1.a. Full Title: Impact of Body Mass Index on Length of Stay for Cardiovascular Disease Hospitalizations in White and African American men and women

b. Abbreviated Title (Length 26 characters): BMI and LOS for CVD

2. Writing Group:
   Writing group members:
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   June Stevens

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. KPT [please confirm with your initials electronically or in writing]

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3. Timeline: Work will begin immediately.
4. Rationale:

Obesity is a known risk factor for cardiovascular disease (CVD); however, little is known about how obesity impacts the length of hospitalization stays for CVD. In a recent article published by our research group using ARIC data (MS proposal # 1133), we found significantly more all-cause hospitalizations and CVD-related hospitalizations among obese adults compared to normal weight adults (1). The impact of weight status tended to be greater in women than men for CVD-related hospitalizations but similar between Whites and African Americans. That manuscript did not compare the length of stay (LOS).

Based on the 2006 National Hospital Discharge Survey (NHDS), approximately 5.8% of Whites and 7.0% of African Americans were hospitalized overall in 2006 (2). The likelihood of being hospitalized increases with age, 6.8% in 45-54 year olds, 9.8% in 55-64 year olds and 14.2% in 65-74 year olds. During middle adulthood (45-64 years of age), women have slightly higher overall rates of hospitalization than men (7.4% in women 45-54 years of age and 10.0% in women 55-64 years of age versus 6.3% in men 45-54 years of age and 9.6% in women 55-64 years of age). The average length of stay for all hospitalizations in adults aged 45-64 years was 5.0 days and 5.5 days for adults aged 65 and over (3).

In 2006, heart disease (ICD9: 391-392.0, 393-398, 402, 404, 410-416, 420-429) was the primary discharge diagnosis for approximately 16% (2.2 million) of men and 10% (2.0 million) of women (3). The LOS for heart disease was 3.9 days in adults 45-64 years of age and 4.7 days in adults 65 years old and over. The LOS was slightly longer for cerebrovascular disease (ICD9: 430-438) – 5.1 and 4.8 days in adults 45-64 years old and 65 years old and over, respectively.

In general, the LOS has decreased over time (2). For example, the LOS for stroke (ICD9: 430-438) in men 45-64 years of age was 10.0 days in 1990 and decreased to 5.2 days in 2000 and 4.7 days in 2006. The trend was similar in women with 10.7 days, 5.5 days and 5.6 days, respectively. Similar declines (but not as drastic) were found for other specific-causes of CVD hospitalizations. The table below shows the LOS for subcategories of CVD by gender and age for three time points (1990, 2000 and 2006).

<table>
<thead>
<tr>
<th>Subcategory</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>45-64 year olds</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart disease(^a)</td>
<td>5.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Ischemic heart disease(^b)</td>
<td>5.7</td>
<td>3.6</td>
</tr>
<tr>
<td>Heart attack(^c)</td>
<td>7.5</td>
<td>4.7</td>
</tr>
<tr>
<td>Arrhythmias(^d)</td>
<td>4.6</td>
<td>2.8</td>
</tr>
<tr>
<td>Heart failure(^e)</td>
<td>6.9</td>
<td>5.2</td>
</tr>
<tr>
<td>Hypertension(^f)</td>
<td>4.3</td>
<td>2.0</td>
</tr>
<tr>
<td>Stroke(^g)</td>
<td>10.0</td>
<td>5.2</td>
</tr>
<tr>
<td>Subcategory</td>
<td>Male</td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>-------</td>
<td>-------</td>
</tr>
<tr>
<td>65 – 74 year olds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart disease(^a)</td>
<td>7.0</td>
<td>4.7</td>
</tr>
<tr>
<td>Ischemic heart disease(^b)</td>
<td>6.8</td>
<td>4.3</td>
</tr>
<tr>
<td>Heart attack(^c)</td>
<td>8.8</td>
<td>5.3</td>
</tr>
<tr>
<td>Arrhythmias(^d)</td>
<td>5.6</td>
<td>3.8</td>
</tr>
<tr>
<td>Heart failure(^e)</td>
<td>7.9</td>
<td>5.7</td>
</tr>
<tr>
<td>Hypertension(^f)</td>
<td>4.6</td>
<td>2.7</td>
</tr>
<tr>
<td>Stroke(^g)</td>
<td>8.3</td>
<td>4.5</td>
</tr>
<tr>
<td>75- 84 year olds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart disease(^a)</td>
<td>8.1</td>
<td>5.4</td>
</tr>
<tr>
<td>Ischemic heart disease(^b)</td>
<td>8.5</td>
<td>5.2</td>
</tr>
<tr>
<td>Heart attack(^c)</td>
<td>10.1</td>
<td>5.8</td>
</tr>
<tr>
<td>Arrhythmias(^d)</td>
<td>6.5</td>
<td>4.3</td>
</tr>
<tr>
<td>Heart failure(^e)</td>
<td>7.7</td>
<td>6.1</td>
</tr>
<tr>
<td>Hypertension(^f)</td>
<td>*</td>
<td>2.1</td>
</tr>
<tr>
<td>Stroke(^g)</td>
<td>10.0</td>
<td>5.7</td>
</tr>
</tbody>
</table>

