

ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #621

1. **Full Title:** Does vital exhaustion increase the risk of stroke?

Abbreviated Title: (26 letters/space) Vital exhaustion and stroke

2. **Writing Group:**

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3. **Timeline:**

The analysis is contingent on there being at least 200 confirmed incident strokes or TIA's post visit 2. We understand that this is not expected until December, 1999. We hope the manuscript can be submitted very early in the next millennium.

4. **Rationale:**

The Maastricht questionnaire was developed to measure vital exhaustion, defined as "A state which is present when the individual not only complains of decreasing energy but also by feeling dejected or defeated.(1)" In addition to measuring feelings of helplessness, the questionnaire contains symptoms of insomnia (trouble falling asleep and waking up repeatedly during the night) and possible obstructive sleep apnea, a condition in which there is closure of the upper airway tract while the diaphragm continues its breathing effort. Apneic episodes lead to increased intracranial pressure and decreased cerebral perfusion pressure and can cause a marked reduction in cerebral blood flow in some patients(12-14). Exhaustion, obstructive apnea and subjectively reported sleep complaints such as "trouble falling asleep," have all been shown to be risk factors for coronary events (2-10, 15-21). It has been suggested that sleep complaints coupled with exhaustion represent an inability to cope with daily stressors(17) and recently daily stress has been correlated with myocardial ischemia(22). Although related symptoms such as excessive daytime sleepiness have been reported to precede stroke(11), vital exhaustion has not, to our knowledge, been studied in conjunction with stroke. However, McGovern et al. reported that in the ARIC cohort, while an age-adjusted measure of carotid wall thickness was related to excess fatigue, this relationship could be explained by antihypertensive medications, body mass index and conventional risk factors, particularly smoking (23). It is possible that excess fatigue, apnea and insomnia may affect stroke risk by a mechanism other than atherosclerosis.

5. **Main Issues/Hypotheses to be Addressed:**

(1) To determine the ability of the Maastricht questionnaire to predict stroke, after adjustment for conventional risk factors.

(2) To determine the items of the Maastricht questionnaire that are most predictive of stroke, in order to provide clues as to the mechanism.

Methods:

Vital exhaustion and stroke: A proportional hazards regression, using the date of onset of stroke symptoms will be the primary analysis used to determine if vital exhaustion increases the risk of stroke. Analyses will be done overall and by gender and by race.

Determining most predictive items: A logistic discriminant analysis will be used to rank items by predictive ability for stroke.

Power Considerations: If we assume a population of 12,000 individuals with 230 incident strokes, then if 20% of the subjects are considered exhausted, there is about 95% power to detect a risk ratio of 1.75 or higher. The table below varies the prevalence of VE and the risk ratio detected.

Table: Statistical Power Estimates for the association of vital exhaustion and incident stroke, assuming an average sample size of 12,000 persons at risk and 230 incident strokes.

<u>Prevalence of exhaustion</u>	<u>Risk ratio</u>	<u>Power</u>
10% (e.g.: upper decile of questionnaire)	1.5	57%
	1.75	84%
20% (e.g.: upper quintile)	1.5	74%
	1.75	95%
25% (e.g.: upper quartile)	1.5	80%
	1.75	97%

6. Data:

ARIC Data for Visit 2 and later will be required.

Visit 2 data required:

- Visit 2 date
- Individual Items of the Maastricht questionnaire and
- Total score on the Maastricht questionnaire
- Previous/current Stroke indicator
- Previous/current TIA indicator
- Study center
- Gender
- Race
- Age
- Education in years
- Body mass index (kg/m²)
- Smoking category: Current, Former or Never smoker
- Diabetes mellitus indicator
- Systolic blood pressure
- Total Cholesterol
- HDL Cholesterol
- Triglycerides
- Fibrinogen

All Visits post Visit 2

- Stroke indicator

TIA indicator
Stroke onset date
TIA onset date
1st stroke versus not

Also characteristics of the strokes or TIAs for a sentence in the test
1st stroke versus not
Ischemic or other
Right of Left side

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