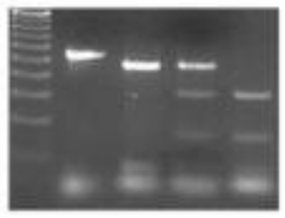
P6 – GENOMICS TO HEALTHCARE

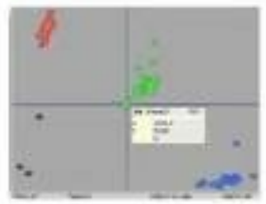
Prevention of common chronic diseases using modern medicine

The march of technology...

single variant
(10^0 SNPs; 10^3 genotypes)

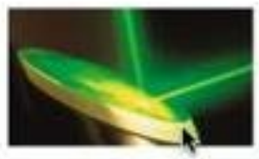


detailed study of individual genes
(10^2 SNPs; 10^{5+} genotypes)



regional studies
(10^4 SNPs; 10^8 genotypes)

genome-wide association
(10^6 SNPs; 10^{10} genotypes)



complete resequencing
(10^8 SNPs / 10^{12} genotypes)

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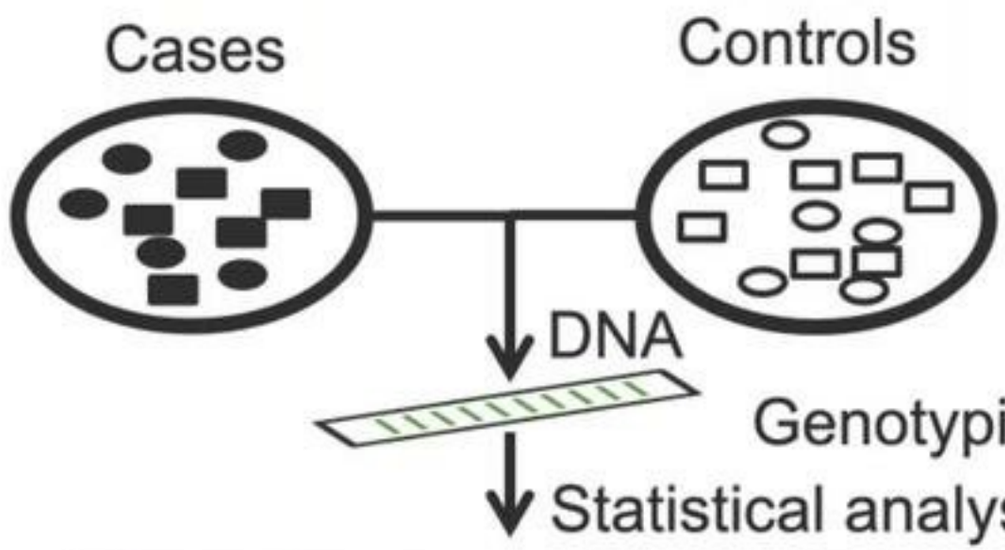
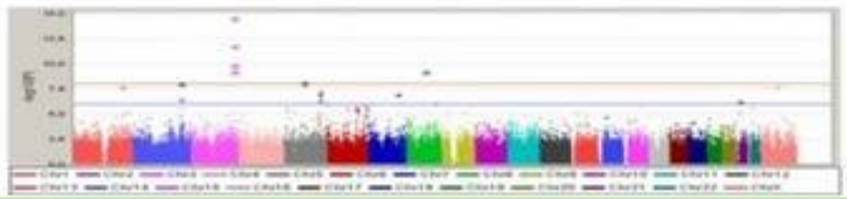
WHAT IS A GWAS?

