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Electrocardiographic Changes Improve Risk Prediction in Asymptomatic Persons Age 65 Years or Above Without Cardiovascular Disease

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ABSTRACT

BACKGROUND Risk prediction in elderly patients is increasingly relevant due to longer life expectancy.

OBJECTIVES This study sought to examine whether electrocardiographic (ECG) changes provide prognostic information incremental to current risk models and to the conventional risk factors.

METHODS In all, 6,991 participants from the Copenhagen Heart Study attending an examination at age ≥65 years were included. ECG changes were defined as Q waves, ST-segment depression, T-wave changes, ventricular conduction defects, and left ventricular hypertrophy based on the Minnesota code. The primary endpoint was fatal cardiovascular disease (CVD) event and the secondary was fatal or nonfatal CVD event. In our study, 2,236 fatal CVD and 3,849 fatal or nonfatal CVD events occurred during a median of 11.9 and 9.8 years of follow-up.

RESULTS ECG changes were frequently present (30.6%) and associated with conventional risk factors. All ECG changes except 1 univariably predicted both endpoints. Event rates of ECG changes versus no ECG changes were respectively 41.4% versus 27.8% and 64.6% versus 50.8%. When added to existing risk scores, ECG changes independently increased the risk of both endpoints. Fatal CVD events: hazard ratio (HR): 1.33 (95% confidence interval [CI]: 1.29 to 1.36; $p < 0.001$) and fatal or nonfatal CVD events: HR: 1.21 (95% CI: 1.19 to 1.24; $p < 0.001$). When added to conventional risk factors, continuous net reclassification improvement was 42.3% (95% CI: 42.0 to 42.4; $p < 0.001$) for fatal and 29.2% (95% CI: 28.4 to 29.2; $p < 0.001$) for fatal or nonfatal events. Categorical net reclassification was 7.1% (95% CI: 6.7 to 9.0; $p < 0.001$) for fatal and 4.2% (95% CI: 3.5 to 5.6; $p < 0.001$) for fatal or nonfatal events.

CONCLUSIONS Simple assessment of the existence of ECG changes improves risk prediction in the general population of persons age ≥65 years. (J Am Coll Cardiol 2014;64:898–906) © 2014 by the American College of Cardiology Foundation.

By 2050, 25% of persons alive in the Western world are expected to be ≥65 years (1). This demographic transition will be a major socioeconomic challenge in the coming decades and all possible efforts undertaken to minimize the morbidity of this increasingly growing population are needed to limit healthcare expenses and facilitate later retirement from the labor market.

Cardiovascular disease (CVD) will remain a leading cause of morbidity in the Western world (2), and in this context, preventing its occurrence in the healthy, older persons at increased risk is essential. However, little is known on how to perform individual risk assessment in this age group. Risk prediction models that are otherwise recommended for this purpose in the middle-age population are not

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suitable in older persons, as they are derived from populations of none or only few persons age ≥65 years (3,4). Moreover, conventional risk factors are not as influential in the development of CVD in this age group as they are in the middle-age population (5), and consequently, other risk markers are needed.

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Electrocardiographic (ECG) changes carry a large potential of such a marker. Their prevalence increases rapidly in this age group (6); they are easily assessed in most clinical settings; and they are a marker of direct pathology, representing at least some level of subclinical, cardiac impairment. In addition, the past 50 years, a number of studies have shown that ECG changes are strongly associated with future CVD in persons who are not previously diagnosed with the condition (7–12).

Although use of the ECG in risk prediction is not currently recommended in asymptomatic individuals (13), it may be very well suited for this purpose in the subgroup of persons age ≥65 years. Therefore, we hypothesized that risk prediction of persons age ≥65 years would be improved by adding ECG changes. To test this, we examined whether adding ECG changes to the European Heart Score (3), the Framingham Global Risk Score (14), and the conventional risk factors would contribute with incremental prognostic information and improve risk prediction.

METHODS

STUDY COHORT. The Copenhagen City Heart Study was initiated during a 2-year period from 1976 to 1978. At that time, a random sample of 19,329 mainly white Caucasians living within a well-defined area of the inner Copenhagen City Boundary was randomly selected and invited to participate (participation rate: 74% [n = 14,223]). In the subsequent examinations, the surviving participants were invited again, and the cohort was supplemented with persons from the younger strata (Figure 1). For the present purpose, only persons who have attended an examination at an age ≥65 years and were free from CVD at the time of the examination were included. Persons with missing ECG were excluded.

All subjects gave informed consent to participate, and the Regional Ethical Committee for Medical Research in Copenhagen approved the study.

