1.a. **Full Title:**  Management and outcomes of patients admitted with acute decompensated heart failure on weekend vs. weekday: The Atherosclerosis Risk in Communities Surveillance 2005-2014

b. **Abbreviated Title (Length 26 characters):**  Outcomes from acute heart failure admission on the weekend compared to weekday

2. **Writing Group:**
Louisa Mounsey, Carla Sueta, Patricia Chang, Kunihiro Matsushita, Stuart Russell, Edgar Miller, Melissa Caughey

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

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**ARIC author** to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).  
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3. **Timeline:**
Abstract to be completed for October 10th submission to either the AHA Epi Lifestyle conference or the ACC Scientific Sessions. Manuscript to be completed within 1 year of proposal approval.
4. **Rationale:**

According to the Healthcare Cost and Utilization Project sponsored by the Agency for Healthcare Research and Quality, heart failure is the third most common diagnosis for inpatient stays, after osteoarthritis and septicemia (excluding maternal/neonatal stays). In 2014, there were over 900,000 hospital stays for this reason. Due to reductions in staffing over the weekends, outcomes may differ for patients admitted with acute decompensated heart failure (ADHF) on the weekends vs. the weekdays. However, previous studies have been conflicting. A study of 9657 patients in Italy between 2002 and 2009 admitted for acute heart failure, determined by ICD-9 codes, found a higher mortality in patients admitted over the weekend.\(^1\) Similarly, a study of 81,810 heart failure admissions (2005-2008) from the GWTG-HF study found increased in-hospital mortality for patients admitted over the weekend for heart failure.\(^2\) Conversely, a study of 1620 patients in Japan found that while patients admitted on the weekend with worsening heart failure were significantly older with more comorbidities, there was no difference in mortality compared to those admitted on weekdays.\(^3\) Similarly, a report from the OPTIMIZE-HF registry of 48,612 patients between 2003 and 2004 hospitalized for heart failure found no difference in mortality among patients admitted on weekends compared to weekdays, but did find an extended length of stay for weekend admissions.\(^4\)

It is particularly noteworthy that two large registries of heart failure patients in the United States, GWTG-HF and OPTIMIZE-HF, report conflicting results on whether in-hospital mortality is significantly greater for weekend compared to weekday admissions. The reason for these conflicting results is uncertain given that the two registries included similar patients admitted at diverse types of medical institutions. The GWTG-HF cohort reported a statistically significant increase in mortality among patients admitted over weekends compared to those admitted on weekdays (3% vs 3.3%, \(p=.008\)). This small difference and the low event rate of in-hospital mortality indicates large sample sizes are required for this analysis, and GWTG may have been underpowered. It is also possible the disparity in in-hospital mortality between weekend vs. weekday admissions was largely driven by a small subgroup of patients more susceptible to death when admitted during weekend conditions. Notably, these two large registries both utilized admission and discharge diagnoses for determination of heart failure cases, with no additional adjudication process. In the ARIC Community Surveillance, we can examine inpatient, 28-day, and 1-year mortality in patients classified by physician review as either “definite” or “probable” ADHF, in both academic and community hospitals from urban, rural, and suburban areas with more minority representation. We will also be able to uniquely compare patients with preserved and reduced ejection fraction (HFP EF and HFrEF), and potential differences in weekend vs. weekday outcomes among demographic subgroups. Hospital record abstractions for patients admitted over 10 years (2005-2014) will allow an analysis of trends over time and provide a more contemporary sample.
5. Main Hypothesis/Study Questions:

1. Do outcomes, development of complications, length of stay, and mortality (inpatient and post-hospitalization) differ for patients admitted with acute decompensated heart failure (ADHF) over the weekend (and holidays) compared to a weekday?

2. Do outcomes, including length of stay, mortality, and development of complications, differ for patients admitted with ADHF during normal business hours compared to after hours?

3. Does post-hospitalization mortality differ for ADHF patients discharged on weekends (and holidays) vs. weekdays? Typically, more resources are in place for patients discharged on the weekdays, whereas patients discharged over the weekend must rely on someone to set things up the following Monday.

4. Do associations differ by HFpEF vs. HFrEF, by demographics (age, race, gender), and by season (winter, spring, summer, fall)?

5. Have mortality and ADHF hospitalization rates, according to weekend vs weekday admission, changed over time, from 2005 to 2014?

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).

Population: ARIC community surveillance, specifically patients admitted with definite or probable acute decompensated heart failure from 2005-2014.

Exclusion criteria: patients with no recorded date of admission

Outcomes Variables: in-hospital mortality, 28-day mortality, 1-year mortality, length of stay, treatments received in inpatient setting, medications during hospitalization and at discharge, development of complications (acute kidney injury, ventricular arrhythmias), need for inotropes, further cardiac testing (transthoracic echo, cardiac catheterization, stress testing).