- Genetic (chip) information is used to evaluate whether the genetic marker(s) are assocated with a phenotype (qualitative or quantitative)





Manhattan-plot

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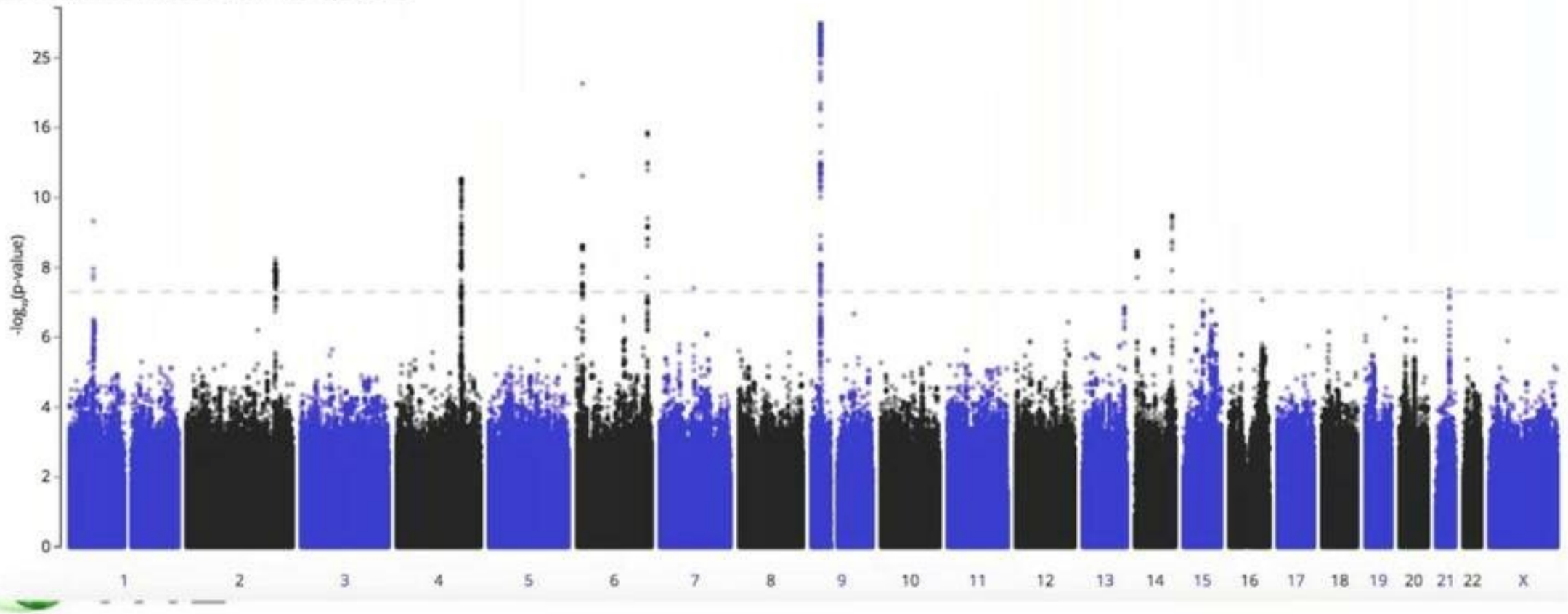
CORONARY HEART DISEASE GWAS

Major coronary heart disease event

Category: Circulatory system

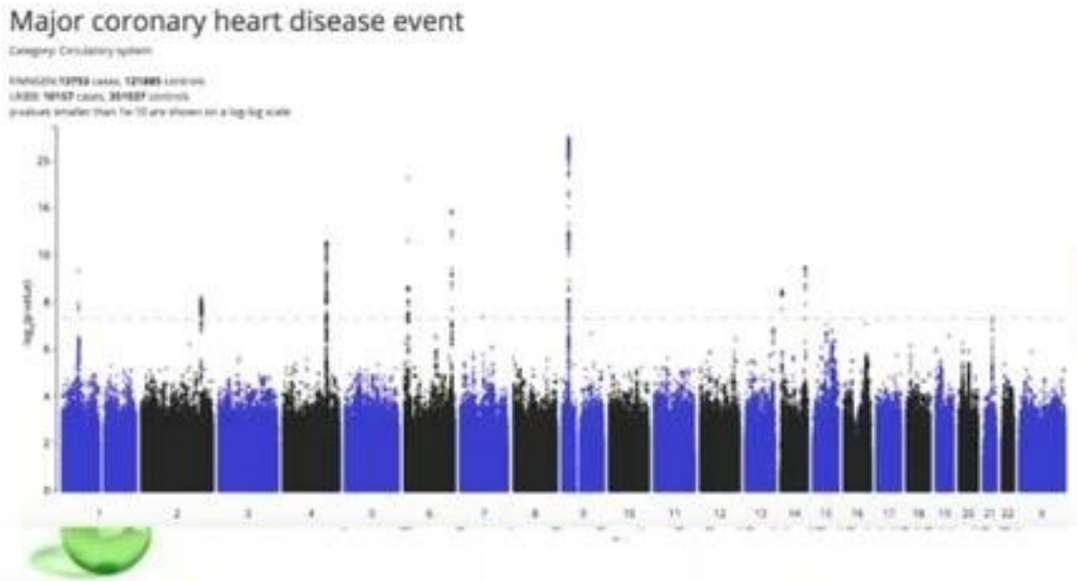
FINNGEN:**13753** cases, **121885** controls
UKBB: **10157** cases, **351037** controls
p-values smaller than 1e-10 are shown on a log-log scale

