HHS Public Access

Author manuscript

Eur J Prev Cardiol. Author manuscript; available in PMC 2016 July 18.

Published in final edited form as:

Eur J Prev Cardiol. 2012 December ; 19(6): 1430–1436. doi:10.1177/1741826711426091.

Prognostic Significance of Serial Q/ST-T Changes by the Minnesota Code and Novacode In the Atherosclerosis Risk in Communities (ARIC) Study

Zhu-ming Zhang, MD, MPH[1], **Ronald J. Prineas, MD, PhD**[1], **Elsayed Z. Soliman, MD, MSc, MS**[1], **Chris Baggett, PhD**[2], **Gerardo Heiss, MD, PhD**[2], and **for the ARIC Research Group**

[1]Epidemiologic Cardiology Research Center (EPICARE), Department of Epidemiology and Prevention, Division of Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA

[2]Department of Biostatistics, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

Abstract

Aims—To compare the value of serial electrocardiographic (ECG) changes by the 2 most widely used ECG classification systems--the Minnesota Code (MC) and Novacode (Nova) for the prediction of subsequent coronary heart disease (CHD) and total mortality.

Methods and Result—We studied 12-lead ECGs from 12,477 participants (average age 54 years at baseline; 58% women; 76% non-Hispanic white) in the Atherosclerosis Risk in Communities (ARIC) Study, who were free of CHD at baseline in 1987, had both good quality ECGs at baseline and at first study-scheduled follow up visit, and had ECG QRS duration < 120ms. A total 2,119 participants died (17%), including 280 CHD deaths during an average of 17 years follow-up. Cox regression models assessed outcome associated with significant serial ECG changes by MC and Nova separately. For CHD death the Hazard ratio was 6.8 (95% confidence interval 3.5-13.3) for incident Nova myocardial infarction (MI), and 5.7 (95% confidence interval 2.7-11.9) for MC-MI in a multivariable model adjusted for clinical, demographic characteristics, and ECG left ventricular hypertrophy. The increased risk for total mortality doubled for both Nova and MC serial ECG MI. Major evolving ST-T wave abnormalities alone were associated with a ≥132% increased risk for CHD death and a 50% increased risk for total mortality by either Nova or MC.

Conclusion—ECG serial change by both MC and Nova are equally valuable predictors for future fatal cardiac events and total mortality and hence equally useful prognostic indicators in clinical trials and epidemiologic studies.

Keywords

cardiovascular disease; electrocardiography; serial change; mortality; Minnesota Code; Novacode

Correspondence: Zhu-ming Zhang, MD, MPH, Division of Public Health Sciences, Wake Forest University School of Medicine, Medical Center Blvd., Winston Salem, North Carolina 27157, Tel: 336-716-0835; Fax: 336-716-0834, zmzhang@wfubmc.edu.

DISCLOSURES: The authors declare they have no potential conflicts of interests.

INTRODUCTION

Well-defined criteria for clinically significant evolution of electrocardiographic (ECG) abnormalities are frequently called for.[1–4] The Minnesota Code (MC) was originally developed to determine cardiac-related disease prevalence in population studies in the early 1960s.[5] Later, criteria were developed to document incident events using objective side-by-side ECG comparison rules.[6–7] The Novacode (Nova) is an extension of the MC,[8–9] which provides a comprehensive hierarchical set of criteria for both prevalent ECG abnormalities and clinically significant serial ECG changes. Both systems have been used in many epidemiologic studies and clinical trials. We have previously compared MC and Nova in terms of their ability to detect prevalent ECG abnormalities in men and women separately and how these ECG abnormalities are predictive of future cardiovascular disease (CVD) events.[10,11] In the present study, we compared the value of serial ECG changes as detected by MC and Nova to predict subsequent incident fatal cardiac events and total mortality.

METHODS

Study Population

The Atherosclerosis Risk In Communities (ARIC) Study, is a population-based, multicenter prospective study to investigate the natural history and etiology of atherosclerotic and CVD events from 4 U.S. communities in Maryland, Minnesota, Mississippi, and North Carolina (n=15,792 men and women aged 45–64 years at enrollment). Participants were interviewed at home, and invited to a baseline clinical examination (1987–1989). They attended three further clinical examinations at approximately 3-year intervals, and received a follow-up telephone call yearly. Details of study design, protocol, sampling procedures, and selection and exclusion criteria have been published.[12] After excluding the participants with prevalent coronary heart disease (CHD) (ECG evidence or a history of myocardial infarction [MI]), angina, coronary artery bypass surgery, coronary angioplasty, or congestive heart failure at baseline, we only focused on those participants who had both good quality ECGs at baseline and at first study-scheduled follow up visit (at year-4), and had ECG QRS duration <120ms. There remained 12,477 participants for the present study (Supplementary-Figure.1).

