

Global Leaders in Genomic Medicine 2014

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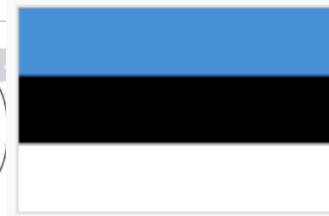
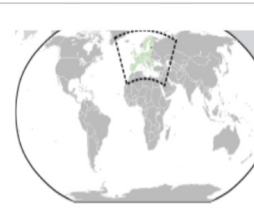
Washington, DC
January 8-9, 2014



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Republic of Estonia

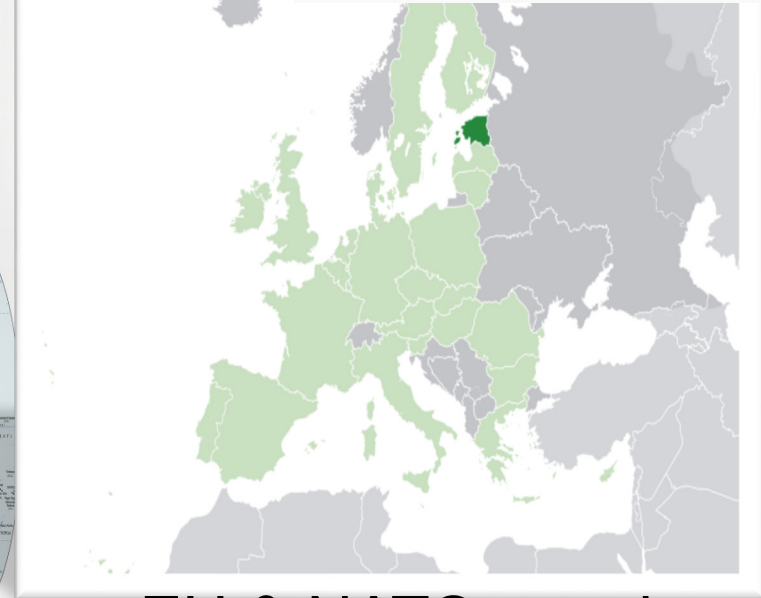
Political Map of the World, September 2008



Flag



Coat of arms



EU & NATO member
since 2004

Schengen Treaty since
2007

EUR as our currency
since 2011

- Population size: ~1.3 million
- Territory: 45 000 km²

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



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)