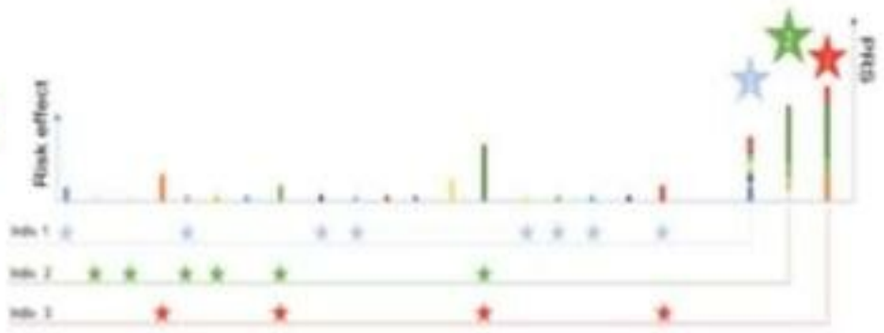


KP
Yhteiskäsittely:...
https://tila.tiimeri.fi/User%20Guide/I
Vastaus

PRS = A NOVEL TOOL TO ESTIMAT GENOMIC RISK

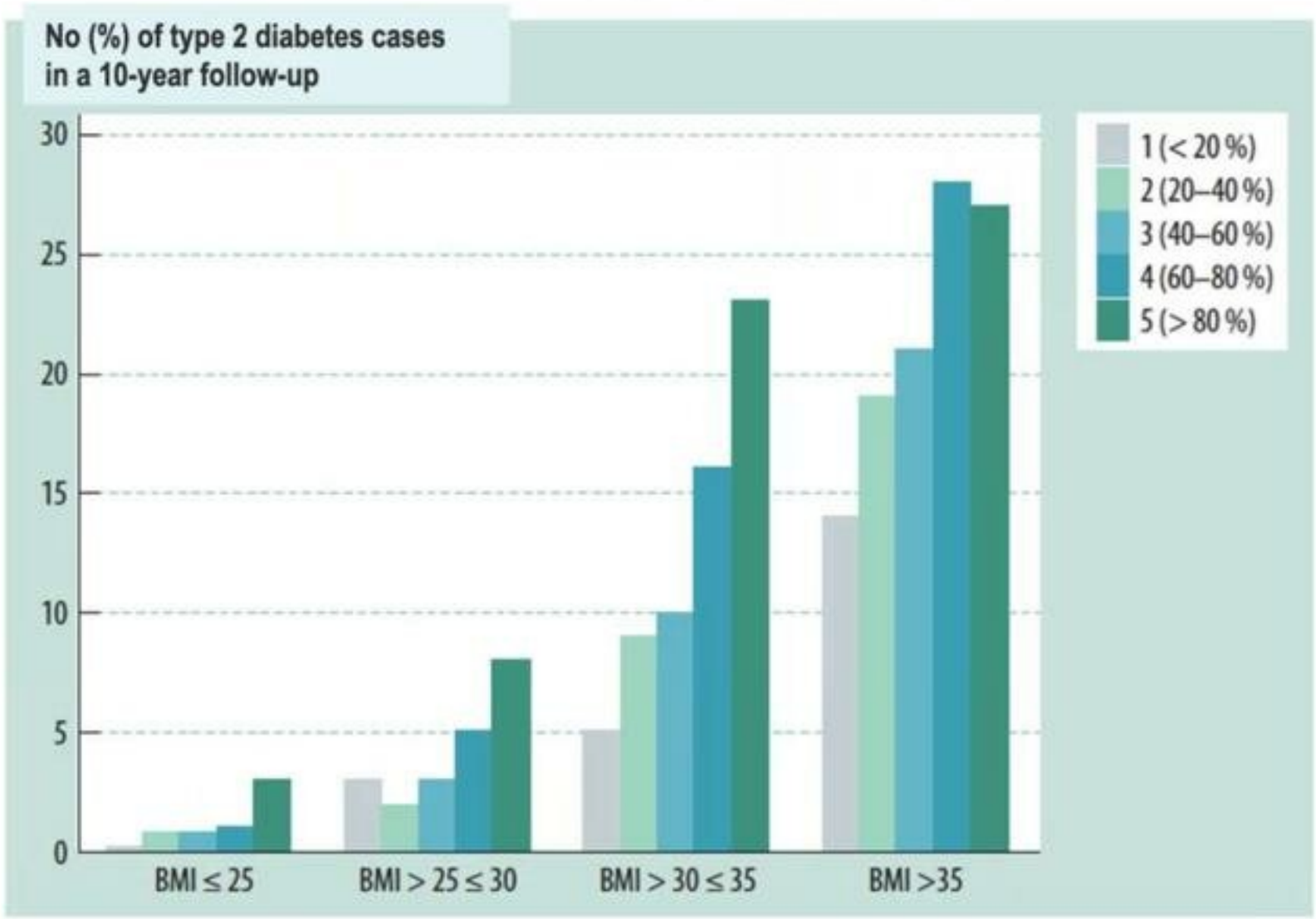
- Most common diseases are multifactorial and polygenic
- GWAS data can be used to form so-called Polygenic Risk Scores (PRS) which condense the risk produced by her/his genomic variation of an individual to a single number for a given phenotype.





