PATIENT AND SOCIAL DETERMINANTS OF HEALTH TRAJECTORIES FOLLOWING CORONARY EVENTS

A Dissertation Presented

By

LISA NOBEL

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ABSTRACT

More than 1.2 million Americans are hospitalized annually with an acute coronary syndrome (ACS); many impaired quality of life after discharge with an ACS. This dissertation focuses on two novel aspects of patient health status (PHS) after ACS: how it can be predicted based on the socioeconomic status (SES) of the patient, and how it evolves over time. We used data from TRACE-CORE, a longitudinal prospective cohort of patients hospitalized with ACS. We measured PHS using both the SF-36 mental and physical component subscales (MCS and PCS) and the Seattle Angina Questionnaire (SAQ) health-related quality of life (HRQoL) and physical limitations subscales at the index hospitalization and at 1, 3, and 6-months post-discharge. Firstly, after adjusting for individual-level SES, we found that individuals living in the neighborhoods with the lowest neighborhood SES had significantly worse PHS. Secondly, we found that each of the components of PHS had subgroups with distinct patterns of evolution over time (trajectories). Both the PCS and the SAQ physical limitations subscale had two trajectories; one with average and one with impaired health status over time. For the HRQoL subscale of SAQ, we found three trajectories: Low, Average, and High scores. For MCS, we found four trajectories: High (consistently high scores), Low (consistently low scores), and two with average scores at baseline that either improved or worsened over time, referred to as Improving and Worsening, respectively. All PHS trajectories, except for MCS, predicted readmission and mortality during the 6 months to 1 year post-ACS discharge.

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LIST OF ABBREVIATIONS

Abbreviation	**Meaning**
ACC	American College of Cardiology
ACS	Acute Coronary Syndrome(s)
AHA	American Heart Association
ANOVA	Analysis of Variance
BIC	Bayesian Information Criterion
CABG	Coronary Artery Bypass Graft
CHD	Coronary Heart Disease
FPL	Federal Poverty Level
GAD-7	Generalized Anxiety Disorder 7
GRACE	Global Registry of Acute Coronary Events
HRQoL	Health-Related Quality of Life
IQR	Interquartile Range
IPR	Income-to-Poverty Ratio
LOS	Length of Stay
MCS	Mental Component Subscale
NDI	Neighborhood Deprivation Index
NHLBI	National Heart Lung and Blood Institute
NIH	National Institutes of Health
NSES	Neighborhood Socioeconomic Status
NSTEMI	Non-ST Elevated Myocardial Infarction
PCI	Percutaneous Coronary Intervention
PCS	Physical Component Subscale
PHQ-9	Patient Health Questionnaire - 9
PHS	Patient Health Status
QGIS	Quantum Geographic Information Systems
SAQ	Seattle Angina Questionnaire
SD	Standard Deviation

SES	Socioeconomic Status
SF-36	36-Item Short Form Survey (SF-36)
STEMI	ST-Elevated Myocardial Infarction
TICS	Telephone Interview for Cognitive Status
TRACE-CORE	Transitions, Risks, and Actions in Coronary Events – Center for Outcomes Research and Education
UA	Unstable Angina

PREFACE

Chapter II of this dissertation is under review for publication as: Neighborhood Socioeconomic Status Predicts Health After Hospitalization for Acute Coronary Syndromes: findings from TRACE-CORE (Transitions, Risks, and Actions in Coronary Events – Center for Outcomes Research and Education)

CHAPTER I : INTRODUCTION

Epidemiology of Acute Coronary Syndrome (ACS) in the US

ACS is the acute form of coronary heart disease (CHD), a highly prevalent and morbid chronic condition. In 2012, about 1.2 million patients were hospitalized with ACS, including 813,000 hospitalizations for acute myocardial infarction (AMI) and 322,000 hospitalizations for unstable angina (UA) .[1] While ACS mortality has been decreasing in the past several decades, the prevalence of ACS has increased.[2] *However, patients are living longer, but not necessarily better*. For example, almost 30% of patients have frequent angina (weekly or more frequent) and moderately to severely diminished quality of life due to ACS at six months following discharge.[3] Only 58% of patients return to work within the first 3 months after discharge for ACS.[4] Returning to work following a cardiovascular disease event has not only economic benefits, but also benefits the quality of life of those affected with ACS.[5] The costs associated with lost productivity and absenteeism 1-year after ACS are about $6000-10,000 per patient.[6]

Patient-Reported Health Status Among Patients with Cardiovascular Disease

The American Heart Association (AHA) defines patient health status (PHS) according to symptom burden, functional status, and health-related quality of life (HRQoL).[7] We will use the term PHS to refer to both functional status and HRQoL. There are 2 types of measures of PHS: generic (e.g., SF-36) and disease-specific, such as the Seattle Angina Questionnaire (SAQ). Disease-specific measures capture important domains of patient well-being directly related to specific disease pathophysiology. Thus, they may be more responsive to clinical interventions than generic measures.[7] Generic measures complement disease-specific measures by capturing the global picture of multi-morbidity in patients with cardiovascular disease.[8] However, both generic and disease-specific measures seem to be equally predictive of death or readmission among patients with coronary artery disease.

Conceptual Framework

The Wilson-Cleary model of Quality of Life sees health status as resulting from complex interactions of socio-demographic and psychosocial factors and the environment (neighborhood socioeconomic status) .[9] The AHA has adopted this model,[7] and this allows for possible relationships between neighborhood and clinical characteristics and their effect on patient health status (Figure I.1).

Predictors of Patient- Health Status Among Patients with Cardiovascular Disease

The AHA, recognizing critical gaps in the existing literature, has called for additional research into determinants of patient health status.[7] A number of studies have examined predictors of PHS for outpatients,[10,11] individuals undergoing cardiac catheterization,[12-19] patients with myocardial infarction, [20-25] and after ACS hospitalization.[26] [27-29] To date, however, no studies have examined trajectories (subgroups with distinct longitudinal patterns) of PHS and their predictors.

Women,[11,14] individuals with low socio-economic status,[16,30] and those who live alone[31] are more likely to have worse HRQoL. Also, those with additional co-morbidities[27] fare worse than those with CHD alone, while increasing age and coronary revascularization are associated with better HRQoL.[29] Several psychosocial variables including depression,[22] and anxiety[32] are associated with worse HRQoL in patients with CHD. **However, we lack even a basic understanding of whether there are subgroups with distinct longitudinal patterns (trajectories) of patient health status and the sociodemographic, medical history, psychosocial, and clinical characteristics associated with different trajectories.**

Trajectories of HRQoL

Group-based trajectory analysis determines whether there are subgroups of individuals with distinct longitudinal patterns of a phenomenon over time. The emerging science of trajectory analysis offers the potential of rich insights from longitudinal data that could inform the organization and delivery of healthcare with expectations about the likely duration and shape of individual patient's illness progression. This would allow patients, caregivers, and providers to anticipate and address changing needs, possibly preventing future adverse clinical events. In cancer, distinct trajectories of health status trigger different care patterns and healthcare expenditures.[33] Whether analogous patterns apply in ACS has never been examined.

Neighborhood deprivation as a predictor of adverse health outcomes

Neighborhood "deprivation" or low neighborhood socioeconomic status (NSES), may affect health through several pathways. Indeed, the built environment, such as the presence or absence of walkways, parks and urban sprawl, may contribute to chronic disease development.[34,35] Areas with higher neighborhood deprivation may have less access to healthy food[36] and be associated with other cardiovascular risk factors.[37,38] Also, many health policies can affect health by changing residential neighborhoods. Because place of residence is highly correlated with race and social position, it could serve as a proxy for health disparities due to race and individual-level socio-economic status (SES).[39] [40] Several studies have shown that areas with higher neighborhood deprivation have higher rates of heart disease and stroke.[40-42] Moreover, areas with higher neighborhood deprivation are more likely to have adverse self-rated health and quality of life in the general population.[43-45] Despite evidence that both individual and neighborhood-level SES are important predictors of quality of life in the general population, **no study has examined the effect of neighborhood deprivation on quality of life after ACS hospitalization beyond the effect of individual-level SES. Large neighborhood effects on quality of life after ACS by neighborhood characteristics would point towards neighborhood deprivation as a "driver" of health disparities**. It will be important to know how much of the observed variation in quality of life after ACS by hospital admission site is identified through neighborhood-level effects.[46]

Patient Health Status - A Quality Metric

In their seminal work, Crossing the Quality Chasm: A New Health System for the 21st century, the Institute of Medicine declared that we should aim to provide care that is safe, effective, timely, efficient, equitable and patient-centered.[47] PHS measures are key to the efforts towards patient-centered care, as they allow patients to be more involved in their own care and can help providers to focus on patient concerns regarding functional status and HRQoL.[47] Thus, PHS measures have been proposed as a quality metric for patients with cardiovascular disease by several different organizations including the American Heart Association[48] and the International Consortium for Health Outcomes Measurement.[49] Moreover, both the Veterans Affairs Administration and the Centers of Medicare and Medicaid Services are exploring using patient health status measures as quality metrics among patients who have received elective percutaneous coronary intervention (PCI).[50]

Although PHS measures may be useful quality metrics, there are some potential pitfalls in their use. Healthcare providers have expressed concerns that the data collection would be too great and it is unclear whether these measures can discriminate between providers and institutions with high and low quality of care.[51] To create a "level playing field" quality measures must be risk-adjusted among providers who serve very different patients.[48] The International Consortium for Health Outcomes Measurement has suggested a set of measures that include neither psychosocial nor socio-economic measures. If NSES predicts patient health status, and is not included in risk adjustment measures, then that could lead to unfairly penalize safety-net hospitals and those who serve patients from lower NSES neighborhoods. Our study aims to determine the relationship between neighborhood socio-economic status and patient health status, to be able to inform this risk adjustment process in the future.

Patient Health Status as a Predictor of Clinical Outcomes

Patients with higher symptom burden, more physical limitations and worse HRQoL are more likely to die.[52-59] However, relatively few studies have characterized the relationship between patient health status and hospital readmission among patients with coronary artery disease.[53-55,59] The samples of these studies were mixed with individuals without ACS (e.g., individuals with stable coronary artery disease, heart failure,[53] or patients undergoing PCI) ,[59] whereas others only included patients with myocardial infarction.[60] The risk for hospital admissions and pathophysiology among the aforementioned patients may differ markedly from those of ACS patients. **Our study will be first to quantify how trajectories of PHS over the first 6 months post-discharge affect the risk of all-cause readmission during the second 6 months post-discharge, a time when further negative health events are likely to occur.**

Specific Aims

Our study will leverage the availability of rich data already collected for the NHLBI-funded TRACE-CORE, a longitudinal prospective cohort study of 2,183 patients hospitalized with ACS. TRACE-CORE includes robust and carefully collected and abstracted data on psychosocial and patient-centered outcomes and geo-coded census-level characteristics. Patient-centered outcomes (including generic and disease-specific HRQoL, and physical limitations) are measured longitudinally: at the index hospitalization and again at 1, 3, 6, and 12-months post-discharge. We will first seek to determine the extent to which neighborhood socioeconomic status (NSES) predicts post-ACS patient health status. Then, we will seek to identify subgroups of patients with distinctive HRQoL trajectories during the first 6 months following their index event, as well as factors (measures of neighborhood deprivation, in addition to patient morbidities and socio- demographic characteristics) that are associated with these patterns. We will also explore these early HRQoL trajectories as potential predictors of readmissions in the second 6-months post-discharge.

Aim 1: Determine whether **neighborhood SES is** associated with **patient health status (SAQ and SF-36)**, after discharge for ACS, independently of individual-level SES.

H1a. Neighborhood deprivation will independently predict poor health-status, even after accounting for patient morbidities and SES factors.

Aim 2: Determine associations between **individual level** socio-economic, clinical, in-hospital and psychosocial factors and **trajectories of patient health status post-ACS discharge** (physical limitations and angina specific quality of life as measured by the Seattle Angina Questionnaire [SAQ]) and generic quality of life by the SF-36 at baseline, 1-, 3-, and 6-months following hospital discharge for ACS.

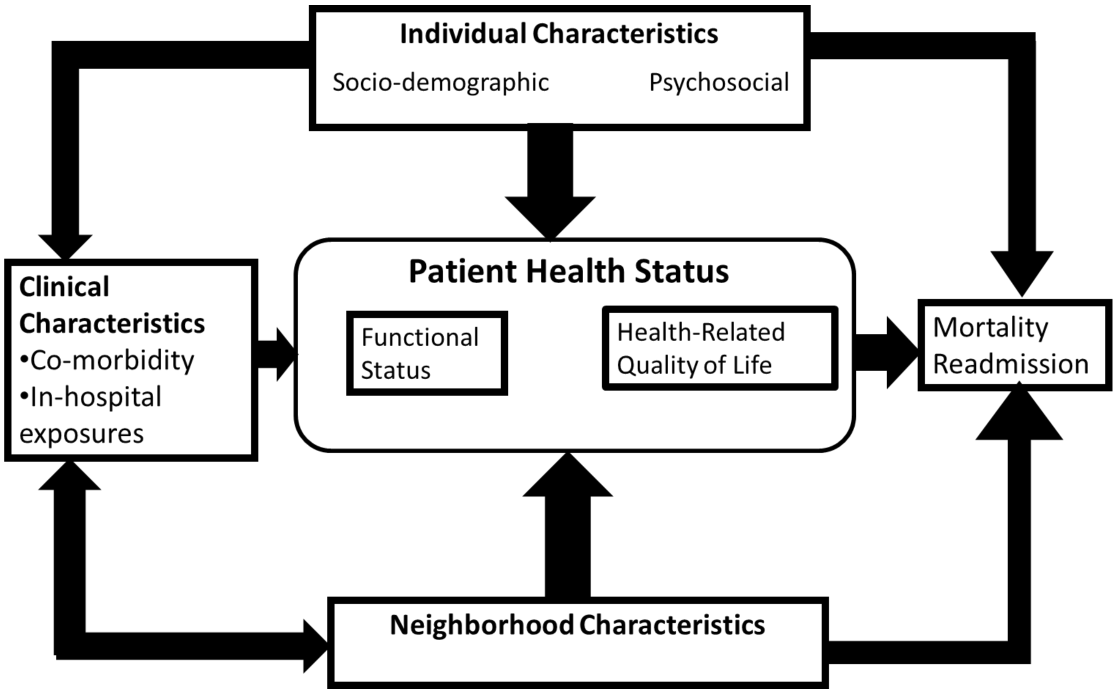
H2a. Trajectories will include stable, improving, and decreasing patient health status over time

H2b. Individuals who have more co-morbidity and worse psychosocial well-being will be less likely to improve than younger healthy adults.

Aim 3: Identify the extent to which **trajectories** of the generic quality of life (SF-36) and the 5 SAQ domains (physical limitations and disease-specific quality of life) at baseline, 1, 3, and 6 months predict **mortality or readmission 6 months to 1 year** post-ACS discharge.

H3a. Unfavorable health status trajectories (SF-36 and SAQ) will increase the probability of subsequent death and readmission.

Figure I.1: Adapted Wilson-Cleary Model[9]



CHAPTER II : NEIGHBORHOOD SOCIOECONOMIC STATUS PREDICTS HEALTH STATUS AFTER HOSPITALIZATION FOR AN ACUTE CORONARY SYNDROME

Abstract

Objective: To explore the influence of contextual factors on health-related quality of life (HRQoL), which is sometimes used as an indicator of quality of care, we examined the association of neighborhood socioeconomic status (NSES) and HRQoL after hospitalization for acute coronary syndromes (ACS).

Methods: We studied 1,481patients hospitalized with ACS in Massachusetts and Georgia querying HRQoL via the mental and physical components of the SF-36 (MCS and PCS) and the physical limitations and angina-related HRQoL subscales of the Seattle Angina Questionnaire (SAQ) during hospitalization and at 1-, 3-, and 6-months post-discharge. We categorized participants by terciles of the Neighborhood Deprivation Index (a census tract-based measure) to examine the association of NSES with HRQoL after adjusting for individual SES and clinical characteristics.

Results: Participants had a mean age of 61.3 (SD: 11.4) years; 33% were female; 76% were non-Hispanic white; and 11.2% had household incomes below the federal poverty level. Living in lower NSES neighborhoods was associated with lower mean PCS scores (1.5 points for intermediate NSES; 1.8 for low) and SAQ scores (2.4 and 4.2 points) versus living in high NSES neighborhoods. Neighborhood SES was more consequential for patients with lower individual SES. Individuals living below the federal poverty level had lower average MCS and SAQ physical scores (3.7 and 7.7 points, respectively) than those above the federal poverty level.

Conclusions: Neighborhood deprivation was associated with worse health status. Using HRQoL to assess quality of care without accounting for individual and neighborhood SES may unfairly penalize safety net hospitals.

Word count: 249

Introduction

Every year, about 1.2 million adults in the United States are hospitalized with acute coronary syndrome (ACS).[1] While most patients are discharged alive, almost 30% have diminished quality of life for 6 months post-ACS discharge.[3] Thus, the American Heart Association (AHA) has called for additional research into the determinants of functional status and health-related quality of life (HRQoL) among adults with cardiovascular disease.[7]

It is known that individuals with low socioeconomic status (SES) have worse HRQoL than the general population,[61,62] especially those with cardiovascular disease.[63-65] The few studies that have examined neighborhood socioeconomic status (NSES) and HRQoL have mostly focused on the general population; [66-68] however, none have studied HRQoL following hospitalization for an ACS. Neighborhood SES is a risk factor for heart disease [69] and death,[70] and is associated with many factors that affect cardiovascular health, such as the built environment, access to healthy foods,[36] smoking and physical activity.[37,38] Thus, neighborhood SES deserves study as a contributor to health following hospitalization for ACS.

Additionally, most hospitals' patients are geographically concentrated, with safety net hospitals treating a disproportionate share of people from poor neighborhoods. Given that post-discharge patient health may become a hospital quality metric,[47,50] if NSES predicts variations in quality of life after an ACS,[46] this would have important implications for a health outcome quality metric. We could not, however, find any study of the relationship between neighborhood SES and health status in patients with cardiovascular disease.

While there are many plausible explanations for why living in a better-resourced neighborhood is typically associated with better health, the relationships between quality of life and individual and neighborhood SES remain unclear. Therefore, we conducted this study to examine the independent effect of NSES on health status post ACS hospitalization. We hypothesized that low neighborhood SES would predict poor health-status trajectories even after accounting for patient co-morbidities and individual SES, and that the effect of low NSES would be worse for low-SES ACS patients than for those with more individual resources.

Methods

Study Sample and Design

We used data from TRACE-CORE (Transitions, Risks, and Action in Coronary Events – Centers for Outcomes Research and Education), a prospective longitudinal cohort study of adults who survived hospitalization for an acute coronary syndrome. Patients were recruited from April 2011 to May 2013 from 6 community and teaching hospitals in central Massachusetts and Georgia. Further details regarding study design and recruitment and retention of TRACE-CORE participants are available.[71,72]

TRACE-CORE participants were interviewed at discharge either during the index hospitalization for ACS or via telephone 72 hours after discharge. Patients were then followed via structured computer-assisted telephone interviews at 1, 3, and 6 months post-discharge. Trained study personnel abstracted clinical characteristics from medical records. The University of Massachusetts Medical School Institutional Review Board approved this study.