CONVENTIONAL RISK FACTORS. Conventional risk factors were defined as risk factors from either the European Heart Score or the Framingham Global Risk Score, which include the following: increasing age; systolic blood pressure; total cholesterol; male sex; current smoking; and diabetes. They were assessed as follows. Blood pressure was measured after 5 min of rest using the left arm with a cuff adjusted to arm circumferential. Smoking status was self-reported. Total cholesterol was measured at all examinations,

ABBREVIATIONS AND ACRONYMS

CI = confidence interval
CVD = cardiovascular disease
ECG = electrocardiogram/electrocardiographic
HR = hazard ratio
ICD = International Classification of Diseases
IQR = interquartile range
NRI = net reclassification index

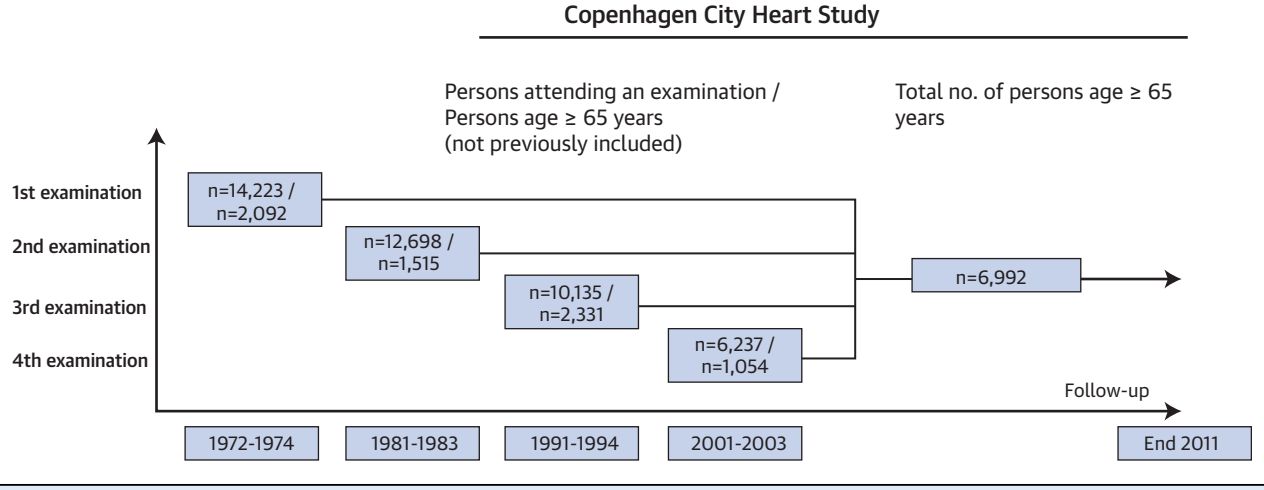
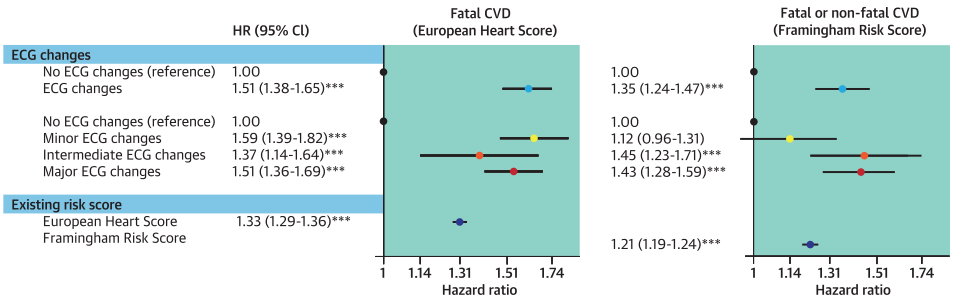


FIGURE 1 Participants Included in the Present Cohort of Persons Age ≥65 Years

For each examination, the total number of persons attending and the total number of persons age ≥65 years are shown. The persons age ≥65 years were pooled in the present cohort. A person could only be included once in the present cohort.



CENTRAL ILLUSTRATION Forest Plots of Different Risk Models, All With Information on ECG Changes With Regard to Fatal and the Combination of Fatal or Nonfatal CVD in Persons Age ≥65 Years

The effect of electrocardiographic (ECG) changes when adjusted for estimates of calculated risks of either the European Heart Score model or the Framingham Global Risk Score. Hazard ratios (HR) displayed: European Heart Score and Framingham Global Risk Score per 10% increase in predicted risk by the corresponding model. Levels of significance: *p < 0.05, **p < 0.01, and ***p < 0.001. CI = confidence interval; CVD = cardiovascular disease.

