

Supplementary Online Content

Shah AJ, Vaccarino V, Janssens ACJW, et al. An electrocardiogram-based risk equation for incident cardiovascular disease from the National Health and Nutrition Examination Survey. *JAMA Cardiol*. Published online August 3, 2016. doi:10.1001/jamacardio.2016.2173.

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Supplementary Information:

Traditional Risk Factors in NHANES I

Questionnaires assessed baseline medical history and included information about previous medical conditions, smoking status, and medication use in the past 6 months. Blood pressure was measured manually by a physician using standard techniques.¹ Frozen blood samples were sent to the Centers for Disease Control and Prevention for measurement of total serum cholesterol using standard techniques.²

Traditional Risk Factors in NHANES III

Diabetes mellitus and smoking status were defined by self-report during an interview by a trained examiner. Additional diabetes criteria included glucose \geq 126, or hemoglobin A1c of \geq 6.5%. Blood pressure was determined by the average of 3 measurements in the examination centers and 3 measurements during the interview. Total cholesterol was measured using commonly available reagents (cat. no 816302 from Boehringer Mannheim). Missing covariate data were imputed based on established methods.³

ECG Processing for NHANES I

Participants who received an ECG were part of a pre-specified subgroup who received an extended examination. Twelve-lead ECG's were collected using Beckman Digicorders, which recorded at 500 samples per second (resolution 2 milliseconds, ms). Visual inspection of the ECG was performed in real time, and recording was repeated if necessary. Digital measurement of intervals and vectors was performed by a trained technician on a large-screen Tektronix

computer terminal. The ECG segments were processed by the Dalhousie Novacode ECG program, which used selective averaging to derive a representative P-QRS-T complex for calculation of vector angles.⁴

Major ECG abnormalities were defined based on Minnesota codes as follows:

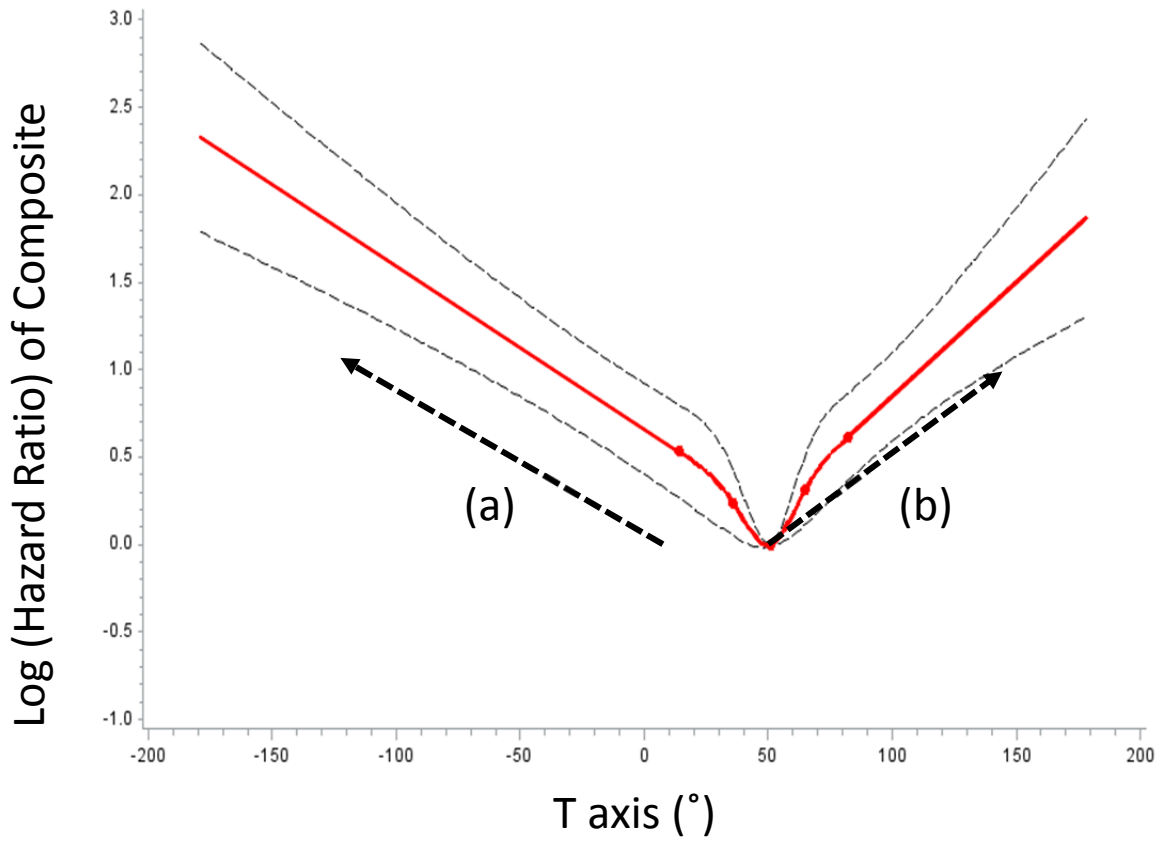
Major Q/QS waves (1.1, 1.2), ST depression (4.1, 4.2), negative T waves (5.1, 5.2), ventricular conduction defect (7.1, 7.2, or 7.4), atrial fibrillation/flutter (8.3), or ST elevation (9.2). Minor ECG abnormalities were defined as having