COMPARISON OF PRS AND BMI IN TYPE 2 DIABETES

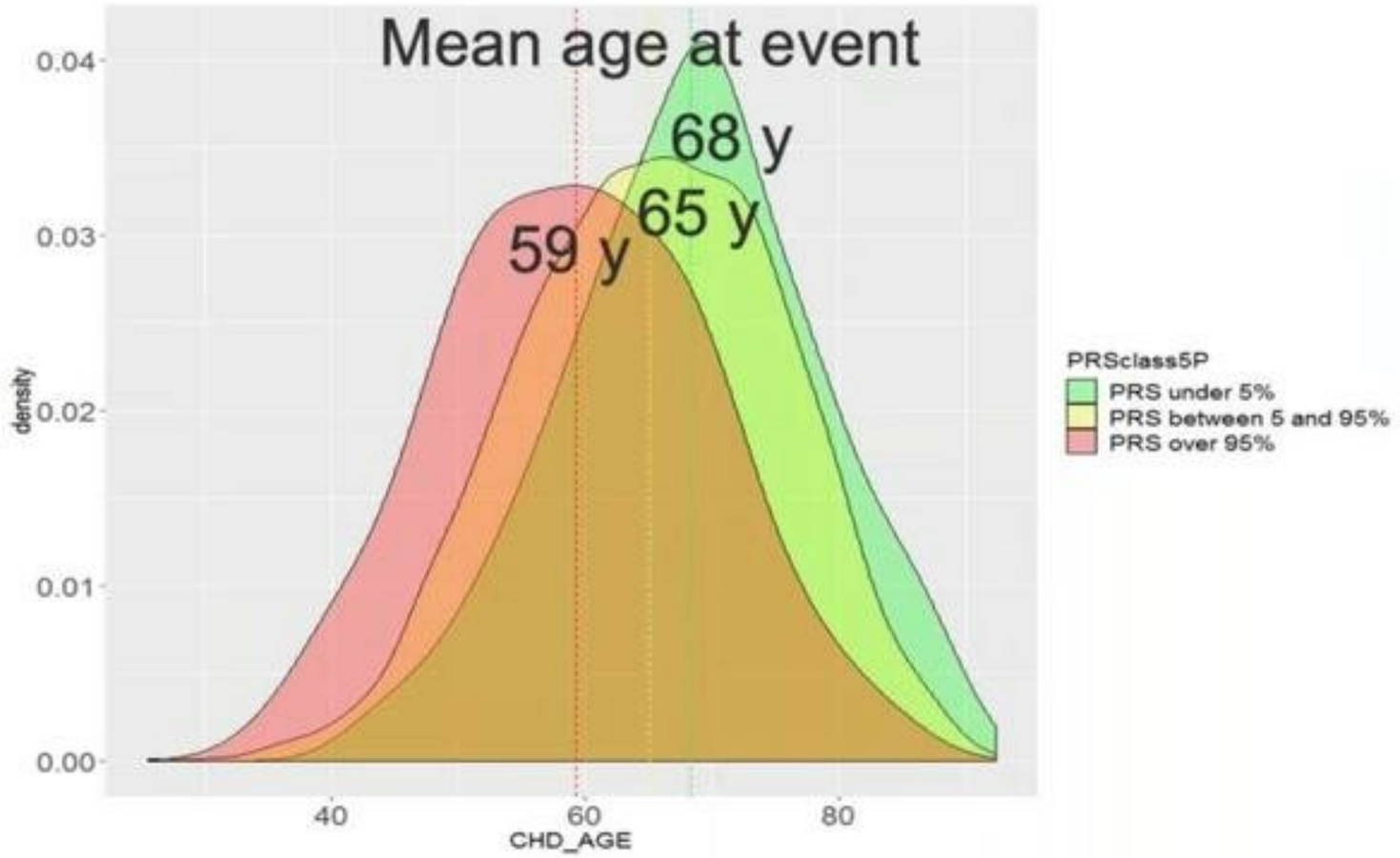
Genetic risk brings added personalized value to the disease prevention regardless of lifestyle



Perola et al Duodecim 2019