Measures

Health-Related Quality of Life (HRQoL)

Study outcomes included generic health-related quality of life (HRQoL), disease-specific HRQoL, and a disease-specific measure of physical limitations. We used the SF-36[73] as our generic measure of HRQoL and the Seattle Angina Questionnaire (SAQ)[74] a disease-specific measure. The SF-36 contains two subscales, Mental Component

Subscale (MCS) and Physical Components Subscale (PCS), each with a range of 0-100, with higher scores indicating better HRQoL. Each subscale is calibrated to a population mean of 50 and standard deviation of 10, with higher scores representing better health. The SF-36 has strong psychometric properties[75] and has been validated in patients with cardiovascular disease.[76] The SAQ is designed to capture disease-specific HRQoL, including physical limitations. The SAQ has strong psychometric properties[77] and has been validated for use with patients with coronary artery disease, including those undergoing coronary angiography,[78] and those with chronic stable angina.[77]

Neighborhood Socioeconomic Status (SES)

We used the neighborhood deprivation index (NDI)[40] based on American Community Survey's 2010 census data to measure neighborhood SES. The NDI includes 5 domains: neighborhood poverty rate, occupational characteristics, housing tenure, employment, and educational distribution.[40] The NDI is calculated from these factors, based on a principal components analysis. It has a mean of 0 and a standard deviation of 1; higher scores indicate greater deprivation (i.e. lower NSES).[40] For analysis, we categorized neighborhood deprivation in terciles: high (NDI score -1.51 to -0.59), intermediate (NDI score -0.59 to 0.30) and low neighborhood SES (NDI score 0.30 to 3.75).

Assigning an NDI score to an individual started with geocoding their self-reported address at discharge to a 2010 census tract. Geocoding involved two steps. First, we used the Google maps application programming interfaces through the R package "geocode" to determine longitude and latitude.[79] This program uses fuzzy matching algorithms to match addresses with geographic co-ordinates and has a database of places that is continuously being updated.[79] The R package also specifies the accuracy with which it was able to match an address to a set of geographic coordinates [79]. There are three levels of accuracy including: rooftop or building-level accuracy, range-interpolated, and approximate [79]. For range-interpolated locations, the algorithm used that information to estimate geographic co-ordinates. Addresses that could only be matched by zip code are classified as approximate matches, so we excluded these from our study. For the second step, we used the open-sourced Quantum Geographic Information Systems (QGIS)[80] to match geographic coordinates for each patient's address to a census tract. Census tracts were defined using 2010 shapefiles from the US census. [81] Information needed to calculate the NDI for each census tract was downloaded and matched to TRACE-CORE participants.

Potential Confounding Variables

Potential patient-level confounders included: demographics (including individual-level SES), co-morbidities, and in-hospital factors. Demographic covariates were age, sex, race/ethnicity, marital status, and whether living alone prior to the index hospitalization. All demographic characteristics were self-reported at baseline, except age which was abstracted from the medical record. Individual-level SES variables included: educational attainment, household income relative to the federal poverty level, usual source of care, and health insurance status. Patients self-reported their highest level of educational attainment, household size and categories of household income (<$10,000, $10,000-19,999, $20,000-34,999, $35,000-49,000, $50,000-$74,999, $75,000-99,999, $100,000-149,999 or $150,000 or more). Based on reported household income and size we calculated the income to poverty ratio (IPR), a measure of the extent, to which individuals were above the federal poverty level set by the Department of Health and Human Services.[82] For example, an IPR score of 1 means that the patient's household income is at 100% of the federal poverty level (FPL); and a score of 3, that it is at 300% of FPL.

Patients were asked at one month following discharge, "Is there a place that you usually go to when you are sick or need advice about your health?". We coded those reporting "no place to go for healthcare" as having no usual source of care. Insurance status was captured from medical record abstraction at discharge as: employer or individual paid insurance, Medicare, Medicaid, or none. Medical record review provided information regarding co-morbidities present before the index hospitalization including lung disease, anemia, high blood pressure, peripheral vascular disease, arthritis, history of heart disease, diabetes, stroke or transient ischemic attack, and heart failure. Information regarding in-hospital exposures included in-hospital procedures, in-hospital complications, type of ACS, length of stay (LOS), and the Global Registry of Acute Coronary Events (GRACE) risk score.[83] In-hospital procedures included Coronary Artery Bypass Graft (CABG) surgery and Percutaneous Coronary Intervention (PCI). In-hospital complications included developing a major-medical condition during the index hospitalization (e.g., acute kidney injury, atrial fibrillation or atrial flutter, heart failure, cardiogenic shock). We categorized ACS type during the index admission as: non-ST segment elevation myocardial infarction (NSTEMI), ST-segment elevation myocardial infarction (STEMI) or unstable angina (UA) according to ACC/AHA criteria.[84] Cases in which ACS type was not clear were decided by a physician panel. Length of hospital stay was abstracted from the medical record.

Statistical Analysis

We first examined distributions, means and standard deviations for all variables, and then bivariate relationships of demographic, individual socioeconomic factors, and medical factors with neighborhood SES categories (high, intermediate, and low NSES) with quality of life, separately for each outcome (MCS, PCS, SAQ HRQoL, and SAQ physical limitations), after accounting for potential confounder using hierarchical linear models. The models included random intercepts to address clustering of observations within patients (repeated measures) and patients within census tracts. We did not include random intercepts for slopes. Due to our primary focus on relationships among health trajectories, and individual and neighborhood SES, we chose *a priori* to study interactions between NSES and individual-level SES and between NSES and time using likelihood ratio tests of statistical significance in models that predict health over time. All models included age, sex, race/ethnicity and the household-specific IPR. We added other covariates when their inclusion changed the estimate for the coefficient for NSES by at least 10%.

We used multiple imputation with predictive mean matching and chained equations to create 20 imputed datasets.[85] Imputation was carried out for both covariates and outcomes. Imputation models relied on all variables described above and: census tract ID, subscales of the SAQ (angina frequency, angina stability and treatment satisfaction subscales), body mass index categories, and information on several psychosocial variables (depression, anxiety, and cognitive impairment). Estimates were combined using Rubin's rules.[86] Analyses were performed using Stata 13 (StataCorp, College Station, TX).

Results

Sample Characteristics

Among 2187 TRACE-CORE participants, we excluded those who died during the 6-month follow-up period (n=55), those with missing baseline MCS SF-36 scores (n=2), those missing subtype of ACS (n=51), and patients who were readmitted during the 6 months following discharge (n=477). An additional 108 patients (6.5%) were excluded from the analysis because they could not be matched to a census tract; of these, 89% were unmatched because their home address was given as a post office box. Thus, the present analysis included 1,481 TRACE-CORE participants. Many values of the health status measures were missing, mostly due to loss to follow-up; 1,002 patients had these data at 1 month, 916 at 3 months and 890 at 6 months.

Patients were on average 61.0 (SD 11.4) years old (Table II.1). Approximately 67% were male, and 76% were non-Hispanic white. About half of participants had a high school degree or less education, and 40% had an annual household income of less than $35,000. Eleven percent (11.2%) of patients were living under the federal poverty level. More than half of the patients were admitted for an NSTEMI, roughly a third were admitted for unstable angina, and 16% were admitted for a STEMI (Table II.2). About two thirds of patients stayed less than 4 days for their initial hospitalization of ACS, and 68% had undergone a percutaneous coronary intervention (PCI) during their initial hospitalization.

Neighborhood Characteristics

TRACE-CORE participants came from 508 census tracts (median of 2 patients per tract (IQR 1-4)). Almost all census tracts were in Massachusetts (53.1%) or Georgia (41.6%). For all components of the NDI except for median house value, neighborhoods in the lowest neighborhood SES tercile had the lowest NDI scores on each component (Supplemental Table II.1). Neighborhoods (not TRACE-CORE participants) with low SES had an average of 23% of individuals with less than a high school degree, 29% under the federal poverty level, and 25% on supplemental nutrition assistance.

Patient Characteristics Associated with Living in Neighborhoods with Low SES

Patients in neighborhoods with the lowest NSES were younger, more likely to be female, to live alone and be Hispanic or non-white (Table II.1). Patients living in lower NSES neighborhoods were also more likely to have lower individual SES including having less than a high school degree, a lower IPR, and more likely to be on Medicaid or Medicare (Table 1) than patients who lived in high NSES neighborhoods. Participants living in lower NSES neighborhoods were more likely to have a history of diabetes, several cardiovascular conditions (high blood pressure, history of heart disease and heart failure) and drug abuse (Table II.2). During their initial hospitalization, participants in lower NSES neighborhoods were less likely to have had a STEMI and more likely to have no procedures (PCI or CABG) during their initial hospitalization (Table II.2).

Trends in Patient Health Status Over Time

Overall, all components of patient health status (MCS, PCS, SAQ HRQoL, and SAQ Physical Limitations) improved over the 6 months following hospital discharge. Much of the improvement in PHS score occurred within 1 month of discharge. Individuals living in high SES neighborhoods had higher average PHS scores (Figure II.1) at discharge that did not attenuate during follow-up.

Interactions

The interaction between NSES and individual SES was significant for both MCS ($p<0.001$) and SAQ Physical Limitations ($p=0.03$), but not for SAQ HRQoL ($p=0.08$) or PCS ($p=0.85$) (Figure II.2). The interactions all indicate larger HRQoL NSES-associated deficits for poorer patients living in poor neighborhoods than for patients with higher individual SES. There were no statistical interactions present between NSES and time (i.e. slopes) for any components of patient health status (MCS $p=0.74$, PCS $p=0.58$, SAQ physical limitations $p=0.38$, SAQ HRQoL $p=0.26$).

Association between Neighborhood SES and Patient Health Status

Figure 3 illustrates the models of Table II.3. Figure II.3 shows predicted PHS over time for several exemplary values of Income to Poverty Ratio or IPR and NSES. For IPR we consider being either in a household at the federal poverty level (IPR=1) or at 300% of the FPL (IPR=3). For NSES, we considered those living in neighborhoods with high vs. low SES terciles. In all models, the association of HRQoL with NSES was weaker (a smaller coefficient) than the association with individual SES in multivariate models (Table II.3 and Figure II.3).

Discussion

We examined the association between NSES and patient health status in the 6 months following hospitalization for an ACS, finding that patients who lived in *neighborhoods* with lower NSES had significantly worse patient health status at discharge, even after adjusting for individual SES and a rich array of clinical characteristics. The discrepancy was maintained throughout the 6-month follow-up, with residing in a poorer neighborhood being associated with worse patient health. Both individual and neighborhood SES mattered for health, with individual SES mattering more than NSES. Moreover, for two of our health status measures, MCS and SAQ physical limitations, combined individual and neighborhood poverty was worse than adding their individual effects would suggest.

Associations between NSES and health were strong and consistent, with low NSES neighborhoods associated with reductions in health. The effect on MCS was almost as large as the minimally important clinical difference among those with no income, e.g., a 5-point deficit in MCS.[87] However, the magnitude of the association with other health outcomes was more modest. For example, the mean PCS score for individuals living in neighborhoods in the lowest NSES tercile was 1.8 lower than the mean for those living in the highest NSES tercile. Although a difference of this size may not be clinically important for an individual, it could matter at the population level.

The literature regarding NSES and HRQoL in the general adult population has found small effects for neighborhood deprivation on patient health status.[68,88] For example, one study estimated reductions of 0.5 and 0.3 points for PCS and MCS scores, respectively, for each standard-deviation-sized increase in the neighborhood deprivation index, after controlling for several individual-level SES measures.[88] This parallels our finding that patients living in the tercile with low NSES neighborhoods, whose mean neighborhood deprivation index was 2.5 SD lower than those in the high NSES tercile, averaged 1.8 points lower on the PCS. We confirmed other previous findings as well, in that individual SES was more consequential for HRQoL than NSES[67] and that the NSES effect held steady over time.[68]

Our finding that individual SES is associated with poorer HRQoL in patients with cardiovascular disease is also consistent with prior work.[63-65] Despite the vast literature on individual SES and HRQoL we found only four studies that examined the interaction between individual SES and NSES: three did not find a statistically significant relationship [89-91] and one did.[67] However, these studies were conducted in the general population. It is plausible that the combination of low individual and low neighborhood SES is particularly problematic for HRQoL following hospitalization, when patients are likely to need substantial social and material support.

Our study found statistically significant interactions between NSES and individual SES for MCS and SAQ physical limitations. This is also as described in the literature based on the general population, where some studies have found significant effects of neighborhood SES on MCS but not PCS or vice versa.[66,89]

NSES could affect HRQoL after an ACS through several mechanisms. Individuals who live in lower SES neighborhoods may be more likely to engage in lifestyle behaviors that inhibit recovery after an ACS. This is plausible, since poorer neighborhoods are associated with more cardiovascular risk factors, such as higher rates of obesity and weight gain in women,[92-94] lower levels of physical activity and higher prevalence of smoking.[95] NSES may also be related to other neighborhood-level risk factors such as a more adverse built environment with fewer parks, sidewalks or grocery stores with fresh fruits and vegetables;[96] and poor social cohesion,[97] and an elevated level of daily stress that may contribute to allostatic load or bodily "wear and tear".[98]

Neighborhood could also influence patient health after ACS through access to health care. For example, low NSES neighborhoods often have too few primary care doctors or clinics, or limited public transportation for getting to clinics. This could contribute to poorer outcomes either through later presentation to the hospital for an ACS or less access to preventive and follow-up services. Further research on the mechanisms by which NSES affects HRQoL might point to neighborhood-based policies that could improve health equity following an acute health event.

The American Heart Association has proposed PHS as a quality metric,[48] and both the Veterans Affairs Administration and the Centers of Medicare and Medicaid Services are exploring using PHS measures as quality indicators after elective PCI.[50] To create a "level the playing field" quality measures must be risk-adjusted among providers who serve very different patients.[48] However, providers have expressed concern about how well these measures (even when risk-adjusted for differences in medical complexity) can discriminate between providers and institutions with high and low quality of care.[51] Our study adds to these concerns, since hospitals that serve patients from low NSES neighborhoods may be unfairly judged. Regardless of that, healthcare providers and hospitals can try to anticipate the needs of ACS patients as they are discharged home to high-risk neighborhoods. Actions could include: more intense discharge planning, post-discharge follow-up, and discussions of neighborhood resources, barriers to self-care and access to follow-up medical care. Policy makers should keep the relationship between NSES and patient health status in mind as they consider using quality metrics based on measures of patient health.

Study Strengths and Limitations

This study has several limitations. First, participants with post office boxes listed for their home addresses were excluded from the analysis since we were unable to match these participants to a census tract. However, this number of individuals was small (~6%) and matched and unmatched participants were similar in their patient health status scores (MCS p=0.980, PCS p=0.204, SAQ HRQoL p=0.628, SAQ physical limitations p=0.06). Second, since our patients came from just 6 hospitals in the eastern US, these findings might not be generalizable to other areas. Third, much data was missing, both due to loss to follow-up and about 20% of participants not reporting individual-level income data. However, a complete analysis and one using multiply-imputed data provided substantively similar findings. Fourth, while patients could have moved during the follow-up period, this was probably quite uncommon, since the follow-up period was only 6 months and only 4.7% of participant's zip codes changed during that time. Fifth, we did not study any "environmentally-oriented" neighborhood characteristics, such as pollution or segregation. Sixth, our findings only apply to ACS patients who were discharged but not readmitted, since we excluded patients who were readmitted within 6 months. However, since neighborhood SES was not associated with readmission (p=0.840), it seems unlikely that our findings would be affected. Seventh, we did not have a pre-ACS measure of patient health status and thus, it is possible that the differences in patient health status are not attributable to the actual ACS event. In compensation for these limitations, these rich longitudinal data from patient interviews and medical and administrative records allowed us to explore important relationships among personal and contextual patient factors and patient health following hospitalization for an ACS.

In summary, we found that patients living in neighborhoods with lower NSES had worse health following discharge for an ACS, even after adjusting for individual SES and clinical characteristics. This difference was present at discharge and sustained during 6 months of follow-up. For the mental health-related quality of life and physical limitations due to angina, the deleterious effect of NSES on patient health status was significantly worse for patients with lower individual-level SES.

We draw two main lessons from these findings: 1) caution should be used when interpreting post-discharge health status as a measure of healthcare quality, and 2) research is needed to identify interventions at the provider, hospital, neighborhood, and municipal levels to address the disparities associated with both individual and community-level socioeconomic stress.