Minnesota codes for Minor Q waves (1.2.8 or 1.3), high R waves (3.1 or 3.3), minor ST changes (4.3 or 4.4), minor T wave changes (5.3 or 5.4), prolonged PR interval (6.3), RR' in V1 or V2 (7.3 or 7.5), or left anterior fascicular block (7.7).

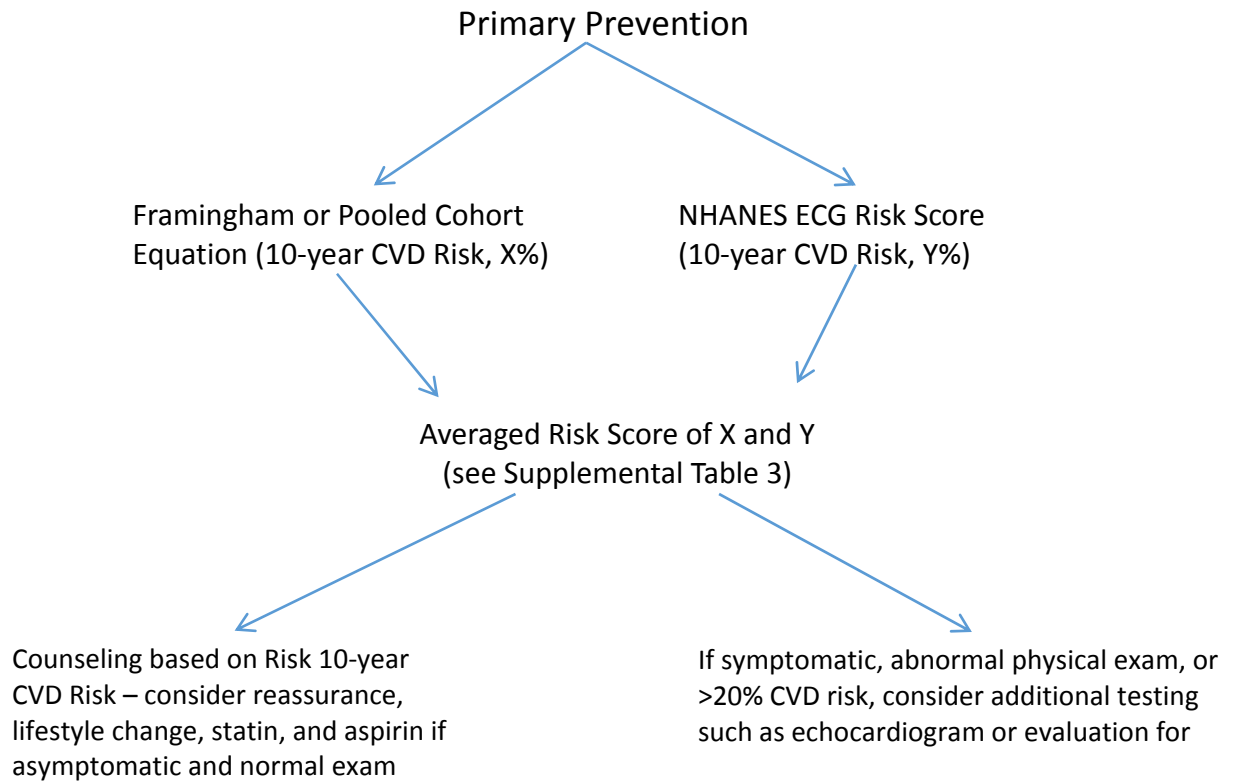
References

1. Pergola PE, White CL, Graves JW, et al. Reliability and validity of blood pressure measurement in the Secondary Prevention of Small Subcortical Strokes study. *Blood Press Monit.* 2007;12(1):1-8.
2. Myers GL, Cooper GR, Winn CL, Smith SJ. The Centers for Disease Control-National Heart, Lung and Blood Institute Lipid Standardization Program. An approach to accurate and precise lipid measurements. *Clinics in laboratory medicine.* 1989;9(1):105-135.
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4. Rautaharju PM, MacInnis PJ, Warren JW, Wolf HK, Rykers PM, Calhoun HP. Methodology of ECG interpretation in the Dalhousie program; NOVACODE ECG classification procedures for clinical trials and population health surveys. *Methods of information in medicine.* 1990;29(4):362-374.

eFigure 1. Association Between T Axis and Major Adverse Cardiovascular Events in the NHANES I Cohort (spline knots at 1%, 25%, 50%, 75%, and 99%)



eFigure 2. Potential Integration of NHANES ECG Risk Score Into Clinical Workflow



eTable 1. Model Coefficients With Traditional Risk Factors and New ECG in Derivation NHANES I Cohort

	B	SE	Chi-Square	p	Hazard Ratio
Age (years)	0.068	0.006	152	<.0001	n/a
Male Sex	1.543	0.427	13	0.0003	n/a
Age x Male	-0.016	0.007	5	0.0219	n/a
Diabetes	0.624	0.115	29	<.0001	1.867
Systolic Blood Pressure (mmHg)	0.012	0.001	71	<.0001	1.012
Blood Pressure Medication	0.139	0.102	2	0.1719	1.15
Current Smoker	0.487	0.067	52	<.0001	1.628
Total Cholesterol (mg/dL)	0.003	0.001	22	<.0001	1.003
T Axis (positive deflection > 45°)	0.006	0.002	17	<.0001	1.006
T Axis (negative deflection < 45°)	0.006	0.002	13	0.0003	1.006