PRS ASSOCIATES WITH THE AGE OF THE FIRST CHD EVENT

High PRS may identify individuals who get a disease at early age



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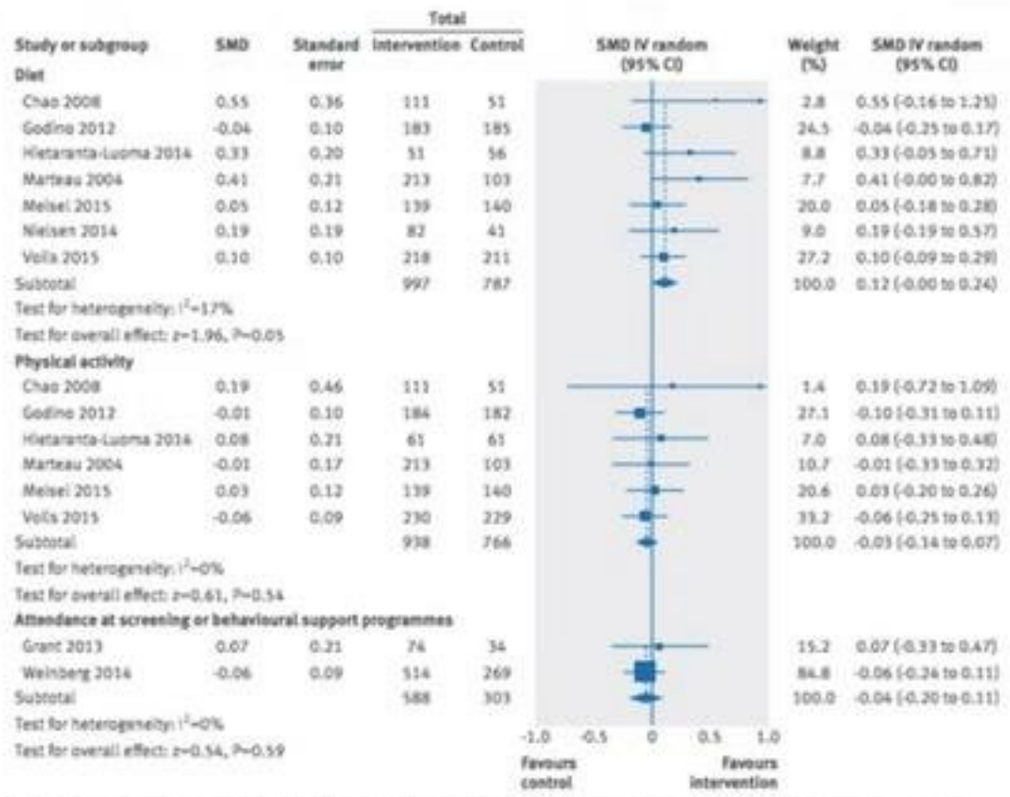
PRS IS NOT INSIGNIFICANT