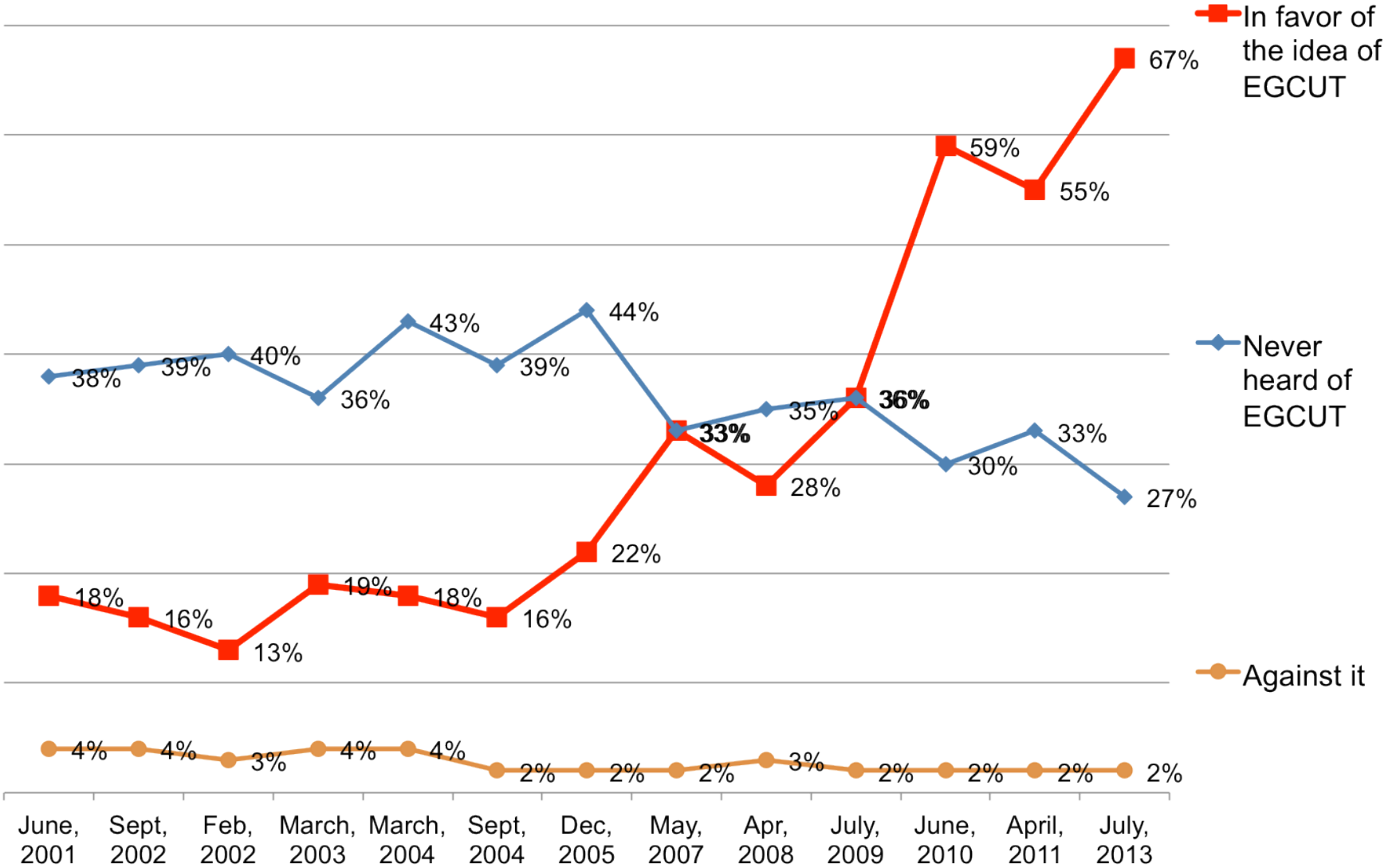
Estonian Human Genes Research Act

§ 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.



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



eHealth



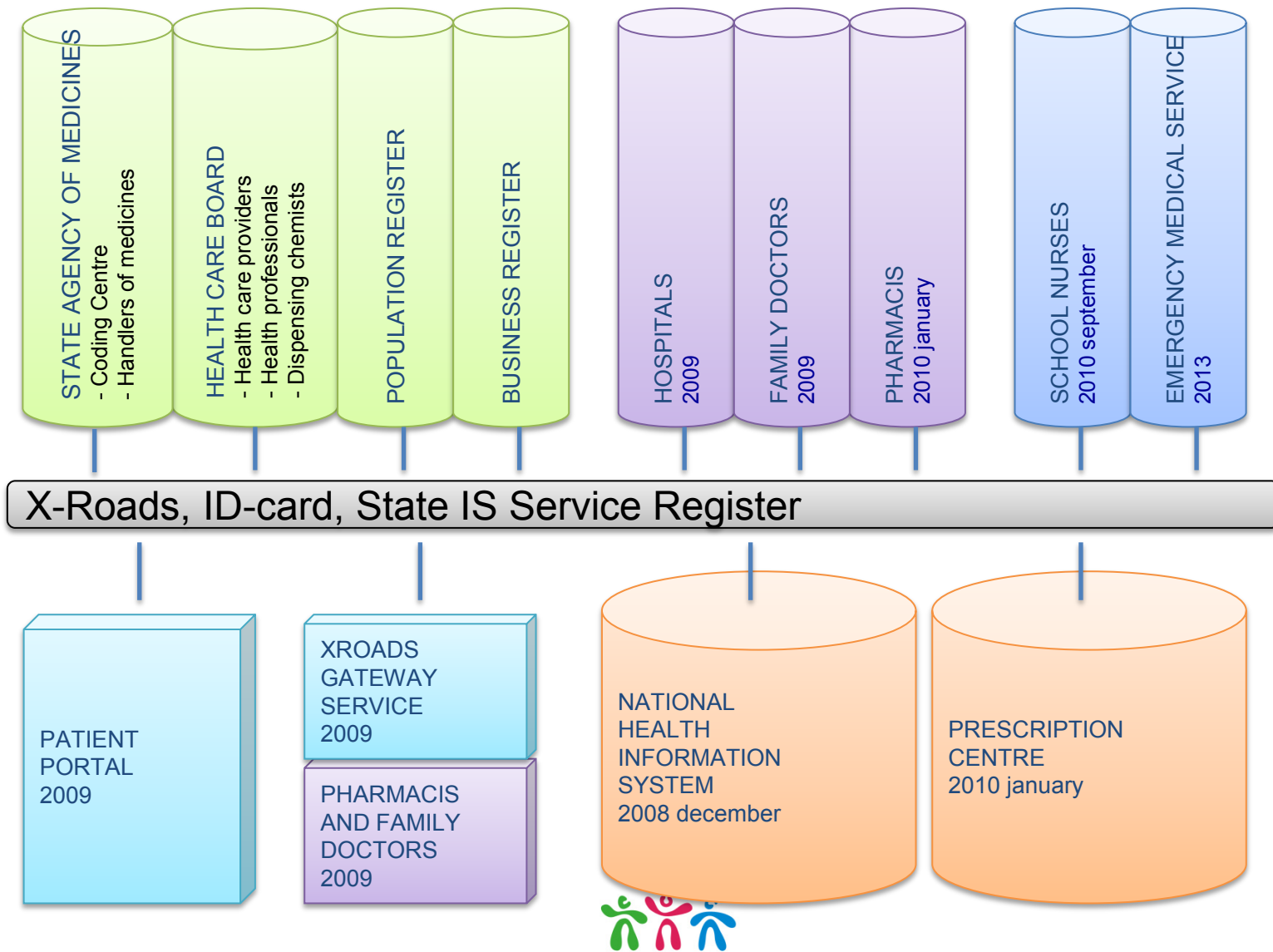
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The Estonian ID card