Table II.1: Socio-demographic and individual-level socioeconomic characteristics associated with neighborhood socioeconomic status* tercile among 1,481 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

		Neighborhood SES			
	Full Sample (n=1481)	**High (n=498)**	**Intermediate (n=490)**	**Low (n=493)**	**P-value**
Socio-demographic					
Average Age (SD)	61.0 (11.4)	61.9 (11.5)	60.9 (11.7)	60.2 (11.0)	0.041
Male, %	66.5	73.5	65.5	60.5	<0.001
Race/ethnicity, %					
Asian or Pacific	0.9	1.8	0.4	0.4	<0.001
Black	15.3	2.4	11.4	32.1	
Native American or	0.9	0.6	1.0	1.0	
White	77.3	89.4	81.2	61.1	
More than one race	4.2	4.2	5.1	3.3	
Hispanic, %	3.2	2.8	2.3	4.0	<0.001
Lives Alone, %	22.0	18.9	19.0	28.0	0.001
Marital status, %					
Single	11.4	8.2	12.0	13.8	<0.001
Married	58.7	67.9	60.0	48.1	
Separated/divorced	18.8	13.3	17.1	26.0	
Widowed	11.2	10.6	10.8	12.0	
Socioeconomic Status					
Education, %					
Less than high-school	17.8	7.9	16.5	29.0	<0.001
High-school	30.0	24.4	32.5	32.1	
Some college, trade	27.6	28.0	30.0	24.8	
College graduate	25.1	39.8	21.0	14.2	
Household Income, %					
<34,999$	40.1	26.1	37.2	57.8	<0.001
35,000-74,999$	31.3	28.5	38.0	27.2	
>75,000	28.6	45.5	24.8	15.0	
Income to Poverty Ratio, %	2.5	2.6	2.3	2.0	<0.001
Less than 1	11.2	11.4	11.4	18.7	<0.001
1-2.9	19.0	15.3	22.2	19.7	
At least 3	69.8	81.1	66.3	61.7	
No usual source of care, %	13.9	12.7	10.2	19.2	0.134
Insurance status, %					
Employer or Individual	69.4	78.5	73.1	56.4	<0.001
Medicare	16.8	12.1	13.5	24.8	
Medicaid	5.1	3.0	4.1	8.1	
None	8.9	6.4	9.4	10.8	

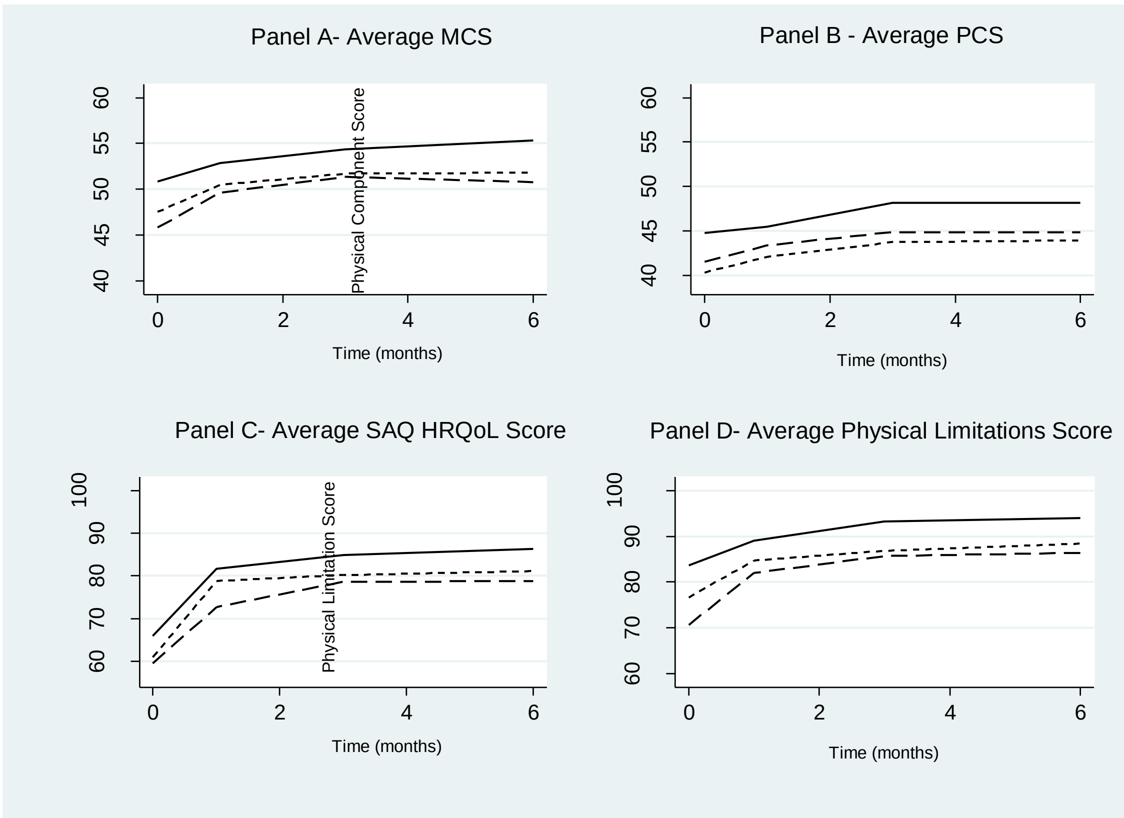
*Neighborhood SES, was measured using the NDI, as in Messer et. al.[40] It has a mean of 0 and a standard deviation of 1; higher scores indicate greater deprivation, that is, worse NSES.[40]

Table II.2: Clinical characteristics and in-hospital management of acute coronary syndrome by neighborhood socioeconomic status* tercile for 1,481 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

		Neighborhood SES			
	Full Sample (n=1481)	**High (n=498)**	**Intermediate (n=490)**	**Low (n=493)**	**P-value**
Co-morbidities					
Lung disease, %	16.3	14.3	15.9	18.7	0.061
Anemia, %	4.3	5.0	4.1	3.9	
High blood pressure, %	73.6	68.1	73.9	78.9	<0.001
Peripheral Vascular Disease, %	8.6	9.0	8.2	8.7	0.859
Arthritis, %	19.3	19.1	18.4	20.5	0.575
History of Heart Disease, %	46.8	39.8	47.0	53.8	<0.001
Diabetes, %	34.6	25.9	32.5	45.4	<0.001
History of Spinal Diseases, %	5.7	6.4	4.7	6.1	0.815
Stroke, %	7.9	5.2	8.6	10.8	0.001
Heart failure, %	11.8	8.0	11.6	15.8	<0.001
Cancer, %	11.6	11.5	12.0	11.4	0.967
Renal failure, %	8.9	8.0	7.8	11.0	0.107
Atrial fibrillation, %	6.4	6.2	5.7	7.1	0.574
Hyperlipidemia, %	68.1	69.5	67.1	67.6	0.513
History of Alcohol Abuse, %	4.7	3.8	5.7	4.7	0.526
History of Drug Abuse, %	4.5	2.8	3.1	7.7	<0.001
Family history of heart disease, %	53.8	54.0	53.5	53.8	0.933
In hospital factors					
Type of ACS, %					
STEMI	15.9	18.3	16.9	12.4	0.028
NSTEMI	54.0	52.0	55.7	54.2	
UA	30.2	29.7	27.4	33.5	
Length of stay, %					
0-1 day	21.7	25.3	18.8	21.1	0.067
2-3 days	45.0	44.8	45.7	44.6	
4+ days	33.2	29.9	35.5	34.3	
Any in hospital complications, %	19.8	18.3	23.1	18.1	0.936
Any in hospital procedures, %					
None	20.5	17.1	18.6	25.8	0.001
Percutaneous Coronary	67.3	69.9	67.8	64.3	
Coronary Artery Bypass Graft	12.2	13.1	13.7	9.9	
Average GRACE risk score (SD)	93.7 (27.7)	93.4 (27.8)	94.6 (28.1)	93.2 ((27.1)	0.667

*Neighborhood SES, was measured using the NDI, as proposed by Messer et. al.[40]. It has a mean of 0 and a standard deviation of 1; with higher scores indicating greater deprivation or worse NSES[40].

Figure II.1: Patient health status by terciles of neighborhood socioeconomic status (SES) among 1,481 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013



*Neighborhood SES, was measured using the NDI, as proposed by Messer et. al.[40] It has a mean of 0 and a standard deviation of 1; with higher scores indicating greater deprivation or worse neighborhood socioeconomic status[40].

†Long dash lines represent the average patient health status among those living in the tercile of neighborhoods with the lowest NSES, the short dash represents those in average neighborhoods, and the solid line represents those living in neighborhoods with the highest NSES.

Table II.3: Association between neighborhood socioeconomic status (SES)[*] and patient health status among 1,481 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	Mental Components Subscale†	**Physical Component Subscale‡**	**Seattle Angina Quality of Life§**	**Seattle Angina Physical Limitations‖**
	beta (95% CI)	**beta (95% CI)**	**beta (95% CI)**	**beta (95% CI)**
Neighborhood Socioeconomic Status (SES)				
High	Referent	Referent	Referent	Referent
Average	**-2.28 (-3.81, -0.75)**	**-1.53 (-2.52, -0.55)**	**-2.37 (-4.30, -0.44)**	**-4.84 (-7.96, -1.72)**
Low	**-4.24 (-5.78, -2.71)**	**-1.83 (-2.90, -0.77)**	**-4.21 (-6.45, -1.97)**	**-8.04 (-11.31, -4.77)**
Individual -level Socioeconomic Status				
Income to Poverty Ratio or IPR (per one unit change)	**0.29 (0.06, 0.53)**	**0.35 (0.13, 0.57)**	**0.69 (0.18, 1.19)**	**0.70 (0.21, 1.18)**
Interaction terms				
High Neighborhood SES*IPR	Referent	Referent	Referent	Referent
Average Neighborhood SES *IPR	0.14 (-0.18, 0.46)	- -	- -	0.52 (-0.19, 1.22)
Worst Neighborhood SES*IPR	**0.50 (0.10, 0.90)**	- -	- -	**1.09 (0.24, 1.94)**

*Neighborhood SES, was measured using the NDI, as proposed by Messer et. al[40]. It has a mean of 0 and a standard deviation of 1; with higher scores indicating greater deprivation or worse NSES[40].

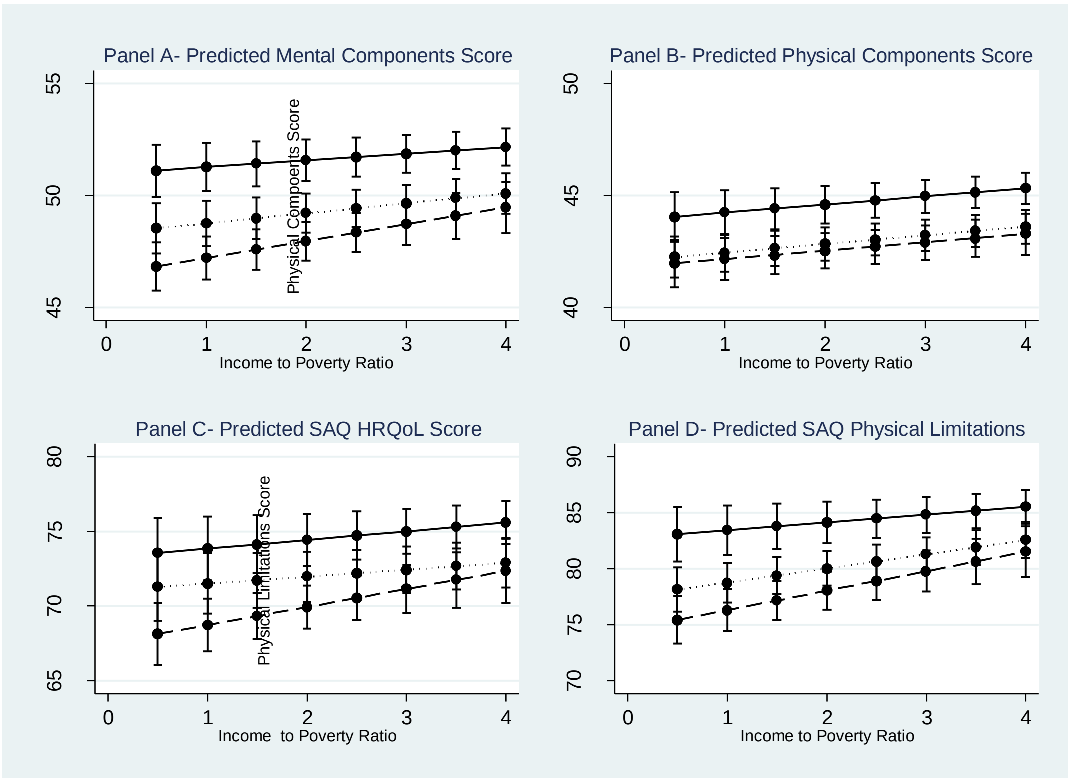
†Adjusted for age, sex, race, GRACE risk score, living alone, history of high blood pressure and length of stay. Multiple imputation was utilized to adjust for missing data.

‡Adjusted for age, sex, race, diabetes, history of heart disease and length of stay. Multiple imputation was utilized to adjust for missing data.

§ Adjusted for age, sex, race, living alone, history of high blood pressure and length of stay. Multiple imputation was utilized to adjust for missing data.

‖ Adjusted for age, sex, race, history of heart disease, heart failure and length of stay. Multiple imputation was utilized to adjust for missing data.

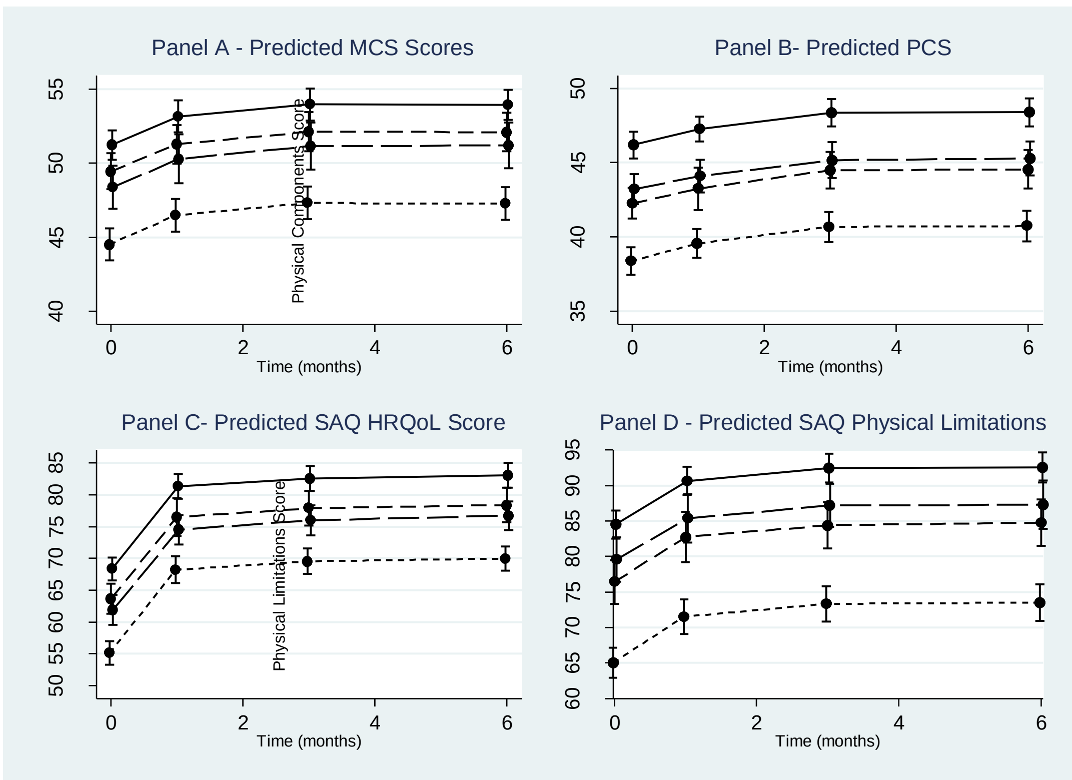
Figure II.2: Predicted patient health status vs. Income to Poverty Ratio by terciles of neighborhood socioeconomic status (SES)* among 1,481 adults hospitalized with Acute Coronary Syndrome, TRACE-CORE, 2011-2013



*Neighborhood SES, was measured using the NDI, as proposed by Messer et. al[40]. It has a mean of 0 and a standard deviation of 1; with higher scores indicating greater deprivation or worse neighborhood socioeconomic status.[40]

†Dashed lines represent the predicted patient health status among those living in the tercile of neighborhoods with the lowest NSES, dotted lines represent those in average neighborhoods, and the solid line represents those living in neighborhoods with the highest NSES. Bars represent 95% confidence intervals.

Figure II.3: Predicted patient health status over time for those in the lowest and highest terciles of neighborhood socioeconomic status (SES)* and those below the federal poverty level and those at least 300% of the federal poverty level among 1,481 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013



*Neighborhood SES, was measured using the NDI, as proposed by Messer et. al[40]. It has a mean of 0 and a standard deviation of 1; with higher scores indicating greater deprivation or worse NSES[40].

†Short dashed lines represent the predicted patient health status among those living in the tercile of neighborhoods with the lowest neighborhood socioeconomic status and whose individual-level income is under the federal poverty level. Long dashed lines represent the predicted patient health status among those living in the tercile of neighborhoods with the lowest NSES and whose individual-level income is at least 300% of the federal poverty level. Medium dashed lines represent the predicted patient health status among those who living in the tercile of neighborhoods with the highest NSES and whose individual-level income is under the federal poverty level. Solid lines represent the predicted patient health status among those living in the tercile of neighborhoods with the highest NSES and whose individual-level income is at least 300% of the federal poverty level.

Supplemental Table II.1: Characteristics of 50 neighborhoods included in the TRACE-CORE study by terciles of neighborhood socioeconomic status (SES)*

		Neighborhood SES			
	All Census Tracts (n=508)	**High (n=160)**	**Intermediate (n=176)**	**Low (n=172)**	**p-value**
Average % of Individuals in Each Census Tract (SD)					
Males in managerial positions	31.8 (14.7)	46.3 (11.5)	30.3 (9.2)	19.7 (9.4)	<0.001
Households with an income < 30k	34.4 (17.6)	17.9 (6.5)	30.9 (8.4)	53.2 (13.6)	<0.001
Individuals < high school degree	13.6 (8.8)	5.8 (2.9)	12.0 (4.5)	22.5 (7.8)	<0.001
Households with > 1 person per room	1.7 (2.0)	0.77 (1.2)	1.3 (1.3)	2.9 (2.4)	<0.001
Unemployment	6.4 (3.0)	4.7 (1.7)	6.1 (2.1)	8.3 (3.7)	<0.001
Under federal poverty line	15.8 (12.8)	5.4 (3.1)	12.0 (5.3)	29.3 (12.1)	<0.001
On cash assistance welfare	2.4 (2.8)	1.3 (1.1)	1.8 (1.5)	4.1 (3.8)	<0.001
On Supplemental Security Income	5.4 (4.1)	2.3 (1.5)	4.6 (2.1)	9.0 (4.6)	<0.001
On Supplemental Nutrition Assistance Program	13.2 (11.4)	4.1 (2.6)	9.9 (4.0)	25.1 (11.4)	<0.001
Female headed households with dependents under 18	12.5 (9.3)	6.1 (3.5)	10.6 (5.2)	20.3 (10.6)	<0.001
Average Median Home Value ($)	236,610 (137, 589)	267,200 (82,622)	169,960 (124,598)	276,355 (163,878)	0.491

*Neighborhood SES, was measured using the NDI, as proposed by Messer et. al.[40] It has a mean of 0 and a standard deviation of 1; with higher scores indicating greater deprivation or worse NSES.[40]

CHAPTER III : TRAJECTORIES OF PATIENT HEALTH STATUS FOLLOWING HOSPITALIZATION FOR ACUTE CORONARY SYNDROMES

Abstract

Objective: We identified trajectories of patient health status (health-related quality of life (HRQoL) and physical limitations) following hospitalization for an acute coronary syndrome (ACS) and examined predictors of these trajectories.

Methods: We used data from TRACE-CORE, a prospective cohort of patients hospitalized with ACS. We measured patient health status using the physical components (PCS) and mental component summaries (MCS) of the SF-36 and the Seattle Angina Questionnaire (SAQ) HRQoL and physical limitations measure. We measured patient health status during hospitalization and at 1-, 3-, and 6-months post-discharge. High scores on each measure are best. We identified trajectories and their predictors using group-based trajectory models.

Results: Participants (n=1,589) were of mean age 61.1 (SD 11.4) years, 33.4% were female, and 77.0% were non-Hispanic white. We found 4 MCS trajectories: High (64.4%), Improving (16.3%), Worsening (10.5%) and Low (8.9%). We found 2 trajectories for each of PCS and SAQ physical limitations: Average (PCS (66.4%); SAQ (67.8%)) and Impaired (PCS (33.6%); SAQ (32.2%)). Also, we found 3 SAQ HRQoL trajectories: High (36.4%), Average (53.9%) and Low (9.7%). For all measures, those in the worst trajectories never caught up to those in the better trajectories. We found that being female, having more co-morbidities, and worse depressive symptoms were associated with having worse trajectories for all components of patient health status except for MCS.

Conclusion: Identifying patients with worse expected trajectories based on patient health status scores and other information may help target interventions for patients with ACS who would otherwise do poorly going forward.

