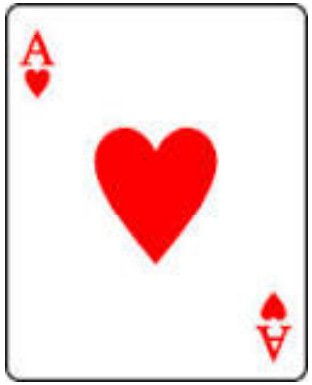
Cardiovascular risk scores: where are we?



Mark Woodward
The George Institute

WHICH PREDICTION VARIABLES?

Estimating modifiable coronary heart disease risk in multiple regions of the world: the INTERHEART Modifiable Risk Score

Catherine McGorrian[1,2], Salim Yusuf[1], Shofiqul Islam[1], Hyejung Jung[1], Sumathy Rangarajan[1], Alvaro Avezum[3], Dorairaj Prabhakaran[4], Wael Almahmeed[5], Zvonko Rumboldt[6], Andrzej Budaj[7], Antonio L. Dans[8], Hertzel C. Gerstein[1], Koon Teo[1], and Sonia S. Anand[1]* on behalf of the INTERHEART Investigators

	'Short' INTERHEART Modifiable Risk Score	'Full' INTERHEART Modifiable Risk Score	'Cholesterol' risk score	'Non-laboratory-based' INTERHEART Modifiable Risk Score
Validation studies within the 2/3 derivation set				
Odds increase of MI for a 1-point increase in score (95% CI)	15.2% (14.4%, 16.1%)	14.3% (13.5%, 15.1%)	12.9% (12.2%, 13.7%)	14.4% (13.9%, 15.3%)
ROC *c*-statistic (95% CI)	0.71 (0.70, 0.72)	0.72 (0.71, 0.73)	0.69 (0.68, 0.70)	0.71 (0.70, 0.72)
Brier score	0.21	0.21	0.22	0.21
Validation studies within the 1/3 test set				
Odds increase of MI for a 1-point increase in score (95% CI)	15.8% (14.7%, 17.0%)	14.0% (13.0%, 15.1%)	13.0% (12.0%, 14.3%)	14.2% (13.1%, 15.3%)
ROC *c*-statistic (95% CI)	0.71 (0.70, 0.73)	0.71 (0.71, 0.73)	0.69 (0.68, 0.71)	0.71 (0.70, 0.72)
Brier score	0.21	0.21	0.22	0.21

Framingham

General Cardiovascular Risk Profile for Use in Primary Care

The Framingham Heart Study

Ralph B. D'Agostino, Sr, PhD; Ramachandran S. Vasan, MD; Michael J. Pencina, PhD;
Philip A. Wolf, MD; Mark Cobain, PhD; Joseph M. Massaro, PhD; William B. Kannel, MD

