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OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

Additional information needed to predict CHD and cardiovascular events in stabilized patients.

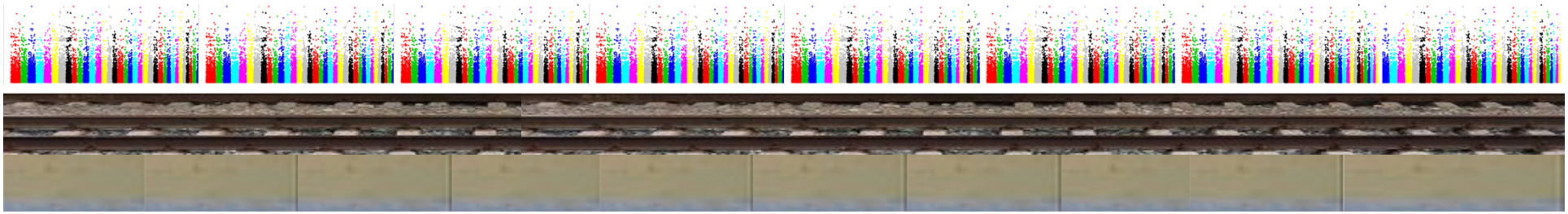
What we know today and what we should know

Svetlana GOROKHOVA

MD, PhD, professor

Research Clinical Center of Russian Railways

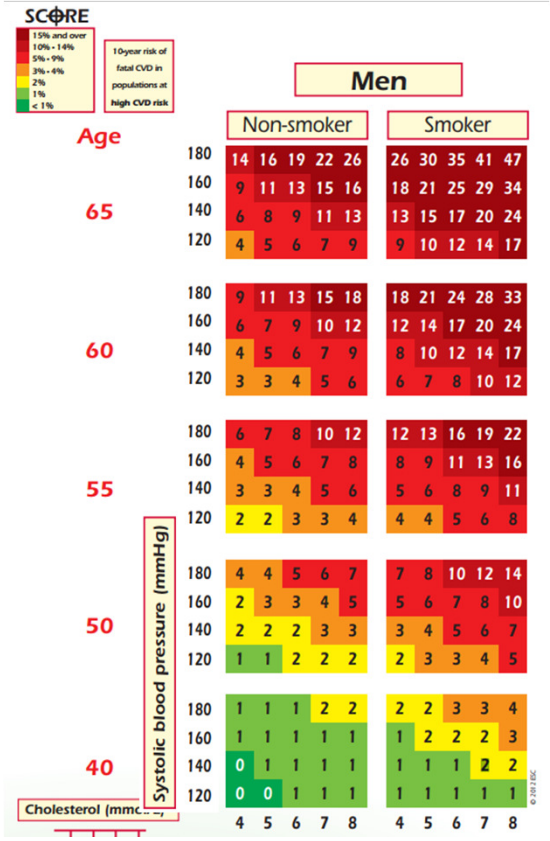
Moscow, Russia



Case 1

Patient G., 41 y.o.

- *Blood pressure* – 140/80
- *No diabetes*
- *Ventricular extra beats*
- *Total cholesterol* – 294 mg/dl
- *HDL cholesterol* - 36 mg/dl



European Score

Risk Factor	Your Answer	Points	Relative Risk
Sex:	Male / Female		
Age:	41 years	1	
Smoker:	Yes / No	2	High
Diabetes:	Yes / No	0	Low
Blood Pressure:	140 / 80 mm Hg	2	High
Total Cholesterol	294 mg/dl	3	Very High
HDL Cholesterol:	36 mg/dl	1	High

Calculate, with Incomplete Values | Calculate

Total Points: 9 = 20 **% risk of heart disease in 10 years**

Average 10-year risk = 7 % *(for others in your age group)*

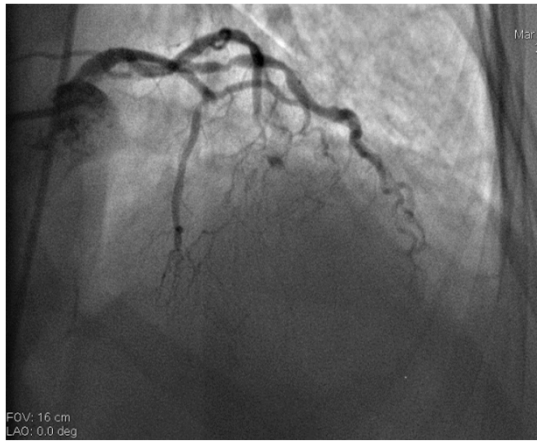
Low 10-year risk = 4 % *(for others in your age group)*

Framingham Risk Score

which revealed an,, and.

Case 1





Patient G., 41 y.o.

Coronary stenosis

- occlusion of the *left anterior descending artery*;
- sub-occlusion of the *left circumflex artery*;
- 75% stenosis of the *right coronary artery.*

WHAT IS KNOWN

Disagreement among Cardiovascular Disease Risk Calculators

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y
A		86	69	97	45	91	75	88	55	94	86	94	92	30	61	59	64	64	59	70	73	70	58	44	45
B	86		64	86	38	86	83	77	56	89	91	89	91	27	63	47	53	52	47	67	59	61	59	39	41
C	69	64		69	58	69	48	69	70	66	61	66	67	41	70	67	67	69	67	73	72	63	73	59	61
D	97	86	69		42	94	75	88	55	91	86	91	89	28	61	56	63	61	56	70	70	67	58	42	44
E	45	38	58	42		38	36	52	77	45	41	45	44	73	69	84	77	80	84	69	72	70	70	69	69
F	91	86	69	94	38		78	81	56	84	83	84	86	27	63	52	58	56	52	67	64	61	58	41	41
G	75	83	48	75	36	78		69	48	78	86	78	80	22	55	45	50	50	45	53	48	53	45	30	30
H	88	77	69	88	52	81	69		58	88	83	88	86	34	63	66	70	70	66	73	77	64	61	48	52
I	55	56	70	55	77	56	48	58		55	53	55	56	56	77	70	73	78	70	81	56	55	70	56	56
J	94	89	66	91	45	84	78	[illegible]	55		92	100	98	30	61	58	63	63	58	69	70	67	58	42	44
K	86	91	61	86	41	83	86	83	53	92		92	94	27	59	52	56	56	52	66	63	61	55	38	39
L	94	89	66	91	45	84	78	88	55	100	92		98	30	61	58	63	63	58	69	70	67	58	42	44
M	92	91	67	89	44	86	80	86	56	98	94	98		30	63	56	61	61	56	70	69	66	59	42	44
N	30	27	41	28	73	27	22	[illegible]	56	30	27	30	30		59	63	58	55	63	47	50	52	59	75	72
O	61	63	70	61	69	63	55	63	77	61	59	61	63	59		72	75	70	72	67	58	58	73	56	55
P	59	47	67	56	84	52	45	[illegible]	70	58	52	58	56	63	72		92	89	100	61	80	72	66	66	66
Q	64	53	67	63	77	58	50	[illegible]	73	63	56	63	61	58	75	92		94	92	64	72	64	61	61	61
R	64	52	69	61	80	56	50	70	78	63	56	63	61	55	70	89	94		89	69	75	64	59	61	61
S	59	47	67	56	84	52	45	[illegible]	70	58	52	58	56	63	72	100	92	89		61	80	72	66	66	66
T	70	67	73	70	69	67	53	73	81	69	66	69	70	47	67	61	64	69	61		75	66	77	59	63
U	73	59	72	70	72	64	48	77	56	70	63	70	69	50	58	80	72	75	80	75		81	70	66	69
V	70	61	63	67	70	61	53	64	55	67	61	67	66	52	58	72	64	64	72	66	81		72	64	67
W	58	59	73	58	70	58	45	61	70	58	55	58	59	59	73	66	61	59	66	77	70	72		67	70
X	44	39	59	42	69	41	30	48	56	42	38	42	42	75	56	66	61	61	66	59	66	64	67		97
Y	45	41	61	44	69	41	30	52	56	44	30	44	44	72	55	66	61	61	66	63	69	67	70	97	

	Calculator	Endpoint
A	Edinburgh (BNF)	10 year CVD
B	Edinburgh (Framingham CVD)	10 year CVD
C	Edinburgh (ASSIGN)	10 year CVD
D	Primary CVD Risk Calculator	10 year CVD
E	Reynolds Risk Score	10 year CVD
F	JBS Assessor	10 year CVD
G	JBS Risk Charts Assessment	10 year CVD
H	Framingham Heart Study (CVD)	10 year CVD
I	Q-RISK2 2011	10 year CVD
J	American Heart Association CVD Risk	10 year CVD
K	Total CVD Risk (High risk for HDL)	10 year CVD
L	Total CVD Risk (Low risk for HDL)	10 year CVD
M	CVD Risk Check	10 year CVD
N	Progetto CUORE	10 year CVD
O	SCORE	10 year CVD mortality
P	Australian Absolute CVD Risk	5 year CVD
Q	New Zealand Cardiovascular Risk Chart	5 year CVD
R	Australian Risk Chart	5 year CVD
S	New Zealand Know Your Numbers	5 year CVD
T	UKPDS	10 year CHD
U	Edinburgh (Framingham CHD)	10 year CHD
V	Framingham Heart Study (CHD)	10 year CHD
W	PROCAM (Health Check)	10 year CHD
X	I-phone STAT ATP III Lipid Management	10 year CHD
Y	National Cholesterol Education Program.	10 year CHD

CVD = Cardiovascular Disease; CHD = Coronary Heart Disease

Agreement Among Cardiovascular Disease Risk Calculators

G. Michael Allan, MD; Faeze Nouri, MD; Christina Korownyk, MD; Michael R. Kolber, MD, MSc; Ben Vandermeer, MSc; James McCormack, PharmD

specific calculators. (*Circulation*. 2013;127:1948–1956.)