Heart Rate (beats/min)	0.009	0.003	14	0.0002	1.009
Corrected QT interval (ms)	0.006	0.002	13	0.0003	1.006

eTable 2. Summary of Performance Improvement by Addition of the NHANES ECG Risk Equation to Models

Baseline Model, Including FRS	C-statistic			Net Reclassification Index Total (Event, Non-Event)		IDI	
	Baseline Model	Baseline + NHANES ECG Score	Difference	Categorical	Continuous	Abs.	Rel.
Left Ventricular Hypertrophy	0.76 (0.73-0.78)	0.80 (0.78-0.83)	0.04 (0.02-0.06)	25% (12%, 13%)	57% (22%, 35%)	1.6%	34%
Major/Minor ECG Abnormalities	0.77 (0.74-0.79)	0.80 (0.78-0.82)	0.03 (0.02-0.05)	21% (10%, 11%)	52% (21%, 31%)	1.3%	25%
Cardiac Injury/Infarction Score	0.78 (0.76-0.81)	0.81 (0.78-0.84)	0.03 (0.02-0.05)	21% (11%, 10%)	50% (21%, 29%)	1.1%	20%
ECG Simple Score	0.77 (0.75-0.80)	0.80 (0.78-0.83)	0.03 (0.02-0.04)	21% (11%, 10%)	49% (18%, 31%)	1.1%	23%

Models Include the Framingham Risk Score and Left Ventricular Hypertrophy, Major/Minor ECG Abnormalities, Cardiac Infarct/Injury Score, and the ECG Simple Score.

Abbreviations: FRS=Framingham Risk Score; IDI=Integrated Discrimination Improvement; Abs.=Absolute, Rel.=Relative

eTable 3. Automated ECG Risk Calculator for Clinical Practice

Age	65
Sex (male=1, female=0)	1
Heart Rate (BPM)	60
QT interval (ms)	400
T axis (degrees)	45
10 year risk of Fatal/Non-Fatal CVD	13.5%
10 year risk of CVD Death	2.9%
10 year risk of Death	10.8%
CVD Risk Based on Traditional Risk Factors (from Framingham or Pooled Cohort Equation, if available)	8.0%
Cumulative Risk of Fatal/Non-Fatal CVD	10.4%

Located online <http://1drv.ms/1Ket2zI>.

Instructions: The user inputs age, sex, heart rate, QT interval, and T axis. The 10-year risks of various outcomes can then be calculated as shown. Furthermore, if the risk from FRS or the Pooled Cohort Equation is available, then this can be averaged together with the ECG risk to provide a cumulative risk by multiplying the odds ratios.