Outcome Ascertainment

Relevant outcomes were incident CHD deaths and all-cause mortality. Deaths and hospitalization events were ascertained using annual follow-up calls to the cohort members, review of vital records, and community surveillance of hospitalized and fatal events. A CHD death was defined as lacking a probable non-CHD cause, and occurring in the context of a recent MI, chest pain within 72 hours of death, or a history of CHD occurring from the first triennial follow-up visit to December 31, 2006 with an average17 year follow-up. Events were classified independently by a separate committee. Detailed definitions for the diagnosis of acute MI and death due to CHD have been published.[13,14]

ECG Methodology

Identical electrocardiographs (MAC PC, Marquette Electronics, Inc., Milwaukee, Wisconsin) were used in all clinic sites, and resting, 10-second standard simultaneous 12-lead ECGs were recorded in all participants using strictly standardized procedures. The chest electrodes were located in precise positions. All ECGs were processed in a central ECG laboratory (EPICORE Center, University of Alberta, Edmonton, Alberta, Canada, and later at EPICARE Center, Wake Forest University, Winston-Salem, North Carolina), where they were visually inspected for technical errors and inadequate quality. The ECGs first processed by the Dalhousie ECG program were repeated for the present study using the 2001 version of the GE Marquette 12-SL program (Marquette 12SL ECG Physician Guide, available at www.ge-healthcare.com). ECGs were classified according to the Nova and MC using variables derived from the median complex of the Marquette measurement matrix.

ECG Serial Classification Criteria for Incident MI/Ischemia

Serial change Nova classification of incident MI/ischemia is based on the change of a score in the appearance of the duration and/or voltage of the Q wave exceeding specified limits and on whether an ST segment and T wave abnormality have evolved significantly from the reference ECG.[7,9] Nova classifies incident MI/Ischemia as I-Nova-5 (I for ‘incident’) with 8 hierarchies: Incident Nova-MI was identified by I-Nova-5.1 to I-Nova-5.4, and I-Nova-5.5/5.6 was for isolated incident ECG ischemia by Nova (Table-1 and Supplementary-1).

MC for classification of incident MI/ischemia incorporates 4 MC codes: Code 1 for Q and QS patterns, Code 4 for ST segment depression, Code 5 for T wave negativity and Code 9–2 for ST segment elevation. All serial changes were confirmed by side-by-side ECG comparison of Q and ST-T change between the first and subsequent examinations. Serial change MC categorizes evolving Q codes as Q1 to Q8, and for evolving ST-T codes as STE-1, ST-T1 to ST-T7.[5–7] Additionally, in order to achieve equivalency with the I-Nova-5 code, 8 hierarchic levels from I-MC-C.1 to I-MC-C.7 were combined as illustrated in Table-1 and Supplementary-2. Incident MC-MI was identified either by Q1 to Q7, or I-MC-C.1 to I-MC-C.4, and I-MC-C5/C.6 was for isolated incident ECG ischemia by MC.

One difference between the Nova and MC is that Q wave smaller than 100μV are ignored in the MC, whereas Nova scores Q waves that are at least 20ms in duration and 75μV in amplitude.

Statistical Analysis Methods

Frequency distributions of all ECG and non-ECG variables were first inspected to rule out anomalies and outliers possibly due to measurement artifacts. Descriptive statistics were used to determine mean, standard deviations, and percentiles for continuous variables, and frequencies and percents for categorical variables. Cox's proportional hazards analysis was used to assess the effects of serial change ECG variables on the risk of CHD death and total mortality, and comparison of MC or Nova predictors. Univariate and multivariate models were used in the analysis. Multivariate mode adjusted for the key demographic and clinical characteristics which included education, smoking status, alcohol use, hypertension, diabetes

mellitus, history of cancer, body mass index, systolic blood pressure, white blood cell, HDL, LDL, baseline glucose, insulin, fibrinogen, uric acid, creatinine, geographic regions, and ECG left ventricular hypertrophy (ECG-LVH) by MC/Nova –all defined in previous reports.[7,12–14] Analyses were performed with SAS version 9.1.3 (SAS Institute, Cary, North Carolina).