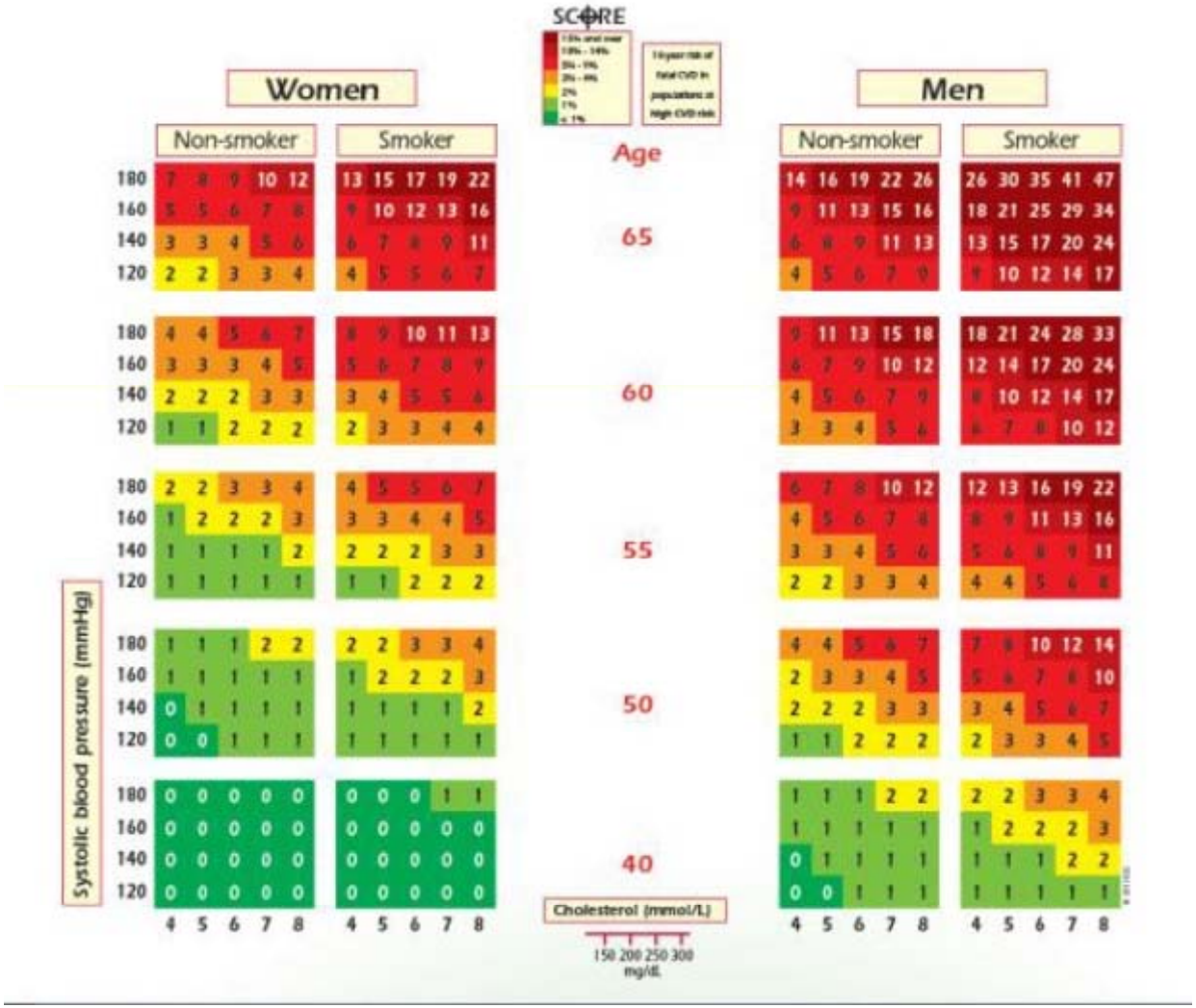
Table 2. Regression Coefficients and Hazard Ratios