<table>
<thead>
<tr>
<th>Variable of Interest</th>
<th>Variable Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>SEX</td>
</tr>
<tr>
<td>Race/Ethnic group</td>
<td>RACE1</td>
</tr>
<tr>
<td>Age</td>
<td>AGE</td>
</tr>
<tr>
<td>HFpEF or HFrEF</td>
<td>LVEF_CUR or SHF</td>
</tr>
<tr>
<td>Definite or probable designation of HF</td>
<td>HFDIAG</td>
</tr>
<tr>
<td>First admission or readmission for ADHF</td>
<td>HFAA7B, HF_HX</td>
</tr>
<tr>
<td>Procedure</td>
<td>Code(s)</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Transthoracic echo performed, date, and resulting EF</td>
<td>HFAA29, HFAA29A, HFAA29B</td>
</tr>
<tr>
<td>Right heart catheterization performed, date</td>
<td>HFAA31, HFAA31A</td>
</tr>
<tr>
<td>Coronary angiography performed, date, and EF</td>
<td>HFAA32, HFAA32A, HFAA32B1</td>
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<tr>
<td>Stress test performed, date</td>
<td>HFAA36, HFAA36A</td>
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<tr>
<td>Chest X-ray performed</td>
<td>HFAA27</td>
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<tr>
<td>ECG performed</td>
<td>HFAA25</td>
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<tr>
<td>IV diuretics</td>
<td>HFAA73B</td>
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<tr>
<td>IV inotropes</td>
<td>HFAA73A</td>
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<tr>
<td>Medications during hospitalization or at discharge</td>
<td>HFAA59-HFAA72</td>
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<tr>
<td>Creatinine (worst)</td>
<td>HFAA44A</td>
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<tr>
<td>BUN (worst)</td>
<td>HFAA45A</td>
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<tr>
<td>Ventricular arrhythmias</td>
<td>HFAA26F</td>
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<tr>
<td>Mortality</td>
<td>HFAA0C, HFAA0D, DDAYS_HF2, DOD F28_HF2, F365_HF2</td>
</tr>
<tr>
<td>Length of stay</td>
<td>Date of admission: CHIA6A</td>
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<tr>
<td></td>
<td>Date of discharge or death: HFAA03</td>
</tr>
<tr>
<td></td>
<td>Time of Admission: CHIA6B</td>
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</tbody>
</table>

**Analytical Plan**

All analyses will be carried out using SAS Survey Analysis procedures. Analyses will be weighted by the inverse of the sampling probability and will account for the stratified sampling design. Dates of admission will be converted to days of the week using SAS formats. SAS formats will also be used to identify dates national holidays were observed, as these are subject to change from year to year. Weekends will be considered Saturday and Sunday. Federal holidays are those designated by the United States Government Office of Personnel Management and include New Year’s Day, Martin Luther King Day, President’s Day, Memorial Day, Independence Day, Labor Day, Columbus Day, Veterans Day, Thanksgiving Day, and Christmas Day. Normal business hours will be considered admission times from 8 am – 5 pm. After-hours admissions will be from 5:01 pm – 7:59 am.

Management and mortality outcomes of weekend vs. weekday admission, and after-hours vs. business hours admission will be analyzed using logistic regression and Cox regression. Subgroup analyses will be carried out, in HFpEF and HFrEF, race-gender groups, older (>75 years) vs. younger patients, and season of admission.

As a sensitivity analysis, associations will also be examined in the subset of hospitalizations with a “definite” classification of ADHF.

We will perform a meta analysis to determine presence of an association between weekend vs. weekday admission and in-hospital mortality when combining results from ARIC, GWTG, OPTIMIZE, and other appropriate registries and cohorts.
Limitations
- Transfer of patients to or from another hospital may be a source of confounding, influencing both classification of “weekend/weekday” admission, and inpatient services and mortality outcomes. For this reason, we will omit patients who are transferred.
- The in-hospital event rate is expected to be low, and the ARIC study may be underpowered to detect differences in this outcome for weekend vs. weekday admission. To overcome this limitation, a random effects meta-analysis with other appropriate ADHF registries and cohorts will be considered.

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 ICTDER03 must be used to exclude persons with a value RES_OTHER = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used? ____ Yes  ____ No

(This file ICTDER 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 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.cscc.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)?

There are no manuscript proposals to examine outcomes of weekend vs. weekday admission in patients with ADHF.
MS #1264 proposes an analysis of weekend vs. weekday admission outcomes in stroke patients but not ADHF.
MS #966 proposes an analysis of after-hours admission times and outcomes for acute MI patients but not ADHF.
MS #2287 proposes an analysis of seasonal trends in ADHF admissions. The first author is no longer leading this proposal. With the permission of senior ARIC author (S. Russell), we will include this analysis in the current proposal; and ARIC authors of MS #2287 (S. Russell, P. Chang, E. Miller) are also authors of the current proposal.
11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ____ Yes  X No

11.b. If yes, is the proposal
___ A. primarily the result of an ancillary study (list number* __________)
___ 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.csc.unc.edu/aric/forms/

12a. 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.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is your responsibility to upload manuscripts to PubMed Central whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.csc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed Central.

13. Per Data Use Agreement Addendum, approved manuscripts using CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript ____ Yes  X No.

References:

