Initiatives based on genomes and e-health databases in Estonia

Lili Milani, PhD

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Estonian Biobank

- Prospective, longitudinal, volunteer-based
- 52,000 participants - 5% of the adult population of Estonia
- Health records, diet, physical activity, etc.
- DNA, plasma and cell samples
- Estonian Human Genes Research Act
- Broad informed consent
- Open for research: Clear access rules

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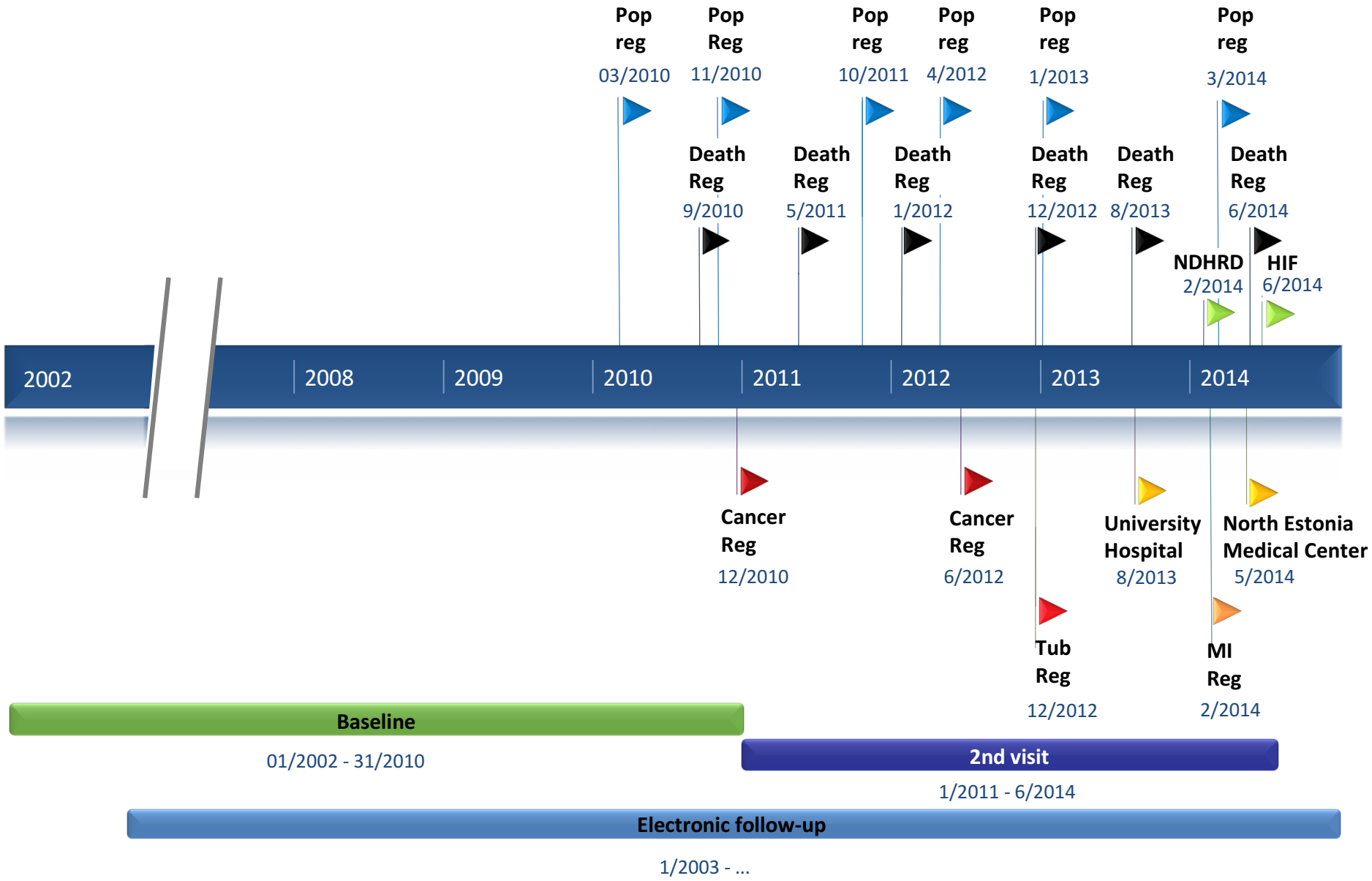
Estonian biobank: omics profiling

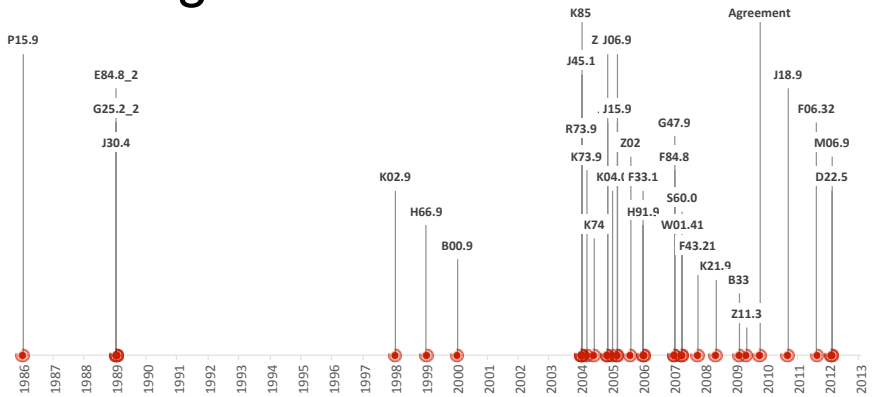
Method	Sample size
Whole genome sequencing	2,400
Whole exome sequencing	2,500
Genome-wide genotyping arrays	50,000
Genome-wide methylation arrays	700
Genome-wide expression arrays	1,100
mRNA sequencing	600
Total RNA sequencing	50
Metabolomics (NMR)	11,000
Metabolomics (MS/MS)	1,100
Telomere length	5,200
Clinical biochemistry	2,700
IgG glycosylation	1,000