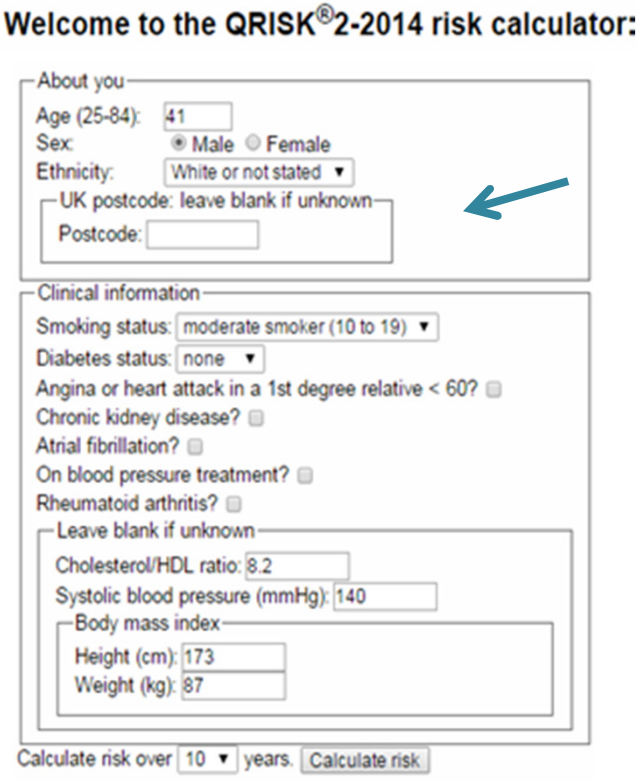
ıtion has an important impact on both risk guidelines recommending therapies based on

Modern trends in improvement of prediction of summary cardiovascular risk

Adapted scales of CHD risk and cardiovascular events

Implement new risk markers

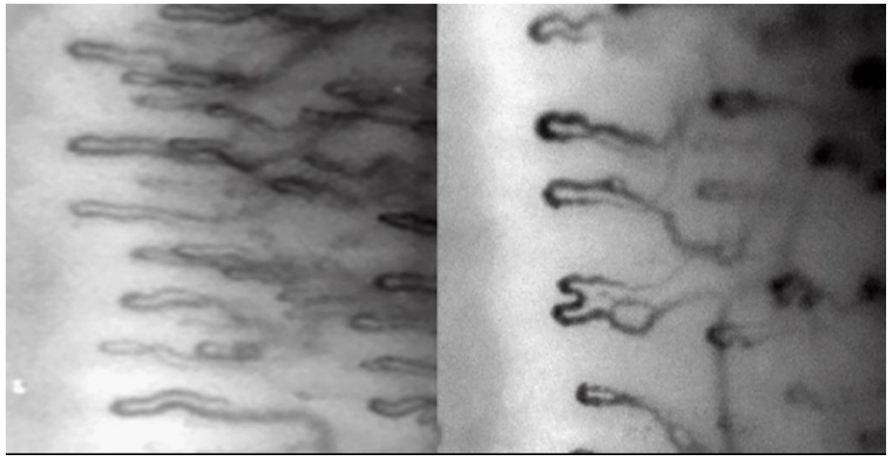




Digital capillaroscopy and the integral assessment of cardiovascular status

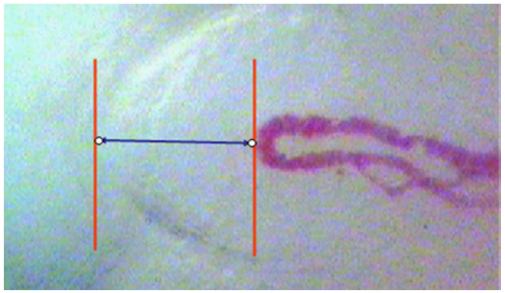


Digital capillaroscopy



normal structure and density of capillary network

abnormal density and rarefaction that characterize stable hypertension

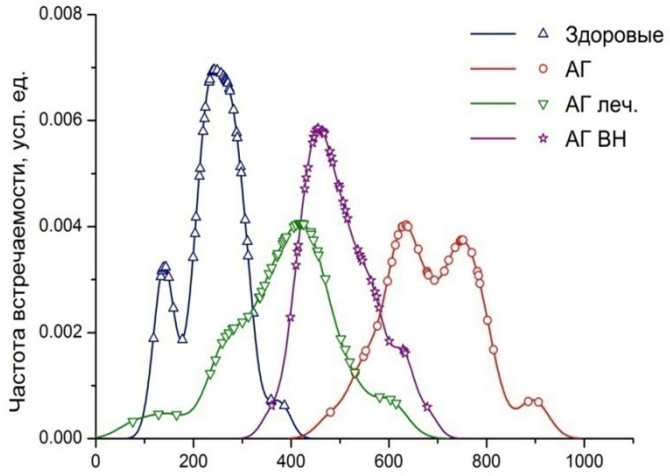


The linear size of the perivascular zone

Калькулятор интегрального индекса состояния ССС

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1														
2	ФИО пациента	ПЗ	ПО	К во/ао	ИМТ	СРПВ	ΔСРПВ	ФЭНД	САД	ДАД	ЧСС		Значение индекса	
3	И-ва	107.8	13.1	1.45	32	6.1	-12.8	2.6	125	75	68		402	
4	Е-ва	118.2	11.8	1.21	26.5	5.6	-0.7	6.5	112	63	98		185	
5	С-ва	121	20.5	1.46	27	7.6	-13.7	76.3	115	67	59		339	
6														
7														
8														
9														
10														
11														
12														
13														
14														
15														

Готово



An integral index of cardiovascular system status

2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

6.1.2. Recommendations for CQ1: Use of Newer Risk Markers After Quantitative Risk Assessment

Recommendation 1. If, after quantitative risk assessment, a risk-based treatment decision is uncertain, assessment of 1 or more of the following—family history, hs-CRP, CAC score, or ABI—may be considered to inform treatment decision making.

Table 4. Summary of Recommendations for Risk Assessment

Recommendations	NHLBI Grade	NHLBI Evidence Statements	ACC/AHA COR	ACC/AHA LOE
Assessment of 10-Year Risk of a First Hard ASCVD Event				
1. The race- and sex-specific Pooled Cohort Equations* to predict 10-year risk of a first hard ASCVD event should be used in non-Hispanic African Americans and non-Hispanic whites, 40–79 years of age.	B (Moderate)	N/A	I	B[4–8]
2. Use of the sex-specific Pooled Cohort Equations for non-Hispanic whites may be considered for estimation of risk in patients from populations other than African Americans and non-Hispanic whites.	E (Expert Opinion)	N/A	IIb	C
CQ1: Use of Newer Risk Markers After Quantitative Risk Assessment				
1. If, after quantitative risk assessment, a risk-based treatment decision is uncertain, assessment of ≥1 of the following—family history, hs-CRP, CAC score, or ABI—may be considered to inform treatment decision making.	E (Expert Opinion)	Appendix 4	IIb†	B[9–17]
2. Routine measurement of CIMT is not recommended in clinical practice for risk assessment for a first ASCVD event.	N (No recommendation for or against)	Appendix 4	III: No Benefit†	B[12,16,18]
3. The contribution of ApoB, CKD, albuminuria, and cardiorespiratory fitness to risk assessment for a first ASCVD event is uncertain at present.	N (No recommendation for or against)	Appendix 4	—	—
CQ2: Long-Term Risk Assessment				
1. It is reasonable to assess traditional ASCVD risk factors‡ every 4–6 years in adults 20–79 years of age who are free from ASCVD and to estimate 10-year ASCVD risk every 4–6 years in adults 40–79 years of age who are free from ASCVD.	B (Moderate)	Appendix 5 CQ2/ES7	IIa	B[19,20]
2. Assessment of 30-year or lifetime ASCVD risk on the basis of traditional risk factors‡ may be considered in adults 20–59 years of age who are free from ASCVD and are not at high short-term risk.	C (Weak)	Appendix 5 CQ2/ES2, CQ2/ES3, CQ2/ES4, CQ2/ES5, CQ2/ES6	IIb	C[20–22]

ABI indicates ankle-brachial index; ACC, American College of Cardiology; AHA, American Heart Association; ApoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CAC, coronary artery calcium; CIMT, carotid intima-media thickness; CKD, chronic kidney disease; COR, Class of Recommendation; CQ, critical question, ES, evidence statement; hs-CRP, high-sensitivity C-reactive protein; LOE, Level of Evidence; NHLBI, National Heart, Lung, and Blood Institute; and —, not applicable.