TABLE 1 Baseline Characteristics

	No ECG Changes (n = 4,851)	ECG Changes (n = 2,140)	p Value	Minor ECG Changes (n = 624)	Intermediate ECG Changes (n = 353)	Major ECG Changes (n = 1,163)	p Value
Conventional risk factors							
Age, yrs	69.5 ± 3.5	70.2 ± 4.1	<0.001	69.9 ± 3.7	70.4 ± 4.0	70.3 ± 4.4	<0.001
Males	1,893 (39.0)	986 (46.1)	<0.001	276 (44.2)	125 (35.4)	585 (50.3)	<0.001
Current smoking	2,232 (46.4)	1,017 (47.8)	0.28	293 (47.4)	174 (49.6)	550 (47.5)	0.63
Systolic BP, mm Hg	146.9 ± 20.5	157.4 ± 24.2	<0.001	154.1 ± 22.0	154.6 ± 22.8	160.1 ± 25.5	<0.001
Diastolic BP, mm Hg	83.5 ± 11.6	87.2 ± 13.4	<0.001	85.9 ± 12.6	86.6 ± 12.3	88.1 ± 14.2	<0.001
Total cholesterol, mmol/l	6.3 ± 1.2	6.3 ± 1.3	0.21	6.5 ± 1.3	6.5 ± 1.4	6.2 ± 1.2	<0.001
Body mass index, kg/m^2	26.0 ± 4.3	26.2 ± 4.3	0.25	27.0 ± 4.5	26.1 ± 4.4	25.8 ± 4.2	<0.001
Diabetes mellitus	208 (4.4)	151 (7.2)	<0.001	55 (9.0)	20 (5.8)	76 (6.7)	<0.001
Resting heart rate, beats/min	73.3 ± 13.2	75.3 ± 14.0	<0.001	75.6 ± 13.1	75.2 ± 13.2	75.3 ± 14.7	<0.001
Estimated risks using existing scores							
SCORE risk model, %	13.1 (8.0–21.1)	18.3 (10.7–29.6)	<0.001	16.8 (10.5–30.0)	17.4 (9.9–27.6)	19.5 (11.1–32.3)	<0.001
Framingham Global Risk, %	25.9 (16.9–39.9)	33.4 (21.6–51.1)	<0.001	33.7 (21.6–51.9)	32.4 (20.2–48.5)	33.9 (22.0–51.4)	<0.001
ECG changes							
Q waves							
Present		161 (7.5)		53 (8.4)	60 (17.0)	48 (4.1)	
Minor		81 (3.8)		53 (8.4)	10 (2.8)	18 (1.6)	
Intermediate		62 (2.9)			50 (14.2)	12 (1.0)	
Major		18 (0.8)				18 (1.6)	
ST-segment depressions							
Present		616 (28.8)		106 (17.0)	248 (70.3)	262 (22.5)	
Minor		204 (9.5)		106 (17.0)	55 (15.6)	43 (3.7)	
Intermediate		294 (13.7)			193 (54.7)	101 (8.7)	
Major		118 (5.5)				118 (10.1)	
T waves							
Present		1,255 (58.6)		577 (92.5)	313 (88.7)	365 (31.4)	
Minor		845 (39.4)		577 (92.5)	117 (33.1)	151 (13.0)	
Intermediate		388 (18.1)			196 (55.5)	192 (16.5)	
Major		22 (1.0)				22 (1.9)	
Ventricular conduction defects		254 (11.9)					
Left ventricular hypertrophy		850 (39.7)					

Values are mean ± SD, n (%), or median (interquartile range).
BP = blood pressure; ECG = electrocardiogram; SCORE = Systematic Coronary Risk Evaluation.