Timeline: linking to registries

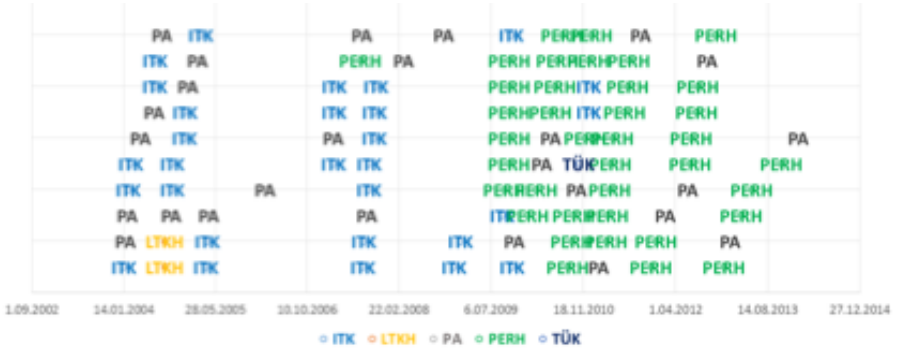


Disease trajectories

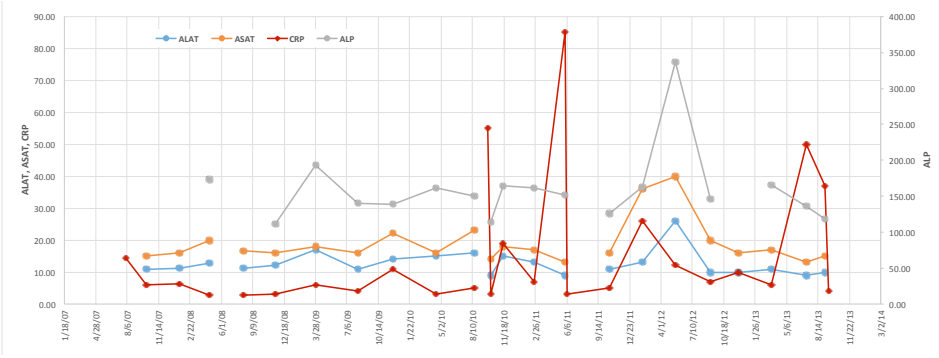
- Diagnosed diseases



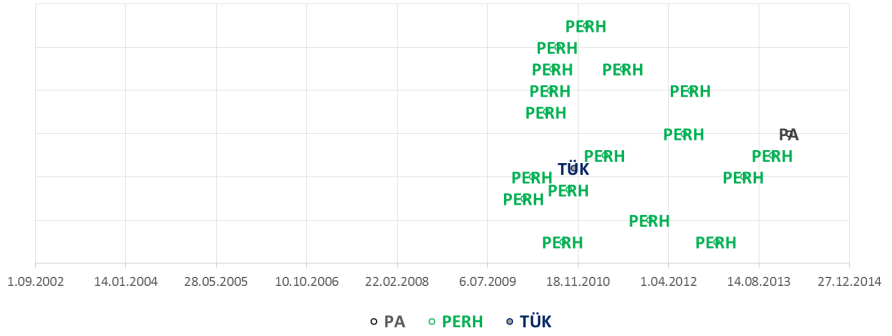
- Health insurance bills



- Clinical lab measurements



- Full free-text records



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RESEARCH

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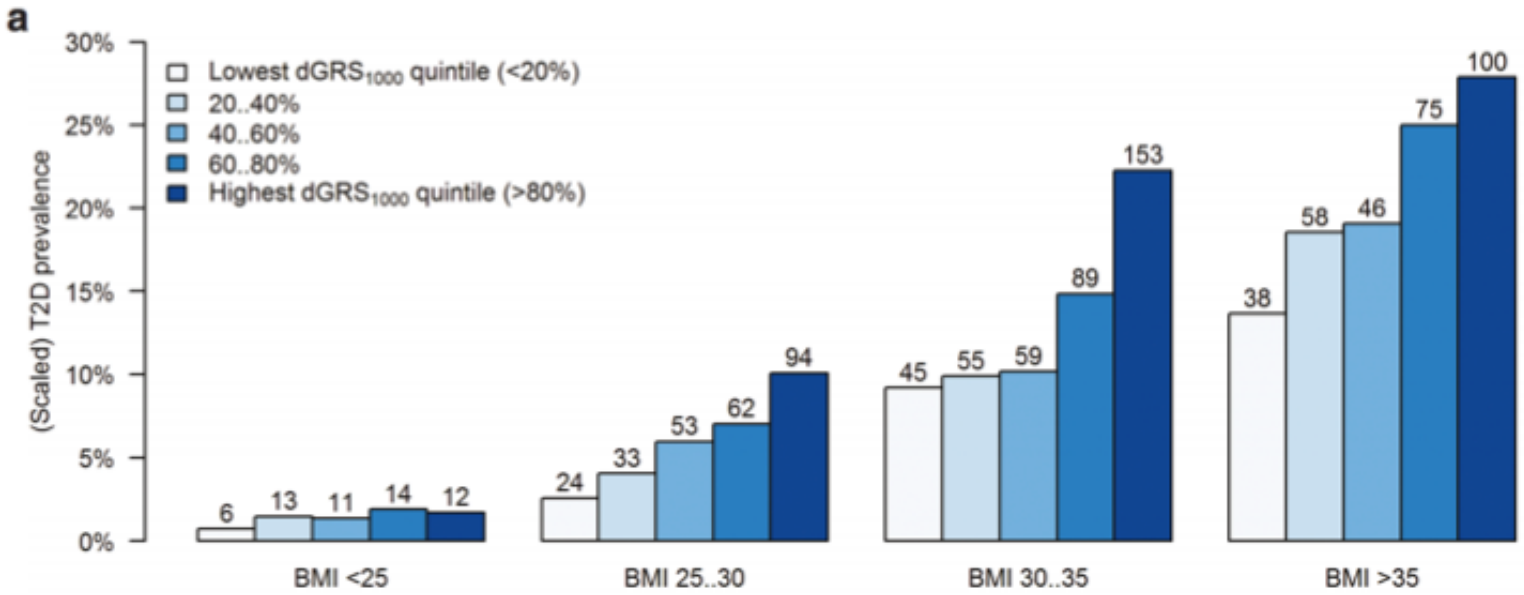
Official journal of the American College of Medical Genetics and Genomics **ORIGINAL RESEARCH ARTICLE** Genetics inMedicine

Open

Personalized risk prediction for type 2 diabetes: the potential of genetic risk scores

Kristi Läll, MSc[1,2], Reedik Mägi, PhD[1], Andrew Morris, PhD[1,3,4], Andres Metspalu, MD, PhD[1,5] and Krista Fischer, PhD[1]

Prevalence in biobank



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GRS for Type 2 Diabetes: incident cases