Abstract word count: 250

Introduction

The prevalence of acute coronary syndrome (ACS) has been increasing,[2] with about 1.2 million Americans hospitalized for ACS annually.[1] The vast majority of individuals with ACS survive but about 30% of survivors are left with moderately to severely impaired health-related quality of life (HRQoL) in the 6 months following hospitalization.[3] The importance of HRQoL post-ACS was highlighted by the American Heart Association (AHA), who called for additional research on patient health status (HRQoL and functional status) and its determinants among ACS survivors.[7]

Several studies have examined determinants of the average evolution of HRQoL after an ACS over time. Women,[11,14] individuals with low socio-economic status,[16,30] those who live alone,[31] and patients with more co-morbidities are more likely to have worse HRQoL; older patients have better HRQoL.[29] Both depression[22] and anxiety[32] are associated with worse HRQoL in coronary heart disease (CHD) patients. However, no prior study has examined trajectories (subgroups of individuals with distinct longitudinal patterns) of HRQoL after an acute ACS event.

Identifying trajectories of patient health status after an ACS is important for these varying trajectories may allow caregivers and providers to anticipate and address future impaired recovery and complications. Distinct trajectories of health status have been associated with differences in healthcare expenditures and care patterns in patients with cancer.[33] Whether there are similar patterns in patients discharged from the hospital after an ACS, and whether they may be provide a useful paradigm to help care for patients with ACS, remains poorly understood. Thus, we determined the associations between individual-level socio-demographic, clinical, and in-hospital factors and trajectories of patient health status at baseline, 1, 3, and 6months following hospital discharge for an ACS. We hypothesized that trajectories will include stable, improving and worsening patient health status over time and that individuals who have more co-morbidities, worse in-hospital courses and a less favorable psychosocial profile will be more likely to belong to trajectories with worse patient health status.

Methods

Study Design and Setting

Details of the study design, recruitment, and retention of the TRACE-CORE (Transitions, Risks, and Action in Coronary Events – Center for Outcomes Research and Education) cohort have been described elsewhere.[71,72] TRACE-CORE is a prospective multi-site longitudinal cohort of adult patients diagnosed with an ACS. Patients were recruited from April 2011 to May 2013 at 6 community and teaching hospitals (3 hospitals in Worcester, MA and 3 hospitals in Georgia). [71,72]

Study Sample

Active surveillance identified all ACS patients at participating hospitals admitted with ICD-9 codes consistent with a possible ACS (ICD-9 codes: 410, 411, 412 and 786.5). Inclusion in the TRACE-CORE cohort required study participants to be at least 21 years old, alive at discharge and have symptoms suggestive of ACS. Participants also had to meet at least one of the following criteria: serial ECG changes (including either ST-segment changes, new bundle branch blocks, T-wave inversions, new Q waves consistent with ACS), elevated cardiac biomarkers (creatinine kinase- MB or troponins), a cardiac catheterization with more than 70% stenosis in at least one coronary artery, or admission for an urgent PCI/ CABG.[71] When unclear, 2 cardiologists independently adjudicated eligibility. Exclusion criteria included: ACS secondary to demand ischemia or aortic dissection, dementia, pregnancy, admission for trauma, receipt of hospice/palliative care or incarceration. For this study, we further excluded individuals who were readmitted or died during the first six months post-ACS care and individuals whose subtype of ACS could not be determined (ST-elevated myocardial infarction (STEMI), non-ST-elevated myocardial infarction (NSTEMI) and unstable angina (UA)).

Data collection

Participants were interviewed at discharge and followed through structured computer-assisted telephone interviews at 1, 3, and 6 months. Baseline interviews for most participants were conducted during the initial hospitalization; those unable to complete it while hospitalized were interviewed by telephone within 72 hours of discharge. Interviews varied from an average of 30 minutes to 1 hour. Detailed medical record review was also undertaken for each participant. Medical record review used downloaded electronic health record data and manual abstraction by trained abstractors to standardized forms. All information was inserted into a web-based collection system. A randomly selected 5% of medical records were abstracted twice to calculate inter-rater agreement. Further detail is in the methodological paper on the TRACE-CORE cohort by Waring et. al.[71]

Measures

Outcome Ascertainment

Our main outcome was patient health status, including functional status, and HRQoL,[7] measured using the SF-36, a generic measure of quality of life[73] and the Seattle Angina Questionnaire[74] or SAQ. The SF-36 represents HRQoL over a 4-week recall period [73] and has two subscales: the physical component summary (PCS) and the mental component summary (MCS). Each subscale has a range of 0-100, standardized to have a mean of 50 and a standard deviation of 10, with higher scores representing better quality of life.[73] The SF-36 has strong psychometric properties.[75,76] The SAQ includes information on other aspects of patient health status: including physical limitations and a disease-specific measure of HRQoL.[74] Each subscale of the SAQ is scored so that higher scores represent better HRQoL and less physical impairment.[74] The SAQ has been validated in CHD patients[78] and has good psychometric properties.[77] From this point forward, we will use “patient health status” to mean: MCS, PCS, SAQ physical limitations and SAQ HRQoL.

Exposure Ascertainment

We measured several socio-demographic, socio-economic, and clinical exposures from both medical record abstraction and interview at discharge. Patients reported sociodemographic information (age, sex, race, marital status) and information on their socioeconomic status, including highest level of education and pre-tax family income in increments of $10,000. Clinical variables included co-morbidities, type of ACS, the Global Registry of Acute Coronary Events or GRACE risk score,[83] length of stay and in-hospital exposures, both of which were measured using medical record abstraction. Type of ACS was categorized using ACC/AHA criteria: NSTEMI, STEMI and unstable angina[84]. This classification was based on the information from medical record abstraction. Whenever there was a question about the type of ACS, the case was reviewed by an adjudicating panel of physicians. Participants whose types of ACS could not be determined were excluded from this study. We used the GRACE risk score to measure the clinical severity of the index ACS hospitalization.[83] The GRACE risk score has good predictive validity and predicts both in-hospital and long-term mortality.[83] Length of stay was calculated from the medical record (days from admission till discharge from the index hospitalization). Patients were classified as having in-hospital complications if there was an onset or occurrence of any the following during the initial hospitalization: renal failure, atrial fibrillation, atrial flutter, a major bleed, cardiogenic shock, cardiac arrest, deep vein thrombosis, delirium, falls, heparin-induced thrombocytopenia, pulmonary embolism, pneumothorax, recurrent myocardial infarction, stroke, transient ischemic attack, urinary tract infection, heart failure, and ventricular tachycardia.

We measured the following psychosocial variables at discharge including: depressive symptoms, anxiety symptoms, and cognitive impairment. Depressive symptoms were measured using the Patient Health Questionnaire-9 (PHQ-9) which ranges between 0-27 and where higher scores indicate a greater severity of depressive symptoms.[99] Symptoms of anxiety were measured using the Generalized Anxiety Disorder 7 score (GAD-7) which has a range 0-21 and where higher scores indicate worse anxiety.[100] Cognitive impairment was measured using the Telephone Interview for Cognitive Status (TICS).[101] All measures have strong psychometric properties.[102-106]

Statistical Analysis

Descriptive Statistics

We first described the sample's baseline socio-demographic, socio-economic, co-morbidities and clinical exposures and examined whether these baseline characteristics differed by type of ACS using one-way ANOVA and chi-square tests. We examined the distributions of each patient health status measure and graphically examined their averages over time. To get a feel for the raw data and its variability, we also examined separate time plots of each component of patient health status for each participant, and we graphed time trends of the 4 measures for 30 randomly selected individuals.

Group-based trajectory analysis

We used group-based trajectory models to determine trajectories (subgroups with distinct patterns of patient health status over time of patient health status) of patient health status. These models then assigned every individual a so-called "posterior" probability of belonging in each trajectory. Variables can then be used to predict membership in each trajectory using a multinomial (or logistic in the case of only 2 trajectories) regression. We conducted separate trajectory analyses for each component of patient health status (SF-36 - MCS, SF-36 - PCS, Seattle Angina – physical limitations and Seattle angina – health-related quality of life). We analyzed the subscales of the SF-36 separately as we thought that the underlying trajectories for mental vs. physical functioning might differ following an acute health event such as ACS. We used the traj program developed by Jones *et. al*. [107]

Trajectory analysis requires an iterative procedure with three steps following basic exploratory data analysis are: 1) determine the number of trajectories, 2) determine the shape of each trajectory, and 3) determine the predictors of membership to each trajectory.

We *a priori* decided to examine models with no more than 6 groups, as models with more groups may not be clinically relevant and there was not sufficient data to examine more than 6 groups.[108] To determine the number of trajectories we used both the Bayesian information criterion (BIC) and substantive knowledge.[109] In cases where BIC failed to reach a peak while examining the number of groups, we followed Nagin's recommendation to use substantive knowledge and chose a model with fewer groups.[109]

We then determined the shape or polynomial order of each of the groups by examining every possible combination of polynomials for a set number of groups and choosing the best model based on BIC, significance of polynomial terms and substantive knowledge. Because we only had 4 time points, we could not consider cubic or higher order polynomials.[110] We examined all possible shape combinations with quadratic or lower terms for each group-based trajectory model.

We determined model adequacy using the following two criteria: (1) average posterior probability for membership for each trajectory of at least 0.70; and (2) odds of correct classification of at least 5. To calculate the odds of correct classification, we classified individuals into the group, for which they had the highest posterior probability. Then, we determined the average posterior probability for each group, which was the average of the posterior probabilities for all individuals who were assigned to that group. The odds of correct classification takes into account both the average posterior probability and the percent of participants who were classified into that group. At each of these modeling decision points we examined the results of the model graphically.

Bivariate relationships between predictors and trajectory membership for each patient health status measure were examined using traditional measures of association (one-way ANOVA and chi-square tests). We classified individuals into the trajectory with the highest posterior probability and then used multinomial (or logistic regression in the case of two categories) to determine the relationship between predictors and trajectory membership.

Model building of the multivariate model for prediction of trajectory membership was informed by the adapted Wilson-Cleary Conceptual Model (refer to Figure I.1), [9] clinical knowledge and statistical criteria. Variables that reached a significance level of less 0.10 in bivariate analysis (either traditional or through the trajectory framework) were retained for multivariate analysis in addition to variables chosen based on substantive knowledge. All statistical tests were performed using Stata 13[111].

Missing Data

We quantified the extent of missingness for each variable and examined patterns of missing data. We used multiple imputation[85] to generate plausible values and to account for the variability that missingness contributed to estimates. Multiple imputation is well-accepted method to correct for missing data in latent variable modeling. For example, Bollen compared multiple imputation and direct maximum likelihood, finding that they produced similar results and that each approach had its own strengths.[110] Direct maximum likelihood produces the same results in the hands of any researcher, as it uses the original data set without sampling.[110] However, we chose to use multiple imputation as it allowed us to use variables that were important for the missing variable process, but were not appropriate for the actual trajectory model; it allowed us to leverage the richness of the TRACE-CORE dataset to deal with missing data in our analysis.

Results

Sample Characteristics

There were 2187 TRACE-CORE participants. For the present analysis, we excluded those with: death during the 6-month follow-up period (n=55), negative MCS SF-36 scores (n=2), ACS subtype could not be determined (n=51), or they were readmitted during the 6-months since discharge (n=477). This led to 1,589 TRACE-CORE participants for this study. However, there was a large amount of missingness in patient health status, the majority being due to loss to follow-up between discharge and the 1-month;1065 had data at 1 month, 971 at 3-months and 951 at 6-months.

Average participant age was 61.1 years old (SD 11.4); about one third were female and the majority self-identified as non-Hispanic white (supplemental Table III.1). About half were married and almost a quarter lived alone. The majority had at least a high school education. Most had NSTEMI at baseline (versus unstable angina or STEMI). The majority had a percutaneous coronary intervention. The next largest group had a coronary artery bypass graft, and about a fifth had no procedure during their index hospitalization. Most patients were hospitalized for less than 3 days and about a fifth had some complication during their index hospitalization for ACS.

Average Patient Health Status Over Time

For all four components of patient health status, average health increased (better HRQoL scores and functional status scores) over time (Supplemental Table III.2). Most of the improvement in patient health status scores occurred between the discharge and 1-month time points and not much improvement occurred at later follow-up time points.

Determination of Trajectory Number and Shape

We used BIC values to determine the number of trajectories. For MCS, we found that the model with 4 trajectory groups had the highest BIC and met all other criteria related to average posterior probabilities and odds of correct classification (Supplemental Table III.3). For all other components of patient health status, BIC failed to peak and thus we chose the smallest number of trajectories for PCS and SAQ physical limitations (Supplemental Tables III.4-III.6). For SAQ health-related quality of life we chose 3 trajectories as opposed to 2 trajectories, based on the model fit to the data and our visualization of graphs with 30 random participants, which suggested a group of participants who were doing very poorly after their ACS episode (a SAQ score of less than 30) and continued to do very poorly.

In terms of shape, we found that all trajectories from all components of patient health status fit better with quadratic terms. For all models, the intercept, linear and quadratic terms were statistically significant, and the BIC never suggested that the quadratic models were overfit (data not shown).

Trajectories of all Components of Patient Health Status

Figure III.1 shows the trajectories identified for each patient health status measure. For MCS, we found four trajectories: High, Improving, Worsening and Low. Most participants belonged to the High group (64.4%) who had a high MCS score at baseline (54.5) which stayed high over time. Approximately, 16.3% and 10.5% of participants were classified into the Improving and Worsening groups, respectively. Initially the Improving group had lower scores than the Worsening group (average MCS scores of 34.9 and 47.7 at discharge, respectively), however, by 3-months the Worsening group had lower MCS scores compared to the Improving group. The Low MCS trajectory had a minority of participants (8.9%) who had the worst MCS scores over all 6 months following discharge (average MCS 26.8 at discharge).

For both PCS and SAQ physical limitations, we found two trajectories: Average and Impaired. For PCS, approximately two thirds of participants were in the Average group (average PCS score at discharge 47.1) and the remaining third were in the Impaired group (average PCS score at discharge 31.8). Both groups had improving scores over time, however the Impaired group never caught up to the Average group. A similar pattern was found for the SAQ physical limitations, where we found two trajectories, Average and Impaired with approximately two thirds and one third of the sample, respectively (average SAQ physical limitations score 96.5 and 53.1, respectively).

We found three trajectories for the SAQ health-related quality of life score: High, Average, and Low. Most participants were in the Average group (53.9%), about a third were in the High group (36.4%) and under 10% were in the Low group. All three trajectories showed improvement over time, however, they never improved enough to have comparable scores to the next highest group (average SAQ health-related quality of life scores of 86.9, 56.4 ad 28.9 for the High, Average, and Low groups, respectively at discharge).

Overlap Between Trajectories of All Patient Health Status Components

We found some overlap between trajectory classifications for all four components of patient heath status (Supplementary Table III.7). Specifically, just under a half of participants (48.1%) were classified in the top-performing trajectory for all 4 measures (PCS: Average, MCS: high, SAQ health-related quality of life: high, and SAQ physical limitations: Average).

Predictors of Trajectory Membership

Bivariate relationships between trajectory membership and predictors (socio-demographic, clinical, and psychosocial factors) are presented in Tables III.1 and III.2. For all measures, all of the following were associated with membership in better trajectories: being male, white, married, and having more education. In general, people in worse trajectories had more co-morbidity and had a longer length of stay for their incident hospitalization with ACS. Patients who had been admitted with a STEMI were more likely to be in better trajectories while those who received a percutaneous coronary intervention were more likely to be in better trajectories for all components of patient's health, except for MCS. Higher PHQ-9 and GAD-7 scores were associated with membership in worse trajectories for all components of patient health status.

Multivariate models for the SAQ physical limitations and HRQoL subscales are presented in Table III.3. Individuals who were male, college graduates and those initially admitted for a STEMI were less likely to belong to the worse SAQ trajectories. Higher PHQ-9 scores (worse depressive symptoms) was also associated with a higher likelihood of being in the worst SAQ trajectories.

Multivariate models for the PCS and MCS subscales are presented in Tables III.4 and III.5, respectively. For PCS, women, and those with more co-morbidities, and who had higher depressive symptoms were more likely to be in the Impaired PCS trajectory. For MCS, after psychosocial factors were included, they became the main predictors of MCS trajectory with patients with more depressive and anxiety symptoms and more cognitive impairment being more likely to be in worse MCS trajectories.

Discussion

This is the first study, to our knowledge, to examine trajectories of patient health status after an ACS. We found that, for all four components of patient health status (MCS, PCS, SAQ HRQoL and SAQ physical limitations), most of the patients were doing well. However, a minority of patients had much poorer patient health status. Although the majority of groups identified experienced improvement in patient health status scores over time (except for the Worsening MCS trajectory), the minority of patients with worse patient health status never improved sufficiently to catch up with the rest of their peers. For all components of patient health status except for MCS, patients' scores at discharge determined their score for the next six months of follow-up. There was very little overlap between membership in poor trajectories from one component of patient health status to another. In other words, there was no evidence that the same individuals who were categorized in worse trajectories for one component of patient health status were necessarily categorized into poorly performing trajectories for the other components of patient health status. We also found that for all components of patient health status, except for MCS, being female and having more co-morbidities was associated with being more likely to be in worse trajectories before adjusting for psychosocial factors. Also, worse depressive symptoms were also always associated with a higher risk of being in worse trajectories for all components of patient health status.

Trajectories in Relation to Minimally Important Clinical Differences

In general, there was a considerable amount of separation between the different patient trajectories in health status. For example, the average difference between those classified in the impaired versus average PCS trajectories was greater than 15 points at 6 months after discharge, which is considered to be an important clinical difference.[112] Moreover, even the closest two MCS trajectories (worsening and improving) were above the threshold for a minimally important difference in the MCS scale. For the SAQ scales, all trajectories were separated by much more than the 10 point minimally important clinical difference.[74] The fact that the separation between the trajectories was so large reinforces the consequences of trajectory membership for patients with ACS.

Comparisons with Previous Literature

These findings are consistent with previously published work. For example, one study by Le Grande et. Al. who examined trajectories of health-related quality of life among who had recently undergone coronary artery bypass graft surgery (CABG).[113] Similar to our study, they found that individuals belonged to two trajectories for PCS, described as improvers and non-improvers. However, unlike our study these authors only found two groups for MCS, and that much of the improvement in generic HRQoL scores occurred between 2-6 months after their CABG. One possible explanation for the differences in findings between our study and that conducted by Le Grande et. al. might follow from the characteristics of enrolled patients. Namely patients with stable angina, in addition to those with ACS, may receive a CABG and CABG may be an elective procedure. Moreover, there is some evidence to suggest that the effect of CABG on HRQoL may differ between those with and those without ACS.[114]

Similar to the results of other studies, we found that most of the improvement in patient health status scores occurred shortly after discharge.[115] We also found that women had worse patient health status (except MCS) which has been substantiated by other studies.[116-118] We also found that the effect of gender on SAQ was attenuated by including depressive symptoms.[117] Our findings that patients with a history of cardiovascular disease,[119] unstable angina[13] and more depressive symptoms have worse patient health status has also been previoulsy reported.

Underlying Reasons for Heterogeneity in Patient Health Status

In contrast to analyses based on "average response," as might be reported from longitudinal generalized linear models, there are advantages to focusing on patient trajectories over varying time periods. First, trajectory analysis allows for heterogeneity within the general population related to factors beyond the immedicate ACS clinical event. In our case, this heterogeneity is mostly because of the separation between the trajectories began at discharge (except for worsening and improving trajectories for MCS). Furthermore, differences between belonging to one trajectory versus another are created by the way individuals react to a stressful event, in this case ACS. This theory posits that vulnerable individuals are less likely to improve after an ACS due to a lack of physical and psychosocial reserve (exercise capability, social support etc.). It is possible that the reason that there were so many more (and distinct) MCS trajectories compared with other components of patient health status, is that mental status is may be affected differently by an ACS compared withmore physical aspects of health.