RESULTS

Among 12,477 participants with ECGs both at baseline and at first triennial visit, the mean age at baseline was 54 years, 58% women and 76% non-Hispanic white. Of these, 32% had hypertension, 10% diabetes, and 5% major ECG ST-T abnormalities by either Nova or MC (3.6% by Nova and 3.8% by MC). During an average 17 years post first follow-up visit: total mortality 17.0% (2,119) and CHD death 2.2% (280) (Table-2).

Table 2 shows 0.43% (54) had new incident ECG MI by Nova (I-Nova-5.1 to I-Nova-5.4) and 0.39% (49) by MC (I-MC-C.1 to I-MC-C.4) at first follow-up visit. Furthermore, 4.0% (499) had any new Q/ST-T change by Nova (i.e. codes I-Nova-5.1 through I-Nova-5.7), and 8.2% (1,017) had new codable MC serial change (codes I-MC-C.1 through I-MC-C.7). The agreement coefficient by Kappa for new incident MI by Nova and by MC was 0.678, P=0.384, where the disagreement was related to codable Q wave and their scores.

Prognosis of new ECG MI for CHD death and total mortality

New incident ECG MI categories were strong predictors for CHD death and all-cause mortality (Table 3–4). Incident ECG MI by MC/Nova criteria had at least a 5.6 times higher [Hazard ratio (HR) 6.81, 95% confidence interval (CI) 3.49-13.3 for Nova, and HR 5.66, 95% CI 2.70-11.9 for MC] in the multivariate models adjusted for demographic, clinical variables and ECG-LVH. Incident ECG MI by MC/Nova criteria doubled the risk for total mortality in all models (Table 4).

Isolated incident ECG ischemia independently predicting CHD death and total mortality

Compared with incident ECG MI, major evolution of ST-T change alone was also a strong predictor for CHD death and total mortality (Tables 3 and 4). There was a 2–4 times increased risk for CHD death (HR 2.32, 95% CI 1.31-4.08 for I-Nova-5.5/5.6; and HR 2.55, 95% CI 1.69-3.84 for I-MC-C.5/C.6). There was about 50% increased risk for total mortality by I-MC-C.5/C.6 or I-Nova-5.5/5.6 in the multivariate model. In summary, any new Q/ST-T serial change has ≥168% increased risk for CHD death and ≥47% increase risk for total mortality by either Nova or MC serial classification compared with no new Q/ST-T change group.

There was an interaction between the diagnosis of a clinical MI by the diagnostic committee and the appearance of a serial ECG MI or major Q/ST-T evolution at the first follow-up visit. ECG evolving new MI or major Q/ST-T with diagnostic clinic CHD MI (Supplementary 3-4) increased the risk of CHD death by 7.5 times (HR 8.57, 95% CI 5.04-14.6) and doubled risk for total mortality (HR 2.29, 95% CI 1.61-3.24) (Supplementary-5). Noteworthy, evolving ECG major Q/ST-T by MC or Nova was also predictive of CHD and total mortality regardless of having adjudicated clinical MI at the same period or not. Evolving major Q/ST-

T change in the absence of adjudicated clinical MI at first follow-up visit increased by 119% the risk for CHD death and indicated a 54% increased risk for total mortality as great as that for a clinic adjudicated MI without major serial ECG change (a 35% increase in risk).

DISCUSSION

Cardiovascular disease is a major cause of death and disability worldwide[15] with the ECG contributing independent diagnostic and prognostic information.[16–21] Serial change classification for incident MI/ischemia by MC or Nova has played an important role in numerous clinical trials and epidemiologic studies.[5–11,21] Coding by either Nova or MC has been well suited for incorporation in computer analysis programs as well as by visual review.

This is the first study to evaluate and compare the predictive power of serial change criteria by these 2 ECG classification systems. The relative strength of the 2 systems for prediction of the separate endpoints of CHD death and total mortality varied slightly.