- 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



Architectural “Big picture”



Tools and enablers of information exchange

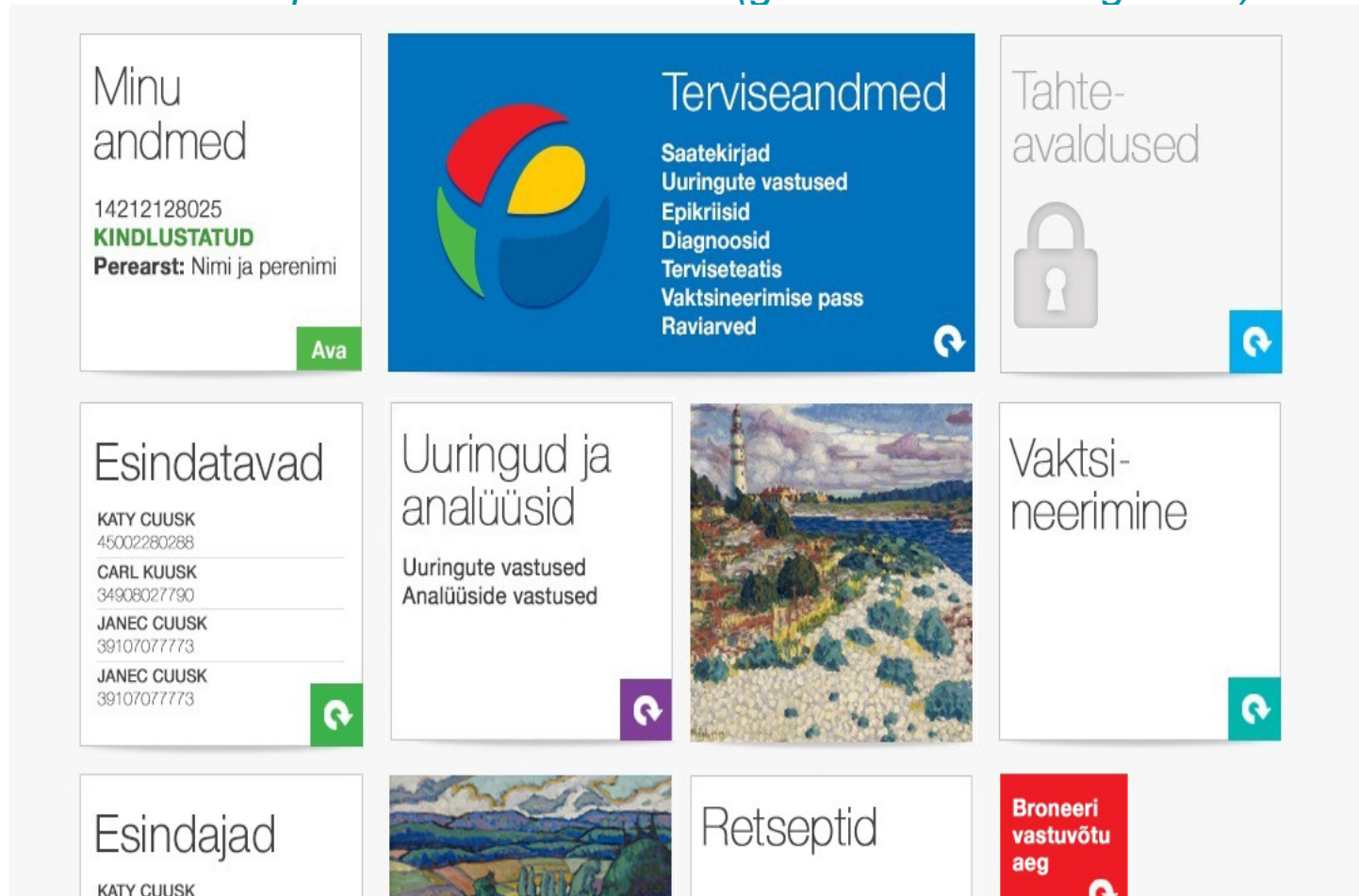
- One universal national identification code
 - Registries and databases use same code to uniquely identify persons
- National PKI infrastructure
- The Estonian ID card
 - Smartcard with two digital certificates
 - Also Mobile-ID – safe digital ID with mobile phone
- National Data Exchange Layer X-Road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