Implications

Trajectories are also potentially important not only because they give patients and their caregivers an idea of what to expect in the near or more ling-term future, but also because they give healthcare providers a way to target interventions to those who seem likely to be on a worse trajectory. It has been shown that individuals who have the worst patient health status tend to benefit the most from interventions such as PCI.[120] However, there are several other examples of interventions that may be helpful in improving the health status of individuals on worse trajectories. For example, a meta-analysis found that depression treatment (pharmacologic, psychotherapeutic or a combination) helped improve HRQoL 6 months following an ACS.[121] Moreover, patients who are experiencing frequent angina may improve their health related quality of life through more intensive pharmacotherapy.[122] Prevailing guidelines suggest that cardiac rehabilitation should be offered to the vast majority of patients after an ACS; [123] however, it may be that patients with adverse post-discharge trajectories might benefit from more tailored interventions. Thus, by using trajectories of patient health status providers may be able to target one of these interventions to those who HRQoL will likely be diminished after an ACS.

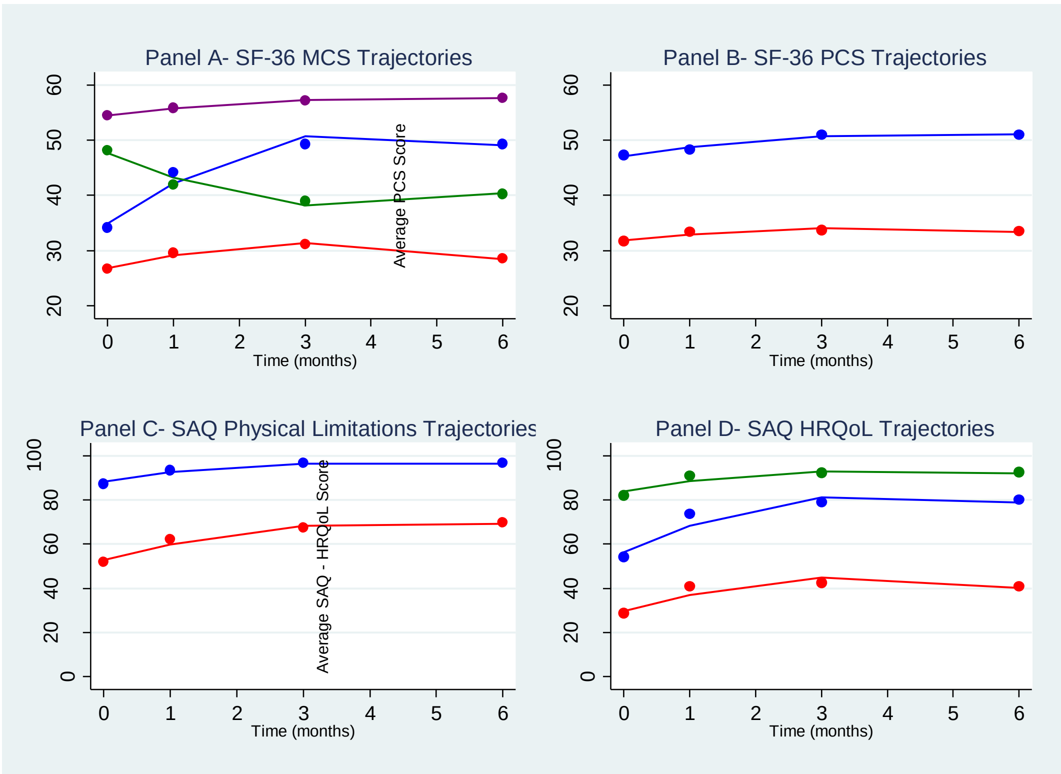
Although trajectories may potentially be used this way in the future, there are some methodological challenges in applying trajectory models in this manner. Currently the Stata programming that implements trajectory analysis, the traj command, does not include a way to determine a way to apply a given trajectory model to a patient without redoing the trajectory model and in the process potentially changing it. This capability will have to be developed before the model can be applied in a clinical setting.

Study Strengths and Limitations

This study has several limitations. First, we needed to use multiple imputation to address missing data due to loss to follow-up. Second, we did not have pre-ACS measure of patient health status and thus could not determine whether the trajectories we found were caused by the ACS episode or were present before the hospitalization. Third, our sample size could have caused us to find fewer trajectories than could be usefully distinguished with a larger patient sample. Fourth, our sample only includes hospitals from 6 urban hospitals and in 2 states and thus may have limited generalizability. Fifth, we excluded all individuals who died or were readmitted during the six months after discharge. Although this limits our generalizability, this exclusion criteria lets us focus on prognosis in a more low-risk patient population. The literature already provides evidence that individuals who have been readmitted have a higher risk of bad outcomes including mortality.[124] However, among patients who have not been readmitted there is more uncertainty about their prognosis. Thus, trajectories may be more useful as a heuristic for prognostication among those who have not been readmitted. Although our study has several limitations, these limitations are mitigated by the strength of our study's rich longitudinal data on both disease-specific (SAQ) and generic (SF-36) patient health status measures.

In conclusion, we found that there are subgroups of patients with different patient health status evolution and that there was little overlap between trajectories. We also found that several risk factors predicted membership in a worse trajectory. Patients and their health care providers might use these findings to target interventions and to give patients' a better idea of their likely prognosis. Future studies should consider incorporating group-based trajectory analysis in their evaluation of HRQoL.

Figure III.1: Trajectories of patient health status over 6 months following discharge among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013



*Panel A shows all MCS trajectories. The Low MCS trajectory (8.9%) is shown in red. The Improving trajectory (16.5%) is shown in blue. The Worsening trajectory (10.5%) is shown in green. The High trajectory (64.4%) is shown in purple.

†Panel B shows all PCS trajectories. The Impaired trajectory (33.6%) is shown in red. The Average PCS trajectory (66.4%) is in blue.

‡ Panel C shows all SAQ physical limitations trajectories. The Impaired trajectory (32.2%) is shown in red. The Average PCS trajectory (67.8%) is in blue.

§Panel D shows all SAQ health-related quality of life trajectories. The Low trajectory (9.7%) is in red. The Average trajectory (53.9%) is in blue and the High trajectory (34.6%) is in green.

Table III.1: Baseline participant characteristics associated with trajectory group membership for SAQ health-related quality of life (SAQL) and SAQ physical limitations (SAPL) among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

Socio-demographic	**SAPL-Average (n=1103)**	**SAPL-Impaired (n=486)**	**p-value**	**SAQL-High (n=551)**	**SAQL- Average (n=911)**	**SAQL- Low (n=127)**	**p-value**
Average Age (SD)	61.0 (11.3)	61.5 (11.5)	0.456	63.8 (11.0)	60.1 (11.4)	57.1 (10.3)	<0.001
Age Categories, N (%)							
50 or younger	212 (19.2)	87 (17.9)	0.700	68 (12.3)	162 (17.8)	31 (24.4)	<0.001
51-60	331 (30.0)	139 (28.6)		123 (22.3)	279 (30.6)	49 (38.6)	
61-70	336 (30.5)	150 (30.9)		187 (33.9)	286 (31.4)	30 (23.6)	
71+	224 (20.3)	110 (22.6)		173 (31.4)	184 (20.2)	17 (13.4)	
Male, N (%)	805 (73.0)	254 (52.3)	<0.001	401 (72.8)	582 (63.9)	76 (59.8)	0.001
Non-Hispanic ±White, N (%)	885 (80.2)	318 (65.4)	<0.001	446 (80.9)	676 (74.2)	81 (63.8)	<0.001
Lives Alone, N (%)	205 (21.1)	105 (26.7)	0.027	96 (20.3)	185 (23.7)	29 (26.4)	0.236
Marital status, N (%)							
Single	124 (11.3)	62 (12.8)	<0.001	41 (7.5)	122 (13.4)	23 (18.1)	<0.001
Married	690 (62.6)	239 (49.2)		359 (65.3)	518 (56.9)	52 (40.9)	
Separated or divorced	190 (17.2)	108 (22.2)		84 (15.3)	178 (19.5)	36 (28.4)	
Widowed	98 (8.9)	77 (15.8)		66 (12.0)	96 (10.2)	16 (12.6)	
Education, N (%)							
Less than high-school	160 (14.5)	121 (24.9)	<0.001	62 (11.3)	176 (19.3)	43 (33.9)	<0.001
High-school or GED	313 (28.4)	161 (33.1)		166 (30.1)	266 (29.2)	42 (33.1)	
Some college, trade school	316 (28.7)	125 (25.7)		165 (30.0)	248 (27.3)	28 (22.1)	
College graduate	313 (28.4)	79 (16.3)		158 (28.7)	220 (24.2)	14 (11.0)	
Co-morbidities							
Lung disease, N (%)	132 (12.0)	123 (25.3)	<0.001	65 (11.8)	162 (17.8)	28 (22.1)	0.002

High blood pressure, N (%)	765 (69.4)	412 (84.8)	<0.001	369 (67.0)	702 (77.1)	106 (83.5)	<0.001
Peripheral Vascular Disease, N (%)	74(6.7)	60 (12.4)	<0.001	37 (6.7)	85 (9.3)	12 (9.5)	0.199
Arthritis, N (%)	185 (16.8)	120 (24.7)	<0.001	98 (17.8)	177 (19.4)	30 (23.6)	0.310
History of Heart Disease, N (%)	450 (40.8)	301 (61.9)	<0.001	223 (40.5)	454 (49.8)	74 (58.3)	<0.001
Diabetes, N (%)	310 (28.1)	241 (49.6)	<0.001	163 (29.6)	341 (37.4)	47 (37.0)	0.008
History of Spinal Diseases, N (%)	53 (4.8)	36 (7.4)	0.038	21 (3.8)	59 (6.5)	9 (7.1)	0.075
Stroke, N (%)	61 (5.5)	64 (13.2)	<0.001	31 (5.6)	80 (8.8)	14 (11.0)	0.037
Heart failure, N (%)	82 (7.4)	106 (21.8)	<0.001	42 (7.6)	120 (13.2)	26 (20.5)	<0.001
Cancer, N (%)	122 (11.1)	68 (14.0)	0.097	72 (13.1)	105 (11.5)	13 (10.2)	0.559
Renal failure, N (%)	76 (6.9)	66 (13.6)	<0.001	41 (7.4)	86 (9.4)	15 (11.8)	0.214
Atrial fibrillation, N (%)	55 (5.0)	47 (9.7)	<0.001	36 (6.5)	62 (6.8)	45 (3.2)	0.287
Hyperlipidemia, N (%)	728 (66.0)	356 (73.3)	0.004	359 (65.2)	634 (69.6)	91 (71.7)	0.144
Anemia, N (%)	36 (3.3)	29 (6.0)	0.012	13 (2.4)	45 (4.9)	7 (5.5)	0.038
History of Drug Abuse, N (%)	37 (3.4)	32 (6.6)	0.004	15 (2.7)	42 (4.6)	12 (9.5)	0.003
In hospital factors							
ACS type, N (%)							
STEMI	204 (18.5)	43 (8.9)	<0.001	111 (20.2)	127 (13.9)	9 (7.1)	<0.001
NSTEMI	603 (54.7)	260 (53.5)		295 (53.5)	499 (54.8)	69 (54.3)	
UA	296 (26.8)	183 (37.7)		145 (26.3)	285 (31.3)	49 (38.6)	
Length of stay, N (%)							
0-1 day	243 (22.0)	104 (21.4)	<0.001	59 (46.5)	51(40.2)	17 (13.4)	<0.001
2-3 days	531 (48.1)	183 (37.7)		334 (36.7)	384 (42.2)	193 (21.2)	
4+ days	329 (29.8)	199 (41.0)		135 (24.5)	279 (50.6)	137 (24.9)	
Any in hospital complications, N (%)	196 (17.8)	115 (23.7)	0.006	99 (18.0)	179 (19.7)	33 (26.0)	0.121
Any in hospital procedures, N (%)							
None	199 (18.0)	125 (25.7)	<0.001	97 (17.6)	196 (21.5)	31 (24.4)	<0.001
PCI	779 (70.6)	289 (59.5)		407 (73.9)	587 (64.4)	74 (58.3)	
CABG	125 (11.3)	72 (14.8)		47 (8.5)	128 (14.1)	22 (17.3)	
Average GRACE risk score (SD)	92.0 (26.5)	98.7 (29.2)	<0.001	96.2 (26.3)	93.3 (28.4)	89.7 (24.9)	0.0305
Psychosocial variables							
Depression (SD)†	4.3 (4.5)	8.6 (5.7)	<0.001	3.2 (3.6)	6.2 (5.1)	11.5 (6.7)	<0.001

Anxiety (SD)*	4.7 (5.1)	8.0 (6.2)	<0.001	3.2 (4.0)	6.5 (5.6)	11.3 (6.3)	<0.001
Cognitive Functioning (SD)‡	32.1 (4.0)	30.2 (4.7)	<0.001	32.3 (3.8)	31.3 (4.4)	30.0 (4.7)	<0.001

†Depression was measured using the Patient Health Questionnaire-9 [99]at baseline. Higher scores indicate worse depression.

*Anxiety was measured using the Generalized Anxiety Disorder-7[100] at baseline. Higher scores indicate worse anxiety.

‡Cognitive Functioning was measured using the Telephone Interview for Cognitive Status or TICS[101] at baseline. Higher scores indicate better cognitive function. The scale ranges from 0 to 41 and. A score over 30 is considered normal.

Table III.2: Baseline participant's characteristics associated with group membership in trajectories of the mental components subscale (MCS) and physical components subscale (PCS) among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	PCS-Average (n=1067)	**PCS-Impaired (n=522)**	**p-value**	**MCS- High (n=1068)**	**MCS-Improving (n=275)**	**MCS-Worsening (n=119)**	**MCS-Low (n=127)**	**p-value**
Socio-demographic								
Average Age (SD)	60.5 (11.3)	62.5 (11.3)	0.0006	61.6 (11.4)	60.5 (11.2)	61.5 (11.8)	58.3 (10.2)	0.0138
Age Categories								
50 or younger	188 (17.6)	73 (14.0)	0.005	194 (18.2)	54 (19.6)	24 (20.2)	27 (21.3)	0.047
51-60	320 (30.0)	131(25.1)		307 (28.8)	80 (29.1)	30 (25.2)	53 (41.7)	
61-70	331 (31.0)	172 (33.0)		326 (30.5)	87 (31.6)	40 (33.6)	33 (26.0)	
71+	228 (21.4)	146 (28.0)		241 (22.6)	54 (19.6)	25 (21.0)	14 (11.0)	
Male, N (%)	769 (72.1)	290 (55.6)	<0.001	750 (70.2)	161 (58.6)	82 (68.9)	66 (52.0)	<0.001
Non-Hispanic ±White, N (%)	848 (79.5)	376 (72.0)	0.001	833 (78.0)	198 (72.0)	81 (68.1)	91 (71.7)	0.018
Lives Alone, N (%)	187 (20.4)	123 (27.5)	0.003	189 (20.3)	67 (29.5)	28 (27.7)	26 (24.5)	0.013
Marital status, N (%)								
Single	131 (12.3)	55 (10.5)	<0.001	120 (11.3)	33 (12.0)	14 (11.8)	19 (15.0)	<0.001
Married	660 (61.9)	269 (51.5)		671 (62.9)	142 (51.6)	61 (51.3)	55 (43.3)	
Separated or divorced	186 (17.5)	112 (21.5)		167 (15.7)	69 (25.1)	31 (26.1)	31 (24.4)	
Widowed	89 (8.4)	86 (16.5)		109 (10.2)	31 (11.3)	13 (10.9)	22 (17.3)	
Education, N (%)								
Less than high-school	159 (14.9)	122 (23.4)	<0.001	145 (13.6)	69 (25.1)	21 (17.7)	46 (36.22)	<0.001
High-school or GED	309 (29.0)	165 (31.7)		311 (29.2)	83 (30.2)	39 (32.8)	41 (32.3)	
Some college	297 (27.8)	144 (27.6)		315 (29.5)	69 (25.1)	34 (28.6)	23 (18.1)	
College graduate	302 (28.3)	90 (17.3)		296 (27.7)	54 (19.6)	25 (21.0)	17 (13.4)	
Co-morbidities								

Lung disease, N (%)	125 (11.7)	130 (24.9)	<0.001	146 (13.7)	57 (20.7)	25 (21.0)	27 (21.3)	0.003
High blood pressure, N (%)	728 (68.2)	449 (86.0)	<0.001	760 (71.2)	221 (80.4)	91 (76.5)	105 (82.7)	0.001
Peripheral Vascular Disease, N (%)	59 (5.5)	75 (14.4)	<0.001	72 (6.7)	30 (10.9)	17 (14.3)	15 (11.8)	0.004
Arthritis, N (%)	146 (13.7)	159 (30.5)	<0.001	195 (18.3)	50 (18.2)	26 (21.9)	34 (26.8)	0.110
History of Heart Disease, N (%)	429 (40.2)	322 (61.7)	<0.001	469 (43.9)	141 (51.3)	64 (53.8)	77 (60.6)	0.001
Diabetes, N (%)	298 (27.9)	253 (48.5)	<0.001	333 (31.2)	120 (43.6)	47 (39.5)	51 (40.2)	<0.001
History of Spinal Diseases, N (%)	50 (4.7)	39 (7.5)	0.023	48 (4.5)	19 (6.9)	11 (9.2)	11 (8.7)	0.035
Stroke, N (%)	52 (4.9)	73 (14.0)	<0.001	65 (6.1)	35 (12.7)	13 (10.9)	12 (9.5)	0.001
Heart failure, N (%)	77 (7.22)	111 (21.3)	<0.001	99 (9.3)	40 (14.6)	20 (16.8)	29 (22.8)	<0.001
Cancer, N (%)	111 (10.4)	79 (15.1)	0.006	128 (12.0)	32 (11.6)	15 (12.6)	15 (11.8)	0.994
Renal failure, N (%)	70 (6.6)	72 (13.8)	<0.001	90 (8.4)	25 (9.1)	14 (11.8)	13 (10.2)	0.619
Atrial fibrillation, N (%)	46 (4.3)	56 (10.7)	<0.001	69 (6.5)	17 (6.2)	9 (7.6)	7 (5.5)	0.927
Hyperlipidemia, N (%)	692 (64.9)	392 (75.1)	<0.001	710 (66.5)	195 (70.9)	92 (77.3)	87 (68.5)	0.073
History of Drug Abuse, N (%)	44 (4.1)	25 (4.8)	0.541	34 (3.2)	14 (5.1)	8 (6.7)	13 (10.2)	0.001
Anemia, N (%)	34 (3.2)	31 (5.9)	0.009	40 (3.8)	15 (5.5)	5 (4.2)	5 (3.9)	0.650
In hospital factors								
ACS type, N (%)								
STEMI	200 (18.7)	47 (9.0)	<0.001	187 (17.5)	29 (10.6)	19 (16.0)	12 (9.5)	0.004
NSTEMI	586 (54.9)	277 (53.1)		587 (55.0)	149 (54.2)	56 (47.1)	71 (55.9)	
UA	281 (26.3)	198 (37.9)		294 (27.5)	97 (35.3)	44 (37.0)	44 (34.7)	
Length of stay, N (%)								
0-1 day	245 (23.0)	102 (19.5)	<0.001	248 (23.2)	59 (21.5)	20 (16.8)	20 (15.8)	0.001
2-3 days	522 (48.9)	192 (36.8)		504 (47.2)	107 (38.9)	51 (42.9)	52 (40.9)	
4+ days	300 (28.1)	228 (43.7)		316 (29.6)	109 (39.6)	48 (40.3)	55 (43.3)	
Any in hospital complications, N (%)	181 (17.0)	130 (24.9)	<0.001	206 (19.3)	54 (19.6)	26 (21.9)	25 (19.7)	0.930
Any in hospital procedures, N (%)								

None	186 (17.4)	138 (26.4)	<0.001	197 (18.5)	69 (25.1)	28 (23.5)	30 (23.6)	0.182
PCI	759 (71.13)	309 (59.2)		741 (69.4)	170 (61.8)	75 (63.0)	82 (64.6)	
CABG	122 (11.4)	75 (14.4)		130 (12.2)	36 (13.1)	16 (13.5)	15 (11.8)	
Average GRACE risk score (SD)	90.9 (26.2)	100.5 (29.0)	<0.001	93.7 (27.0)	95.0 (28.3)	96.6 (27.9)	92.4 (29.6)	0.5812
Psychosocial variables								
Depression (SD)†	4.4 (4.5)	8.1 (5.8)	<0.001	3.5 (3.4)	9.5 (5.2)	6.6 (4.2)	14.1 (6.0)	<0.001
Anxiety (SD)*	4.9 (5.2)	7.4 (6.2)	<0.001	3.7 (4.0)	9.8 (5.9)	6.6 (4.8)	13.8 (5.8)	<0.001
Cognitive Functioning (SD)‡	32.1 (4.0)	30.5 (4.6)	<0.001	32.1 (4.0)	30.7 (4.6)	30.8 (4.6)	29.7 (4.6)	<0.001

†Depression was measured using the Patient Health Questionnaire-9 [99]at baseline. Higher scores indicate worse depression.