Evolving Q wave or ST-T as evidence of an incident MI or ischemic event has been demonstrated previously in publications that have related ECG serial change to CHD death and total mortality. including the Multiple Risk Factor Intervention Trial (MRFIT)[6] and Framingham study.[21] New incident ECG MI (with a major evolving Q wave or evolving minor Q wave plus evolving ST-T change) had a 4 times higher related risk for coronary mortality in the MRFIT. The present study showed that new incident ECG MI increased by 5 times the risk for CHD death compared with those without any evolving Q/ST-T, and doubled the risk for total mortality.

In the present study, 95% (523/552) of MC evolving ST categories were documented as ST-T1, ST-T3, and ST-T7 (major T wave inversion to major T-wave inversion with 100% increase), and showed similar or higher risks than in MRFIT. The adjusted relative risks for CHD death in the present study were HRs of 4.13, 1.82 and 3.31, respectively; and HRs of 2.29, 1.30 and 1.75 for total mortality. The combined code for all of isolated evolving ST-T categories had a HR 2.55 by MC, and 2.32 by Nova for CHD death. According this study, the Minnesota code serial changes include more patients without apparent loss of specificity.

Study Strengths and Limitations

We focused only on electronic ECG data. Also, the serial change was between the baseline examination and the first follow up exam that did not occur until 3 years later, so that it did not test those changes that might have occurred and regressed in the first three years of the study. The strength of the study is the large community-based population, long term follow-up, standardized ECG recording and adjudicated outcomes.

CONCLUSIONS

ECG serial change criteria by both MC and Nova are equally valuable classification systems for detection of incident MI/ischemia in clinical trials and epidemiologic studies. Any

incident ECG MI or isolated major evolving ST-T changes by Nova or MC are independent predictors for fatal cardiac events and all-cause mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The ARIC Study is carried out as a collaborative study supported by National Heart, Lung, and Blood Institute contracts (HHSN268201100005C to HHSN268201100012C). The authors thank the staff and participants of the ARIC study for their important contributions.

REFERENCES

1. Wagner GS, Macfarlane P, Wellens H, Josephson M, Gorgels A, Mirvis DM, et al. American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; American College of Cardiology Foundation; Heart Rhythm Society. ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram part VI: acute ischemia/infarction: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. J Am Coll Cardiol. 2009; 53(11):1003–1011. [PubMed: 19281933]
2. De Backer G, Ambrosioni E, Borch-Johnsen K, Brotons C, Cifkova R, Dallongeville J, et al. European Society of Cardiology Committee for Practice Guidelines. European guidelines on cardiovascular disease prevention in clinical practice: third joint task force of European and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of eight societies and by invited experts). Eur J Cardiovasc Prev Rehabil. 2003; 10(4):S1–S10. [PubMed: 14555889]
3. Luepker RV, Apple FS, Christenson RH, Crow RS, Fortmann SP, Goff D, et al. Case definitions for acute coronary heart disease in epidemiology and clinical research studies. Circulation. 2003; 108(20):2543–2549. [PubMed: 14610011]
4. Thygesen K, Alpert JS. White HD on behalf of the joint ESC/ACCF/AHA/WHF task force for the redefinition of myocardial infarction. Universal definition of myocardial infarction. Circulation. 2007; 116(22):2634–2654. [PubMed: 17951284]
5. Prineas, RJ.; Crow, R.; Blackburn, H. The Minnesota code manual of electrocardiographic findings. Boston, MA: John Wright-PSG; 1982. p. 203-229.
6. Crow RS, Prineas RJ, Hannan PJ, Grandits G, Blackburn H. Prognostic associations of Minnesota Code serial electrocardiographic change classification with coronary heart disease mortality in the Multiple Risk Factor Intervention Trial. Am J Cardiol. 1997; 80(2):138–144. [PubMed: 9230148]
7. Prineas, RJ.; Crow, RS.; Zhang, ZM. The Minnesota Code Manual of Electrocardiographic Findings (including measurement and comparison with the Novacode). 2nd Edition new and enlarged. New York: Springer-London; 2010. p. 226-324.
8. Rautaharju PM, Calhoun HP, Chaitman BR. Novacode serial ECG classification system for clinical trials and epidemiological studies. J Electrocardiol. 1992; 24(S):179–187. [PubMed: 1552254]
9. Rautaharju PM, Park LP, Chaitman BR, Rautaharju F, Zhang ZM. The Novacode criteria for classification of ECG abnormalities and their clinically significant progression and regression. J Electrocardiol. 1998; 31(3):157–187. [PubMed: 9682893]
10. Zhang ZM, Prineas RJ, Eaton CB. Evaluation and comparison of the Minnesota code and Novacode for electrocardiographic Q-ST wave abnormalities for the independent prediction of incident coronary heart disease and total mortality (from the Women's Health Initiative). Am J Cardiol. 2010; 106(1):18–25. [PubMed: 20609641]
11. Zhang ZM, Prineas RJ, Case D, Psaty BM, Suzuki T. Burke GL for the Cardiovascular Health Study Research Group. Gender differences between the Minnesota code and Novacode