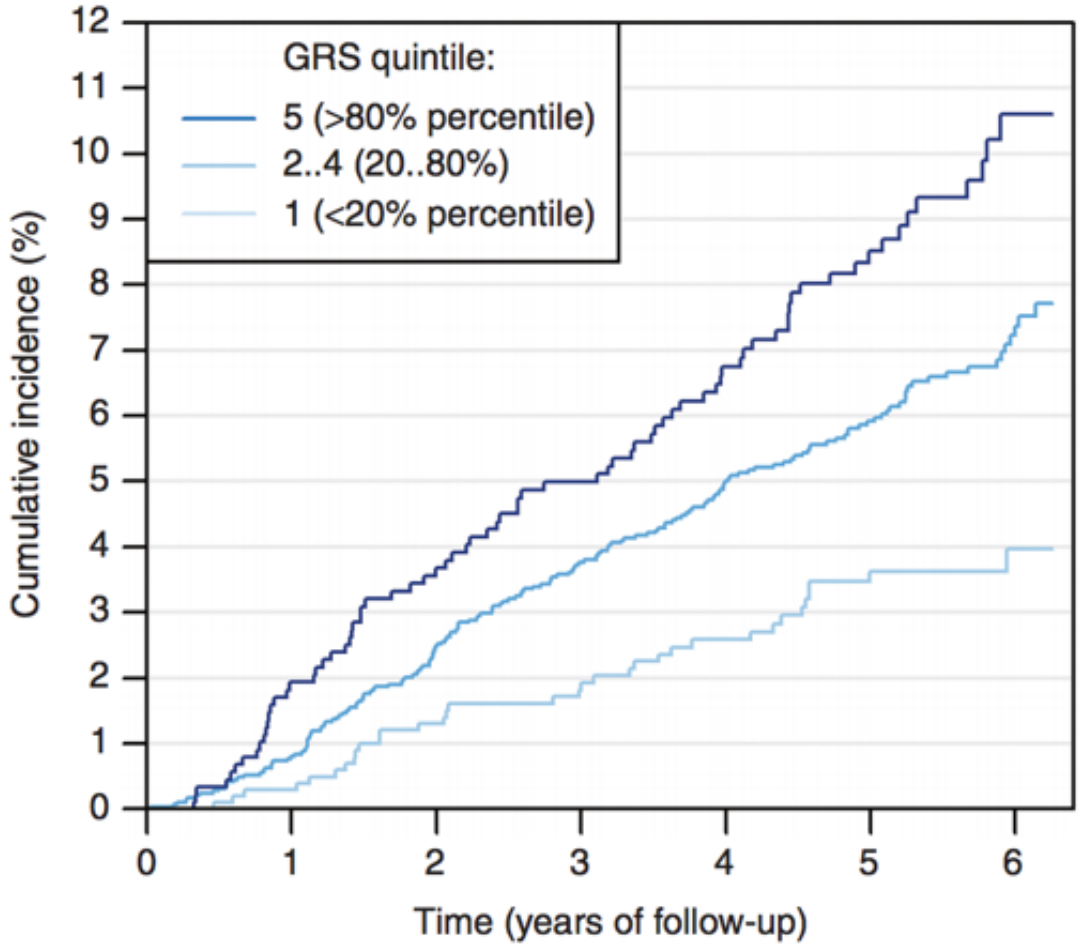
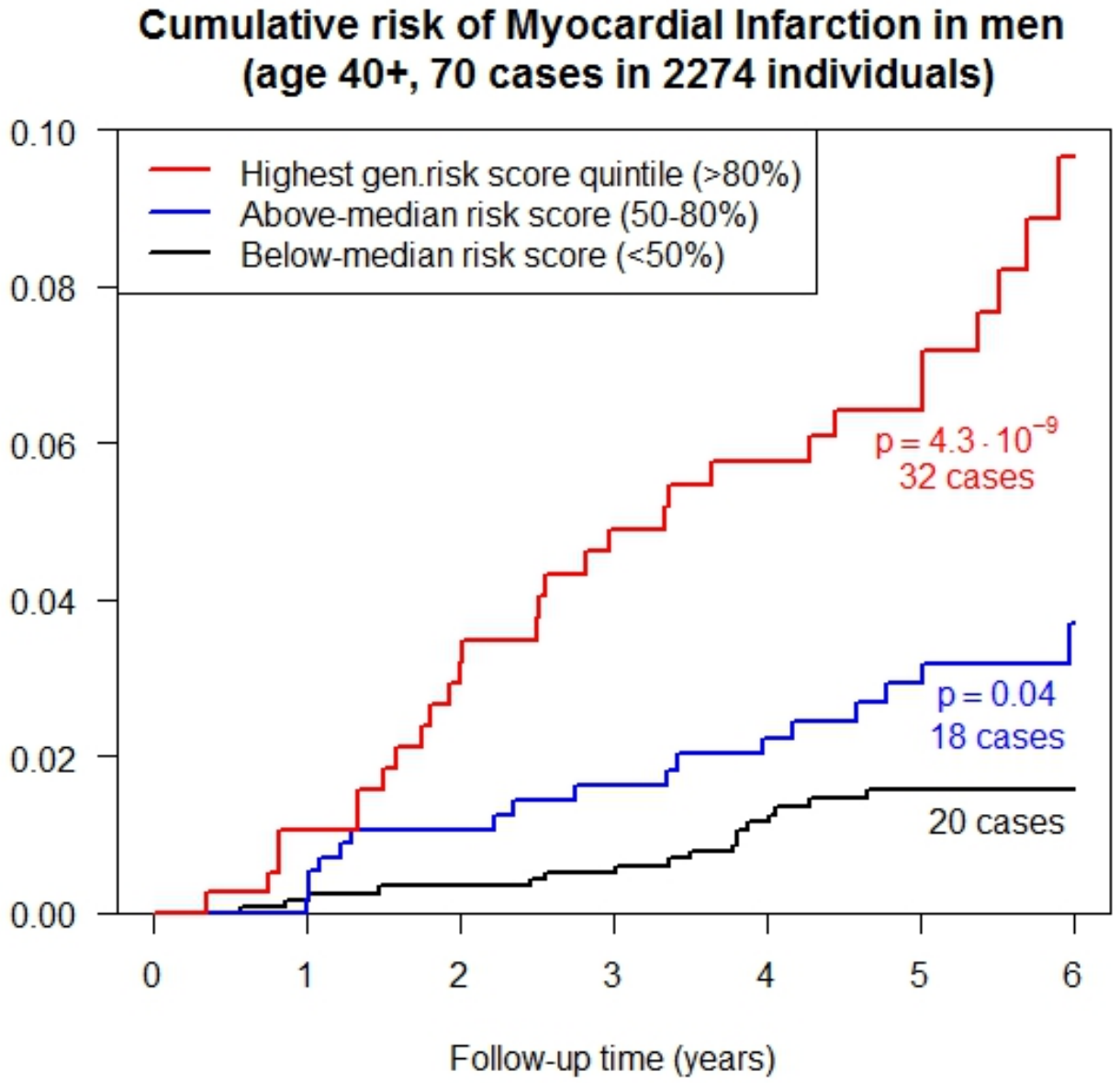