*Anxiety was measured using the Generalized Anxiety Disorder-7[100] at baseline. Higher scores indicate worse anxiety.

‡Cognitive Functioning was measured using the Telephone Interview for Cognitive Status or TICS[101] at baseline. Higher scores indicate better cognitive function. The scale ranges from 0 to 41 and. A score over 30 is considered normal.

Table III.3: Multivariate predictors of trajectory group membership for SAQ health-related quality of life (SAQL) and SAQ physical limitations (SAPL) among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	SAPL- Impaired vs. Average		SAPL- Impaired vs. Average with psychosocial		SAQL- Average vs. High		SAQL- Impaired vs. high		SAQL- Average vs. High with psychosocial		SAQL- Impaired vs. High with psychosocial	
	OR	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Socio-demographic												
Age												
Less than 55	1.37	(0.99-1.89)	1.04	(0.74 – 1.46)	**2.67**	**(1.96 – 3.63)**	**7.61**	**(4.25 –**	**2.08**	**(1.51 – 2.88)**	**4.64**	**(2.49 – 8.64)**
55-65	1.19	(0.88-1.60)	1.01	(0.74 – 1.38)	**1.71**	**(1.30 – 2.24)**	**3.14**	**(1.77 – 5.55)**	**1.50**	**(1.13 – 1.99)**	**2.31**	**(1.25 – 4.24)**
65+	Referent		Referent		Referent		Referent		Referent		Referent	
Male	**0.43**	**(0.34-0.56)**	**0.50**	**(0.38 – 0.65)**	**0.60**	**(0.47 – 0.78)**	**0.56**	**(0.36- 0.88)**	**0.74**	**(0.56 – 0.97)**	0.88	(0.54 – 1.43)
White	**0.66**	**(0.50 – 0.87)**	**0.59**	**(0.44 – 0.79)**	1.00	(0.76 – 1.33)	0.84	(0.54- 1.34)	0.90	(0.67 – 1.20)	0.64	(0.39 – 1.07)
Education												
Less than high-	Referent		Referent		Referent		Referent		Referent		Referent	
High-school or GED	0.81	(0.58 – 1.13)	0.92	(0.64 – 1.31)	**0.59**	**(0.41 – 0.85)**	**0.41**	**(0.24 – 0.71)**	**0.67**	**(0.45 – 0.98)**	**0.53**	**(0.29- 0.96)**
Some college school	**0.67**	**(0.47 – 0.95)**	0.85	(0.59 – 1.23)	**0.58**	**(0.40 – 0.93)**	**0.29**	**(0.16-0.52)**	0.74	(0.50- 1.09)	**0.48**	**(0.25 – 0.92)**
College graduate	**0.52**	**(0.36 – 0.77)**	**0.67**	**(0.45 - 0.99)**	**0.61**	**(0.42 – 0.89)**	**0.20**	**(0.10- 0.41)**	0.77	(0.52 – 1.15)	**0.37**	**(0.17 – 0.78)**
Marital status												
Single	1.21	(0.82 – 1.78)	1.10	(0.73 – 1.66)	**1.84**	**(1.24 – 2.75)**	**2.66**	**(1.40 – 5.04)**	**1.82**	**(1.20 – 2.75)**	**2.50**	**(1.26 – 4.97)**
Married	Referent		Referent		Referent		Referent		Referent		Referent	
Separated or	1.18	(0.86 – 1.62)	1.08	(0.78 – 1.51)	1.23	(0.90- 1.68)	**1.98**	**(1.17 – 3.35)**	**1.22**	**(0.88 – 1.68)**	**1.92**	**(1.09 – 3.38)**
Widowed	1.33	(0.90 – 1.98)	1.27	(0.84- 1.92)	0.84	(0.57 – 1.24)	1.51	(0.74 – 3.09)	0.85	(0.57 – 1.28)	1.38	(0.63 – 3.02)
In-hospital												
Type of ACS												
Unstable angina	Referent		Referent		Referent		Referent		Referent		Referent	
NSTEMI	0.80	(0.61 – 1.05)	0.82	(0.62 – 1.08)	0.84	(0.65 – 1.10)	0.67	(0.42 – 1.05)	0.86	(0.65 – 1.13)	0.69	(0.42 – 1.13)
STEMI	**0.51**	**(0.33-0.78)**	**0.60**	**(0.39 – 0.93)**	**0.62**	**(0.44 – 0.88)**	**0.25**	**(0.11 -0.57)**	**0.65**	**(0.45 – 0.94)**	**0.32**	**(0.13 – 0.74)**
Procedure												

None	Referent		Referent		Referent		Referent		Referent		Referent	
PCI	1.01	(0.74 – 1.36)	0.96	(0.70- 1.31)	-	-	-	-	-	-	-	-
CABG	1.39	(0.91-2.13)	1.30	(0.83 – 2.04)	-	-	-	-	-	-	-	-
Any Hospital	1.33	(0.97-1.81)	1.28	(0.93 – 1.77)	-	-	-	-	-	-	-	-
Length of stay (per	-	-	-	-	1.00	(0.99 – 1.00)	1.00	(0.99 -1.01)	1.00	(0.99 – 1.01)	1.00	(0.99 – 1.02)
Co-morbidities												
Lung disease	**1.88**	**(1.38 – 2.56)**	**1.85**	**(1.35 – 2.55)**	**1.40**	**(1.00 -1.94)**	1.58	(0.92 – 2.72)	1.31	(0.93 – 1.85)	1.42	(0.79 – 2.56)
High blood pressure	**1.52**	**(1.10 – 2.09)**	1.33	(0.96 – 1.86)	**1.57**	**(1.20 – 2.05)**	**2.37**	**(1.35 – 4.16)**	**1.37**	**(1.04 – 1.81)**	**1.89**	**(1.03 – 3.47)**
History of heart	**1.64**	**(1.27 – 2.13)**	**1.65**	**(1.26 – 2.16)**	1.27	(0.99 -1.63)	1.39	(0.88 – 2.18)	1.26	(0.97 – 1.62)	1.31	(0.80 – 2.13)
Diabetes	**1.59**	**(1.24 – 2.05)**	**1.49**	**(1.15 – 1.94)**	1.11	(0.87 – 1.44)	0.80	(0.51 – 1.27)	1.03	(0.79 – 1.34)	0.68	(0.41- 1.11)
Stroke	**1.90**	**(1.26 – 2.86)**	**1.74**	**(1.14 – 2.64)**	1.53	(0.97 – 2.41)	1.87	(0.90 – 3.88)	1.39	(0.86 – 2.24)	1.57	(0.72 – 3.44)
Heart failure	**1.98**	**(1.38 – 2.82)**	**1.81**	**(1.25 – 2.61)**	**1.51**	**(1.01 – 2.25)**	**2.36**	**(1.29 – 4.32)**	1.41	(0.93 – 2.14)	**2.00**	**(1.04 – 3.86)**
Drug Abuse	**2.35**	**(1.33 – 4.13)**	**2.00**	**(1.10 – 3.62)**	-	-	-	-	-	-	-	-
Psychosocial												
Depression†	-	-	**1.13**	**(1.10-1.16)**	-	-	-	-	**1.09**	**(1.05 – 1.14)**	**1.20**	**(1.13 – 1.28)**
Anxiety*	-	-	-	-	-	-	-	-	**1.08**	**(1.05 – 1.12)**	**1.13**	**(1.07 – 1.19)**

†Depression was measured using the Patient Health Questionnaire-9 [99]at baseline. Higher scores indicate worse depression.

*Anxiety was measured using the Generalized Anxiety Disorder-7[100] at baseline. Higher scores indicate worse anxiety.

Table III.4: Multivariate predictors of trajectory group membership for physical components subscale (PCS) of the SF-36 among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	PCS- Impaired vs. Average		**PCS- Impaired vs. Average with psychosocial**	
	OR	**(95% CI)**	**OR**	**(95% CI)**
Socio-demographic				
Age				
Less than 55	1.21	(0.87 – 1.68)	0.88	(0.62 – 1.25)
55-65	1.18	(0.88 – 1.59)	1.00	(0.73 – 1.36)
65+	Referent		Referent	
Male	**0.59**	**(0.45 – 0.77)**	**0.66**	**(0.50 – 0.87)**
White	0.80	(0.60 – 1.08)	0.76	(0.56 – 1.03)
Lives Alone	1.26	(0.93 – 1.69)	1.20	(0.88 – 1.63)
Education				
Less than high-school	Referent		Referent	
High-school or GED	0.78	(0.54 – 1.12)	0.87	(0.60 – 1.27)
Some college, trade school	0.55	(0.52 – 1.08)	0.95	(0.64 – 1.40)
College graduate	**0.55**	**(0.37 – 0.82)**	0.70	(0.46 – 1.07)
Medical				
Type of ACS				
Unstable angina	Referent		Referent	
NSTEMI	0.88	(0.66 – 1.15)	0.83	(0.63 – 1.08)
STEMI	**0.48**	**(0.31 – 0.74)**	**0.61**	**(0.41 – 0.92)**
Length of Stay (per 2 days)	1.00	(0.99 – 1.01)	1.00	(0.99 – 1.00)
Co-morbidities				
Lung disease	**1.71**	**(1.22 – 2.38)**	**1.68**	**(1.19 – 2.37)**
High blood pressure	**1.58**	**(1.13 – 2.22)**	1.38	(0.98 – 1.96)
Peripheral Vascular Disease	**1.81**	**(1.16 – 2.82)**	**2.01**	**(1.28 – 3.16)**
Arthritis	**2.26**	**(1.66 – 3.09)**	**2.23**	**(1.62 – 3.07)**
History of Heart Disease	**1.37**	**(1.04 – 1.79)**	**1.37**	**(1.03 – 1.81)**
Diabetes	**1.41**	**(1.08 – 1.85)**	**1.35**	**(1.02 – 1.78)**
Stroke	**2.41**	**(1.54 – 3.76)**	**2.18**	**(1.38 – 3.44)**
Heart failure	**1.86**	**(1.26 – 2.75)**	**1.70**	**(1.13 – 2.56)**
Psychosocial				
Depression†	-	-	**1.12**	**(1.09 - 1.15)**

†Depression was measured using the Patient Health Questionnaire-9 [99] at baseline. Higher scores indicate worse depression.

Table III.5: Multivariate predictors of trajectory group membership mental components subscale (MCS) of the SF-36 among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	MCS- Low vs. High		**MCS- Worsening vs. High**		**MCS- Improving vs. High**		**MCS- Low vs. High with psychosocial**		**MCS- Worsening vs. High with psychosocial**		**MCS- Improving vs. High with psychosocial**	
	OR	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**	**OR**	**(95% CI)**
Socio-demographic												
Age												
Less than 55	**3.44**	**(2.09 – 5.65)**	**1.59**	**(1.13 – 2.24)**	1.15	(0.71 -1.81)	**1.86**	**(1.00 – 3.48)**	1.21	(0.68 – 1.53)	0.91	(0.55- 1.52)
55-65	**2.35**	**(1.43 – 3.85)**	1.33	(0.96 – 1.86)	1.10	(0.69 – 1.74)	1.75	(0.95 – 3.23)	1.08	(0.73 – 1.59)	1.00	(0.62- 1.61)
65+	Referent		Referent		Referent		Referent		Referent		Referent	
Male	0.41	(0.28 – 0.61)	0.59	(0.44 – 0.78)	0.97	(0.64 – 1.47)	0.72	(0.45 – 1.18)	0.85	(0.61 – 1.18)	1.22	(0.80 – 1.89)
White	1.00	(0.65 – 1.55)	0.86	(0.63 – 1.17)	**0.64**	**(0.42 – 0.98)**	1.10	(0.62 -1.96)	0.89	(0.60 – 1.32)	0.68	(0.43 – 1.09)
Co-morbidities												
History of Heart Disease	**1.93**	**(1.29 – 2.88)**	1.31	(0.99 – 1.74)	1.35	(0.91- 2.02)	1.44	(0.87 – 2.36)	1.11	(0.80 – 1.55)	1.21	(0.81 – 1.82)
Stroke	1.48	(0.75 – 2.91)	**2.15**	**(1.37 – 3.36)**	1.70	(0.90 – 3.23)	1.07	(0.47 – 2.45)	1.70	(0.99 -2.92)	1.46	(0.75 – 2.85)
Heart failure	**2.57**	**(1.56 – 4.23)**	1.48	(0.98 – 2.25)	1.70	(0.99 – 2.94)	1.87	(0.98 – 3.55)	1.17	(0.72 – 1.90)	1.44	(0.82 – 2.54)
Psychosocial												
Depression†	-	-	-	-	-	-	**1.38**	**(1.30 – 1.47)**	**1.24**	**(1.19- 1.30)**	**1.15**	**(1.09- 1.22)**
Anxiety*	-	-	-	-	-	-	**1.17**	**(1.12 – 1.47)**	**1.13**	**(1.09 – 1.17)**	**1.07**	**(1.02 – 1.12)**
Cognitive Functioning‡	-	-	-	-	-	-	**0.93**	**(0.88 – 0.98)**	0.96	(0.93 – 1.00)	0.97	(0.92 – 1.01)

†Depression was measured using the Patient Health Questionnaire-9 [99]at baseline. Higher scores indicate worse depression.

*Anxiety was measured using the Generalized Anxiety Disorder-7[100] at baseline. Higher scores indicate worse anxiety.

‡Cognitive Functioning was measured using the Telephone Interview for Cognitive Status or TICS[101] at baseline. Higher scores indicate better cognitive function. The scale ranges from 0 to 41 and. A score over 30 is considered normal.

Supplemental Table III.1: Baseline characteristics overall and by acute coronary syndrome subtype (ST-elevated myocardial infarction or STEMI, non-ST-elevated myocardial infarction or NSTEMI, Unstable angina or UA) among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	Full sample (n=1,589)	**STEMI (n=247)**	**NSTEMI (n=863)**	**UA (n=479)**	**P-value**
Socio-demographic					
Average Age (SD)	61.1 (11.4)	59.2	60.6 (11.5)	63.2 (10.8)	<0.001
Female, N (%)	530 (33.4)	65 (26.3)	310 (35.9)	155 (32.4)	0.016
Non-Hispanic White, N (%)	1224 (77.0)	202	654 (75.8)	368 (76.8)	0.141
Lives Alone, N (%)	310 (22.7)	51 (23.3)	167 (22.8)	92 (22.3)	0.957
Marital status, N (%)					
Single	186 (11.7)	42 (17.1)	108 (12.5)	36 (7.5)	0.002
Married	929 (58.5)	148	490 (56.8)	291 (60.8)	
Separated or divorced	298 (18.8)	39 (15.9)	165 (19.1)	94 (19.6)	
Widowed	175 (11.0)	17 (6.9)	100 (11.6)	58 (12.1)	
Education, N (%)					
Less than high-school	281 (17.7)	37 (15.0)	161 (18.7)	83 (17.4)	0.707
High-school or GED	474 (29.8)	81 (33.8)	247 (28.6)	146 (30.5)	
Some college, trade school	441 (27.8)	72 (29.2)	234 (27.1)	135 (28.2)	
College graduate	392 (24.7)	57 (23.1)	221 (25.6)	114 (23.9)	
Co-morbidities					
Lung disease, N (%)	255 (16.1)	31 (12.6)	133 (15.4)	91 (19.0)	0.061
High blood pressure, N (%)	1177 (74.1)	150	632 (73.2)	395 (82.5)	<0.001
Peripheral Vascular Disease, N (%)	134 (8.4)	17 (6.9)	69 (8.0)	48 (10.0)	0.280
Arthritis, N (%)	305 (19.2)	44 (17.8)	135 (15.6)	126 (26.3)	<0.001
History of Heart Disease, N (%)	751 (47.3)	74 (30.0)	361 (41.8)	316 (66.0)	<0.001
Diabetes, N (%)	551 (34.7)	51 (20.7)	301 (34.9)	199 (41.5)	<0.001
History of Spinal Diseases, N (%)	89 (5.6)	11 (4.5)	41 (4.8)	37 (7.1)	0.053
Stroke, N (%)	125 (7.9)	12 (4.9)	65 (7.5)	48 (10.0)	0.032
Heart failure, N (%)	188 (11.8)	12 (4.9)	95 (11.0)	81 (16.9)	<0.001
Cancer, N (%)	190 (12.0)	20 (8.1)	94 (10.9)	76 (15.9)	0.003
Renal failure, N (%)	142 (8.9)	15 (6.1)	80 (9.3)	47 (9.8)	0.217
Atrial fibrillation, N (%)	102 (6.4)	7 (2.8)	41 (4.8)	54 (11.3)	<0.001
Hyperlipidemia, N (%)	1084 (68.2)	140	566 (65.6)	378 (78.9)	<0.001
History of Alcohol Abuse, N (%)	74 (4.7)	15 (6.1)	37 (4.3)	22 (4.6)	0.500
In hospital factors					
Length of stay, N (%)					
0-1 day	347 (21.8)	21 (8.5)	131 (15.2)	195 (40.7)	<0.001
2-3 days	714 (44.9)	166	437 (50.6)	111 (23.2)	
4+ days	528 (33.2)	60 (24.3)	295 (34.2)	173 (36.1)	

