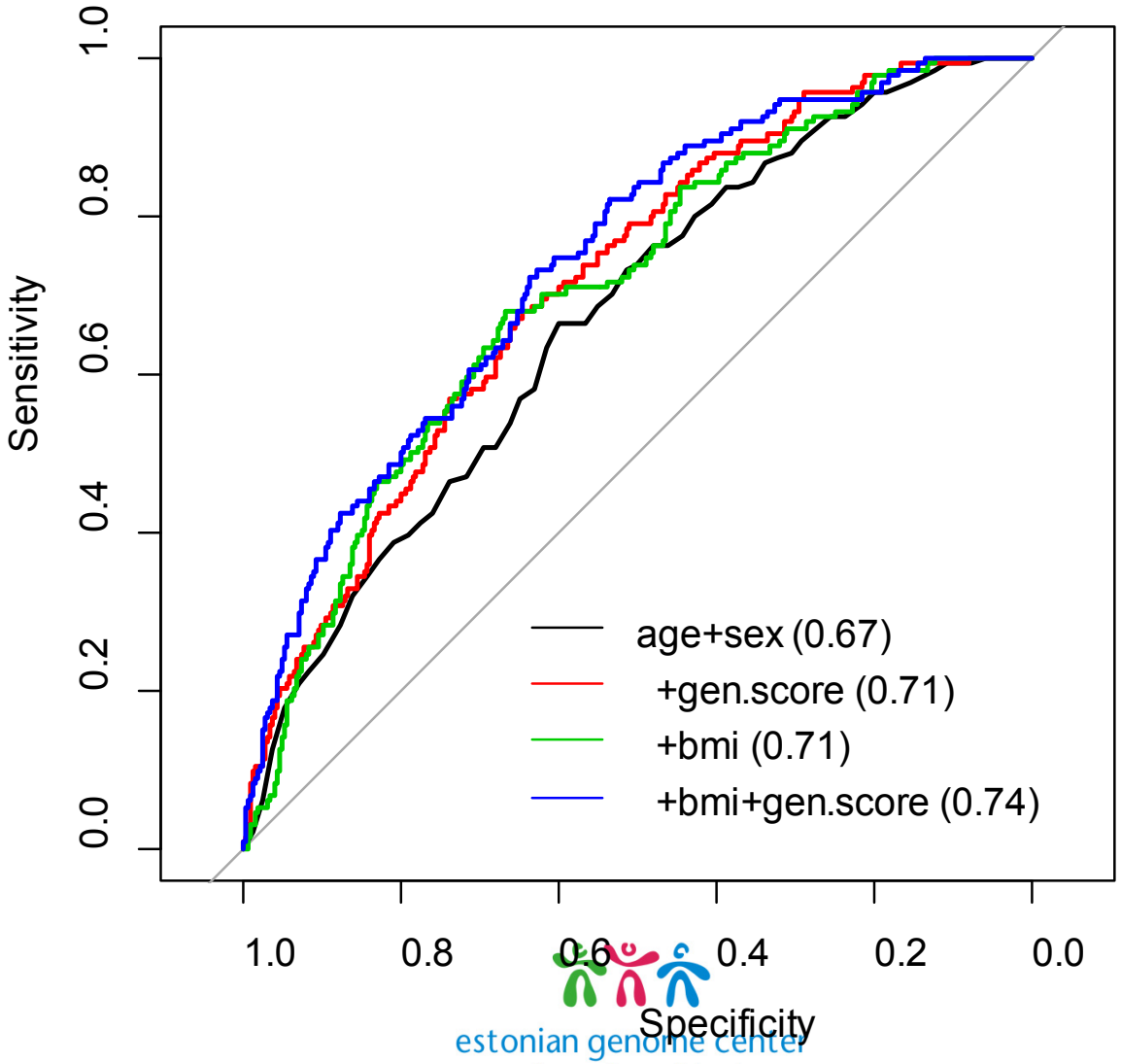
# ROC curves for the subset (T2D, age 45-74, BMI 25-35)

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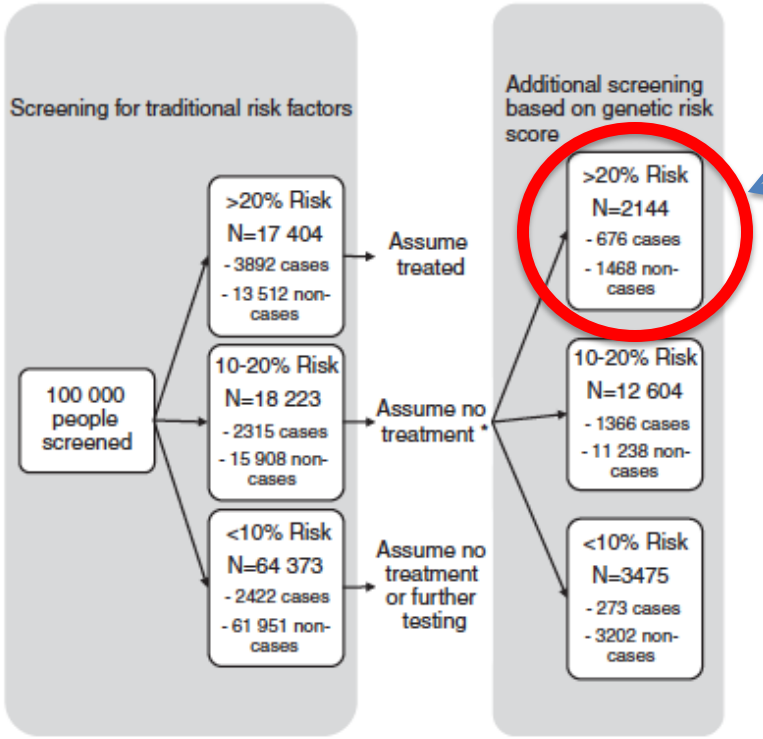
# Prevented deaths of MI?