WHAT WE SHOULD KNOW

Criteria for Evaluation of Novel Markers of Cardiovascular Risk

A Scientific Statement From the American Heart Association

Mark A. Hlatky, MD, FAHA, Chair; Philip Greenland, MD, FAHA, Co-Chair; Donna K. Arnett, PhD, FAHA;

1. Proof of concept—Do novel marker levels differ between subjects with and without outcome?
2. Prospective validation—Does the novel marker predict development of future outcomes in a prospective cohort or nested case-cohort/case-cohort study?
3. Incremental value—Does the novel marker add predictive information to established, standard risk markers?
4. Clinical utility—Does the novel risk marker change predicted risk sufficiently to change recommended therapy?
5. Clinical outcomes—Does use of the novel risk marker improve clinical outcomes, especially when tested in a randomized clinical trial?
6. Cost-effectiveness—Does use of the marker improve clinical outcomes sufficiently to justify the additional costs of testing and treatment?

the Net Reclassification Improvement (NRI)

$$\mathrm{NRI} = \left\{ \begin{array}{l} \mathrm{Proportion}\left(\mathrm{risk}^{\mathrm{exp}} > \mathrm{risk}^{\mathrm{base}} \mid \text{case patients}\right) \\ -\mathrm{Proportion}\left(\mathrm{risk}^{\mathrm{exp}} < \mathrm{risk}^{\mathrm{base}} \mid \text{case patients}\right) \end{array} \right\} + \left\{ \begin{array}{l} \mathrm{Proportion}\left(\mathrm{risk}^{\mathrm{exp}} < \mathrm{risk}^{\mathrm{base}} \mid \text{control subjects}\right) \\ -\mathrm{Proportion}\left(\mathrm{risk}^{\mathrm{exp}} > \mathrm{risk}^{\mathrm{base}} \mid \text{control subjects}\right) \end{array} \right\}$$

M. Pencina et al. ***Circulation*****. 2009;119:2408-2416.**

Job strain as non-medical cardiovascular risk factor

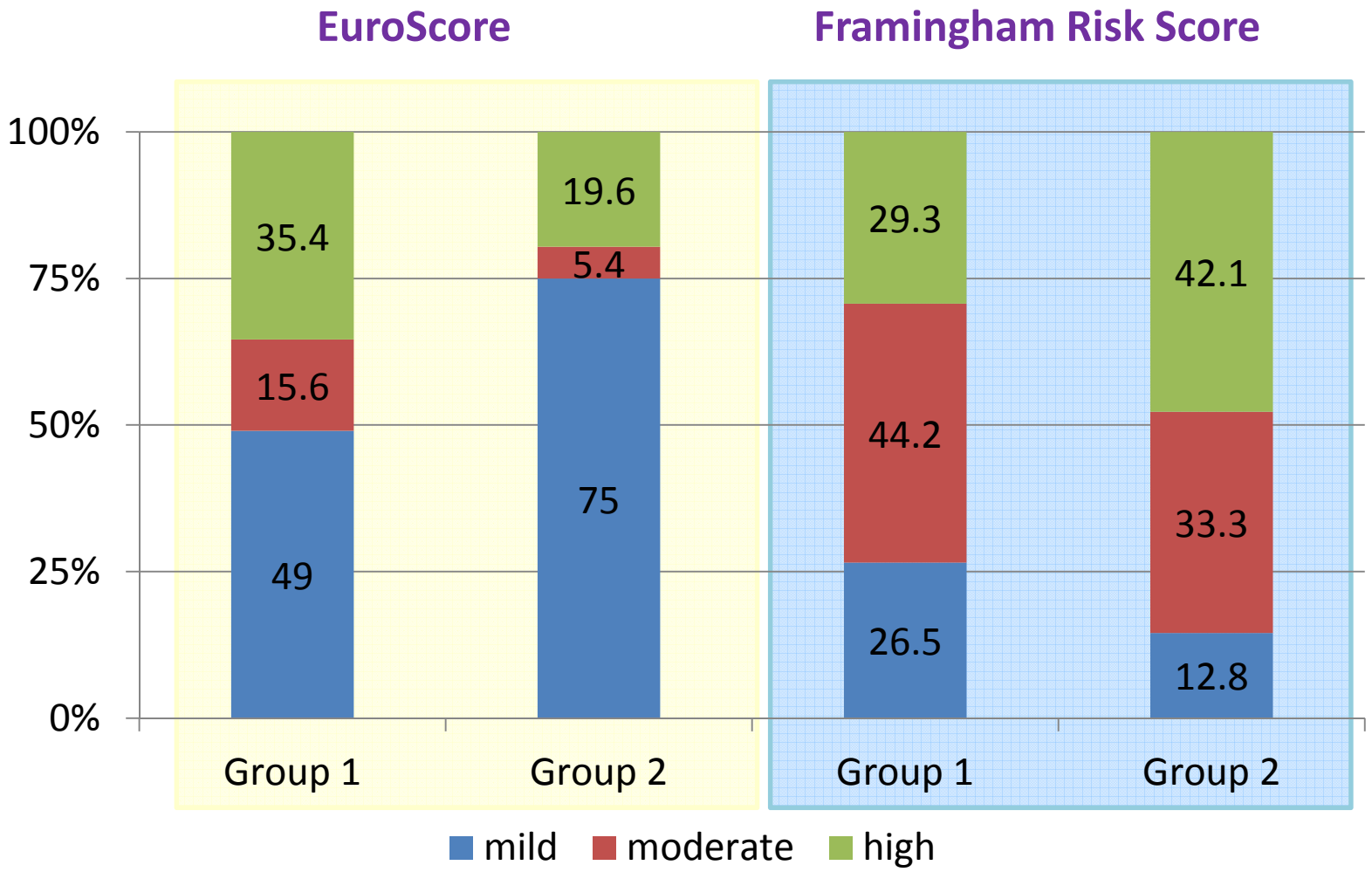
Does adding information on job strain improve risk prediction for coronary heart disease beyond the standard Framingham risk score? The Whitehall II study

Mika Kivimäki,[1,2]* Solja T Nyberg,[2] G David Batty,[1] Martin J Shipley,[1] Jane E Ferrie,[1] Marianna Virtanen,[1,2] Michael G Marmot,[1] Jussi Vahtera,[2,3] Archana Singh-Manoux[4] and Mark Hamer[1]

- **Job strain was associated with an increased risk of developing CHD.**
- **There was no evidence to suggest that adding information on job strain improved risk prediction above the standard Framingham model.**

- For the 160 'hard' endpoint CHD cases and 5373 non-cases, **NRI was very similar, 0.7%** (95% CI: 4.2 to 5.6%), P=0.39.