National Patient Portal

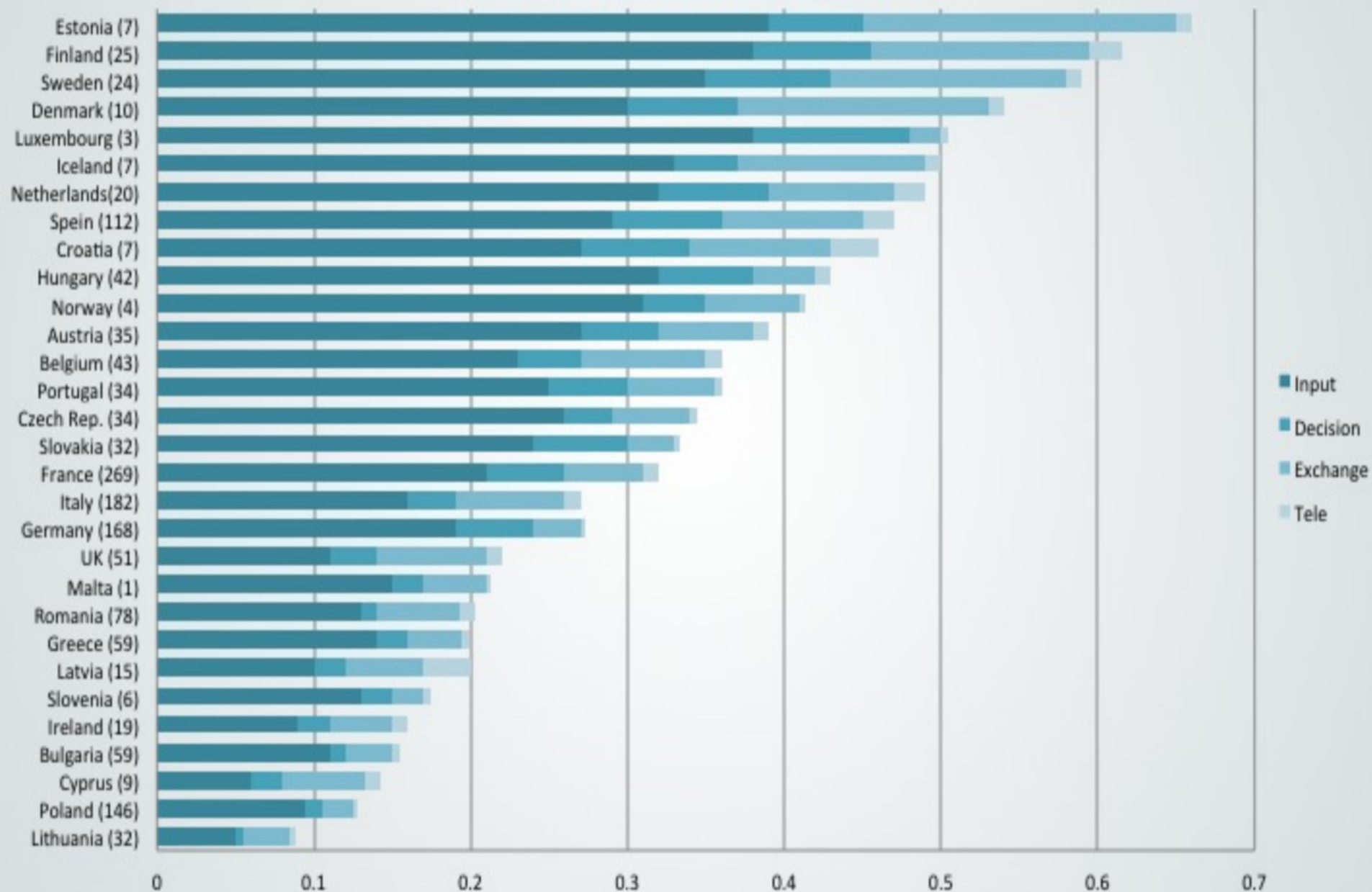
Documents total – 10.8 mio

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



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



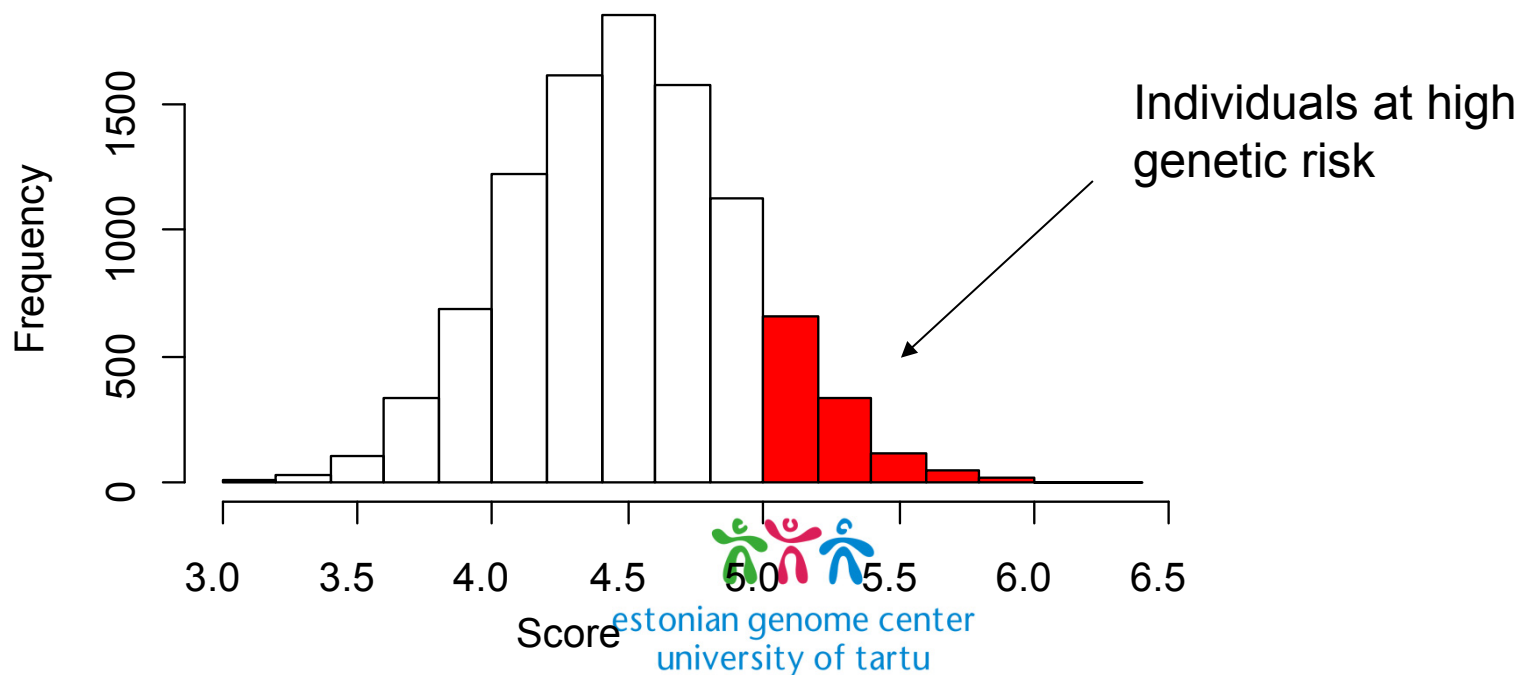