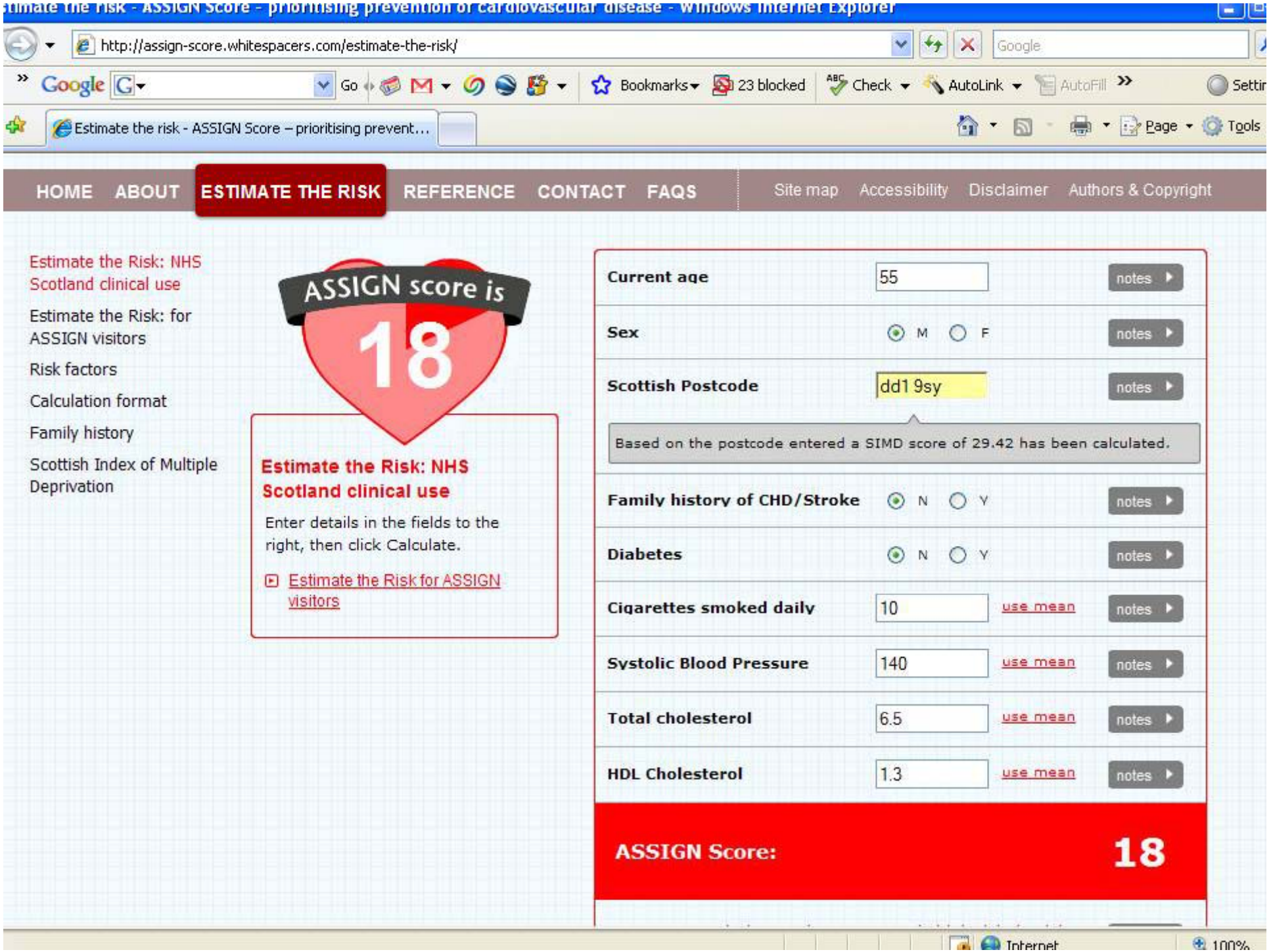
Variable	β*	P	Hazard Ratio	95% CI
Women [So(10)=0.95012]				
Log of age	2.32888	<0.0001	10.27	(5.65–18.64)
Log of total cholesterol	1.20904	<0.0001	3.35	(2.00–5.62)
Log of HDL cholesterol	−0.70833	<0.0001	0.49	(0.35–0.69)
Log of SBP if not treated	2.76157	<0.0001	15.82	(7.86–31.87)
Log of SBP if treated	2.82263	<0.0001	16.82	(8.46–33.46)
Smoking	0.52873	<0.0001	1.70	(1.40–2.06)
Diabetes	0.69154	<0.0001	2.00	(1.49–2.67)
Men [So(10)=0.88936]				
Log of age	3.06117	<0.0001	21.35	(14.03–32.48)
Log of total cholesterol	1.12370	<0.0001	3.08	(2.05–4.62)
Log of HDL cholesterol	−0.93263	<0.0001	0.39	(0.30–0.52)
Log of SBP if not treated	1.93303	<0.0001	6.91	(3.91–12.20)
Log of SBP if treated	1.99881	<0.0001	7.38	(4.22–12.92)
Smoking	0.65451	<0.0001	1.92	(1.65–2.24)
Diabetes	0.57367	<0.0001	1.78	(1.43–2.20)

So(10) indicates 10-year baseline survival; SBP, systolic blood pressure.
*Estimated regression coefficient

SCORE - European High Risk Chart

10 year risk of fatal CVD in high risk regions of Europe by gender, age, systolic blood pressure, total cholesterol and smoking statu




http://assign-score.whitespacers.com/estimate-the-risk/
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Estimate the Risk: NHS Scotland clinical use
Estimate the Risk: for ASSIGN visitors
Risk factors
Calculation format
Family history
Scottish Index of Multiple Deprivation
ASSIGN score is
18
Estimate the Risk: NHS Scotland clinical use
Enter details in the fields to the right, then click Calculate.
Estimate the Risk for ASSIGN visitors
Current age
55
notes
Sex
M
F
Scottish Postcode
dd1 9sy
Based on the postcode entered a SIMD score of 29.42 has been calculated.
Family history of CHD/Stroke
N
Y
Diabetes
Cigarettes smoked daily
10
use mean
Systolic Blood Pressure
140
Total cholesterol
6.5
HDL Cholesterol
1.3
ASSIGN Score:
18

