1. **Full Title:** Methodology for the adjustment of rate of myocardial infarction for the changes in biomarkers/enzymes – the ARIC Study

2. **Abbreviated Title (Length 26 characters):** Adjusting MI Rate for Biomarkers

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

   **Lead:** Lily Wang  
   **Address:** CSCC, Dept. of Biostatistics, UNC-CH, CB# 8030  
   **Phone:** (919) 966-8333  
   **Fax:** (919)962-3265  
   **E-mail:** uccchw@mail.csc.unc.edu  
   **Writing group members:** Lloyd Chambless, Wayne Rosamond, Paul Sorlie, Aaron Folsom

4. **Timeline:** First draft by Oct 31, 2002

4. **Rationale:** Since year 1996, a newly introduced cardiac enzyme troponin which is more sensitive and specific for detecting myocardial infarction than other cardiac enzymes (CK-MB, total CK/LDHs) was used in ARIC surveillance. There were 8%, 62%, 75% and 81% (not adjusted for sampling fractions) of hospitalizations used troponin in 1996-99, respectively. Therefore, one would expect an increase in rates of MI since 1996 for the introduction of troponin. Meanwhile, some hospitals have dropped using other enzymes since 1996 due to using troponin. This also has an impact in detecting an MI.

Moreover, patterns of diagnostic biomarker usage of other enzymes change over the study years. There was a clear trend towards increased addition of CK-MB to total CK/LDHs in 1987-95 when troponin was not used in the ARIC study hospitals. For example, there were 56% hospitalizations using both CK-MB and total CK/LDHs in 1987 while there were 72% in 1995. Changes of the patterns of the usage of CK-MB and/or total CK/LDHs are smaller after 1996 (between 71-75%). Since the more the diagnostic biomarkers are used, the better chance an MI will be detected, one would also expect an increase over time in rates of MI in 1987-1995 due to more hospitalizations having both CK-MB and total CK/LDHS performed. This suggests that a correction for the change in diagnostic biomarker is needed for the interpretation of rates of MI, and is essential for years (1987-95) prior to the introduction of troponin.

Above suggests that for a meaningful interpretation of the trend of MI, adjustment of the rate of MI for the introduction of troponin, the dropping of other enzymes and the changes in patterns of using other enzymes is needed.

We will use 1995 data as the reference year, which is right before ARIC collected troponin data, to standardize the distribution of cardiac enzymes with respect to CK-MB and total CK/LDHs.
for both pre- and after-troponin years. An algorithm to estimate the number of MIs that would have been detected had troponin not been used and other enzymes (CK-MB and total CK/LDHs) ordered as in the reference year for after-troponin years (1996 and after) will be developed.

Note that we have searched the approved ARIC manuscript proposals and found potential overlaps with 2 of them, MS# 725 (Prognosis of hospitalized MI according to degree of myocardial injury assessed by biochemical markers and other risk indicators by Annie McNeill, Wayne Rosamond et. al.) and MS#713 (Effect of troponin on the assessment of trends in coronary heart disease by Wayne Rosamond et. al.). After discussion with Wayne, we determine that there will be no overlaps with MS#725. Though some of the write-up might be overlapped with MS#713, there should be no significant overlaps since the focus of this manuscript is on how to adjust MI rates for troponin. Wayne will also compare MI rates using reclassified troponin (from three categories of troponin classification: Normal, Equivocal and Abnormal to two categories: Normal and Abnormal) in MS#713.

5. **Main Hypothesis/Study Questions:**
The main purpose of this manuscript is not hypothesis testing but to develop a methodology to adjust rates of MI for the introduction of troponin, dropping of other cardiac enzymes and changes of the patterns of the usage of cardiac enzymes with respect to CK-MB and total CK/LDHs.

6. **Data (variables, time window, source, inclusions/exclusions):**
Community Surveillance data in 1987-1999

Variables: ARICDX2, MIDX, FATALDX, MIDATE, DTHDATE, PAINDX, ECGDX2, ENZDX2

7.a. Will the data be used for non-CVD analysis in this manuscript? ___ Yes ___ X 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 ___ X 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/cscs/ARIC/stdy/studymem.html](http://bios.unc.edu/units/cscs/ARIC/stdy/studymem.html)

   ___ X ___ Yes ___ No