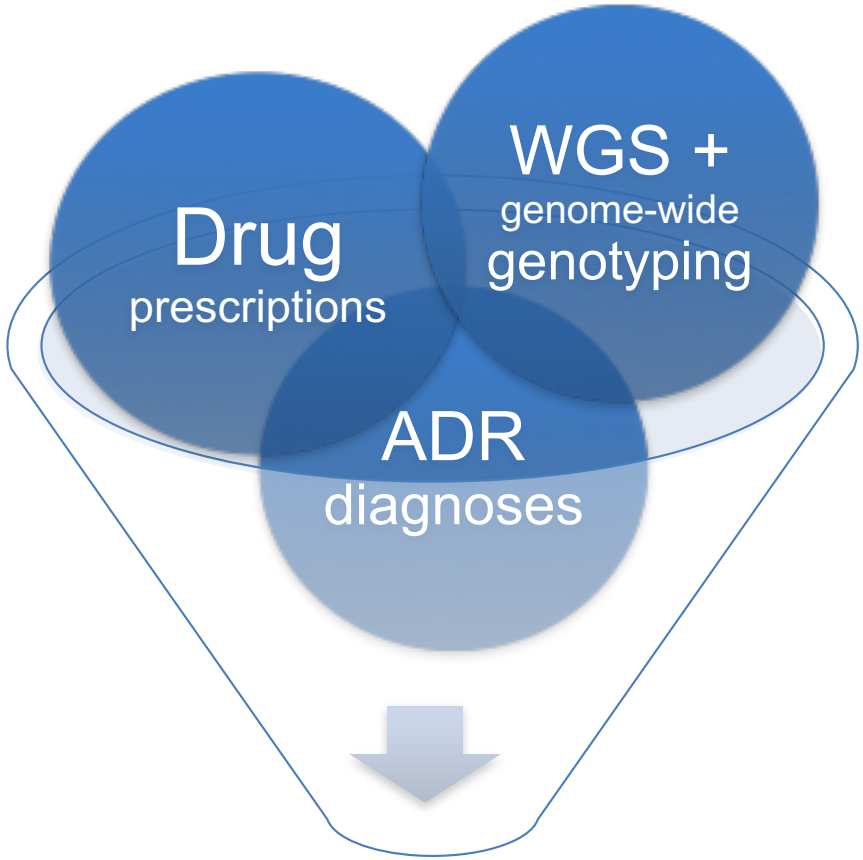
Figure 2 Cumulative incidence of type 2 diabetes in 4,881 genotyped individuals free of T2D aged 35–79 and with BMI >23 at baseline. In the figure, 6.25-year follow-up is presented because only 25% of individuals were followed for more than 6.25 years. Cumulative incidence in presented separately in three $dGRS_{1000}$ categories.