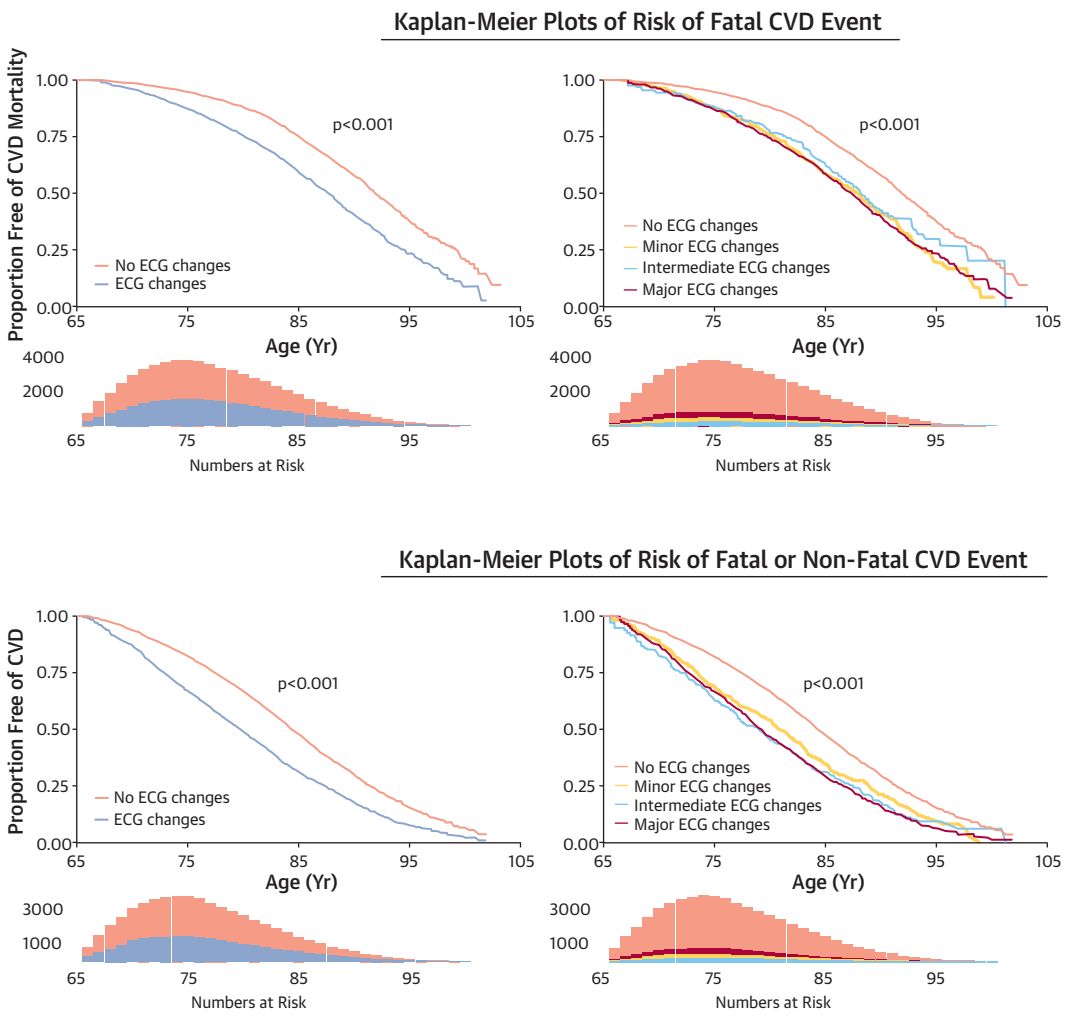


FIGURE 2 Kaplan-Meier Plots

Kaplan-Meier plots of proportion free of fatal cardiovascular disease (CVD) and proportion free of fatal or nonfatal CVD stratified by presence and severity of electrocardiographic (ECG) changes, respectively.

whereas measurement of high-density lipoprotein cholesterol was not available at the first examination and only measured on a subgroup of the persons at the second examination. Diabetes mellitus was defined as plasma glucose concentration ≥11.1 mmol/l, use of insulin, other antidiabetic medicine, or self-reported disease (15,16). Resting heart rate was read from the ECG.

KNOWN CVD. Known CVD was self-reported and cross-validated with the highly validated Danish National Board of Health's National Patient Registry using International Classification of Diseases (ICD)-8 codes (before 1994): 410 to 414 (ischemic heart disease), 430 to 438 (stroke), and 440 to 441 and 444 (peripheral atherosclerotic disease), or ICD-10 codes (after 1994): I20 to I25 (ischemic heart disease), I46 (cardiac arrest), I50 (heart failure), I60 to I68 (stroke), and I70 to -I72 and I74 (peripheral atherosclerotic disease). However, because the National Patient Registry was not established until 1977, validation in the first and second examination was done by reviewing medical files at general practitioners.

ECG. At inclusion, a 12-lead ECG was obtained on all individuals and coded according to the Minnesota Code Classification system (17,18). Two independent reviewers reviewed all, and in cases of disagreement, a third reviewer adjudicated. ECG changes were defined as Q waves (1.1.x to 1.3.x), ST-segment