Polygenic risk scores

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

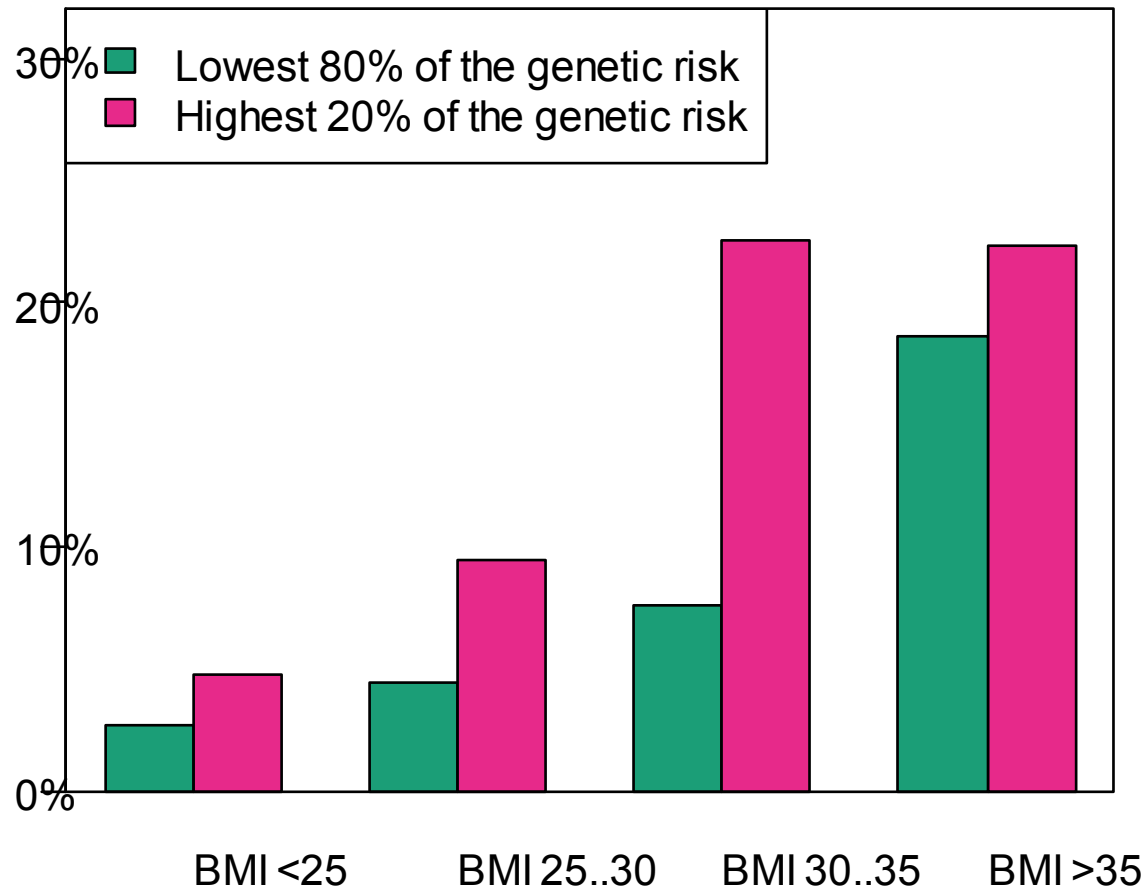
X_2, \dots, X_k - allele dosages for k independent markers (SNP-s), typically the ones with strongest effect