BMJ

RESEARCH

Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2

Julia Hippisley-Cox, professor of clinical epidemiology and general practice,[1] Carol Coupland, senior lecturer in medical statistics,[1] Yana Vinogradova, research fellow in medical statistics,[1] John Robson, senior lecturer in general practice,[2] Rubin Minhas, coronary heart disease lead,[3] Aziz Sheikh, professor of primary care research and development,[4] Peter Brindle, research and development strategy lead[5]

Included variables

- Self assigned ethnicity (white/not recorded, Indian, Pakistani, Bangladeshi, other Asian, black African, black Caribbean, Chinese, other including mixed)
- Age (years)
- Sex (males *v* females)
- Smoking status (current smoker, non-smoker (including ex-smoker))
- Systolic blood pressure[18] (continuous)
- Ratio of total serum cholesterol/high density lipoprotein cholesterol[18] (continuous)
- Body mass index (BMI)[12] (continuous)
- Family history of coronary heart disease in first degree relative under 60 years[12] (yes/no)
- Townsend deprivation score[12] (output area level 2001 census data evaluated as a continuous variable)
- Treated hypertension[12] (diagnosis of hypertension and at least one current prescription of at least one antihypertensive agent)
- Rheumatoid arthritis[29] (yes/no)
- Chronic renal disease[30] (yes/no)
- Type 2 diabetes[18] (yes/no)
- Atrial fibrillation[31 32] (yes/no)

CVD?

INDANA risk score (Pocock, BMJ 2001): CVD death

The Framingham Heart Study defines CVD as a composite of CHD (coronary death, myocardial infarction, coronary insufficiency, and angina), cerebrovascular events (including ischemic stroke, hemorrhagic stoke, and transient ischemic attack), peripheral artery disease (intermittent claudication), and heart failure

QRISK2:

The primary outcome measure was the first recorded diagnosis of cardiovascular disease recorded on the general practice clinical computer system or their linked ONS death certificate during the study period. For this study, we included coronary heart disease (angina and myocardial infarction), stroke, or transient ischaemic attacks in the term cardiovascular disease but not peripheral vascular disease.

Endpoints for the A**SSIGN score** were *deaths from cardiovascular* causes (ICD-9 codes 390–459, ICD-10 codes I00-I99) or any hospital discharge diagnosis for *coronary heart disease* (ICD-9 410–414, ICD-10 I20-I25) or *cerebrovascular disease* (ICD-9 430–438, ICD-10 G45, I60-I69), or for *coronary artery interventions* (CABG or PTCA).

LENGTH?

Mostly 10 years, but…..

Predicting the 30-Year Risk of Cardiovascular Disease
The Framingham Heart Study

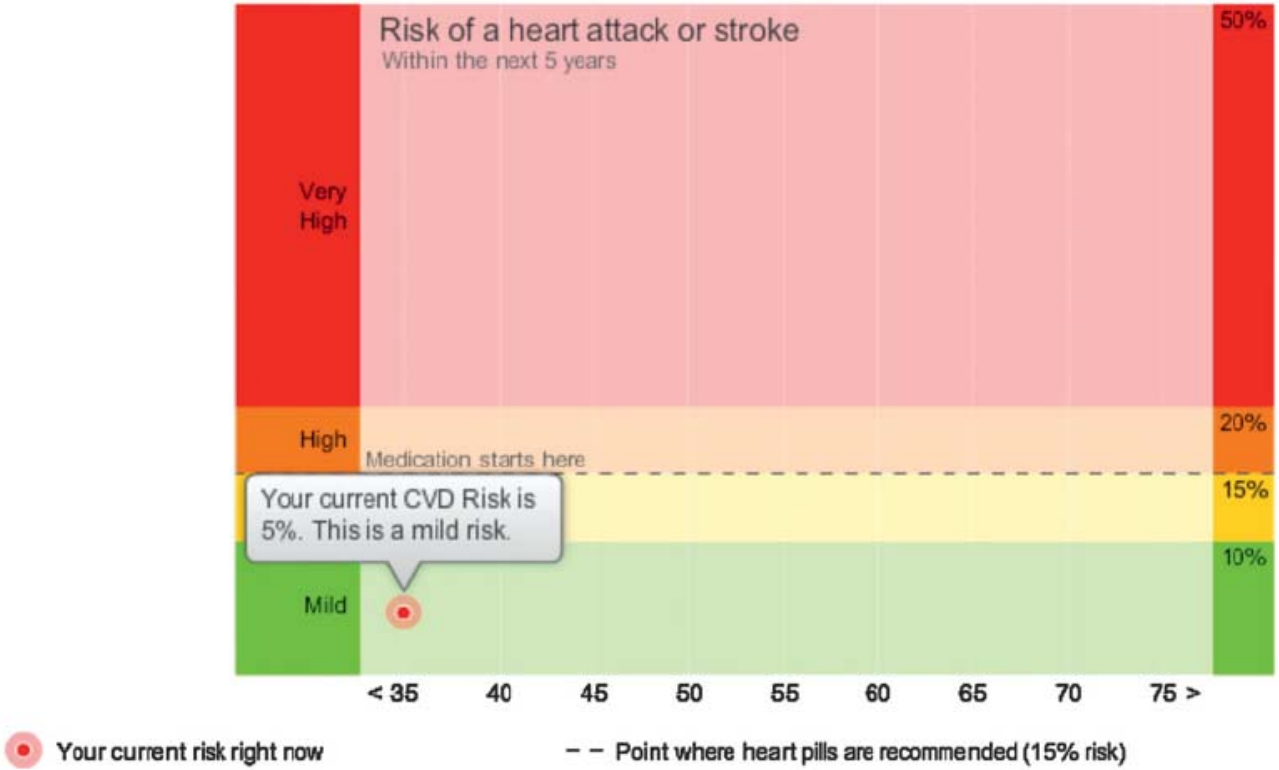
Michael J. Pencina, PhD; Ralph B. D'Agostino, Sr, PhD; Martin G. Larson, ScD; Joseph M. Massaro, PhD; Ramachandran S. Vasan, MD