electrocardiographic prognostication of coronary heart in the Cardiovascular Health Study. Am J Cardiol. 2011; 107(6):817–820. [PubMed: 21247534]

12. ARIC Investigators. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. Am J Epidemiol. 1989; 129(4):687–702. [PubMed: 2646917]
13. Goff DC Jr, Howard G, Wang C-H, Folsom AR, Rosamond WD, Cooper LW, et al. Trends in severity of hospitalized myocardial infarction: the Atherosclerosis Risk in Communities (ARIC) Study, 1987–1994. Am Heart J. 2000; 139(5):874–880. [PubMed: 10783222]
14. White AD, Folsom AR, Chambless LE, Sharret AR, Yang K, Conwill D, et al. Community surveillance of coronary heart disease in the Atherosclerosis Risk In Communities (ARIC) Study: methods and initial two years' experience. J Clin Epidemiol. 1996; 49(2):223–233. [PubMed: 8606324]
15. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, et al. on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics—2011 Update. A report from the American Heart Association. Circulation. 2011; 123(4):e18–e209. [PubMed: 21160056]
16. Kumar A, Prineas RJ, Arnold AM, Psaty BM, Furberg CD, Robbins J, et al. Prevalence, prognosis, and implication of isolated minor nonspecific ST-segment and T-wave abnormalities in older adults: Cardiovascular Health Study. Circulation. 2008; 118(25):2790–2796. [PubMed: 19064684]
17. Rautaharju PM, Grace S, Nelson JC, Marino-Larsen EK, Psaty BM, Furberg CD, et al. Comparison of mortality risk for electrocardiographic abnormalities in men and women with and without coronary heart disease (from the Cardiovascular Health Study). Am J Cardiol. 2006; 97(3):309–315. [PubMed: 16442387]
18. Zhang ZM, Prineas RJ, Case D, Soliman EZ. Rautaharju PM for ARIC Research Group. Comparison of the prognostic significance of the electrocardiographic QRS/T angles in predicting incident coronary heart disease and total mortality (from the atherosclerosis risk in communities study). Am J Cardiol. 2007; 100(5):844–849. [PubMed: 17719331]
19. Rautaharju PM, Kooperberg C, Larson JC, LaCroix A. Electrocardiographic abnormalities that predict coronary heart disease events and mortality in postmenopausal women. The Women's health Initiative. Circulation. 2006; 113(4):473–480. [PubMed: 16449726]
20. Prineas RJ, Grandits G, Rautaharju PM, Cohen J, Zhang ZM, Crow RS. Long-term prognostic significance of isolated minor electrocardiographic T-Wave abnormalities in middle aged men free of clinic cardiovascular disease. The Multiple Risk Factor Study (MRFIT). Am J Cardiol. 2002; 90(12):1391–1395. [PubMed: 12480053]
21. Kannel WB, Anderson K, McGee DL, Degatano LS, Stampfer MJ. Nonspecific ectrocardiographic abnormality as a predictor of coronary heart disease: the Framingham Study. Am Heart J. 1987; 113(2):370–376. [PubMed: 3812192]

Table 1

ECG Serial Change Criteria for Incident Myocardial Infarction and Ischemia by the Minnesota Code and the Novacode

