

## ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #300

1. Title:

Predictive Value of QTc for CHD

2. Writing Group:

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3. Timeline:

ECG measurements March 1995 - Feb 1996

Analysis: March 1996, draft: Summer 1996

4. Rationale:

Long QT syndrome patients are at high risk of sudden death. Also in myocardial infarction patients and patients who had diagnostic 24-hour electrocardiography an association of heart-rate adjusted QT-interval (QTc) with sudden death has been observed. This elevated risk has been attributed to predominance of left sympathetic nerve activity or myocardial membrane defects leading to electrical instability in situations of high sympathetic activity. Whether QTc prolongation predicts coronary heart disease mortality in healthy persons remains to be clarified. In the Framingham Heart Study no significant associations with mortality were observed, whereas a number of Dutch studies have observed more than twofold risks of coronary heart disease mortality in subjects with QTc prolongation. The ARIC data present a possibility to study the subject in another large USA cohort.

5. Main hypothesis:

QTc prolongation is associated with risk of: myocardial infarction incidence, coronary heart disease mortality, and sudden death. The association may partly be explained by indicators of elevated sympathetic activity like high fasting insulin level, and low heart rate variability.

6. Data (variables, time window, source, inclusions/exclusions):

Design: (follow-up data) Case-cohort\*\*: Random sample of 1000 men and 1000 women (without prevalent heart disease) and all incident cases of myocardial infarction, all cases of coronary heart disease death and sudden death. Expected: a total of plus or minus 3000. QT measurements will be taken from rhythm-strips.

Analysis: Survival analysis using poisson-regression for the case-cohort design (Schouten) will be carried out separately for males and females.

Other covariates: (Visit 1 data) age, systolic and diastolic blood pressure, Body Mass Index, height, weight, cholesterol subfractions, smoking, physical activity, triglycerides, waist-hip ratio, insulin, glucose, serum K concentration, ECG-data, rhythm disturbances, use of medication (beta-blockers, antihypertensives), carotid artery wall thickness, prevalent disease variables

\*Incidence data won't be published until released by ARIC.

\*\*The case-base or case-cohort design is similar to the nested case-control design. The difference between the two is that in the case-cohort design, the referent sample is drawn from the total cohort instead of a non-case sample. The advantage is that this cohort sample can be used for every outcome that is investigated. An additional advantage is the case-cohort design allows the estimation of incidence density

ratio's (Schouten, Prentice), in contrast to the case-control design which does not. If the size of this cohort sample is a four or five fold of the number of cases, loss of precision is very low (Miettinen).

## REFERENCES

1. Miettinen OS. Design options in epidemiological research. An update. *Scand J Work Environ Health* 1982; 8:suppl 1:7-14
2. Prentice RL. A case-cohort design for epidemiologic and cohort studies and disease prevention trials. *Biometrika* 1986; 73:1-11
3. Schouten EG, Dekker JM, Kok FJ, le Cessie S, van Houwelingen HC, Pool J, Vandenbroucke JP. Risk ratio and rate ratio estimation in case-cohort designs: hypertension and cardiovascular mortality. *Stat in Med* 1993; 12: 1733-45