GRS for Coronary Artery Disease and prediction of incident Myocardial Infarction



A weaker, but still significant effect seen among females (p=0.005)

98% of Europeans carry ≥ 1 mutation relevant for drug treatment outcome



Pharmacogenomic study

TRANSLATION

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Feedback to participants

1. Risk for common diseases
   - Genetic risk
   - Lifestyle risk factors
2. Incidental findings (BRCA1/2, FH, etc)
   - Cascade screening
3. Pharmacogenetics
4. Carrier status

Reporting disease risk: type 2 diabetes

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Krista Fischer, Kristi Läll, Sulev Reisberg, Tormi Reinson

BRCA1/2 mutations detected by WGS

Gene	cDNA	Prot.	Pathogenic/benign	AC
BRCA1	c.4258C>T	p.Gln1420*	Known pathogenic (BIC)	1
BRCA1	c.1840A>T	p.Lys614*	Known pathogenic (BIC)	1
BRCA1	c.5329dupC (5382insC)	p.Ser1756fs*	Known pathogenic (BIC)	4
BRCA1	c.4035delA (4154delA)	p.Glu1345fs*	Known pathogenic (BIC)	6
BRCA2	c.8572C>T	p.Gln2858*	Known pathogenic (BIC)	2
BRCA2	c.467_468insT	p.Lys157fs*	Expected pathogenic	1
BRCA2	c.9097_9098insT	p.Thr3033Ilefs*10	Expected pathogenic	1

+ WES: 15 + Long-range haplotyping: 18

= **Total 49 cases + cascade screening**

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Dr Neeme Tõnisson,
Dr Liis Leitsalu
Marili Palover

TRAINING

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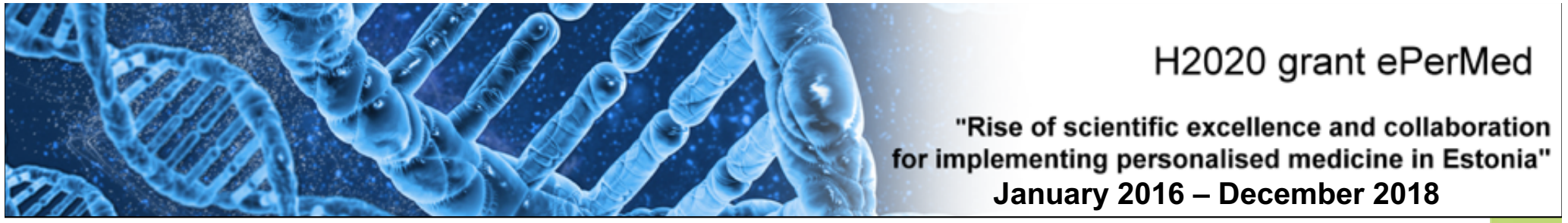


H2020 grant ePerMed

"Rise of scientific excellence and collaboration for implementing personalised medicine in Estonia"

January 2016 – December 2018

ePerMed workshop for clinicians

YOUR INFORMATION

YOUR DISEASE RISK

YOUR CURRENT RISK is average, 2.4 %

EXPLORE how lifestyle changes may affect your risk. The risk graph below will be updated in realtime to reflect changes in your measurements.