\(^a\) – ICD9 codes for heart disease: 391-392.0, 393-398, 402, 404, 410-416, 420-429  
\(^b\) – ICD9 codes for ischemic heart disease: 410-414  
\(^c\) – ICD9 codes for heart attack: 410  
\(^d\) – ICD9 codes for arrhythmias: 427  
\(^e\) – ICD9 codes for heat failure: 428  
\(^f\) – ICD9 codes for hypertension: 401  
\(^g\) – ICD9 codes for stroke: 430-438

Limited research had been conducted examining the relationship between obesity and LOS. Zizza et al (4) used NHANES and NHEFS data and found that obesity was associated with an increase risk of extended stay in the hospital. They did not examine the types of hospitalizations. It is plausible that the LOS for CVD hospitalizations would be longer for obese adults compared to normal weight adults. To our knowledge, no study has examined all CVD hospitalizations (ICD9: 390-459) in a population based cohort. Few studies have examined specific CVD subcategories and obesity. The findings from the available studies are summarized below.

Razinia et al (5) examined BMI and LOS for ischemic stroke in 451 patients. In this study BMI was calculated from three different sources – measured height and weight, self-reported height and weight, and caregiver provider the patient’s height and weight. Patients were classified into 4 BMI status categories – underweight/normal weight (< 25 kg/m^2), overweight (25 - <30 kg/m^2), obese class I (30 - <35 kg/m^2), and obese class II/III (≥ 35 kg/m^2). The majority of the patients were in the underweight/normal weight and overweight categories, 46% and 36%, respectively. Fatal hospitalizations (n=18) were included in the analysis. The median length of stay was 5.2 days (95% CI: 4.6-5.8) among underweight/normal weight, 5.1 days (4.5-5.8) among overweight, 6.4 days (5.4-7.5) among obese class I, and 6.3 days (4.5-8.2) among obese class II/III (p = 0.08).
Reeves et al (6) examined 4,372 patients undergoing Coronary Artery Bypass Surgery (CABG) in the United Kingdom. Fatal hospitalizations were excluded. They classified patients into 5 BMI categories – underweight (< 20 kg/m²), normal weight (20-<25 kg/m²), overweight (25 - <30 kg/m²), obese class I (30 - <35 kg/m²), and obese class II/III (≥ 35 kg/m²). Length of stay was dichotomized as ≤ 7 days or >7 days. They found underweight patients more likely to have a longer LOS than normal weight (OR: 1.60, 95% CI: 1.06 - 2.35). Overweight, obesity class I and obesity class II/III were also associated with longer hospital stays, OR=1.20 (95% CI: 1.02-1.42), OR=1.40 (95% CI: 1.12-1.74), OR=1.50 (95% CI: 1.02-2.21), respectively. Reeves et al hypothesized that obese patients may stay longer in the hospital as a precaution.