Background—Present cardiovascular disease (CVD) risk prediction algorithms were developed for a ≈10-year follow up period. Clustering of risk factors at younger ages and increasing life expectancy suggest the need for longer-term risk prediction tools.

Methods and Results—We prospectively followed 4506 participants (2333 women) of the Framingham Offspring cohort aged 20 to 59 years and free of CVD and cancer at baseline examination in 1971–1974 for the development of "hard" CVD events (coronary death, myocardial infarction, stroke). We used a modified Cox model that allows adjustment for competing risk of noncardiovascular death to construct a prediction algorithm for 30-year risk of hard CVD. Cross-validated survival C statistic and calibration χ^2 were used to assess model performance. The 30-year hard CVD event rates adjusted for the competing risk of death were 7.6% for women and 18.3% for men. Standard risk factors (male sex, systolic blood pressure, antihypertensive treatment, total and high-density lipoprotein cholesterol, smoking, and diabetes mellitus), measured at baseline, were significantly related to the incidence of hard CVD and remained significant when updated regularly on follow-up. Body mass index was associated positively with 30-year risk of hard CVD only in models that did not update risk factors. Model performance was excellent as indicated by cross-validated discrimination C=0.803 and calibration χ^2=4.25 (P=0.894). In contrast, 30-year risk predictions based on different applications of 10-year functions proved inadequate.

Conclusions—Standard risk factors remain strong predictors of hard CVD over extended follow-up. Thirty-year risk prediction functions offer additional risk burden information that complements that of 10-year functions. (*Circulation*. 2009;119:3078-3084.)

Key Words: atherosclerosis ■ competing risk ■ lifetime risk ■ obesity ■ risk factors



NZ Heart Forecast

DATA SOURCE?