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

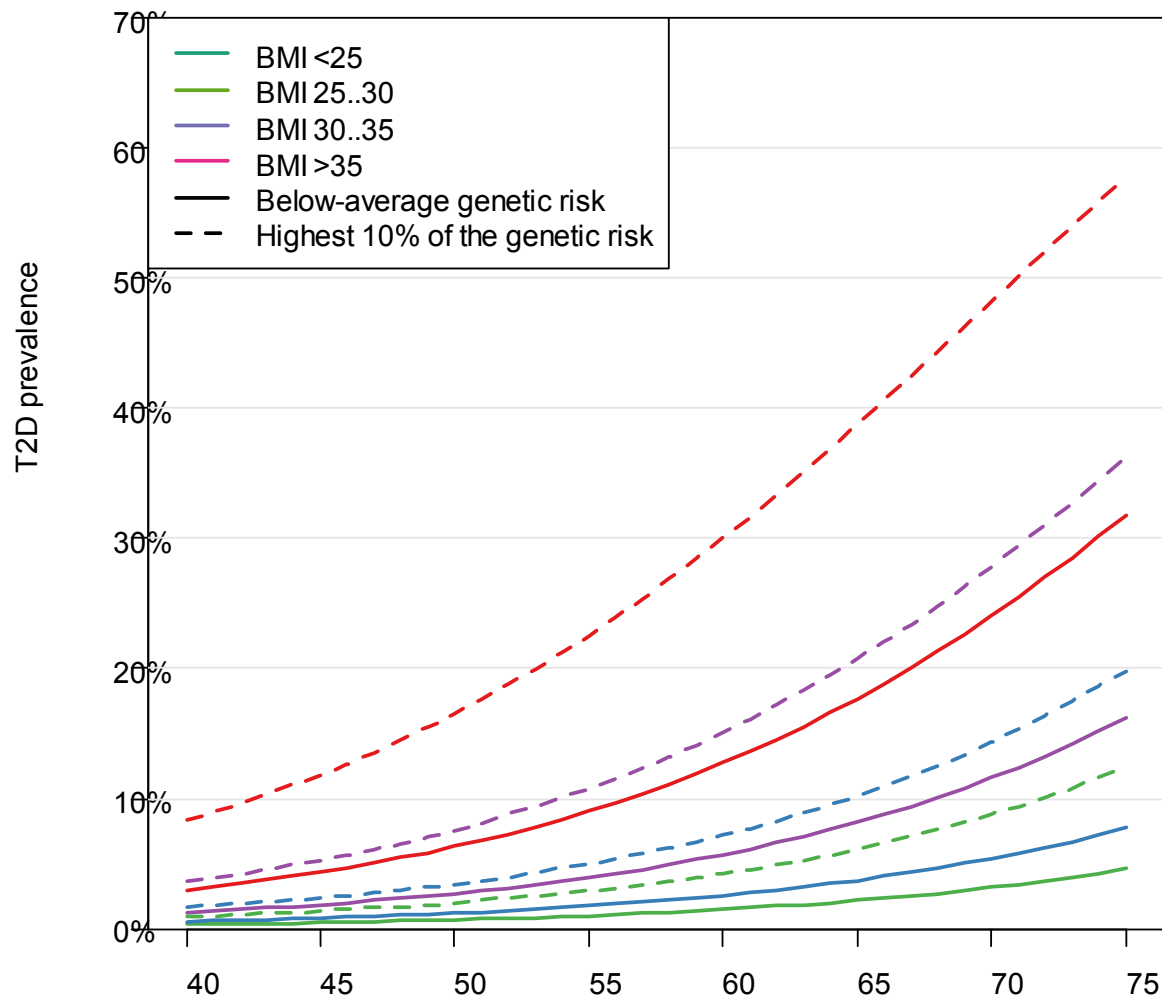
**Polygenic risk score for type II diabetes:
histogram of the score in 7462 individuals (Estonian Biobank)**