Any in hospital complications, N (%)	311 (19.6)	62 (25.1)	170 (19.7)	79 (16.5)	0.021
Any in hospital procedures, N (%)					
None	324 (20.4)	22 (8.9)	195 (22.6)	107 (22.3)	<0.001
PCI	1068 (67.2)	209 [illegible]	577 (66.9)	282 (58.9)	
CABG	197 (12.4)	16 (6.5)	91 (10.5)	90 (18.8)	
Average GRACE risk score (SD)	94.0 (27.5)	91.0	97.9 (28.5)	88.4 (25.3)	<0.001

Supplemental Table III.2: Patient Health Status at baseline, 1-, 3-, and 6-months among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	Baseline			1-month			3 months			6 months			
	N	Average	SD	N	Average	SD	N	Average	SD	N	Average	SD	p-value
Mental Components Subscale	1,589	48.02	12.20	1065	51.22	10.60	971	52.67	10.06	953	52.91	10.61	<0.001
Physical Components Subscale	1,589	42.03	10.70	1065	43.75	9.90	971	45.72	10.32	953	45.72	10.60	<0.001
SAQ – Physical limitations	1420	76.49	25.63	948	85.54	20.57	899	88.79	18.74	863	89.79	18.22	<0.001
SAQ- HRQoL	1588	61.92	26.08	1064	78.05	20.90	970	81.67	18.51	952	82.44	18.90	<0.001

Supplemental Table III.3: Criteria for choosing number of mental components subscales trajectories among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	Bayesian Information Criterion	Average Posterior Probability for Each Trajectory						Odds of Correct Classification for Each Trajectory					
# of Trajectories		1st	2nd	3rd	4th	5th	6th	1st	2nd	3rd	4th	5th	6th
1	-17786.54	1						Infinity					
2	-16982.87	0.916	0.968					31.01	10.64				
3	-16851.47	0.856	0.796	0.946				53.23	12.46	8.98			
4	-16775.73	0.833	0.725	0.816	0.928			49.19	13.38	37.11	7.20		
5	-16792.62	0.833	0.725	0.816	0.928	NA*		49.19	13.38	39.18	7.20	NA	
6	-16756.03	0.788	0.720	0.779	0.706	0.924	NA	114.19	20.23	34.42	12.81	7.94	NA

*NA is not applicable

Supplemental Table III.4: Criteria for choosing number of physical components subscale trajectories among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

# of Trajectories	Bayesian Information Criterion	Average Posterior Probability for Each Trajectory						Odds of Correct Classification for Each Trajectory					
		1st	2nd	3rd	4th	5th	6th	1st	2nd	3rd	4th	5th	6th
1	-17509.09	1						Infinity					
2	-16614.70	0.912	0.946					20.27	8.96				
3	-16422.02	0.847	0.798	0.916				26.68	8.05	10.95			
4	-1636.53	0.853	0.804	0.774	0.903			135.20	15.50	7.69	11.77		
5	-16326.99	0.863	0.781	0.717	0.623	0.878		148.89	14.54	13.14	7.77	9.72	
6	-16321.90	0.839	0.733	0.750	0.795	0.604	0.861	140.05	12.66	16.97	91.36	5.49	10.21

Supplemental Table III.5: Criteria for choosing number of SAQ health-related quality of life trajectories among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	Bayesian Information Criterion	Average Posterior Probability for Each Trajectory						Odds of Correct Classification for Each Trajectory					
# of Trajectories		1st	2nd	3rd	4th	5th	6th	1st	2nd	3rd	4th	5th	6th
1	-18295.57	1						Infinity					
2	-18028.68	0.817	0.897					8.33	8.57				
3	-17944.46	0.796	0.805	0.819				36.37	5.47	8.05			
4	-17910.29	0.807	0.742	0.775	0.820			44.33	3.98	5.09	45.61		
5	-17908.72	0.777	0.627	0.764	0.663	0.795		54.17	4.10	4.53	12.43	39.38	
6	-17867.00	0.764	0.739	0.762	0.794	0.777	0.834	40.51	5.25	47.49	5.23	107.38	83.50

Supplemental Table III.6: Criteria for choosing number of SAQ physical limitations trajectories among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

	Bayesian Information Criterion	Average Posterior Probability for Each Trajectory						Odds of Correct Classification for Each Trajectory					
# of Trajectories		1st	2nd	3rd	4th	5th	6th	1st	2nd	3rd	4th	5th	6th
1	-12607.56	1						Infinity					
2	-12251.22	0.862	0.907					13.11	4.85				
3	-12203.51	0.810	0.718	0.823				19.17	3.59	6.89			
4	-12200.79	0.739	0.687	0.718	0.708			30.24	7.04	3.03	8.59		
5	-12199.83	0.681	0.618	0.584	0.684	0.720		28.13	7.67	9.93	3.30	8.37	
6	-12205.39	0.667	0.626	0.687	0.690	0.668	0.726	8.66	14.76	3.33	238.83	6.60	33.20

Supplemental Table III.7: Overlap of trajectories for all four components of patient health status among 1,589 adults hospitalized with acute coronary syndrome, TRACE-CORE, 2011-2013

Physical Components Subscale	Mental Components Subscale	SAQ Physical Limitations	SAQ HRQoL	Frequency (%)
Average	High	Average	High	764 (48.1)
Average	Improving	Average	Average	76 (4.8)
Impaired	High	Average	Average	86 (5.4)
Impaired	High	Impaired	Average	117 (7.4)
Impaired	Improving	Impaired	Average	64 (4.0)
Other				482 (30.3)

CHAPTER IV : TRAJECTORIES OF PATIENT HEALTH STATUS PREDICT READMISSION AND DEATH AFTER AN ACUTE CORONARY SYNDROME

Abstract

Objective: We determined whether trajectories (subgroups of patients with distinct longitudinal patterns over time) of patient health status (health-related quality of life (HRQoL) and physical limitations) at baseline, 1, 3, and 6 months predict mortality or readmission 6 to 12 months post-acute coronary syndrome (ACS) discharge.

Methods: We used the TRACE-CORE cohort of patients hospitalized with ACS. We measured patient health status using the SF-36 mental and physical components (MCS and PCS) and the Seattle Angina Questionnaire physical limitations and angina-related quality of life subscales (SAQ physical limitations and SAQ HRQoL) during hospitalization and at 1, 3, and 6-months post-discharge. We identified readmissions between 6-12 months post-ACS discharge using both Medicare claims data and self-report, and deaths using the National Death Index. We used logistic regression analysis to model the association between trajectory membership and the composite outcome of death or readmission.

Results: Participants (n=1,589) were, on average, 61.1 (SD 11.4) years old, two thirds were men, and three quarters were non-Hispanic white. Among 1,143 individuals with complete data for the composite outcome of death or readmission, 257 (22.5%) experienced this endpoint (including 13 deaths). Individuals in the worst (compared to the best) patient health status trajectories, except for MCS trajectories, were more likely to experience death or readmission after adjusting for several confounding factors (PCS

OR 2.42 (95% CI (1.75-3.35), SAQ physical limitations OR 1.46 (95% CI 1.06-2.02), SAQ HRQoL OR 2.00 (95% CI 1.00-4.00)).

Conclusions: Trajectories of patient health status may help clinicians to target interventions.

Word count: 248

Introduction

Approximately ninety percent of the 1.2 million Americans hospitalized with an acute coronary syndrome (ACS) survive to discharge.[1,125] However, death and readmission after hospital discharge is not uncommon and upwards of one quarter of patients with ACS either die or are readmitted to the hospital from 6 to 12 months post ACS discharge.[126] Moreover, many experience impaired health-related quality of life (HRQoL) after discharge. Thirty percent of patients experience severely diminished quality of life due to ACS over six months following discharge[3] and only 58% of patients return to work within the first 3 months.[4] Thus, the American Heart Association has highlighted the clinical importance of patient health status (HRQoL and functional status) among patients with cardiovascular disease.[7]

Post-ACS health status impairment also has important implications for patients,[7] since those with more physical limitations and worse HRQoL are more likely to die.[52-59] However, relatively few studies have examined the relationship between patient health status and hospital readmission,[53-55,59] and most of these included individuals without ACS or did not include individuals with unstable angina. To our knowledge, no study has determined whether membership in trajectories or subgroups of individuals with similar longitudinal patterns of patient health status over time is associated with subsequent mortality and hospital readmission.

Trajectories are important not only because they could help ACS survivors, their caregivers, and providers have an idea about what to expect in terms of early patient health status, but also because they may also predict future events such as mortality and health care use.[115,127]. In this study, we examined the extent to which trajectories of patient health status at baseline, and at 1, 3, and 6 months post-discharge predict mortality or readmission in the second 6 months post-ACS discharge. We hypothesized that individuals with more unfavorable trajectories during the first 6 months will be more likely to be readmitted or die from 6 months to 1 year post-ACS.

Methods

Study Design, Setting and Data Sources

We used data from a prospective longitudinal cohort, TRACE-CORE (Transitions, Risks, and Action in Coronary Events – Centers for Outcomes Research and Education), which included patients with ACS who survived to discharge. Patients were hospitalized between April 2011 and May 2013 at 6 community and teaching hospitals from Central Massachusetts and Georgia. Patients were interviewed using computer-assisted interviews at discharge, 1-, 3-, 6- and 12-months post-discharge. Participants' medical records from the index ACS hospitalization were abstracted by trained study personnel. In addition, TRACE-CORE also captures both Medicare claims data (for the subset of patients on Medicare), and National Death Index data for the first year after hospitalization with ACS. The University of Massachusetts Medical School Institutional Review Board approved this study. Further details on the TRACE-CORE cohort including detailed exclusion and inclusion criteria are available.[71,72]

Measures

Outcomes Measures

Our main outcome was a composite of death and all-cause readmission from 6-months to 12-months post ACS discharge, which we will term "late death or readmission". Mortality was ascertained from death certificates from national death records. Re-hospitalization was determined from a combination of Medicare claims data and from self-report data. Individuals with Medicare claims data (n=505) included those with Medicare part B and fee-for-service data. For those individuals, readmission was determined *solely* by the presence/absence of any hospital admission during the relevant timeframe from Medicare claims data. *For other TRACE-CORE participants without Medicare data*, we used the answer to the following question, "Since we last talked to you on [the date of the 6-month interview], have you been admitted to the hospital for any reason? This does not include emergency room or emergency department visits where you were not admitted to the hospital." Response options included: yes, no, I don't know or refusing to answer. Those who answered yes or no were coded as readmitted or not, respectively, and all other responses were coded as missing.

Measurement of Exposures

Our main exposures were trajectories (distinct subgroups with similar patterns over time) of patient health status from discharge to 6-months post-discharge after hospitalization for an ACS. Patient health status included subscales from both the Seattle angina questionnaire (SAQ) and the SF-36. We used the physical limitations and angina health-related quality of life (HRQoL) subscales of SAQ. [74] We also used the mental components subscale (MCS) and physical components subscale (PCS) of the SF-36.[73] All patient health status components were measured at discharge, 1-, 3- and 6-months post-discharge. All components of patient health status range from 0-100, with higher scores being associated with better health (better HRQoL and fewer physical limitations) and have strong psychometric properties.[75-78]

We used the trajectories developed from group-based trajectory analysis in aim 2 to ascertain the probability of each patient belonging in each trajectory of each component of patient health status. For this aim, we assigned individuals to the trajectory with which they had the highest probability of membership. For further details on this process refer to aim 2. A brief description of the trajectories for each component of patient health status is provided below.

Based on aim 2, we found that that there were 3 and 2 trajectories for SAQ HRQoL and physical limitations, respectively. For both SAQ HRQoL and physical limitations, all trajectories showed improving scores over the first 6-months post-ACS, but those in poorer performing trajectories never caught up with their counterparts. Most of respondents were classified in either the High (36.4%) or Average (53.9%) SAQ HRQoL trajectories and only a minority were in the Low SAQ HRQoL trajectory. For SAQ physical limitations, we found 2 trajectories: Average (67.8%) and Impaired (32.2%).

From aim 2, we found that MCS and PCS had very different trajectories. For MCS there were four different trajectories: High (64.4%), Improving (16.5%), Worsening (10.5%) and Low (8.9%). The High group had high scores throughout and the Low group had low scores throughout. The Improving group originally had worse scores than the Worsening group, but by six months had better scores. For PCS, there were only the following 2 trajectories that behaved similarly to the trajectories for SAQ physical limitations: Average (66.4%) and Impaired (33.6%). For further details on these trajectories refer to aim 2 results section and figure III.1.

Measurement of Covariates

We measured several socio-demographic, co-morbidity and clinical co-variates at discharge. Patients reported all sociodemographic information including sex, race, marital status, and highest level of attained education at discharge. Age was abstracted from medical record. Co-morbidities and clinical variables related to the incident hospitalization were abstracted from the medical record.

Clinical variables included ACS type, the Global Registry of Acute Coronary Events or GRACE risk score,[83] length of stay, in-hospital procedures and any in-hospital complications. Type of ACS was categorized using American College of Cardiology/American Heart Association criteria: NSTEMI, STEMI and unstable angina[84] based on the information from medical record abstraction. A panel of adjudicating physicians reviewed any questionable cases and those whose subtypes of ACS could not be determined were excluded. We used the GRACE risk score as a proxy measure for the clinical severity of the ACS event.[83] In-hospital procedures included percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG). Patients who had of any the following during the index hospitalization for ACS were classified as having in-hospital complications: renal failure, atrial fibrillation, atrial flutter, a major bleed, cardiogenic shock, cardiac arrest, deep vein thrombosis, delirium, falls, heparin-induced thrombocytopenia, pulmonary embolism, pneumothorax, recurrent myocardial infarction, stroke, transient ischemic attack, urinary tract infection, heart failure, and ventricular tachycardia.

We measured depressive and anxiety symptoms using the Patient Health Questionnaire-9 (PHQ-9)[128] and the Generalized Anxiety Disorder 7 score (GAD-7).[100] For both scales, higher scores indicate worse symptoms and both have strong psychometric properties.[100,102-106] Cognitive impairment was measured using the Telephone Interview for Cognitive Status (TICS) with higher scores being associated with better cognitive function.[101]

Statistical Analysis

We examined the relationship between late death or readmission and trajectory membership using chi-squared statistics. We also determined the relationship between co-variates and late death or readmission using chi-squared statistics and analysis of variance. We used logistic regression to assess the multivariate relationship between trajectory membership and late death or readmission. We used separate models for each component of patient health status, as we found in aim 2 that there was not an overwhelming amount of overlap between membership in trajectories for each of the components of patient health status. Moreover, we wished to determine the separate predictive ability of each of the components of patient health status. All models included age, sex, and race/ethnicity. We added other covariates when their inclusion changed the estimate for the odds ratios between trajectory membership and late death or readmission by at least 10%. To address missing data, we used multiple imputation with predictive mean matching and chained equations to create 20 imputed datasets.[85] Multiple imputation was used to address missingness in exposures, covariates and outcomes. All analyses were performed using Stata 13 (StataCorp, College Station, TX).

Results

Sample Characteristics

From 2187 TRACE-CORE participants, we excluded 55 who died during the 6-month follow-up period, 2 without baseline MCS SF-36 scores, 51 whose subtype of ACS was missing, and 477 patients who were readmitted during the 6 months following discharge. Thus, we had a final analytic sample of 1,589 TRACE-CORE patients, with 505 patients also having information from Medicare claims data. For longitudinal analysis, we had the following numbers of participants from each follow-up: 1065 patients with data at 1 month, 971 at 3 months, 953 at 6 months and 950 at 12 months.

Patients were on average 61.1 years old (SD 11.4); 66.7% were male and about three quarters were non-Hispanic white (table 1). About a half of patients were married and the majority had a high school degree. Just over half of the participants were admitted with an NSTEMI, the majority had a PCI and only about a third had a hospital stay of more than 3 days.

Late Readmission or Death

There were 13 deaths as well as 244 readmissions out of 1143 individuals with information on readmissions, yielding a 22.5% risk of death or readmission from 6-months to 1-year post-discharge. Information on approximately 60% of all readmissions amongst the entire sample came from Medicare claims data. Individuals who died or were readmitted were more likely to be older, male, be less educated and have more co-morbidities (Table IV.1). Those who had longer lengths of stay, more in-hospital complications and who did not have a PCI or CABG were also more likely to die or be readmitted. Individuals who died or were readmitted had higher depressive and anxiety symptoms and worse cognitive function.

Association between Trajectory Membership and Late Death or Readmission

In general, individuals belonging in worst trajectories were more likely to have died or been readmitted when compared to those in the best trajectories (Table IV.2). However, for MCS, those in the Worsening and Improving trajectories had very similar rates of death or readmission. For SAQL however, those in the Low trajectory did have more deaths and readmissions when compared to those in the Average SAQL trajectory.

Table IV.3 shows the multivariate logistic regression models of the association between trajectory membership status and death or readmission based on multiply imputed data. Before adjusting for depressive symptoms, membership in the worse trajectories of patient health status (except for the low trajectory of MCS) was associated with a higher risk of death or readmission when compared to belonging to the best trajectory (Table IV.3). However, after adjusting for depressive symptoms, membership in any of the worse MCS trajectories was not associated with a higher risk of death or readmission (Table IV.3). Yet membership in worse trajectories for all other components of patient health, aside from MCS, was still associated with a significantly increased risk of death.

Discussion

This study is the first to examine the ability of trajectories of patient health status after an ACS (based on data from discharge to 6-months post discharge) to predict a composite endpoint of death or readmission from 6-months to 1-year post-discharge. The risk of readmission or death from 6-months to 1-year post-ACS discharge was 22.5%. We found that membership in worse trajectories, for every component of patient health status except for MCS, predicted late death and readmission after adjustment for multiple confounders. Membership in worse MCS trajectories was associated with a higher risk of late death or readmission until depressive symptoms were considered.

Comparison to Existing Literature on Patient Health Status and Death or Readmission

Our findings are similar to other studies that have shown that generic physical HRQoL (not specific to a certain disease or condition) is a good predictor of total mortality, cardiovascular disease incidence in the general population[128] and outcomes in patients with cardiovascular disease.[129] In addition, many studies among those with myocardial infarction,[56] ACS[130] or recipients of PCI[131] have found that worse scores on PCS are associated with higher mortality[56,130,131] at a variety of time points and higher rates of readmission.[60,129] Similarly, our study found that membership in worse PCS trajectories was associated with a higher risk of death or readmission.