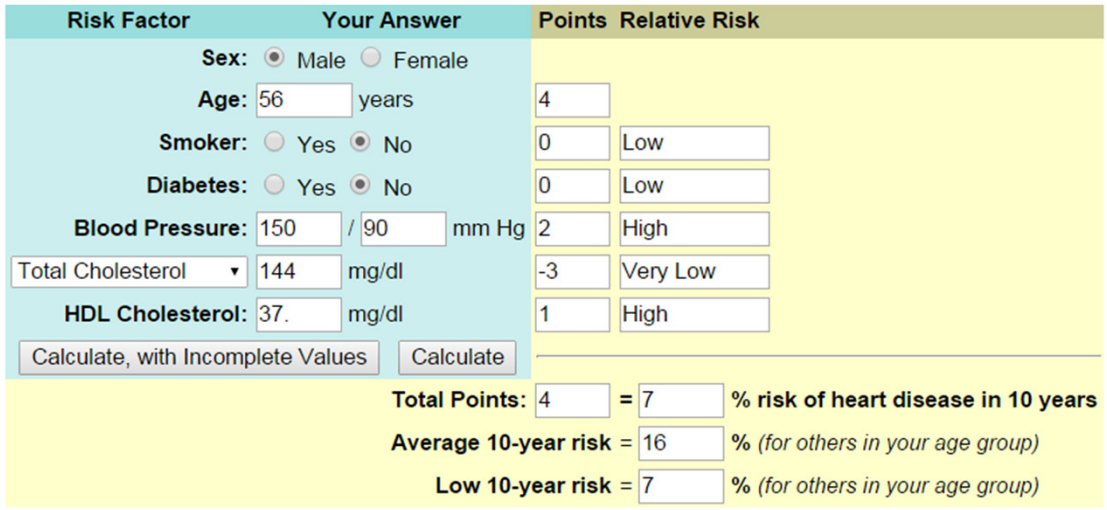
Job status and Risk Scores



a higher risk of coronary artery atherosclerosis in group 1 (railroad workers)

Case 2

Patient P., 56 y.o.
locomotive driver



Risk Factor	Your Answer	Points	Relative Risk
Sex:	Male / Female		
Age:	56 years	4	
Smoker:	Yes / No	0	Low
Diabetes:	Yes / No	0	Low
Blood Pressure:	150 / 90 mm Hg	2	High
Total Cholesterol	144 mg/dl	-3	Very Low
HDL Cholesterol:	37. mg/dl	1	High

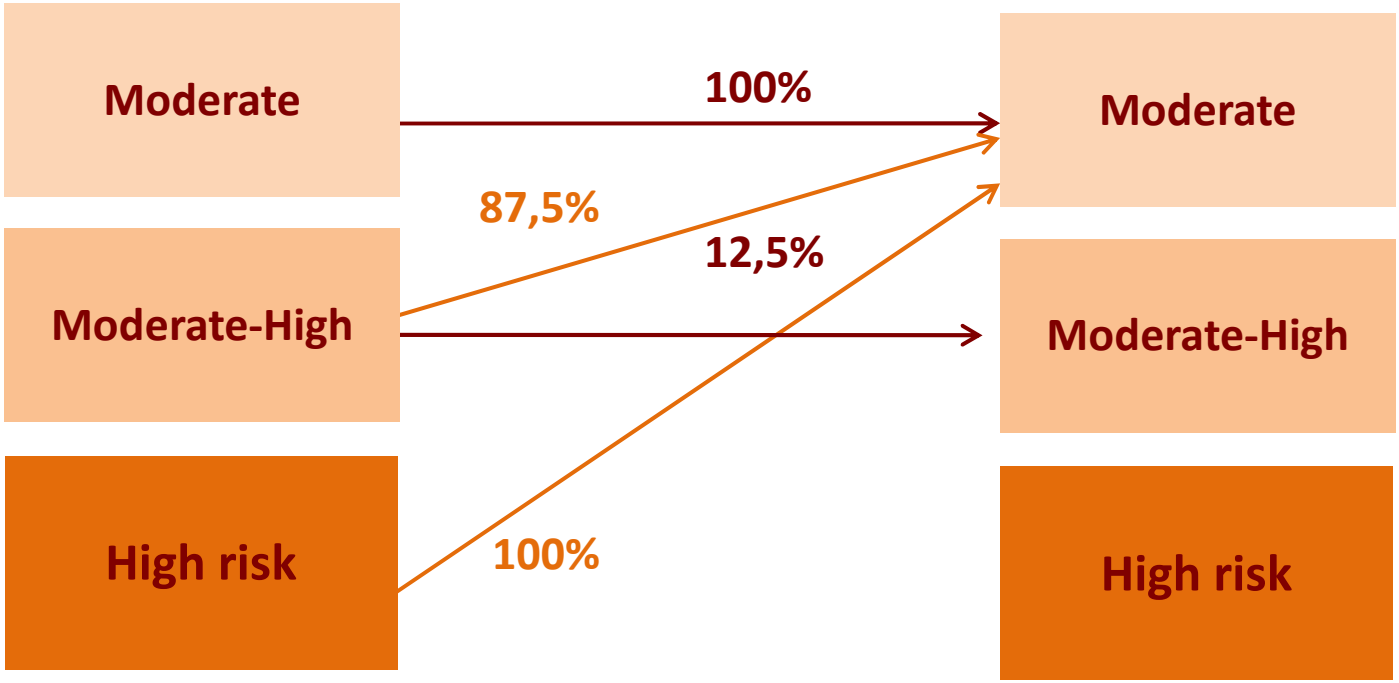
Calculate, with Incomplete Values | Calculate

Total Points: 4 = 7 % risk of heart disease in 10 years
Average 10-year risk = 16 % *(for others in your age group)*
Low 10-year risk = 7 % *(for others in your age group)*

Coronary stenosis

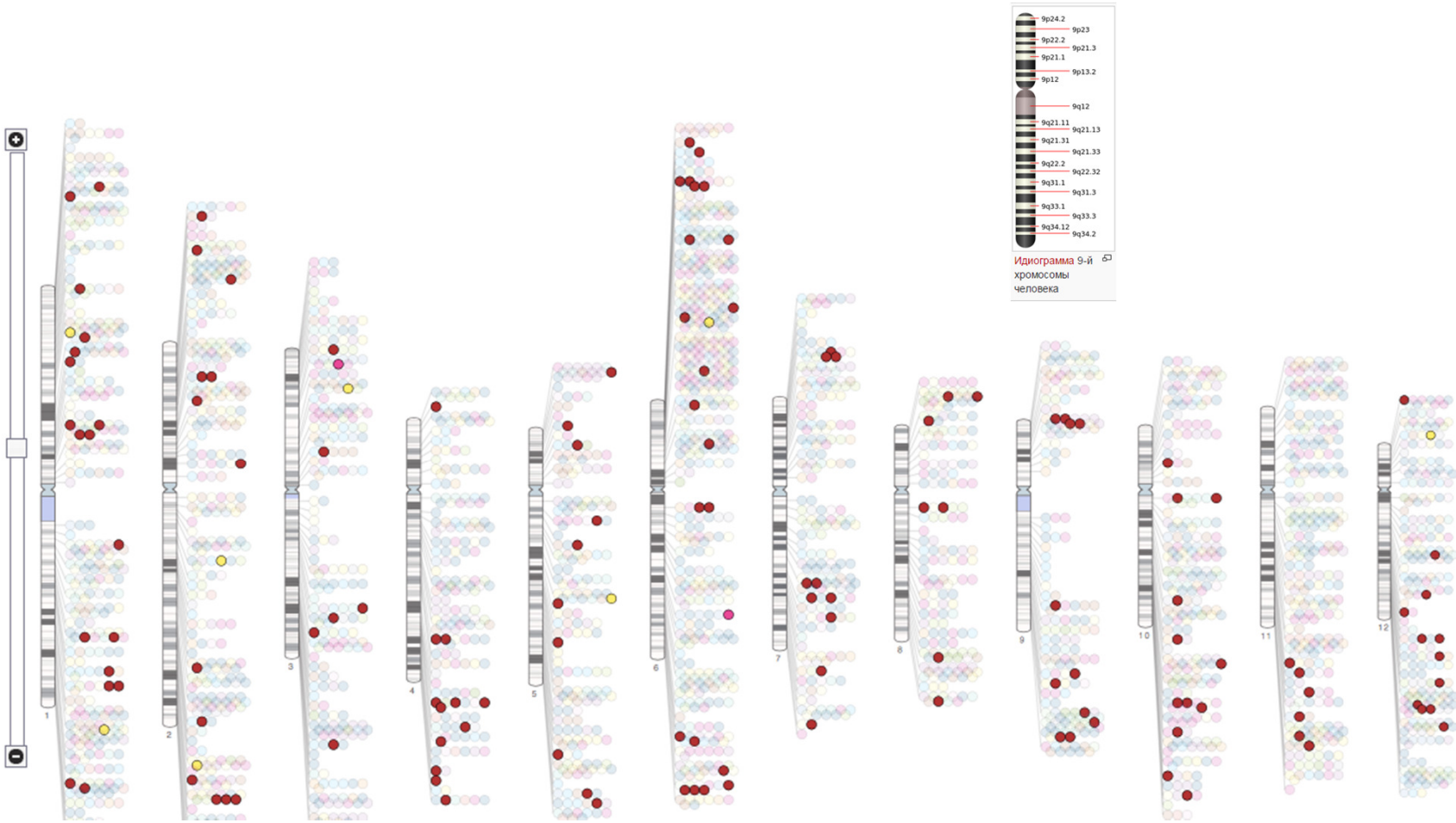
- *60-75%* stenosis of the *circumflex branch of the left coronary artery*;
- *60-70%* stenosis of the *obtuse marginal artery*;
- sub-occlusion of the *right coronary artery*