By treating 2144 persons who have >20% risk when the genetic information is known 135 deaths would be prevented in 10 years!

Slide from Prof. Markus Perola

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# The Estonian Program for Personal Medicine

Approved at the Estonian Government Research and Development Council on 17.12.2013.

- **Health care**

  - Educating health care professionals
  - Educating the patients
  - Further development of the eHealth incl. decision support systems

- **Research and Development**

  - Sequencing 5000 individuals, Estonian Chip and analysis software
  - International collaboration

- **Commercialization**

  - IPR
  - Business agreements

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# Research and Development

**PILOT PROJECT**

-Sequence 5000 – we'll get SNV up to 0.1%
-Estonian chip – ca 0.7 – 1.0 mio SNVs
-Pilot with 50 000 gene donors from the Estonian Biobank during one year using PCP, eHealth database and decision support software

**MAIN PROJECT**

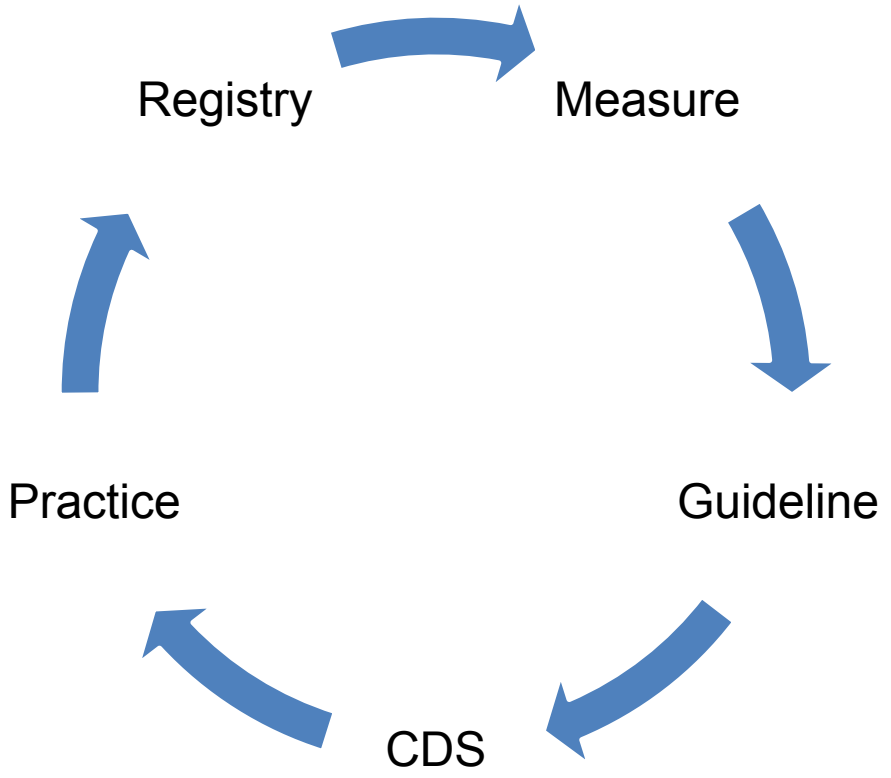
-Offer to everyone from 35 to 65 year old as a disease risk and drug response prediction test (75-80% will accept)
-We'll have ca 500 000 people in the database with EMR, genotypes, samples and prescription data recorded longitudinally

**This system could be used as a additional "instrument" for physicians in diagnosing, treating and preventing disease, but also for research.**

# What is Clinical Decision Support Engine (CDSE)?

- CDSE provides clinicians with knowledge presented at appropriate times
- It encompasses a variety of tools such as computerized alerts, clinical guidelines, and order sets
- CDSE has the potential provide the necessary level of personalized guidance to providers at the point of care that will be necessary in the era of genomic medicine

# Virtuous Cycle of Clinical Decision Support




http://www2.eerp.usp.br/Nepien/DisponibilizarArquivos/tomada_de_decis%C3%A3o.pdf

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# Evidence Generating Medicine

- The next step beyond evidence-based medicine
- The systematic incorporation of research and quality improvement considerations into the organization and practice of healthcare
- To advance biomedical science and thereby improve the health of individuals and populations.

# Survey of PCPs

- Survey sent to 130 PCPs collaborating with the EGCUT, 65 responded
  - 96.3% - either strongly agree or agree that a training program in genetics and genomics is necessary
  - 75% - reported having patients show interest in their genomic health data
  - 96.4% - believe that predictive genetic testing will improve health care
  - 73.3% - believe that predictive genetic testing will be used in their practice in the next 5 years
  - 35.8% - believe that individualized medicine will be used in their practice in the next 5 years

# Challenges and issues

- Awareness doctors and patients
- New technologies and data empower patient with more possibilities to manage own health
- Ethical issues
  - Right to know and right not to know
  - Treatable and non-treatable conditions
- Not enough knowledge about associations between DNA variants and diseases
- Large work-load to keep database of known risk markers updated

# Are we fready for the personalized medicine?

- E-health, EMR and other e-based infrastructures are in place
- Genome analysis technology can do the task
- Scientific and medical expertiese is here
- Genomic variations are excisting and they have an effect on human health and behavior
- People are interested in personalized, genome based health realted information

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# Thank you!

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