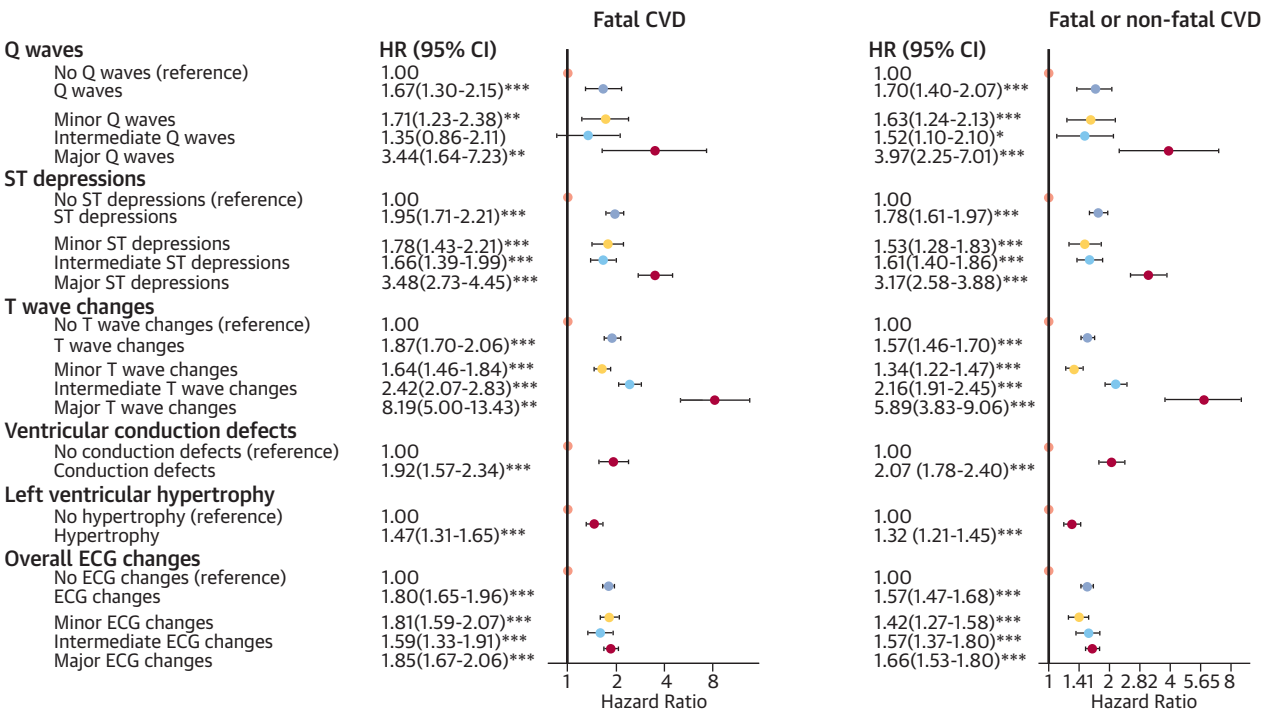


FIGURE 3 Forest Plots of Univariable Analyses of ECG Changes

Univariable analyses of the associations of each ECG change and the combined ECG changes with the endpoints of fatal CVD and the combination of fatal or nonfatal CVD. Levels of significance: *p < 0.05, **p < 0.01, and ***p < 0.001. CI = confidence interval; HR = hazard ratio; other abbreviations as in Figure 2.

depressions (4.1 to 4.3), T-wave changes (5.1 to 5.3), left ventricular conduction defects (7.1.x and 7.2.x), and left ventricular hypertrophy (3.1 and 3.2). If present, the 2 latter changes were regarded as major ECG changes. In case >1 ECG change was coded, the lowest value (i.e., the largest ECG change) determined the class.

ENDPOINTS. Two equal endpoints were used to reflect both European and U.S. guidelines: fatal CVD and the combination of fatal or nonfatal CVD. Additionally, all-cause mortality was used in supplemental analyses. The Danish National Board of Health's National Patient Registry and Register of Cause of Death was used to obtain the CVD events defined as death or admission with the above-mentioned ICD-8 and ICD-10 codes.

STATISTICAL ANALYSES. Absolute 10-year risk of fatal CVD and 10-year risk of the combination of fatal or nonfatal CVD as estimated by the European Heart Score and the Framingham Global Risk Score, respectively, were calculated on all participants using previously published formulas (3,14). Missing values of high-density lipoprotein cholesterol for calculation of Framingham Global Risk Score was set to the mean value of the remaining participants.

Multivariable analyses shown in the **Central Illustration** were performed using Cox proportional hazards regression models using all available follow-up and with adjustments for European Heart Score, Framingham Global Risk Score (with corresponding endpoints), or conventional risk factors with both endpoints (fatal CVD and the combined endpoint of fatal or nonfatal CVD). Non-CVD mortality also was considered as a competing risk, the results of which are shown in Online Figure 1.

MODEL VALIDATION AND DISCRIMINATION. Cox models were internally validated using bootstrapping with 10,000 samples, and the estimates were corrected for optimism. Confidence intervals were calculated using bias-corrected and accelerated

TABLE 2 Comparison Between Models With and Without ECG Changes and Resting Heart Rate