Dynamics of a total cardiovascular risk in conditions of complete correction of BP and dyslipidemia



N = 236

World experience in genetic modelling



Genetic associations with different cardiovascular diseases

Genetic risk score

WHAT WE SHOULD KNOW

Atherosclerosis 240 (2015) 305–310

Contents lists available at ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

A genetic risk score of 45 coronary artery disease risk variants associates with increased risk of myocardial infarction in 6041 Danish individuals

N.T. Krarup [a, *], A. Borglykke [b], K.H. Allin [a], C.H. Sandholt [a], J.M. Justesen [a], E.A. Andersson [a], N. Grarup [a], T. Jørgensen [b, c, d], O. Pedersen [a], T. Hansen [a, e]

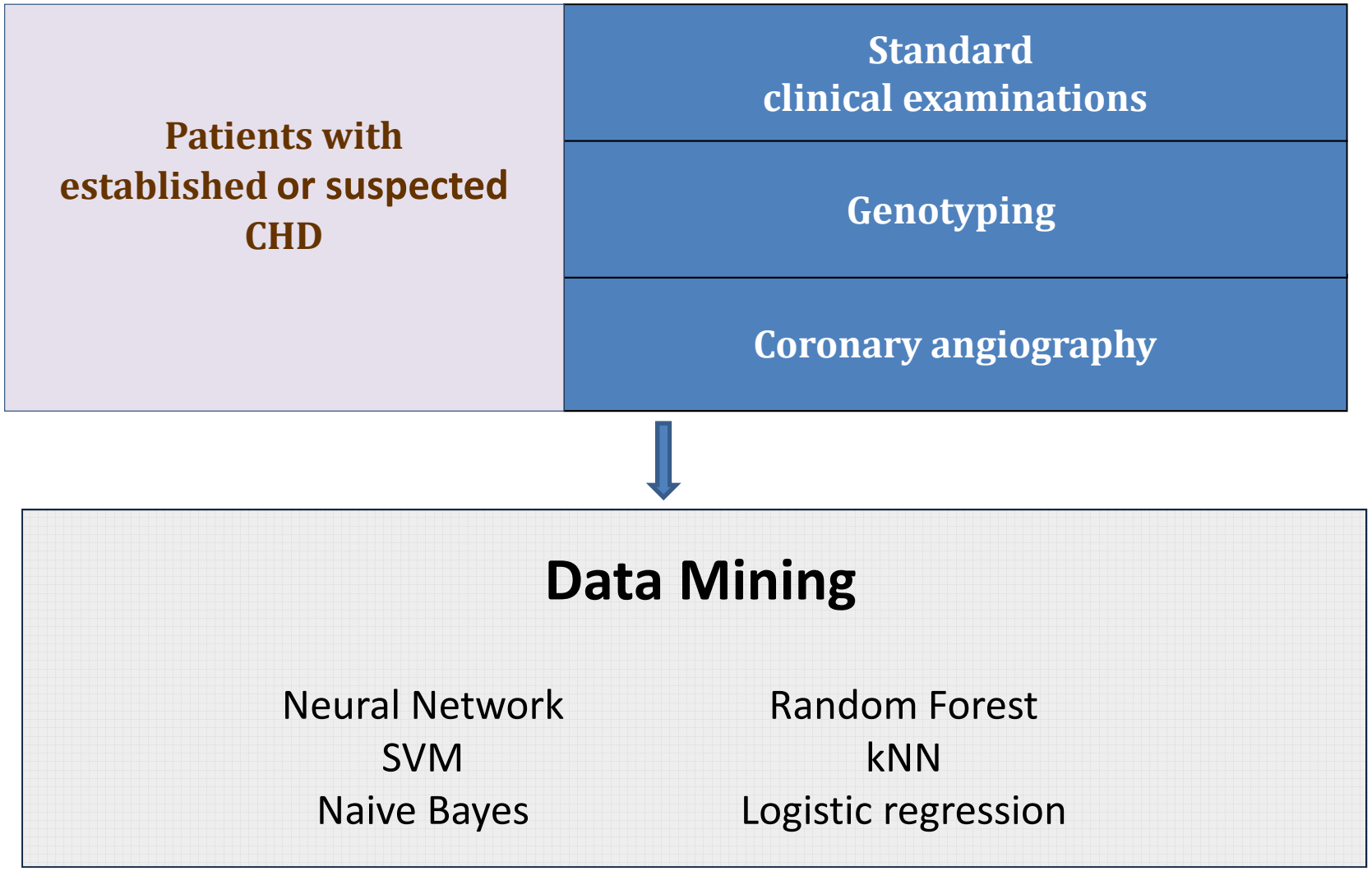
[a] The Novo Nordisk Foundation Center for Basic Metabolic Research, Section of Metabolic Genetics, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
[b] Research Center for Prevention and Health, Glostrup University Hospital, Glostrup, Denmark
[c] Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
[d] Faculty of Medicine, University of Aalborg, Aalborg, Denmark
[e] Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark

Table 3
C-index, Net Reclassification Index and Integrated Discrimination Improvement of GRS on incident MI.

Trait	Models compared	C-index	p	NRI (95%CI)	p	IDI (95%CI)	Relative IDI	p
MI	CAD risk factors vs. CAD risk factors + GRS	0.68 (0.62–0.73) vs. 0.69 (0.64–0.75)	0.002	−0.02 (−0.08 to 0.04)	0.5	0.001 (−0.0002–0.003)	0.07	0.09

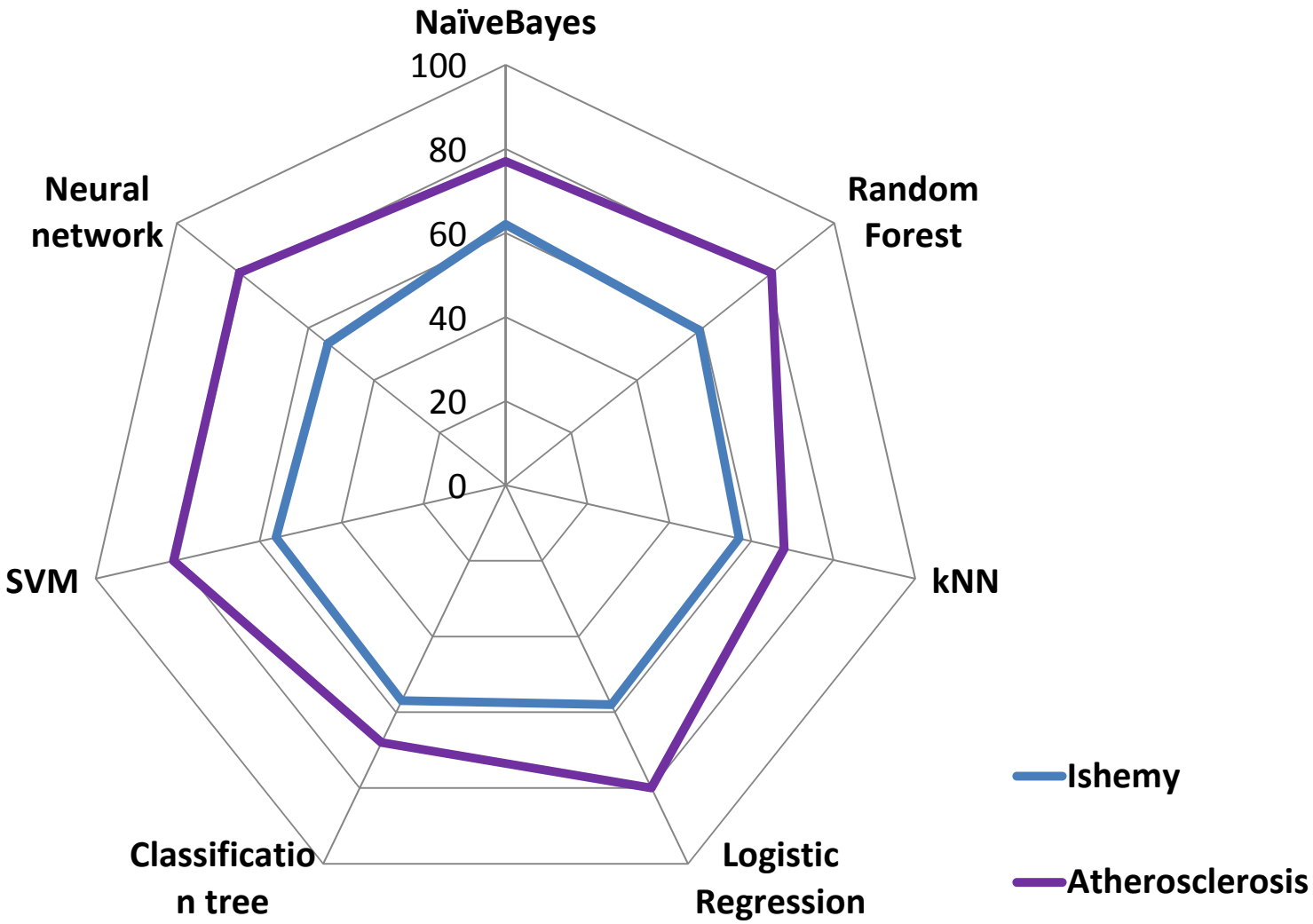
The table shows the predictive capacity of GRS added to conventional CAD risk factors on the incidence of myocardial infarction (MI). Analyses were done in the complete data set. C-index represents the concordance of the models on risk of developing MI during the follow-up time in Inter99. The calculated p-value is derived from statistical significance of means in two groups with 5 degrees of freedom. CAD risk factors are the European SCORE risk factors (age, sex, BMI, type 2 diabetes and smoking status). NRI: net reclassification index; IDI: integrated discrimination improvement; C-index: concordance index; MI: myocardial infarction; GRS: genetic risk score.