Wells et al (7) examined 284 patients with acute myocardial infarction (ICD9: 410) in Augusta, Georgia. They compared the mean length of stay across 5 BMI categories (underweight (< 20 kg/m²), normal weight (20-<25 kg/m²), overweight (25 - <30 kg/m²), obese class I (30 - <35 kg/m²), and obese class II/III (≥ 35 kg/m²)). The mean LOS (across BMI categories) was 7.1± 8.4 days, 8.2 ± 7.6 days, 5.3 ± 4.8 days, 8.4 ± 11.3 days, and 7.5 ± 8.0 days, respectively. They found no significant correlation (p=0.093) between BMI and LOS for acute myocardial infarction.

Yap et al (8) investigated the relationship between obesity and post-operative stay following cardiac surgery in Australia. Patients (n=4,053) were categorized into 3 BMI categories – non-obese (20 - <30 kg/m²), obese (30 - <40 kg/m²), and morbid obese (≥ 40 kg/m²). Patients with a BMI <20 kg/m² were excluded from the analysis. The majority of the patients (69.1%) were in the referent BMI group (non-obese). They found no association between obesity and post-operative stay > 14 days among obese (OR= 1.13, 95%CI: 0.87-1.47) and morbid obese (OR=1.33, 95%CI: 0.63-2.83).

Only one of the studies (6) summarized above found a significant association between BMI and LOS. Two other studies (5, 9) showed trends but were limited by sample sizes (n<500). In addition, none of the studies examined BMI as a continuous variable instead created 3 to 5 categories. It is important to note, that the NIH/WHO definition of normal weight (18.5 - <25.0 kg/m²) was not used in any of these studies. The outcome (length of stay) was only examined as a continuous variable in two studies (5, 9).

The purpose of this study is to conduct a longitudinal analysis to determine if obesity is associated with longer length of stay for CVD hospitalizations. We will examine LOS for all primary CVD hospitalizations and cause-specific CVD hospitalizations. The cause-specific CVD hospitalizations that we will examine include, but are not limited to:

<table>
<thead>
<tr>
<th>First listed diagnosis</th>
<th>ICD-9 codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>401</td>
</tr>
<tr>
<td>Heart disease</td>
<td>391-392.0, 393-398, 402, 404, 410-416, 420-429</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>410</td>
</tr>
<tr>
<td>Coronary atherosclerosis</td>
<td>414.0</td>
</tr>
<tr>
<td>Other ischemic heart disease</td>
<td>411-413, 414.1-414.9</td>
</tr>
<tr>
<td>Cardiac dysrhythmias</td>
<td>427</td>
</tr>
</tbody>
</table>
First listed diagnosis | ICD-9 codes
---|---
Congestive heart failure | 428.0, 428.2-428.4
Cerebrovascular disease | 430-438

5. **Main Hypothesis/Study Questions:**

- Determine the association between body mass index (BMI) and length of hospital stays for cardiovascular disease. We hypothesize that adults with a higher BMI will have a longer length of stay (LOS) in the hospital.
- Determine the association between other anthropometric measurements (waist circumference, hip circumference, waist-to-hip ratio) and length of hospital stays for cardiovascular disease. We hypothesize that adults with larger anthropometric measurements will have a longer LOS.
- Determine the association between BMI and length of hospital stays for cause-specific CVD hospitalizations (e.g. heart disease, stroke). We hypothesize that adults with a higher BMI will have a longer LOS.
- Determine if associations between anthropometric measures and length of hospital stay for CVD differ by race and gender. We hypothesize that associations will differ by race and gender in that obesity will be associated with longer hospital stays in African Americans and women than in Whites and men.