Total cholesterol: 5.3

My measured value 5.3
Target value < 5 mmol/l

HDL cholesterol (HDL): 2.3

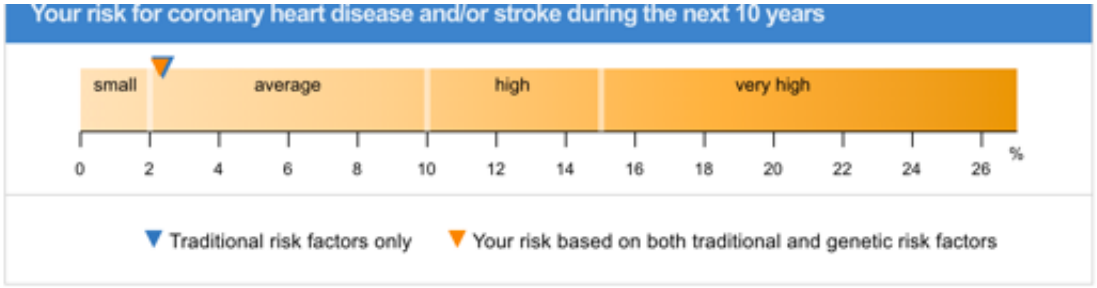
My measured value 2.3
Target value > 1.2 mmol/l

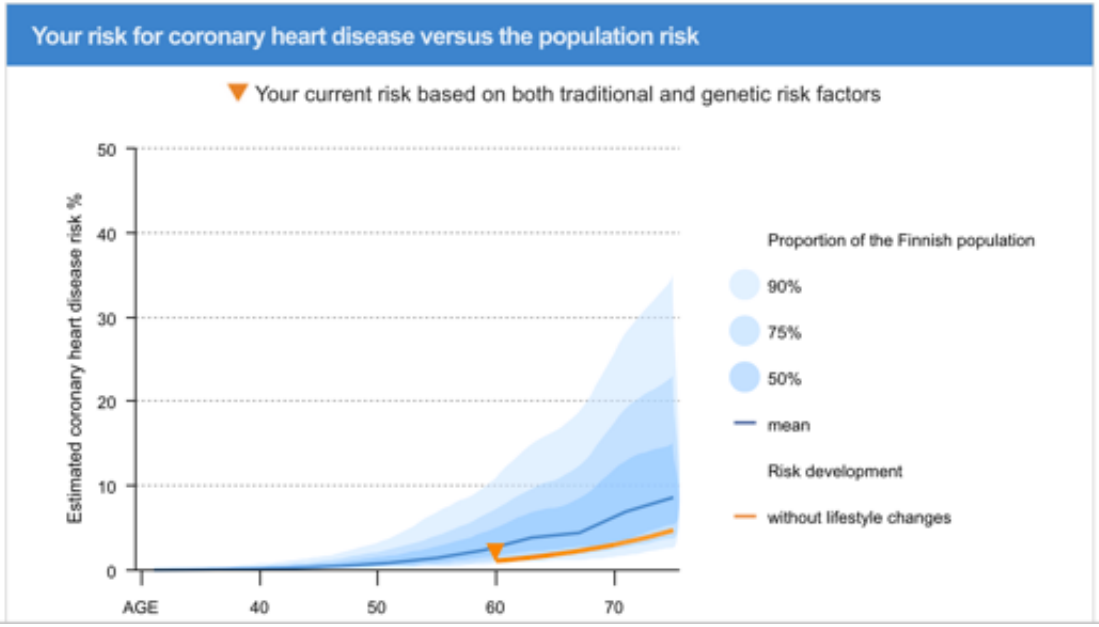
Systolic blood pressure: 102

My measured value 102
Target value < 120 mmHg

Non-smoker:

Your genetic risk score for coronary heart





H2020-TWINN-2015

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Prof. Andres Metspalu, Tõnu Esko, Krista Fischer, Reedik Mägi, Maris Alver, Kristi Läll, Kristi Krebs, Tõnis Tasa, Mart Kals, Tom Haller, Neeme Tõnisson, Anu Reigo, Liis Leitsalu, Helene Alavere, Kristjan Metsalu, Kairit Mikkel, Mari-Liis Tammesoo

BIIT

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TARTU ÜLIKOOLI KLIINIKUM A.D. 1804

Prof. Jaak Vilo, Hedi Peterson, etc.

QureTEC

Regionaalhaigla

BioMed@STACC: the health data mining team

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Marek Oja · Margus Jäger · marje johanson · Markus Lippus · Mihkel Manguse · monika soosaar · Raul Sirel

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