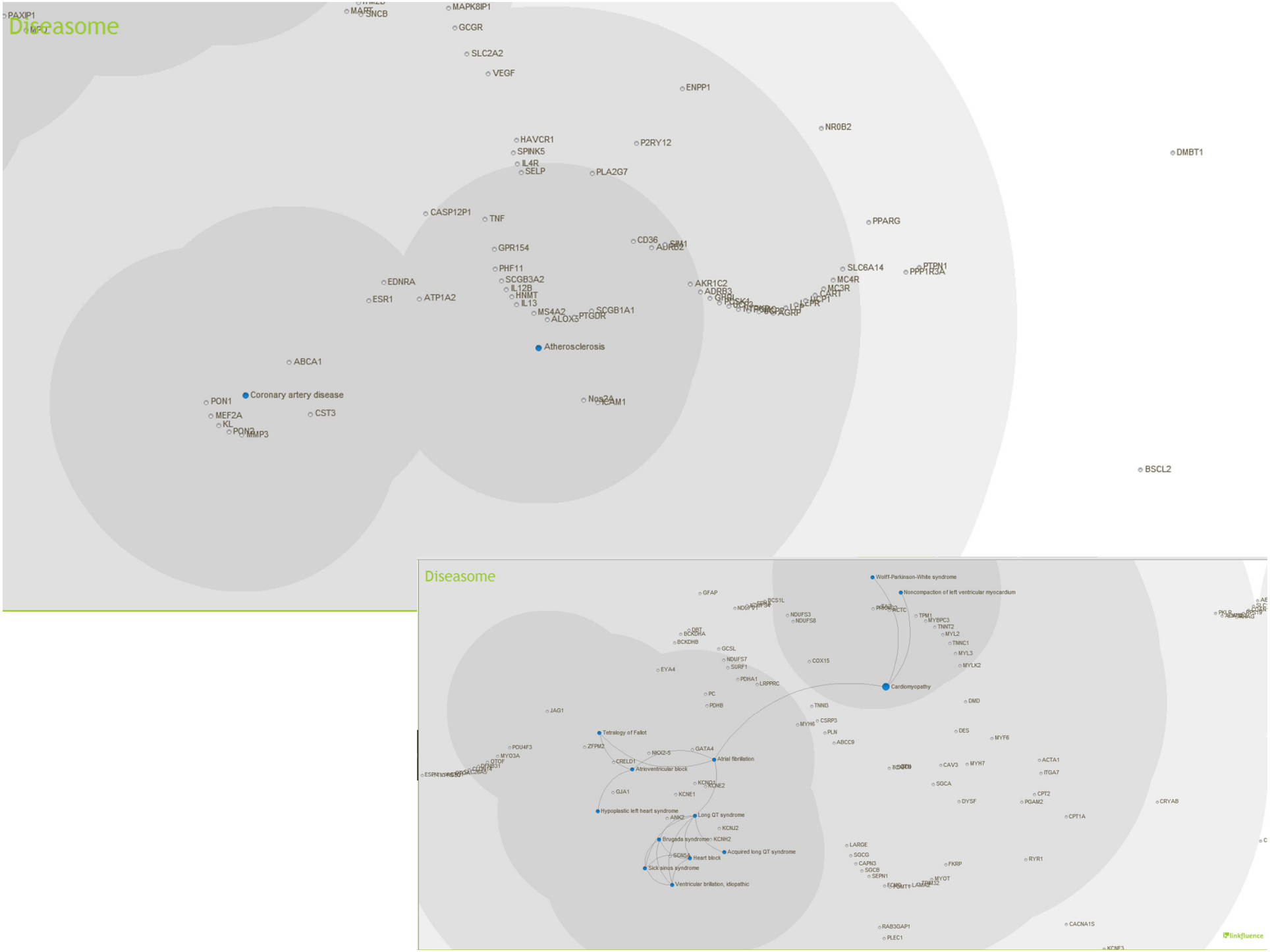
Data Base


Patients with established or suspected CHD
Standard clinical examinations
Genotyping
Coronary angiography
Data Mining
Neural Network
SVM
Naive Bayes
Random Forest
kNN
Logistic regression

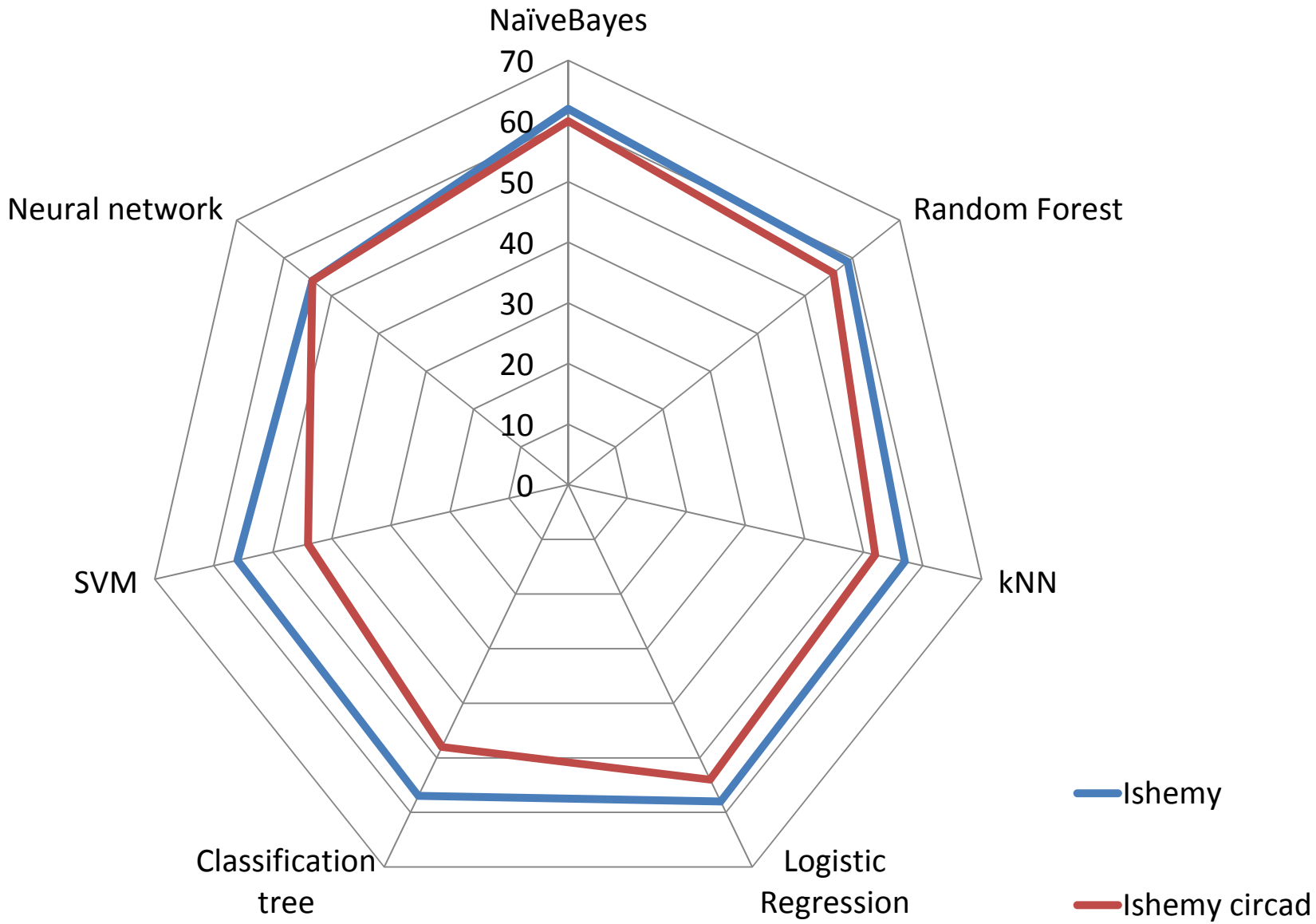
Genetic risk score

ROC curves for classifications CHD (different endpoints using different methods)