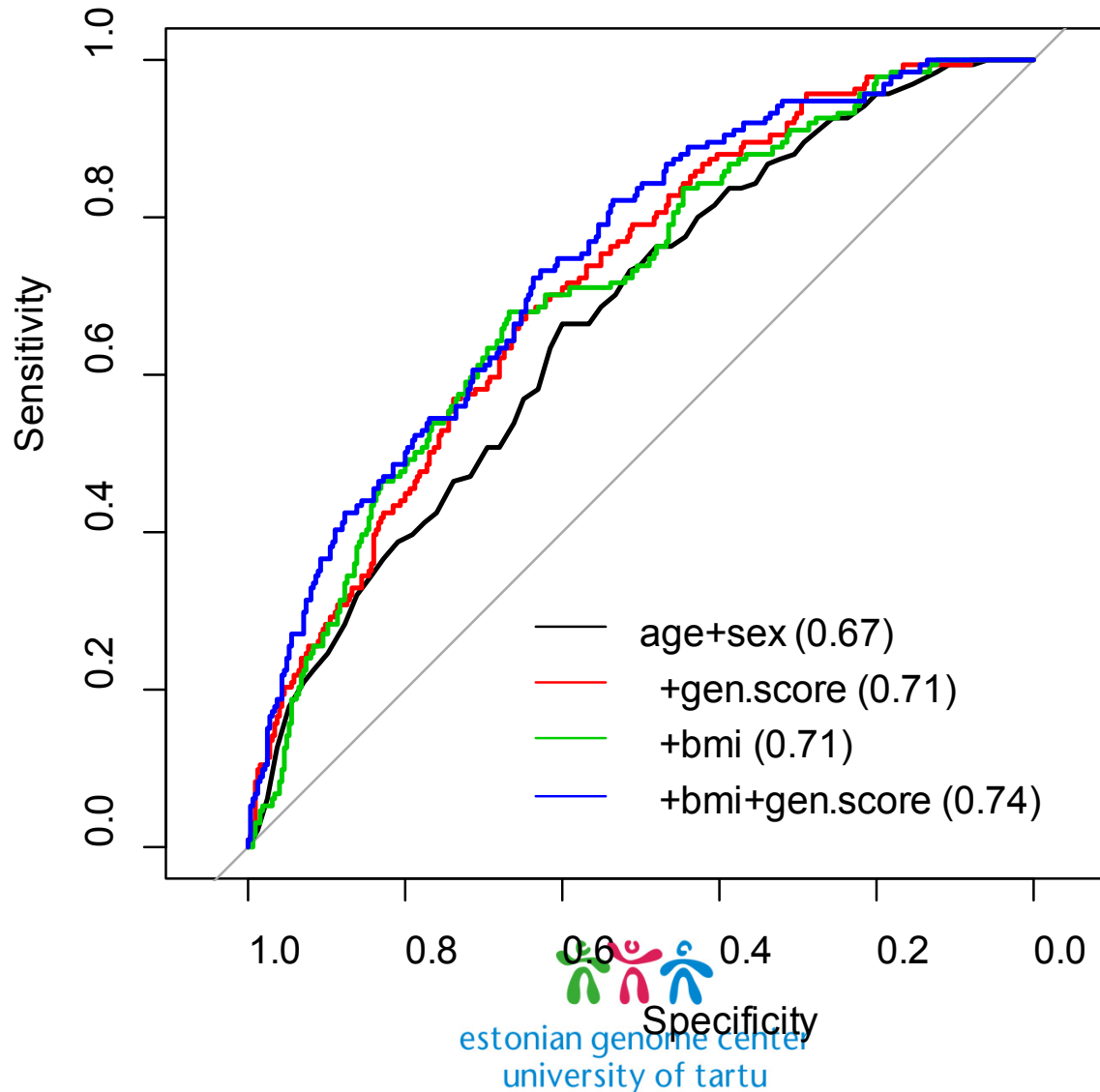
Prevalence of type 2 diabetes aged 40-79