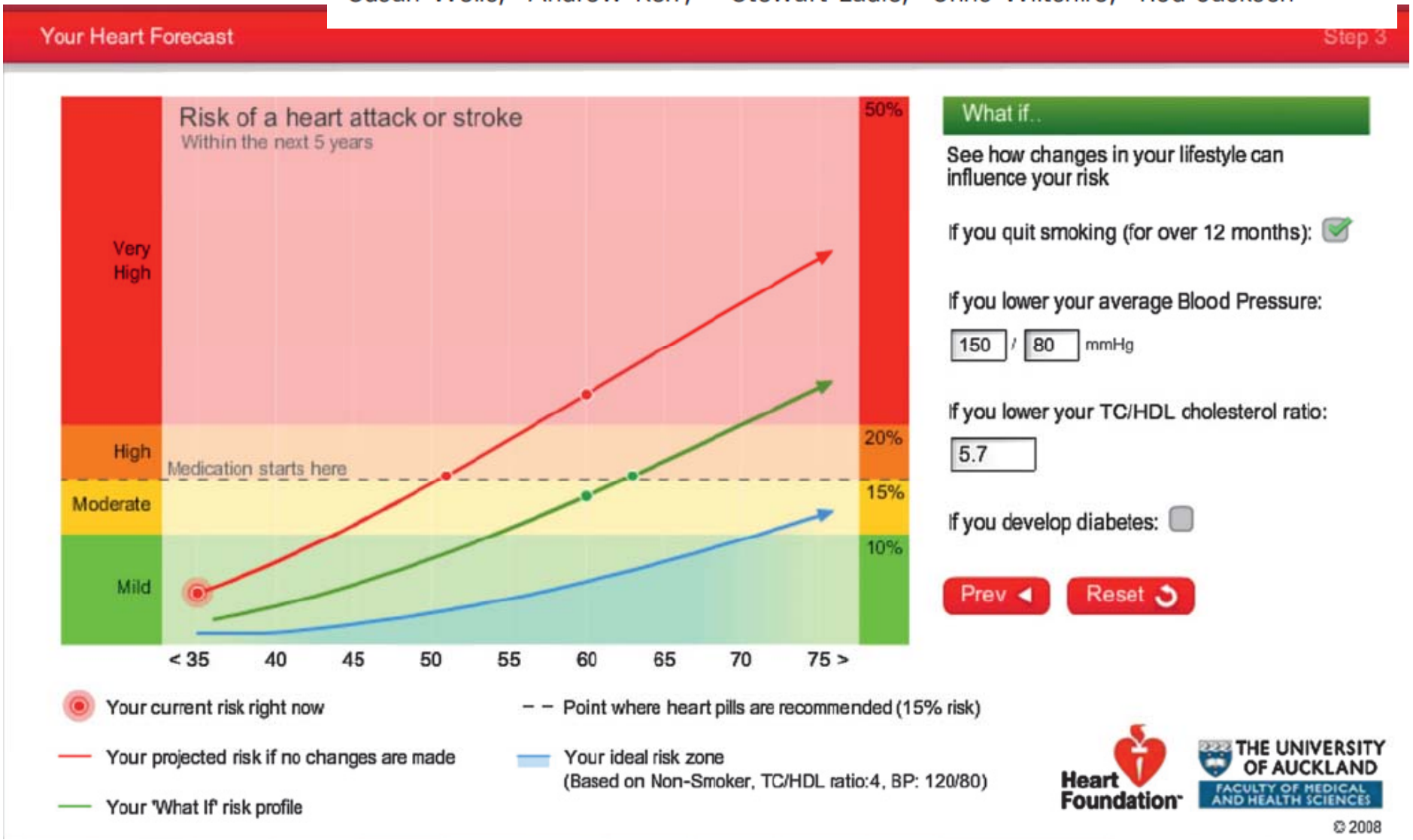
ASSIGN: cohort study in a general national population
Framingham: cohort study in a general regional population
INDANA risk score: 8 randomized clinical trials
INTERHEART score: Case-control study across multiple hospitals
QRISK: general practice register

NON-STANDARD USES OF RISK SCORES

- Shocking patients regarding harm
- Estimating benefit of change
- Balancing harm and benefit

'Your Heart Forecast': a new approach for describing and communicating cardiovascular risk?

Susan Wells,[1] Andrew Kerr,[1,2] Stewart Eadie,[3] Chris Wiltshire,[4] Rod Jackson[1]



Benefit score
(in preparation)

A Cardiovascular Disease Policy Model for Scotland: Part 1 – predicting life expectancy accounting for socio-economic deprivation

JD Lewsey[1], KD Lawson[1], I Ford[2], K Fox[3], LD Ritchie[4], H Tunstall-Pedoe[5], GCM Watt[6], M Woodward[7], S Kent[1], M Neilson[1], AH Briggs[1]

BMJ 2011;343:d5888 doi: 10.1136/bmj.d5888

Jupiter trial

RESEARCH

Johannes A N Dorresteijn *epidemiologist and medical doctor*[1], Frank L J Visseren *professor of vascular medicine, epidemiologist, and internist*[1], Paul M Ridker *Eugene Braunwald professor of medicine, epidemiologist, and cardiologist*[2], Annemarie M J Wassink *internist and postdoctoral researcher*[1], Nina P Paynter *assistant professor of epidemiology*[2], Ewout W Steyerberg *professor of medical decision making, and methodologist*[3], Yolanda van der Graaf *professor of epidemiology and imaging*[4], Nancy R Cook *associate professor of biostatistics and epidemiology*[2]