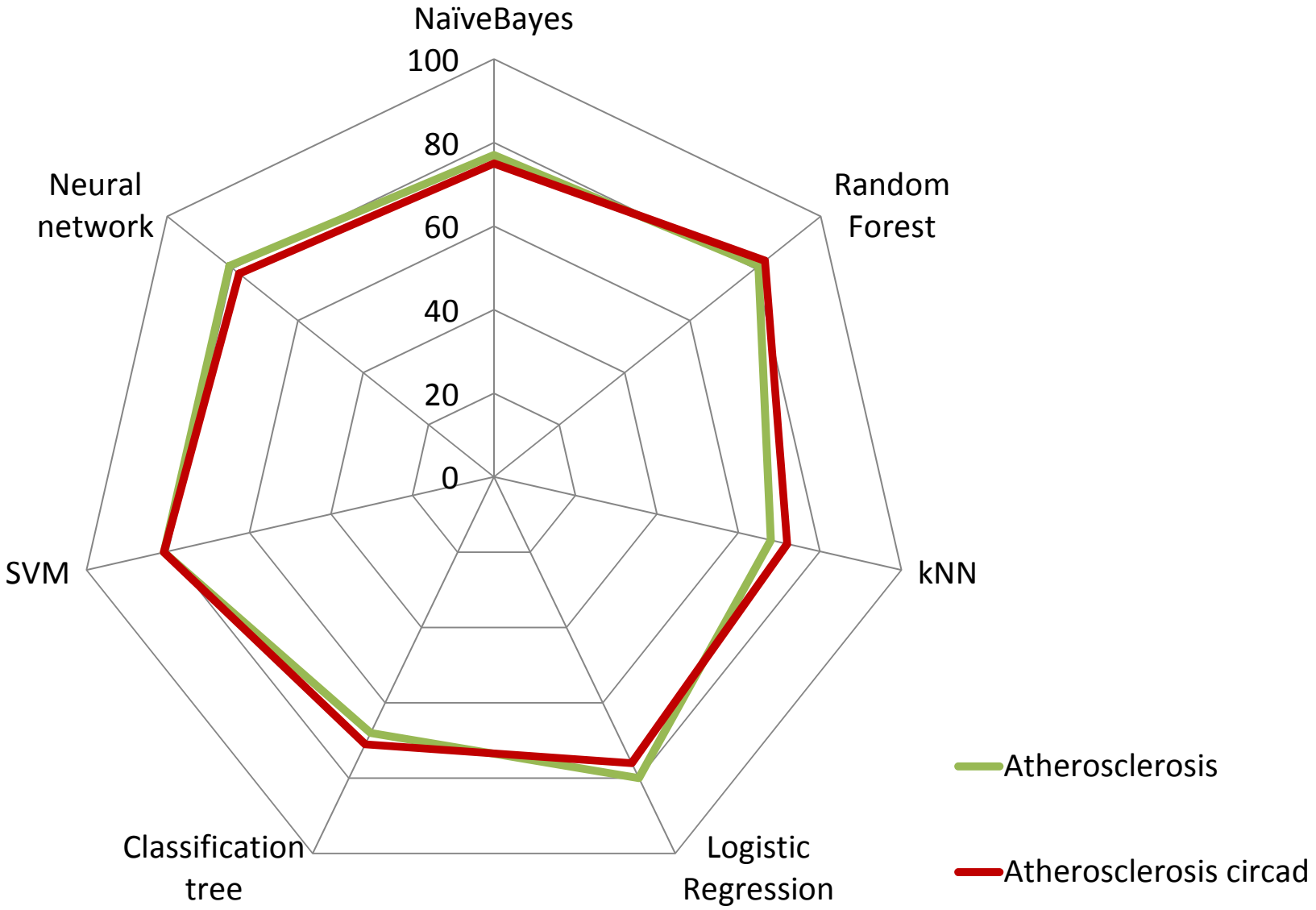



Diseasome
PAXIP1
MART
SNCB
MAPK8IP1
GCGR
SLC2A2
VEGF
ENPP1
NR0B2
HAVCR1
SPINK5
IL4R
SELP
P2RY12
PLA2G7
DMBT1
CASP12P1
TNF
PPARG
CD36
GPR154
PHF11
SCGB3A2
IL12B
HNMT
IL13
EDNRA
ESR1
ATP1A2
MS4A2
ALOX5
PTGDR
SCGB1A1
SLC6A14
PTPN1
PPP1R3A
MC4R
MC3R
CART
AKR1C2
ADRB3
Atherosclerosis
ABCA1
Coronary artery disease
PON1
MEF2A
KL
PON2
MMP3
CST3
Nos2A
ICAM1
BSCL2
Diseasome
Wolff-Parkinson-White syndrome
Noncompaction of left ventricular myocardium
GFAP
NDUFS3
NDUFS8
TPM1
MYBPC3
TNNT2
MYL2
TNNC1
MYL3
MYLK2
DBT
BCKDHA
BCKDHB
GCSL
NDUFS7
SURF1
COX15
EYA4
PDHA1
LRPPRC
Cardiomyopathy
PC
PDHB
JAG1
TNNI3
DMD
MYH6
CSRP3
PLN
ABCC9
DES
MYF6
Tetralogy of Fallot
ZFPM2
POU4F3
MYO3A
DTOF
GATA4
NKX2-5
CRELD1
Atrial fibrillation
Atrioventricular block
CAV3
MYH7
ACTA1
ITGA7
SGCA
KCND1
KCNE2
KCNE1
GJA1
DYSF
PGAM2
CPT2
CRYAB
CPT1A
Hypoplastic left heart syndrome
ANK2
Long QT syndrome
KCNJ2
Brugada syndrome
KCNH2
Acquired long QT syndrome
SCN5A
Heart block
Sick sinus syndrome
Ventricular brillation, idiopathic
LARGE
SGCG
CAPN3
SGCB
SEPN1
FKRP
RYR1
MYOT
RAB3GAP1
PLEC1
CACNA1S
linkfluence

ROC curves for myocardial ischemia using different methods with the addition of circadian genes



ROC curves for coronary atherosclerosis using different methods with the addition of circadian genes