The impact of communicating genetic risks of disease on risk-reducing health behaviour: systematic review with meta-analysis

Gareth J Hollands,[1] David P French,[2] Simon J Griffin,[3] A Toby Prevost,[4] Stephen Sutton,[3] Sarah King,[1] Theresa M Marteau[1]

BMJ: first publi

"…communicating DNA based risk estimates changes behaviour is not supported by existing evidence … do not support use of genetic testing or the search for risk-conferring gene variants for common complex diseases on the basis that they motivate risk-reducing behaviour."



Study or subgroup	SMD	Standard error	Total intervention	Total control	SMD IV random (95% CI)	Weight (%)	SMD IV random (95% CI)
Diet							
Chao 2008	0.55	0.36	111	51		2.8	0.55 (-0.16 to 1.25)
Godino 2012	-0.04	0.10	183	185		24.5	-0.04 (-0.25 to 0.17)
Hietaranta-Luoma 2014	0.33	0.20	51	56		8.8	0.33 (-0.05 to 0.71)
Marteau 2004	0.41	0.21	213	103		7.7	0.41 (-0.00 to 0.82)
Meisel 2015	0.05	0.12	139	140		20.0	0.05 (-0.18 to 0.28)
Nielsen 2014	0.19	0.19	82	41		9.0	0.19 (-0.19 to 0.57)
Volk 2015	0.10	0.10	218	211		27.2	0.10 (-0.09 to 0.29)
Subtotal			997	787		100.0	0.12 (-0.00 to 0.24)
Test for heterogeneity: I^2=17%							
Test for overall effect: z=1.96, P=0.05							
Physical activity							
Chao 2008	0.19	0.46	111	51		1.4	0.19 (-0.72 to 1.09)
Godino 2012	-0.01	0.10	184	182		27.1	-0.10 (-0.31 to 0.11)
Hietaranta-Luoma 2014	0.08	0.21	61	61		7.0	0.08 (-0.33 to 0.48)
Marteau 2004	-0.01	0.17	213	103		10.7	-0.01 (-0.33 to 0.32)
Meisel 2015	0.03	0.12	139	140		20.6	0.03 (-0.20 to 0.26)
Volk 2015	-0.06	0.09	230	229		33.2	-0.06 (-0.25 to 0.13)
Subtotal			938	766		100.0	-0.03 (-0.14 to 0.07)
Test for heterogeneity: I^2=0%							
Test for overall effect: z=0.61, P=0.54							
Attendance at screening or behavioural support programmes							
Grant 2013	0.07	0.21	74	34		15.2	0.07 (-0.33 to 0.47)
Weinberg 2014	-0.06	0.09	514	269		84.8	-0.06 (-0.24 to 0.11)
Subtotal			588	303		100.0	-0.04 (-0.20 to 0.11)
Test for heterogeneity: I^2=0%							
Test for overall effect: z=0.54, P=0.59							

Fig 4 | Primary outcome analysis: diet; physical activity; attendance at screening or behavioural support programmes. SMD=standardised mean difference