Category	Novacode	Minnesota Code*	
Evolving Q wave			
Major Q wave evolution	I-Nova-5.1	I-MC-C.1	Q1
Moderate Q wave evolution with evolving ST-T	I-Nova-5.2	I-MC-C.2	Q2,Q3,Q4
Moderate Q wave evolution with nonevolving ST-T	I-Nova-5.3	I-MC-C.3	N/A
Borderline Q wave evolution with evolving ST-T	I-Nova-5.4	I-MC-C.4	Q5,Q6,Q7
Evolving ST-T change			
Profound ST-T evolution without evolving Q waves	I-Nova-5.5	I-MC-C.5	ST-T1,ST-T3,STE-1
Evolving ST-T with nonevolving Q waves	I-Nova-5.6.1	I-MC-C.6	ST-T2,ST-T4
Isolated ST-T evolution	I-Nova-5.6.2	I-MC-C.6	ST-T5,ST-T6,ST-T7
Borderline Q wave change			
Borderline Q wave evolution with nonevolving ST-T	I-Nova-5.7	I-MC-C.7	Q8
No significant Q or ST-T evolution			
No significant Q wave or ST-T evolution	I-Nova-5.0	I-MC-C.0	Q0
New Incident Myocardial Infarction/Ischemia			
New Incident myocardial infarction	I-Nova-5.1 to I-Nova-5.4	I-MC-C.1 to I-MC-C.4	Q1 through Q7
New isolated major ischemia	I-Nova-5.5/5.6	I-MC-C.5/C.6	ST-T1 to ST-T7,STE-1
Any new Q/ST-T change	I-Nova-5.1 to I-Nova-5.7	I-MC-C.1 to I-MC-C.7	Q1 through Q7 or ST-T1 to ST-T7,STE-1

Note:

* including evolving Q/ST code by the Minnesota code, and combined MC serial change code (I-MC-C.X). See Supplementary 1–2 and Reference# 7&9.

Table 2

Characteristics of study participants including the outcomes during average 17 years follow-up

Characteristics at baseline (N=12,477)			
Age (year)	54±6	Current smoking	3321 (26.66%)
Body mass index (kg/m^2)	28±5	Hypertension	4001 (32.20%)
Systolic blood pressure (mmHg)	120±18	Diabetes mellitus	1259 (10.17%)
Diastolic blood pressure (mmHg)	73±11	LVH by Nova or MC *	650 (5.21%)
Women	7248 (58.09%)	CHD Death **	280 (2.24%)
African-American	3048 (24.43%)	Total Mortality **	2119 (16.98%)
ECG ischemia by Nova#		**ECG ischemia by combined MC#**	
Nova-5.5	194 (1.55%)	MC-C.5	133 (1.07%)
Nova-5.6	254 (2.04%)	MC-C.6	343 (2.75%)
Nova-5.7	509 (4.08%)	MC-C.7	644 (5.16%)
Nova-5.8	2043 (16.37%)	MC-C.8	1188 (9.52%)
Nova-5.0	9477 (75.96%)	MC-C.0	10169 (81.50%)
ECG serial change for MI/Ischemia by Nova/ MC at first scheduled follow-up visit##			
ECG serial change by MC			
Q1	44 (0.35%)	STE-1	17 (0.14%)
Q2	1 (0.01%)	ST-T1	81 (0.65%)
Q3	0	ST-T2	2 (0.02%)
Q4	0	ST-T3	247 (1.98%)
Q5	1 (0.01%)	ST-T4	2 (0.02%)
Q6	3 (0.02%)	ST-T5	5 (0.04%)
Q7	0	ST-T6	3 (0.02%)
Q8	416 (3.33%)	ST-T7	195 (1.56%)
Q0	11460 (91.85%)		
ECG serial change by Nova		**ECG serial change by combined MC**	
I-Nova-5.1	11 (0.09%)	I-MC-C.1	44 (0.35%)
I-Nova-5.2	9 (0.07%)	I-MC-C.2	1 (0.01%)
I-Nova-5.3	22 (0.18%)	I-MC-C.3	N/A
I-Nova-5.4	12 (0.10%)	I-MC-C.4	4 (0.03%)
I-Nova-5.5	48 (0.38%)	I-MC-C.5	328 (2.63%)
I-Nova-5.6	169 (1.35%)	I-MC-C.6	224 (1.80%)
I-Nova-5.7	228 (1.83%)	I-MC-C.7	416 (3.33%)
I-Nova-5.0	11978 (96.0%)	I-MC-C.0	11460 (91.85%)

Note:

See Reference#11;

See Table-1 for serial change criteria.