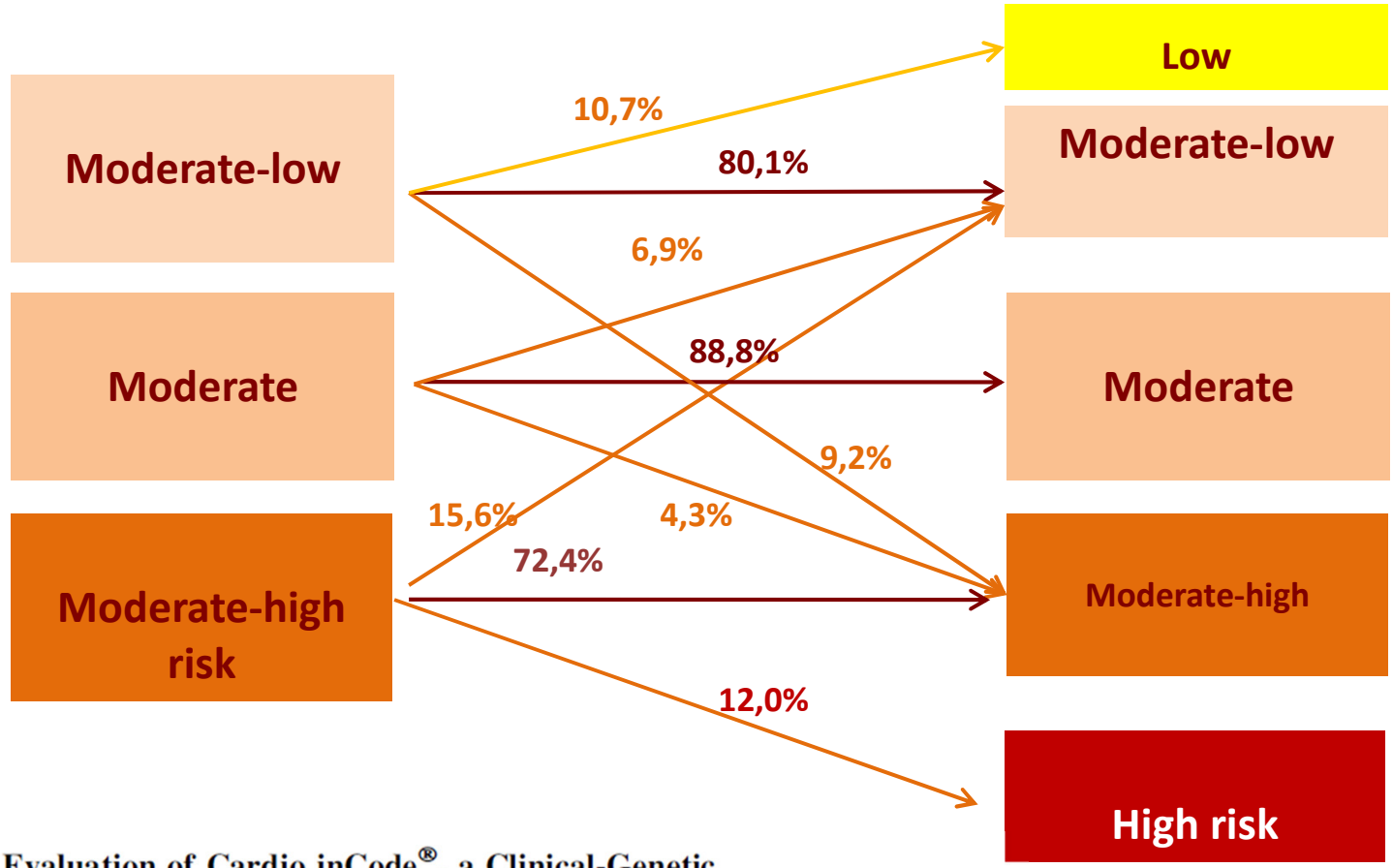


Accuracy of ANN models for CAD diagnosis

Model	Factors	Accuracy, %
I	Age, profession, diabetes, arterial hypertension, smoking, obesity, family anamnesis of CHD, glucose, cholesterol	64
VI	*NOS, ACE, AGT-235, AGT-174, AGTR, CRP-1, CRP-2, CRP-3* SNPs, SCORE index	83
X	*NOS, ACE, AGT-235, AGT-174, AGTR, CRP-1, CRP-2, CRP-3* SNPs, age, smoking, obesity, family anamnesis of CHD, HDL, LDL	88

Addition of the information on genes may improve accuracy of the prediction model for coronary artery disease

Cardiovascular risks reclassification in case of addition genetic risk



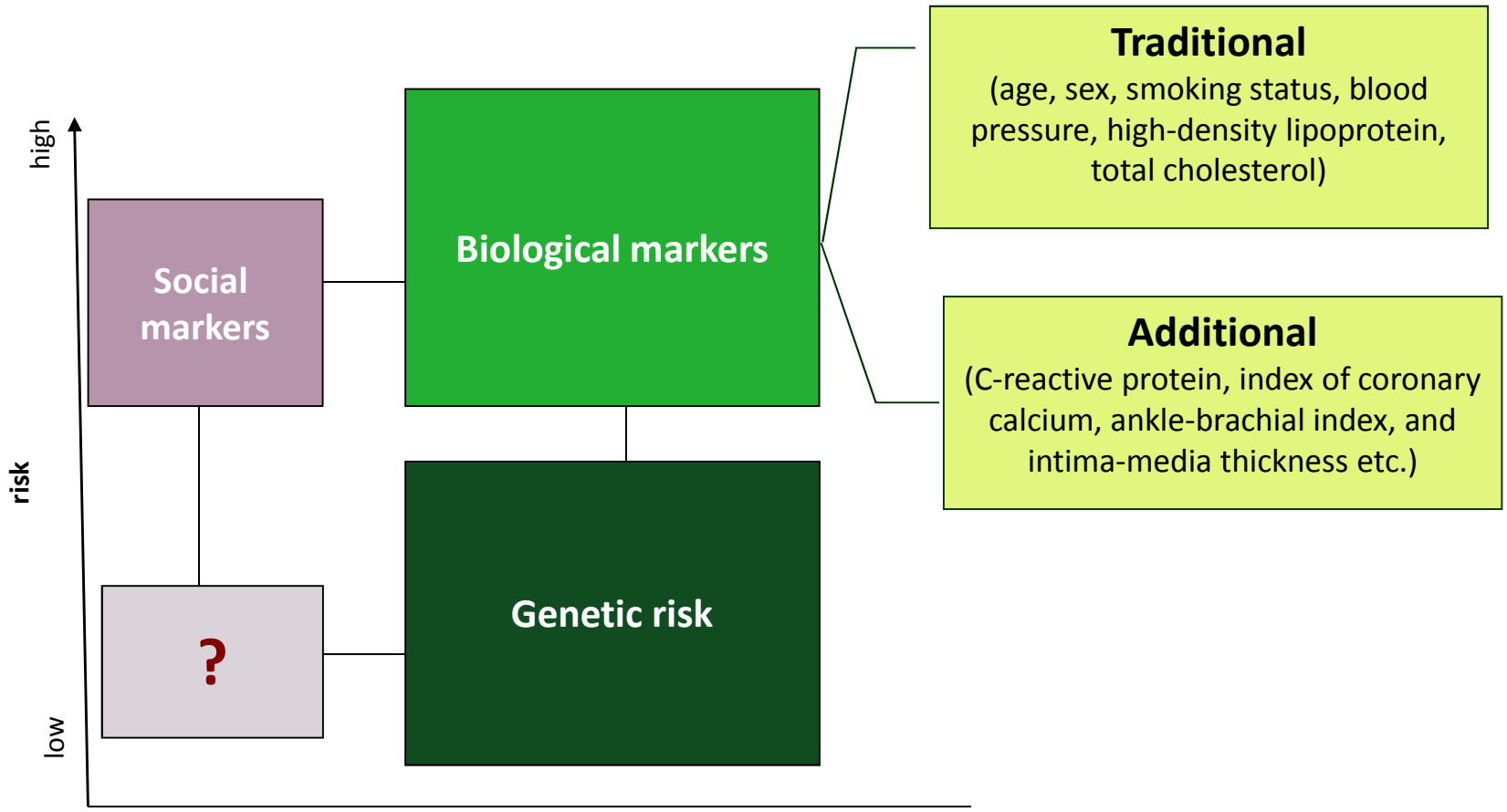
Economic Evaluation of Cardio inCode®, a Clinical-Genetic Function for Coronary Heart Disease Risk Assessment

A. Ramírez de Arellano · A. Coca · M. de la Figuera · C. Rubio-Terrés · D. Rubio-Rodríguez · A. Gracia · A. Boldeanu · J. Puig-Gilberte · E. Salas

Appl Health Econ Health Policy (2013) 11:531–542

N = 3537

Cardiovascular risk's quadrant



Conclusions

- The issue of precise prediction of a disease and its complications cannot be resolved only with traditional non-genetic risk factors such as sex, age, smoking, diabetes and cholesterol.
- Inclusion of genetic and non-medical factors (for example, duration of the working day and occupational factors) into risk models can increase accuracy of prognostic models for cardiovascular diseases.
- Individual total risk should include the following components / groups of factors:1) basic (genetic, sex, race/ethnicity and other non-modifiable factors), 2) additional variable (modifiable) factors such as smoking, cholesterol, blood pressure etc.

WHAT WE SHOULD KNOW

Circulation
Cardiovascular Genetics

American Heart Association

A Genetic Risk Score Is Associated With Incident Cardiovascular Disease and Coronary Artery Calcium: The Framingham Heart Study

George Thanassoulis, Gina M. Peloso, Michael J. Pencina, Udo Hoffmann, Caroline S. Fox, L. Adrienne Cupples, Daniel Levy, Ralph B. D'Agostino, Shih-Jen Hwang and Christopher J. O'Donnell

Table 2. The HRs for the Association Between a GRS (per Allele) and Incident Events

GRS	No. of SNPs	Age- and Sex-Adjusted HR (95% CI)	*P* Value	Risk Factor–Adjusted HR (95% CI)*	*P* Value	Fully Adjusted HR (95% CI)†	*P* Value
Incident hard CHD							
1	13	1.09 (1.02–1.17)	0.02	1.07 (1.00–1.15)	0.04	1.07 (1.00–1.15)	0.04
2	102	1.02 (0.99–1.04)	0.14	1.01 (0.99–1.03)	0.48	1.01 (0.99–1.03)	0.47
Incident CVD							
1	13	1.06 (1.02–1.10)	0.006	1.05 (1.01–1.09)	0.03	1.05 (1.01–1.09)	0.03
2	102	1.01 (1.00–1.03)	0.07	1.01 (1.00–1.02)	0.54	1.00 (0.99–1.02)	0.52

- **Addition of genetic risk to traditional risk factors improves prognostic value, but not all genetic markers are clinically useful.**

Thanks' for your kind attention!!!!!!



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