P6 – GENOMICS TO HEALTHCARE

Prevention of common chronic diseases using modern medicine

PUBLIC HEALTH PROGRAMMES

e.g. North Karelia Project 1972–, Finnish Allergy Program 2008–2018, Suicide Prevention Project, Indoor Air and Health

INTERVENTION STUDIES

e.g. Diabetes Prevention Study (DPS), FINGER, vaccine trials

HEALTHCARE

Focus heavily on treatment instead of prevention

Ageing population; increasing costs resulting from the chronic diseases

P6

GENOMICS

A plethora of genomic regions found to associate with various diseases and traits (e.g. coronary heart disease, type 2 diabetes)

Costs of genome analyses rapidly decreasing

POPULATION FOLLOW-UP STUDIES

e.g. HES-surveys: Mobile Clinic, FINRISK, Health 2000/2011, FinHealth

DATA RECORDS AND SAMPLE COLLECTIONS

e.g. national registries, biobanks

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P6 – GENOMICS TO HEALTHCARE

Prevention of common chronic diseases using modern medicine

Objectives of the P6 initiative

- Improved public health
- Cost-effective use of the healthcare resources
- Health equality of citizens
- Finland as a healthcare pioneer
- Improved prevention and early care of the common chronic diseases
- Professionally directed use of genetic information in the clinical care
- Novel opportunities for research, public-private co-operation and businesses in the health sector

Healthcare professionals have a new predcitive, preventive, personalized and participatory tool for their clinical work that is ethically sound and simple to use

PURPOSE

Management and coordination	P6 Study	Communications	Health-economic evaluations	Public-private collaboration	Technology and biobanks	Training

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P6 – GENOMICS TO HEALTHCARE

Prevention of common chronic diseases using modern medicine

Disease endpoints selected to the P6 study

gout
venous thrombosis
coronary heart disease
prostate cancer
colorectal cancer
atrial fibrillation
rheumatoid arthritis
parodontitis
caries
smoking
type 2 diabetes
asthma
breast cancer
hyperlipidaemia
inflammatory bowel diseases
dementia
stroke
COPD
retinal degeneration
lung cancer
D-vitamin level

Forming polygenic risk scores (PRS) based on previous high-quality research. Evaluation of PRSs in a large prospective Finnish population sample collection

Recruitment of 100.000 participants from the Finnish biobanks. Returning disease risk information (genetic and lifestyle) via a secure web portal
900.000 registry controls

Invitation of 4.000 high-risk individuals to an active intervention (RCT)

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P6 – TIMELINE

Strategic planning of the P6 initiative

2019

P5 FinHealth pilot

2018-2019

Recruitment of P6 study subjects via a biobank portal

2021-2022

P6 PRS analyses in the THL cohorts

2020

P6 interventions

2021-2023

Returning P6 risk information via a secure web portal

2022-2023

Analyses of the P6 results

2022-2024

Follow-up through national healthcare registries

Follow-up studies

2024 ->

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P6 – SUMMARY

1. **A large-scale study** returning information to 100.000 participants on their genetic risk for selected common chronic diseases.
   - 900.000 registry controls
2. A novel **operations model** for the healthcare professionals for using genetic infomation in their day-to-day clinical work
   - Predictive, preventive, personalized and participatory
   - Training and guidance to be provided
3. **Biopank portal**
4. **Novel opportunities** for research and public-private collaboration, incl. drug development and wellbeing services

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Precision Public Health based on (Gen)omic data - P6 Genomics to Healthcare

P5

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BF Co-creation; genomics to healthcare

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PROFITU

PreMed

VTT, Data-driven precision medicine ecosystem

Done/On-going

1M Cohort

thl

***CleverP**chd*
***CleverP**dm2*

Genomic Medicine Board

Genome Center Finland

Genome directed interventions
- Genoventions (BF Co-innovation)

Planning

Sote-uudistus

Digitalisaation edistämisen ohjelma

Ecosystem

P5 FINHEALTH PILOT

Polygenic risk score (PRS)

- Coronary artery disease
- T2 diabetes
- Venous thromboembolism

Single Clinical Variants (SCV)