	Fatal CVD Events			Fatal or Nonfatal CVD Events		
	C-Index (95% CI)	Continuous NRI (%) (95% CI)	Categorical NRI (%) (95% CI)	C-Index (95% CI)	Continuous NRI (%) (95% CI)	Categorical NRI (%) (95% CI)
Conventional risk factors	0.705 (0.687-0.723)			0.651 (0.639-0.663)		
Conventional risk factors and						
Q waves						
As present or not	0.709 (0.691-0.727)*	5.3 (-0.02 to 12.9)	1.9 (0.7-3.1)†	0.655 (0.643-0.667)†	3.9 (-1.6 to 9.5)	0.7 (-0.2 to 1.8)
With increasing severity	0.710 (0.692-0.727)*	6.3 (-0.01 to 14.0)	2.1 (0.9-3.3)‡	0.655 (0.643-0.667)†	5.3 (-0.3 to 10.8)	0.9 (0.0-1.9)*
ST-segment depressions						
As present or not	0.714 (0.697-0.732)‡	18.0 (10.4-25.6)‡	3.1 (0.7-5.4)*	0.660 (0.648-0.672)‡	14.7 (9.1-20.3)‡	2.2 (0.4-4.1)*
With increasing severity	0.717 (0.699-0.734)‡	18.5 (10.8-26.5)‡	3.5 (1.1-6.5)†	0.661 (0.649-0.673)‡	15.2 (9.7-20.8)‡	2.3 (0.5-4.0)*
T-wave changes						
As present or not	0.716 (0.699-0.734)‡	29.2 (21.5-36.8)‡	5.4 (2.2-8.6)†	0.658 (0.647-0.670)‡	20.3 (14.7-25.9)‡	2.7 (0.6-4.8)*
With increasing severity	0.720 (0.702-0.732)‡	29.3 (21.6-36.9)‡	5.0 (1.8-8.3)†	0.662 (0.651-0.674)‡	20.2 (14.6-25.8)‡	3.3 (1.3-5.4)†
Ventricular conduction defect	0.708 (0.690-0.726)	2.8 (-4.9-10.4)	1.1 (0.1-2.1)*	0.655 (0.643-0.667)†	5.5 (-0.1 to 11.1)	0.0 (-1.1 to 1.2)
Left ventricular hypertrophy	0.706 (0.688-0.724)	12.1 (4.5-19.8)†	2.7 (1.0-4.4)†	0.651 (0.639-0.663)	6.7 (1.1-12.3)*	-1.1 (-2.3 to 0.1)
Resting heart rate	0.709 (0.691-0.727)†	14.1 (6.4-21.7)‡	0.9 (-1.8 to 3.7)	0.652 (0.640-0.664)	7.3 (1.8-12.9)*	-0.2 (-1.4 to 1.0)
ECG changes						
As present or not	0.719 (0.702-0.737)‡	42.3 (34.7-50.0)‡	7.1 (3.6-10.6)‡	0.660 (0.648-0.672)‡	29.1 (23.6-34.7)‡	3.8 (1.4-6.3)†
With increasing severity	0.719 (0.702-0.736)‡	42.3 (34.7-50.0)‡	7.2 (3.7-10.7)‡	0.660 (0.648-0.671)‡	29.2 (23.7-34.8)‡	4.2 (1.8-6.7)‡
ECG changes and resting heart rate						
As present or not	0.722 (0.705-0.740)‡	35.6 (28.0-43.3)‡	6.7 (3.0-10.3)‡	0.661 (0.649-0.672)‡	29.9 (24.3-34.5)‡	3.5 (1.0-6.0)†
With increasing severity	0.722 (0.705-0.740)‡	34.8 (27.3-42.5)‡	6.5 (2.9-10.1)‡	0.661 (0.649-0.673)‡	29.5 (24.0-35.1)‡	3.5 (0.9-5.9)†

Levels of significance: *$p < 0.05$, †$p < 0.01$, and ‡$p < 0.001$.
CI = confidence interval; CVD = cardiovascular disease; ECG = electrocardiogram; NRI = net reclassification index.

bootstrapping. Cox model discrimination was assessed using the C-statistics and categorical and continuous net reclassification index (NRI). These statistics require a binary response, so the persons with <10 years of follow-up were excluded. Adding all ECG changes as present or not was marginally better judged by the clinically relevant NRI. For that reason and for the sake of simplicity, the equations presented for calculating absolute risks are based on these models. Also, they were used for creating risk categories for categorical NRI for both endpoints.

All statistical calculations were made using R for Mac (version 2.15.3, R Project for Statistical Computing, Vienna University of Economics and Business Administration, Wien, Austria).

RESULTS

In all, 6,991 persons, age ≥65 years and without known CVD, were identified from the 4 examinations in the Copenhagen City Heart Study (Figure 1). For the additional endpoint of all-cause mortality, follow-up was available until April 23, 2013. There were no persons lost to follow-up, and the median follow-up time was 11.9 years (interquartile range [IQR]: 8.2 to 18.1, range 0.02 to 35.5) for fatal CVD and 9.8 years (IQR: 5.7 to 15.9, range 0.01 to 35.4) for the combination of fatal or nonfatal CVD. During follow-up, 2,236 persons reached the endpoint of fatal CVD, and 3,849 persons reached the combined endpoint of fatal or nonfatal CVD, yielding event rates of ECG changes versus no ECG changes of