* ECG-LVH (Left Ventricular Hypertrophy by Cornell voltage or MC 3.1);

** Outcomes-CHD death and total mortality during first scheduled follow-up visit to average 17 years follow-up;

Table 3

CHD Death by Serial Change for the Novacode and the Minnesota Code During first scheduled follow-up visit to an average 17 Years Follow-up

N=280/12477	Event rates[§] n/N (%)	Univariate HR (95% Cl)	Multivariate[§§] HR (95% Cl)
Nova Serial Change[#]			
I-Nova-5.1 to 5.4	13/54 (24%)	**11.8 (6.76–20.7)**[*]	**6.81 (3.49–13.3)**[*]
I-Nova-5.5 to 5.6	17/217 (8%)	**3.99 (2.44–6.52)**[*]	**2.32 (1.31–4.08)**[**]
I-Nova-5.7	12/228 (5%)	**2.68 (1.50–4.78)**[*]	1.88 (0.96–3.69)
I-Nova-5.0	238/11978 (2%)	ref	ref
Q/ST-T change vs. No-change	42/499 (8%) 238/11978 (2%)	**4.26 (3.07–5.92)**	**2.68 (1.83–3.91)**
Combined MC Serial Change[#]			
I-MC-C.1 to C.4	11/49 (22%)[*]	**11.4 (6.23–21.0)**[*]	**5.66 (2.70–11.9)**[*]
I-MC-C.5 to C.6	40/552 (7%)[*]	**4.06 (2.89–5.70)**[*]	**2.55 (1.69–3.84)**[*]
I-MC-C.7	24/416 (6%)[*]	**3.16 (2.07–4.83)**[*]	**2.55 (1.61–4.03)**[*]
I-MC-C.0	205/11460 (2%)	ref	ref
Q/ST-T change vs. No-change	75/1017 (7%) 205/11460 (2%)	**4.08 (3.13–5.31)**	**2.75 (2.01–3.75)**

Note:

[#] see Table-1 for serial change criteria.

[§] events rates--n (%), the event rate is the number of events (n) divided by the number (N) in that category of ECG MI, or each I-MC-C and I-Nova-5 codes, where rate is n/N (%).

[§§] Adjusted for key demographic and clinical variables of age, gender, race, education, smoking status, alcohol use, diabetes, hypertension, cancer, body mass index, systolic blood pressure, white blood cell count, baseline glucose, insulin, fibrinogen, HDL, LDL, uric acid, creatinine, geographic regions and ECG-LVH by MC/Nova.

[*] P-value <0.001;

[**] P-value <0.01

Table 4

Total Mortality by Serial Change for Novacode and Minnesota Code During First Scheduled Follow-up Visit to a Maximum of 17 Years Follow-up

N=2119/12477	Event rates[§] n/N (%)	Univariate HR (95% CI)	Multivariate[§§] HR (95% CI)
Nova Serial Change[#]			
I-Nova-5.1 to 5.4	27/54 (50%)	**3.03 (2.07–4.43)***	**2.07 (1.31–3.27)****
I-Nova-5.5 to 5.6	83/217 (38%)	**2.38 (1.91–2.96)***	**1.47 (1.13–1.91)****
I-Nova-5.7	71/228 (31%)	**1.94 (1.53–2.46)***	**1.59 (1.23–2.05)***
I-Nova-5.0	1938/11978 (16%)	ref	ref
Q/ST-T change vs. No-change	181/499 (36%) 1938/11978 (16%)	**2.25 (1.93–2.62)***	**1.58 (1.33–1.88)***
Combined MC Serial Change[#]			
I-MC-C.1 to C.4	24/49 (49%)	**2.83 (1.89–4.24)***	**2.16 (1.38–3.27)***
I-MC-C.5 to C.6	185/552 (34%)	**2.13 (1.84–2.48)***	**1.56 (1.31–1.87)***
I-MC-C.7	104/416 (25%)	**1.56 (1.28–1.90)***	**1.28 (1.04–1.58)****
I-MC-C.0	1806/11460 (16%)	ref	ref
Q/ST-T change vs. No-change	313/1017 (31%) 1806/11460 (16%)	**1.93 (1.71–2.18)***	**1.47 (1.29–1.69)***

Note:

[#]see Table-1 for serial change criteria.

*and[§] see Table-3.