1.a. Full Title: Construction and validation of a depression measure in the ARIC study.

b. Abbreviated Title (Length 26 characters): Depression in ARIC

2. Writing Group (list individual with lead responsibility first):

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3. Timeline: Analysis and write-up should be completed in six months.

4. Rationale:

   Depressive symptoms have been associated with increased risk for coronary heart disease (CHD), total mortality, and stroke in previous studies. It is uncertain if depression is causally related to these outcomes, however. It may be that depression is associated with health related behaviors such as smoking, poor diet, high alcohol use, physical inactivity, and non-compliance with medical treatments for hypertension, diabetes, and other conditions, that promote CHD, total mortality, and stroke. These poor health behaviors may result in hypertension, poorly controlled diabetes, high LDL cholesterol, and low HDL cholesterol.

   The ARIC study provides an opportunity to address these issues in a large and well-defined prospective study. However, no standardized measure of depression has been collected in the ARIC study. This proposal concerns the construction and validation of a depression measure in the ARIC study. For example in the Maastricht Questionnaire, there are 21 items assessing "vital exhaustion". Most items overlap with symptoms of depression, i.e., fatigue, hopelessness, thoughts about dying, insomnia, worthlessness, poor coping capacity, problems with concentration, crying spells. None of the items asks directly about depressed mood. However, the first two items of the Interpersonal Support Evaluation List (Health and Life Profile: Part A) ask: "How do you feel about life as a whole" and "On a scale of zero to ten, how satisfied are you
with the meaning and purpose of your life”. Other items in this questionnaire also assess aspects of depressed mood, pessimism, negative thought processes, and social relatedness. We believe it is possible to construct a psychometrically sound and valid measure of depression from items culled from the questionnaires that have been collected in the ARIC data. In addition, external validation can be obtained using data on prescription rates of psychotropic medications, especially antidepressant medications and/or anti-anxiety agents.

5. Main Hypothesis/Study Questions:

- **Goal:** to construct and validate a depression measure
- **Hypotheses:**
  1. It is possible to construct a psychometrically sound measure of depression from items, with sufficient face validity to assess depression, culled from the following questionnaires (Interpersonal Support Evaluation List, Lubben Social Network Scale, and Maastricht Questionnaire).
  2. Information on demographic correlates of depression scores can provide preliminary validating support for this new measure of depression. For example, it is expected that levels of depression are higher in women compared to men, in the ARIC study as in other epidemiological samples.
  3. Further validation of the new depression measure and cut-off scores for "clinically significant" depression can be obtained by comparing depression scores between people who are prescribed psychotropic medications, especially antidepressant medications and/or anti-anxiety agents.

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

- **Study population:** people who completed the Health and Life Profile form (that includes the Interpersonal Support Evaluation List, Lubben Social Network Scale, and Maastricht Questionnaire) at visit 2.
- **Variables (at visit 2):**
  - Items from the Interpersonal Support Evaluation List, Lubben Social Network Scale, and Maastricht Questionnaire will be used to construct a depression measure.
  - Demographic variables (sex, age, racial background).
  - Prescription medication data. Psychotropic agents will be classified into major groups (antidepressants, sedatives/hypnotics, antipsychotics, opiates, stimulants, and mood stabilizers).
  - Other variables: smoking status, alcohol use, level of exercise, diabetes, hypertension, LDL cholesterol, total cholesterol, HDL cholesterol, waist-to-hip ratio.

**Statistical Analysis Approach:**

Factor analysis will be used to analyze the data. Factor analysis is a statistical technique that is appropriate for use when analyzing the structure of the interrelationships (correlations) among a large number of variables (e.g., test scores, test items, questionnaire responses) by defining a set of common underlying dimensions, known as factors. For this study, the items from the Interpersonal Support Evaluation List, the Lubben Social Network Scale, and the Maastricht Questionnaire will be used. There are 50 items in these three questionnaires. Items that will be used in the factor analysis will be based on those items that appear to measure depressive symptoms (based on expert consensus). A confirmatory factor analysis using a separate sample from the ARIC data set will be conducted after the original factor analysis to
confirm the results. A standard latent root criterion (eigenvalues) will be used to determine which factors to retain.

Scores on the new depression measure will be compared between demographic groups and between people who are prescribed antidepressants and/or sedative/hypnotic agents. Cut-off score on that measure for clinically significant depression can be estimated by Receiver Operating Characteristics (ROC) computations. Correlations between depressive scores and selected variables (e.g., smoking, alcohol use, diabetes, etc.) will also be explored. SAS software will be used.

7.a. Will the data be used for non-CVD analysis in this manuscript?  _____ Yes  ____ No

b. If Yes, is the author aware that the file ICTDER02 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used?  _____ Yes  ____ No
(This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?  _____ Yes  ____ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 must be used to exclude those with value RES_DNA = “No use/storage DNA”?  _____ Yes  ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: [http://bios.unc.edu/units/csc/ARIC/stdy/studymem.html](http://bios.unc.edu/units/csc/ARIC/stdy/studymem.html)

_____ Yes  _____ No