TABLE 3 Model Validation

	Conventional Risk Factors	Conventional Risk Factors and ECG Changes	p Value
Fatal CVD events			
C-index	0.705 (0.703-0.707)	0.719 (0.717-0.721)	
Adjusted for optimism	0.706	0.720	<0.001
Continuous NRI, %		42.3 (42.0-42.4)	
Adjusted for optimism		42.3	<0.001
Categorical NRI, %*		7.1 (6.7-9.0)	
Adjusted for optimism		8.6	<0.001
Fatal or nonfatal CVD events			
C-index	0.651 (0.649-0.653)	0.660 (0.658-0.662)	
Adjusted for optimism	0.652	0.660	<0.001
Continuous NRI, %		29.2 (28.4-29.2)	
Adjusted for optimism		29.2	<0.001
Categorical NRI (%)†		4.2 (3.5-5.6)	
Adjusted for optimism		4.7	<0.001

Parenthetical values are 95% CI. Risk categories are based on tertiles of predicted risks using models with ECG changes as present or not. Optimism estimates are obtained by bootstrapping 10,000 samples and CI by bias-corrected and accelerated bootstrapping of 10,000 samples. *Risk categories: low risk: <8.9%; intermediate risk: 8.9% to 14.9%; high risk: >14.9%. †Risk categories: low risk: <25.9%; intermediate risk: 25.9% to 36.6%; high risk: >36.6%.

Abbreviations as in Tables 1 and 2.

41.4% versus 27.8% and 64.6% versus 50.8%, respectively. For the additional endpoint of all-cause mortality, median follow-up was 11.9 years (IQR: 8.2 to 18.7, range 0.02 to 36.8), 5,626 events occurred with event rates of 87.9% (ECG changes) versus 71.2% (no ECG changes). The baseline characteristics of the study population are shown in Table 1.

UNADJUSTED ANALYSES. ECG changes were found in 30.6% of the participants at baseline. The distribution of Q waves, ST-segment depressions, T-wave changes, left ventricular conduction defects, and left ventricular hypertrophy in the combined ECG changes are shown in Table 1. Kaplan-Meier curves with age as the underlying time scale are shown in Figure 2 and Online Figure 2. ECG changes were significantly associated with both endpoints. Stratifying by sex showed similar results. Figure 3 and Online Figure 3 show univariable associations of ECG changes with fatal CVD, the combination of fatal and nonfatal CVD events, and the additional endpoint of all-cause mortality.

ADJUSTED ANALYSES. ECG changes remained significantly associated with both endpoints when included in a model with European Heart Score and Framingham Global Risk Score, respectively (Central Illustration). They remained significantly associated with both endpoints when included in a model with all conventional risk factors. Though less pronounced, the results were similar with the additional

TABLE 4 Calculating 10-Year Risk of Fatal CVD and of Fatal or Nonfatal CVD

Step 1. Calculate *I* using regression coefficients.	Regression coefficients for calculating *I*	
	Fatal CVD	Fatal or nonfatal CVD
$I = B_1 \times$ Age in years+	$B_1 = 0.0891$	$B_1 = 0.0752$
$B_2 \times$ Systolic blood pressure (mm Hg)+	$B_2 = 0.0101$	$B_2 = 0.0072$
$B_3 \times$ Current smoking (1 if "yes," 0 if "no")+	$B_3 = 0.4533$	$B_3 = 0.3424$
$B_4 \times$ Diabetes (1 if "yes," 0 if "no")+	$B_4 = 0.5570$	$B_4 = 0.5738$
$B_5 \times$ Total − cholesterol (mmol/l)+	$B_5 = 0.0337$	$B_5 = 0.0172$
$B_6 \times$ Sex (1 for man, 0 for woman)+	$B_6 = 0.4836$	$B_6 = 0.3728$
$B_7 \times$ ECG changes (1 if present, 0 if not)	$B_7 = 0.4117$	$B_7 = 0.3090$

Step 2. Calculate estimated risks.

Risk of fatal CVD $= 1 - 0.8791^{e^{I-8.4573}}$
Risk of fatal or nonfatal CVD $= 1 - 0.6811^{e^{I-6.8311}}$

Case.
A 70-year-old woman, current smoker, with a systolic blood pressure of 140 mm Hg, a total cholesterol of 5.1 mmol/l, no history of diabetes, and ECG changes

Risk of fatal CVD
$I = 70 \times 0.0891 + 140 \times 0.0101 + 1 \times 0.4533 + 0 \times 0.5570 + 5.1 \times 0.0337 + 0 \times 0.4836 + 1 \times 0.4117 = 8.6879$
Risk of fatal CVD $= 1 - 0.8791^{e^{8.6879-8.4573}} = 15\%$

Risk of fatal or nonfatal CVD
$I = 70 \times 0.0752 + 140 \times 0.0072 + 1 \times 0.3424 + 0 \times 0.5738 + 5.1 \times 0.0172 + 0 \times 0.3728 + 1 \times 0.3090 = 7.0111$
Risk of fatal or nonfatal CVD $= 1 - 0.6811^{e^{7.0111-6.8311}} = 37\%$

Abbreviations as in Tables 1 and 2.

endpoint of all-cause mortality (Online Figure 4). Adjusting for resting heart rate—that was also evaluated as a possible variable in the final model—and examination number in the above-mentioned models did not change the results. The same was the case when stratifying by sex. Also, no interactions were found between ECG changes and examination number on the risk of reaching the endpoints. Testing for interactions with age groups (<75 years, 75 to 84 years, and >85 years), and ECG changes showed a significant interaction of the 75 to 84 years age group with ECG changes for both endpoints.