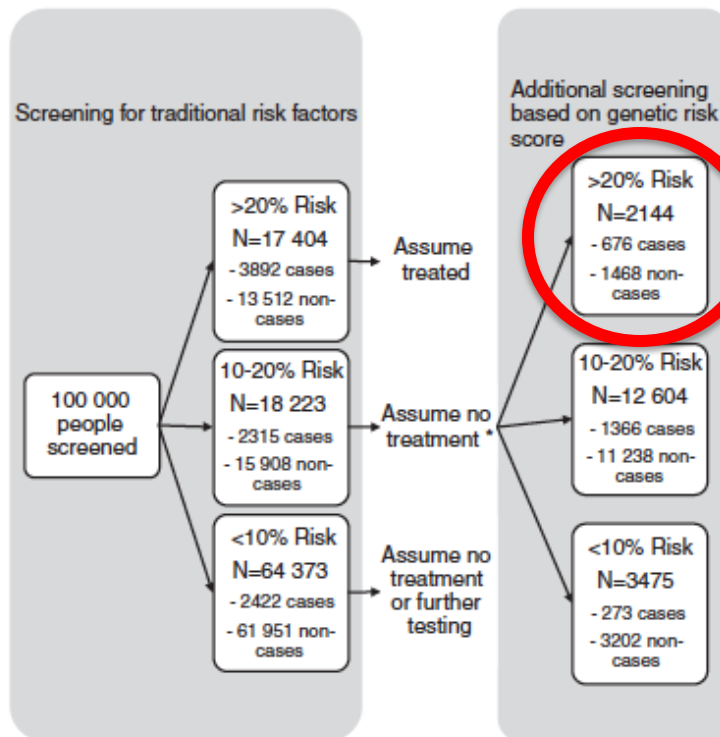
Model-based predictions of T2D risk



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



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!



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.

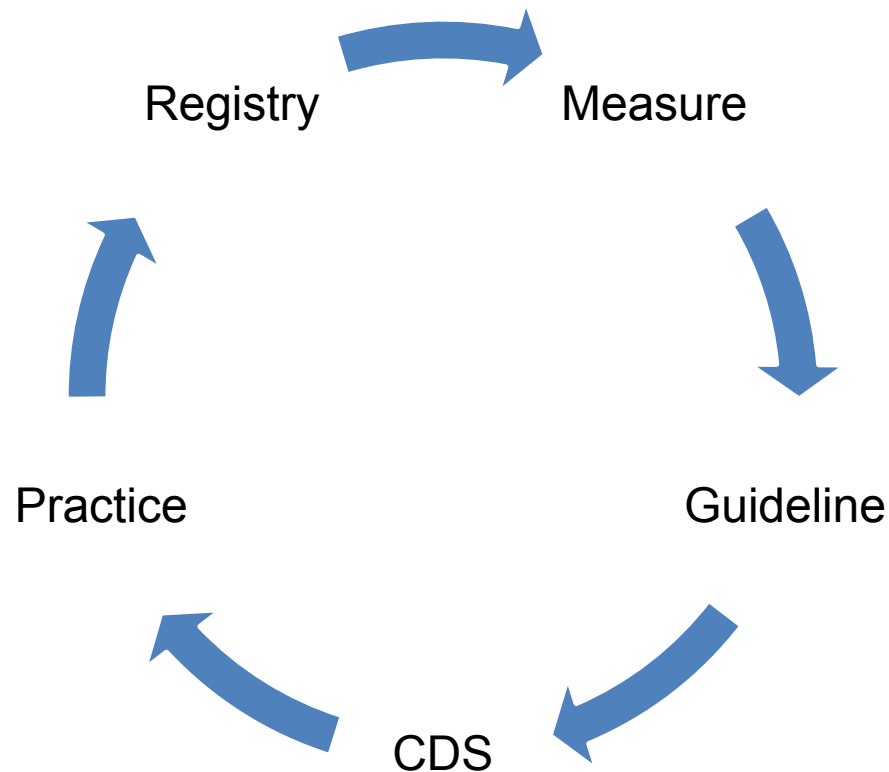


What is Clinical Decision Support Engine (CDSE)?

- 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 ready 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 expertise is here
- Genomic variations are existing and they have an effect on human health and behavior
- People are interested in personalized, genome based health related information



Thank you!

www.biobank.ee

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