Estimating treatment effects for individual patients based on the results of randomised clinical trials

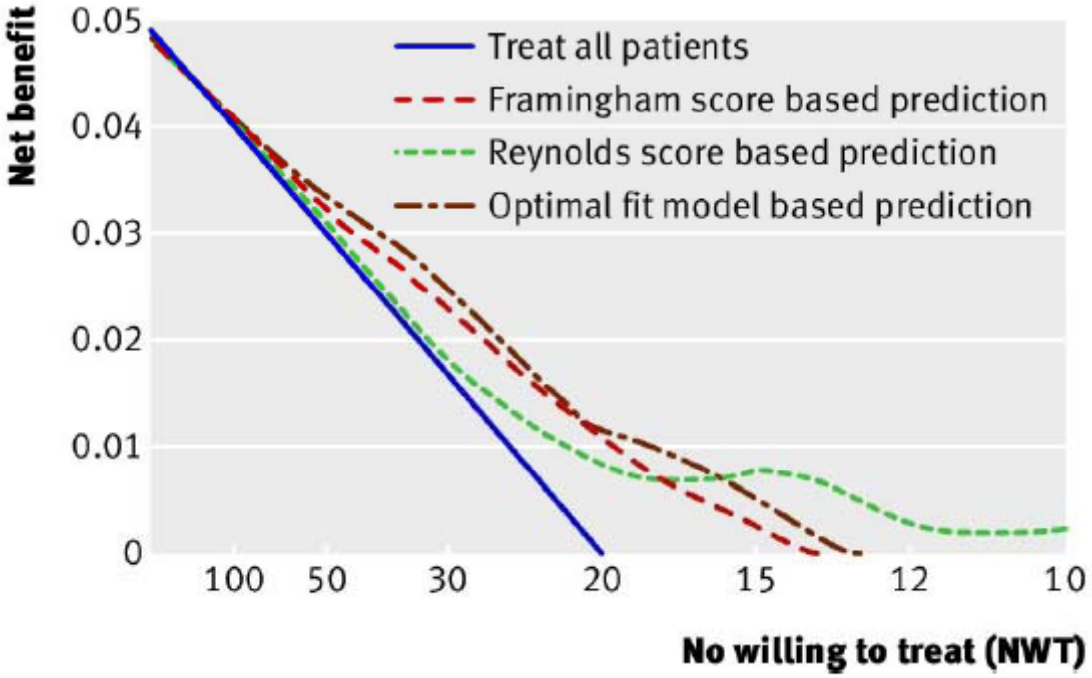


Fig 4 Decision curve: graphical representation of net benefit. For large values of numbers willing to treat (NWT), the net benefit of treating all patients is about equal to the net benefit of prediction based treatment. The net benefit of treating all patients becomes negative if the NWT is less than 20, whereas the net benefit of prediction based treatment is still positive for a NWT of 20 and converges to zero for smaller values of NWT

Problems with risk scores

- Used by busy docs?
- Accuracy at individual level?
- Dynamic?
- Account for treatment?

TREATMENT EFFECTS?

Cardiovascular risk scores do not account for the effect of treatment: a review

S M Liew,[1,2] J Doust,[3] P Glasziou[2,3]

Results 21 risk scores from 18 papers were identified from 3536 papers. Cohort size ranged from 4372 participants (SHS) to 1591209 records (QRISK2). More than half of the cardiovascular risk scores (11) were from studies with recruitment starting after 1980. Definitions and methods for measuring risk predictors and outcomes varied widely between scores. Fourteen cardiovascular risk scores reported data on prior treatment, but this was mainly limited to antihypertensive treatment. Only two studies reported prior use of lipid-lowering agents. None reported on prior use of platelet inhibitors or data on treatment drop-ins.

RELEVANCE?

The New York Times

Risk Calculator for Cholesterol Appears Flawed

By GINA KOLATA

Published: November 17, 2013

Last week, the nation's leading heart organizations released a sweeping new set of guidelines for lowering cholesterol, along with an online calculator meant to help doctors assess risks and treatment options. But, in a major embarrassment to the health groups, the calculator appears to greatly overestimate risk, so much so that it could mistakenly suggest that millions more people are candidates for statin drugs.

The calculator overpredicted risk by 75 to 150 percent, depending on the population.