COMPARING 10-YEAR RISK MODELS WITH AND WITHOUT ECG CHANGES. In all, 4,923 persons with ≥10 years of follow-up for the endpoint of fatal CVD (837 events) and 5,418 persons with ≥10 years of follow-up for the combined endpoint of fatal or nonfatal CVD (2,092 events) were found. For the additional endpoint of all-cause mortality, this number was 6,907 persons (2,225 events). C-index and categorical and continuous NRI for adding each ECG change and resting heart rate to the conventional risk factors are found in **Table 2** and Online Table 1. It is apparent, that though adding resting heart rate to the model with the conventional risk factors and ECG changes improved the C-index, the models without the resting heart rate had superior performance judged by the clinically relevant NRI. For this reason, the models with the conventional risk factors and the ECG changes were chosen as the final models. The results of the statistical tests for these models' discrimination based on 10,000 bootstrap samples are shown in **Table 3** and Online Table 2.

DISCUSSION

In this study, we have shown that CVD risk estimation of persons age ≥65 years can be improved by adding ECG changes to the conventional risk factors. Adding ECG changes as present or not is simplest and performed equally well with adding ECG changes with increasing severity and, therefore, was chosen as the most appropriate approach. Information needed to calculate predicted risks by this model is found in **Table 4**. Estimation of all-cause mortality was only marginally improved by adding ECG changes.

PREVIOUS EVIDENCE OF USE OF THE ECG IN RISK PREDICTION. The U.S. Preventive Services Task Force has recommended against use of routine ECG as a screening procedure based on a lack of evidence of clinical benefit (13). The task force, however, did request studies on how addition of ECG to conventional risk factors affects reclassification. A study by Auer et al. (19) recently examined the effects of major and minor ECG changes added to the conventional risk factors in persons age ≥65 years and found a correct reclassification on the endpoint of coronary heart disease in 7.4% of their population. The present study contributes with longer follow-up and expands the scope by providing means to predicting CVD in general. Additionally, as stated by the investigators, use of minor and major ECG abnormalities is hampered by the complexity of detailed ECG interpretation – a task not easily performed in daily clinical practice. However, just looking for the most well-known ECG changes is simpler and does not require careful division of changes into categories of severity.

CLINICAL IMPLICATIONS: A NEW ERA IN RISK PREDICTION? The only way of estimating individuals' absolute risks of developing CVD is by extrapolating risks from the former generations. Certainly, this is not the optimal solution as changes in absolute risks are affected by time-specific factors, such as contemporary lifestyle habits and health behaviors. The implication of this is that risk estimation should be constantly developing as an adaptation to the overall demographics in the society. The ongoing transition implies that not only does the proportion of the population of persons age ≥65 years continue to increase, it also gets older with a growth rate twice as high of persons ≥80 years as that of persons ≥60 years (1). In connection with this development, the task of primary prevention will no longer only be limited to the current middle-age population, which marks a broadening of focus that will require new approaches to enable efficient CVD risk estimation across all ages.

STUDY LIMITATIONS. The study is strong in that we have a well-described, randomly collected population with long-term follow-up. Using a cohort pooled from examinations performed during a 25-year period is a disadvantage, as it yields large variation in the follow-up period. However, as absolute risks are not stable over time for persons with the same risk factors, using a pooled cohort takes into account this variation caused by changes in lifestyle and health behavior during the 25-year period. Furthermore, we found no interactions between ECG changes and examination attended on the risk of reaching either of the endpoints.

Digital coding of ECG is increasingly used and serves as a valuable assistant in the daily clinical practice and may even be superior to visual assessments (20). However, we did not have access to

digital encodings and could not examine the usefulness of digitally coded ECG changes in relation to improving risk prediction.

CONCLUSIONS

Based on these results, we have shown that CVD risk prediction in persons age ≥65 years is improved significantly by adding ECG changes to the conventional risk factors.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Current risk assessment tools were not designed for specific application to people ≥65 years, in whom other factors may have better predictive value. Among these are electrocardiographic abnormalities recorded at rest.

TRANSLATIONAL OUTLOOK: Additional research is needed to validate other factors that might identify older individuals who might benefit from specific interventions to reduce their risk of cardiovascular events.

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KEY WORDS elderly, electrocardiography, risk prediction

APPENDIX For supplemental figures and tables, please see the online version of this article.