6. **Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).**

We will use data from the ARIC visits 1-4 and annual follow-ups

**Identification information**
- Patient ID
- Date of visit
- Field center

**Anthropometrics**
- Weight
- Weight at age 25
- Height

**Medical History**
- Ever been hospitalized
- Self-rated health
- Prevalent CHD
- Incident CHD
- Prevalent cancer
- Incident cancer
- Prevalent stroke
- Incident stroke

**Demographics**
- Gender
- Ethnicity
- Age
- Education
- Employment
- Insurance status
- Marital status

**Hospitalizations**
- ID number (link)
- Discharge date
- Primary Diagnosis code
- Other diagnosis codes
- Admission date

**Other**
- Smoking status
- Alcohol status
Outcome: The primary outcome for this proposal is length of hospitalization for cardiovascular disease. The type of hospitalization will be determined by the first-listed diagnosis. This analysis is limited to only CVD hospitalizations since admission date was not collected for all hospitalizations. The ICD codes for CVD hospitalizations are 390 to 459. We will also examine the length of hospital stay following CVD subcategories: heart disease (391-392.0, 393-398, 402, 404, 410-416, 420-429), ischemic heart disease (410-414), heart attack (410), arrhythmias (427), heart failure (428), hypertension (401), stroke (430-438). The length of stay (LOS) will be calculated as the number of days between the admission date and discharge date.

Exposures: The exposures are continuous body mass index (BMI), waist circumference, hip circumference, and waist-to-hip ratio. We will examine the exposure using mean measurement prior to CVD hospitalization. Using standard cut points, we examine the exposures as categorical variables.

Covariates: The potential covariates include race, gender, field center, age, physical activity, education level, smoking status, alcoholic beverage consumption, marital status, insurance status and year of hospitalization.

Exclusions:
- Ethnicity other than White or African-American
- African-Americans in Minnesota or Maryland
- Missing exposure at baseline
- Not hospitalized or non-CVD hospitalization (based on the first-listed ICD code, 390-459).
- Missing covariates
- Long term hospitalizations in order to separate them from regular short term stays.
  We will define short term stay as either less than 2 weeks or 1 month.

Brief data analysis plan: We will use mixed models (PROC MIXED in SAS) to account for repeated measures within participants. BMI will be examined continuously. We will test whether or not the quadratic term is significant. We will also test race and gender interactions and, if appropriate, run separate analyses by race and/or gender groups (African American women, White women, African American men and White men).

The analysis will be repeated for the other anthropometric measurements as the main exposure and the length of hospital stay for the subcategories of CVD as the outcome.

One challenge we will have to how to account for linked hospitalizations. Our plan is to examine the hospitalizations that are coded as “linked” to determine whether the lengths
for the different hospitalizations should be added together and analyzed as one occurrence or counted as separate occurrences (repeated measures).

Other challenges include determine the appropriate length cut point to separate short-term stay from long-term stay. We will investigate using 2 weeks and 1 month. The other challenge is whether we should exclude fatal hospitalizations.

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 ICTDER03 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 ICTDER03 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 ICTDER03 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://www.csec.unc.edu/ARIC/search.php

___ x___ Yes  _______ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

MS #1133 – Association between obesity and hospitalizations

This proposal is from our research group and the manuscript has been published (Han E, Truesdale KP, Taber DR, Cai J, Juhaeri J, Stevens J. Impact of overweight and obesity on hospitalization: race and gender differences. Int J Obes (Lond). 2009 Feb;33:249-56). That manuscript examined the association between obesity and hospitalizations. The proposed proposal will expand on that paper and examine the length of stay among a subset of the hospitalizations (CVD hospitalizations) and its association with obesity.
There are no other ARIC proposals related to this proposal.

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  _X___ Yes  ____ No

11.b. If yes, is the proposal

   _X__  A. primarily the result of an ancillary study (list number* 2005.08_)

   ___  B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* __________  __________  __________)

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.
References