There are several reasons why we may not have found an association between MCS trajectories and subsequent death or readmission at 6-12 months post-ACS. First, the literature on the association of MCS and outcomes in patients with cardiovascular disease is more mixed.[129] For, example a study by Thombs et. al. of ACS patients failed to find a statistically significant association between MCS and mortality,[130] while others have found strong associations between worse MCS scores and higher mortality and readmission.[60,131,132] One explanation for this may be the differences in patient populations, since the Thombs et. al. study included only ACS patients,[130] while the other studies included all-comers for PCI (including stable angina),[131] post-myocardial infarction patients with severe left ventricular dysfunction[60] and patients with heart failure.[132] This would explain why our study, which only included patients discharged from the hospital after an ACS, failed to find an association between MCS trajectory membership and subsequent death or readmission. Second, it is possible that it is the depressive symptoms component of MCS that predisposes towards worse outcomes. In as much, after adjustment for depressive symptoms, there was no association between MCS trajectories and death or readmission. Only the study by Thombs et. al. adjusted for depression.[130] Our findings are similar, in that after adjusting for depressive symptoms, there was no significant association between MCS trajectories and readmission or death. Third, the method of scoring the MCS and PCS subscales of the SF-36 may also contribute. Worse responses (in terms of functioning) on a select number of items that contribute to both MCS and PCS scores, tend to push PCS scores lower, but also increase MCS scores towards the mean.[133] This may cause an artificial decrease in the association between MCS and outcomes.[134]

Disease-specific HRQoL measures among patients with cardiovascular disease have consistently been found to predict adverse outcomes among patients with cardiovascular disease including both mortality and readmissions.[135-137] Our study, similar to the findings of others,[137,138] found that worse angina physical limitations scores were associated with a higher risk of our composite outcome. We also found a barely significant association between angina-related HRQoL and our composite outcome. To the best of our knowledge, this is the first time this has been reported in the literature.

Possible Mechanisms

There are several mechanisms of how trajectories of patient health status may be associated with an increased risk in readmission and mortality. One possibility is that worse patient health status is associated with higher mortality and readmission, because worse patient health status has also been associated with underlying inflammation.[139] It is also possible that worse patient health status is associated with lower social support and worse self-care, which could lead an increased risk of recurrent cardiovascular events or mortality. Future research should be done on the mechanisms linking patient health status and mortality and morbidity, as this might give healthcare providers future avenues for intervention.

Implications

The finding that trajectories of most patient health status components can predict death and readmission has several implications. First, the finding that membership in a worse trajectory of all patient health status (except for MCS) can predict subsequent outcomes makes it more likely that these trajectories are really two different populations that recover from ACS in very different ways. Second, providers who find that someone might belong to a worse patient health status trajectory might consider targeting more intensive interventions to them. Moreover, because, only a minority of patients are on these worse trajectories, it makes trajectories an even more practical heuristic for identifying patients with a worse prognosis. There are several interventions from which patients on these trajectories might benefit. If individuals have worse angina, they might benefit more from interventions like PCI and enhanced pharmacological management, both of which have been found to benefit those with worse angina-related patient health status.[120,122] Moreover, tailored cardiac rehabilitation programs could be developed for those on the worse patient health status trajectories. Although trajectories could be applied in the clinical medicine, this application does depend on some needed methodological work. Namely, it would need to be possible to include models reported in the literature and use them to produce posterior probabilities of trajectory membership without having to rerun the model. Methodological work to be able to do this is currently ongoing and would need to be done to be able to have external validation of these models and to incorporate these models into clinical practice.

Study Strengths and Limitations

This study has several limitations. First, we used both Medicare claims and self-report to determine whether someone had been readmitted. Despite self-report not being as reliable as claims data, information regarding 60% of readmissions was obtained from claims. Moreover, our risk of readmission or death was similar to rates that have been reported in the literature on ACS .[126] Because using two different measures in two subsets of a study population can be problematic, we did a sensitivity analysis in which we only used self-reported readmission for all study participants. The results from this sensitivity analysis were substantively similar to the results presented, as we showed that membership in worse trajectories of patient health status (except for MCS) was still associated with a higher chance of subsequent death or readmission. Second, we had a significant amount of missing data. We attempted to mitigate the effect of this by using multiple imputation. However, when we compared the analyses to the complete case analysis, the results were virtually identical except SAQ trajectories were no longer significant predictors of death and readmission. Third, when creating the trajectories, we excluded any individuals who had died or been readmitted from discharge to 6 months. We did this as we envision trajectories to possibly be a useful paradigm for prognostication among those who are at a lower risk for future events. It has already been established that those who are readmitted early will be more likely to have worse outcomes, such as mortality[124] and thus trajectories may not be useful among this subpopulation. However, this means that the trajectories that we found and their increased risk of readmission or death may only be generalizable to the subset of ACS survivors who were not initially readmitted between discharge and 6 months. The study's strengths mitigate these limitations. Our study used a combination of many data sources: longitudinal data on patient health status (to determine trajectories), comprehensive medical record abstraction and claims data. This represents a unique and rich set of data that allowed us to complete this study.

In conclusion, we found that all trajectories of patient health status except for MCS predicted readmission or death. We draw two conclusions from these findings. First, trajectories of patient health status are a useful way to identify patients at increased risk of future bad outcomes. Second, future research should be done to determine if tailored interventions can be deployed to improve outcomes (patient health status, readmissions, and mortality) in patients in the worst trajectories.

Table IV.1: Socio-demographic and clinical characteristics associated with death or readmission from 6-months to 1-year post-ACS discharge among 1,589 adults hospitalized with Acute Coronary Syndrome, TRACE-CORE, 2011-2013

	Total Sample (n=1,589)	Death or Readmission (n=257)	No Death or Readmission (n=886)	p-value
Socio-demographic				
Average Age (SD)	61.1 (11.4)	65.4 (11.7)	63.0 (10.6)	0.002
Male, N (%)	1059 (66.7)	151 (58.8)	590 (66.6)	0.021
Non-Hispanic White, N (%)	1203 (75.7)	94 (75.5)	683 (77.1)	0.593
Lives Alone, N (%)	310 (22.7)	58 (27.0)	73 (22.4)	0.156
Marital status, N (%)				
Single	186 (11.7)	23 (9.0)	93 (10.5)	0.015
Married	929 (58.5)	136 (52.9)	544 (61.4)	
Separated or divorced	298 (18.8)	51 (19.8)	143 (16.1)	
Widowed	175 (11.0)	47 (18.3)	106 (12.0)	
Education, N (%)				
Less than high-school	281 (17.7)	66 (25.7)	111 (12.5)	<0.001
High-school or GED	474 (29.9)	83 (32.3)	255 (28.8)	
Some college, trade school	441 (27.8)	54 (21.0)	276 (31.2)	
College graduate	392 (24.7)	54 (21.0)	244 (27.5)	
Co-morbidities				
Lung disease, N (%)	225 (16.1)	62 (24.1)	139 (15.7)	0.002
High blood pressure, N (%)	1177 (74.1)	210 (81.7)	660 (74.5)	0.017
Peripheral Vascular Disease, N (%)	134 (8.4)	38 (14.8)	66 (7.5)	<0.001
Arthritis, N (%)	305 (19.2)	76 (29.6)	164 (18.5)	<0.001
History of Heart Disease, N (%)	751 (47.3)	164 (63.8)	391 (44.1)	<0.001
Diabetes, N (%)	551 (34.7)	129 (50.2)	288 (32.5)	<0.001
History of Spinal Diseases, N (%)	89 (5.6)	20 (7.8)	55 (6.2)	0.369
Stroke, N (%)	125 (7.9)	42 (16.3)	59 (6.7)	<0.001
Heart failure, N (%)	188 (11.8)	62 (24.1)	88 (9.9)	<0.001
Cancer, N (%)	190 (12.0)	33 (12.8)	116 (13.1)	0.916
Renal failure, N (%)	142 (8.9)	43 (16.7)	73 (8.2)	<0.001
Atrial fibrillation, N (%)	102 (6.4)	23 (9.0)	63 (7.1)	0.325
Hyperlipidemia, N (%)	1084 (68.2)	190 (73.9)	609 (68.7)	0.110
History of Alcohol Abuse, N (%)	74 (4.7)	9 (3.5)	36 (4.1)	0.684
In hospital factors				
Type of ACS				
ST-elevated myocardial	247 (15.5)	24 (15.1)	135 (84.9)	0.051
Non-ST-elevated myocardial	863 (54.3)	148 (24.1)	466 (75.9)	
Unstable angina	479 (30.1)	85 (23.0)	285 (77.0)	
Length of stay, N (%)				

0-1 day	347 (21.8)	39 (15.2)	218 (24.6)	<0.001
2-3 days	714 (44.9)	97 (37.7)	399 (45.0)	
4+ days	528 (33.2)	121 (47.1)	269 (30.4)	
Any in hospital complications, N (%)	311 (19.6)	72 (28.0)	154 (17.4)	<0.001
Any in hospital procedures, N (%)				
None	324 (20.4)	76 (29.6)	168 (19.0)	<0.001
PCI	1068 (67.2)	152 (59.1)	606 (68.4)	
CABG	197 (12.4)	29 (11.3)	112 (12.6)	
Average GRACE risk score (SD)				
Psychosocial variables				
Depression (SD)†	5.6 (5.3)	7.1 (6.1)	4.8 (4.6)	<0.001
Anxiety (SD)*	5.7 (5.6)	6.5 (6.1)	4.9 (5.1)	<0.001
Cognitive Functioning (SD)‡	31.5 (4.3)	30.2 (5.0)	32.0 (4.0)	<0.001

†Depression was measured using the Patient Health Questionnaire-9 [99]at baseline. Higher scores indicate worse depression.

*Anxiety was measured using the Generalized Anxiety Disorder-7[100] at baseline. Higher scores indicate worse anxiety.

‡Cognitive Functioning was measured using the Telephone Interview for Cognitive Status or TICS[101] at baseline. Higher scores indicate better cognitive function. The scale ranges from 0 to 41 and. A score over 30 is considered normal.

Table IV.2: Patient health status trajectories associated with death or readmission from 6-months to 1-year post-ACS discharge among 1,589 adults hospitalized with Acute Coronary Syndrome, TRACE-CORE, 2011-2013

Trajectory Membership	Total Sample (n=1,589)	Death or Readmission (n=257)	No Death or Readmission (n=886)	p-value
Physical Components Score				
Average	1067 (67.2)	112 (43.6)	644 (72.7)	<0.001
Impaired	522 (32.9)	145 (56.4)	242 (27.3)	
Mental Components Subscale				
High	1068 (67.2)	151 (58.8)	638 (72.0)	0.001
Improving	275 (17.3)	52 (20.2)	124 (14.0)	
Worsening	119 (7.5)	29 (11.3)	69 (7.8)	
Low	127 (8.0)	25 (9.7)	55 (6.2)	
SAQ – physical limitations				
Average	1103 (69.4)	140 (54.5)	650 (73.4)	<0.001
Impaired	486 (30.6)	117 (45.5)	236 (26.6)	
SAQ – angina related quality of life				
High	551 (34.7)	65 (25.2)	3358 (40.4)	<0.001
Average	911 (57.3)	163 (63.4)	477 (53.8)	
Low	127 (8.0)	29 (11.3)	51 (5.8)	

Table IV.3: Association between membership in patient health status trajectories and death or readmission from 6-months to 1-year post-ACS discharge among 1,589 adults hospitalized with Acute Coronary Syndrome, TRACE-CORE, 2011-2013

Trajectory Membership	Unadjusted Odds Ratio for Death or Readmission		Adjusted Odds Ratio for Death or Readmission, except for Depression†		Adjusted Odds Ratio for Death or Readmission, with Depression‡	
	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Physical Components Score						
Average	Referent		Referent		Referent	
Impaired	3.37	(2.55 – 4.47)	2.80	(2.08-3.76)	2.42	(1.75 – 3.35)
Mental Components Subscale						
High	Referent		Referent		Referent	
Improving	1.79	(1.08 – 2.96)	1.35	(0.79-2.32)	1.08	(0.70 – 1.65)
worsening	1.83	(1.29 – 2.59)	1.59	(1.10-2.30)	1.28	(0.77 – 2.10)
low	1.67	(1.06 – 2.64)	1.57	(0.98-2.54)	0.67	(0.36 – 1.24)
SAQ – physical limitations						
Average	Referent		Referent		Referent	
Impaired	2.14	(1.63 -2.81)	1.83	(1.37-2.45)	1.46	(1.06 – 2.02)
SAQ – angina related quality of life						
High	Referent		Referent		Referent	
Average	1.76	(1.29 – 2.59)	1.61	(1.13-2.29)	1.81	(1.00 – 2.03)
Low	3.12	(1.82 – 5.34)	2.84	(1.49 –	2.00	(1.00– 4.00)

All models apply to the full population (n= 1,589), use multiple imputation and are adjusted for at least age, sex, and race.

† The physical components model is also adjusted for history of heart disease. The mental component model is also adjusted for educational attainment. The SAQ health-related quality of life model is also adjusted for living alone, a history of heart disease and diabetes.

‡ Each of these models is adjusted for depressive symptoms in addition to the other variables listed in the two notes above. (E.g., this physical components model is adjusted for age, sex, race, the GRACE risk score, history of heart disease and depressive symptoms.)

CHAPTER V : DISCUSSION AND CONCLUSIONS

Patient health status after an ACS has become important as a considerable proportion of patients have shown impaired health status (health-related quality of life and functional status) after an ACS. For example, almost 30% of patients have moderately to severely diminished quality of life due to ACS over six months following discharge.[3] Due to this phenomenon, the AHA has called for more research on patient health status and its' determinants.[7] This dissertation answered that call by exploring both a novel neighborhood-level predictor (neighborhood socioeconomic status) of patient health status after ACS and trajectories (subgroups of individuals with distinct longitudinal patterns over time) of patient's health status. We examined the determinants of these trajectories and their implications for patients' future. Conclusions and implications for future studies based on the work in this dissertation on neighborhood socioeconomic status (aim 1) and trajectories of patient health status are summarized below.

Neighborhood Socioeconomic Status Predicts Patient Health Status

We used hierarchical linear models to examine the association between neighborhood socioeconomic status (NSES) and patient health status in the 6 months following an ACS hospitalization (aim 1 – Chapter II). We found that being in the lowest tercile of NSES consistently predicted having lower patient health status, even after accounting for individual SES and many other covariates. This discrepancy started at discharge and was present during the next six months of follow-up. We also found that lower individual socioeconomic status (SES) was associated with worse patient health status. This association between individual SES and patient health status had a greater magnitude than the association of NSES and patient health status. For both the mental components subscale (MCS) and SAQ physical limitations, combined individual and neighborhood poverty was worse than adding their individual effects would imply.

Patient health status has been proposed as a quality metric[48], and both the Veterans Affairs Administration and the Centers of Medicare and Medicaid Services are considering their use as quality indicators after elective percutaneous coronary intervention.[50] If patient health status becomes a quality metric, then unless proper risk adjustment takes place, it is possible that hospitals that care mostly for patients from neighborhoods with lower NSES could be unfairly penalized. Policy makers should consider the relationship between NSES and worse patient health status, as they explore using patient health status as a quality indicator.

Adjusting for NSES in risk adjustment has been previously proposed for thirty-day readmission rates after an acute myocardial infarction. A study by Kind et. Al. found that neighborhood socioeconomic status, predicted thirty-day all-cause readmissions after a myocardial infarction.[140] They suggested that NSES, gleaned from patient's addresses, be considered for risk adjustment.[140] Although this may be appropriate for readmission measures, our findings suggest that for MCS and SAQ physical limitations this may not be sufficient, as combined low individual and neighborhood SES was worse than adding their individual effects would suggest. We could obtain information on individual SES by using Medicaid status. as proxy measures for low individual SES. Future research should explore what mechanisms adequately measure individual level SES from claims data.

Our findings also have implications for healthcare providers. Healthcare providers should discuss neighborhood resources, barriers to self-care and access to follow-up medical care. Hospitals can also use NSES information based on address to target transitional care interventions to those living in lower NSES neighborhoods, who may need these interventions more.[140] Because NSES can help identify individuals who will have both worse patient health status and be more likely to be readmitted within thirty days[140], it becomes an even better indicator of a worse prognosis.

Although our findings from aim 1 (chapter II) have important implications, there are some limitations. One limitation is that our study only included patients from 6 hospitals in the eastern US and our findings might not generalize to other areas. Future work should be done to confirm not only that the relationship between NSES and patient health status is the same elsewhere in the US, but also in countries with universal healthcare systems and in low- and lower-middle-income countries. For example, one study in Canada found that there were no differences in the use of cardiac medications, use of procedures and readmission according to SES.[141] Thus, it will be important to confirm the association between NSES and patient health status in other healthcare contexts.

Trajectories of Patient Health Status

In aims two and three (chapters III and IV), we investigated trajectories, predictors of trajectory membership and the ability of trajectories to prognosticate for future events. We found 2 trajectories for each of PCS and SAQ physical limitations: Average (PCS (66.4%); SAQ (67.8%)) and Impaired (PCS (33.6%); SAQ (32.2%)). We also found 3 SAQ HRQoL trajectories: High (36.4%), Average (53.9%) and Low (9.7%). MCS had the highest number of trajectories with the following four trajectories: High (64.4%), Improving (16.3%), Worsening (10.5%) and Low (8.9%). For trajectories of all four components of patient health status, those who were female, had more co-morbidity and worse depressive symptoms were associated with membership in worse trajectories for all components of patient health status except for MCS. In terms of the consequences of trajectory membership, we found that for all patient health status components except for MCS, membership in worse trajectories was associated with a higher risk of death or readmission.

There are several implications of these results. The most important is the potential use of trajectories of patient health status after an ACS as a prognostic tool for both patients and healthcare providers. In contrast to analyses that focus on averages, trajectory analysis allows and models heterogeneity, thereby giving patients a better idea of what their recovery may look like within the first six months following an ACS hospitalization. For healthcare providers, trajectories may provide clinicians with a way to target interventions, such as PCI,[120] more intensive angina treatment (if angina symptoms are severe),[122] and perhaps more tailored cardiac rehab interventions.[123] Trajectories not only indicate how a patient is likely to recover in the first six months after hospitalization, but also membership in a trajectory has important implications for the future. Patients in worse trajectories (for all components of patient health status except for MCS) have a higher risk of mortality and readmission in the 6 months to 12 months following an ACS hospitalization. This fact reinforces the potential prognostic importance of trajectories.

Our study had several limitations. First, the patients in our study only came from 6 hospitals in the eastern U.S. Future studies amongst other ACS cohorts from other hospitals and geographic locations should confirm our findings to ensure generalizability of our findings and that the trajectories that we found are not solely due to the patient mix present in our 6 study hospitals. Second, it is possible that our limited sample size may have affected the number of trajectories that we found. In the future, studies with a larger number of participants should examine whether this is the case. Third, we excluded individuals who had been readmitted during the six months following their index ACS hospitalization. This exclusion criterion does limit our generalizability, however, when we examine the use of trajectories as a prognostic tool it sheds new light on the reasoning behind this exclusion criteria. Specifically, we already know that individuals who have been readmitted are more likely to a higher mortality rate[124] etc. Thus, the real use of trajectories as a useful heuristic for prognosis, comes for individuals where there is more uncertainty about their recovery (both patient health status and mortality and readmissions).

There are several areas that future studies should examine in relation to trajectories of patient health status after an ACS. First, it may be useful to know how long trajectories predict death or readmission. Unfortunately, our study only contained information for all study participants on readmission for one year; future studies may want to examine whether trajectories of patient health status continue to predict worse outcomes after longer lengths of time. Second, it may be useful to conduct additional analyses that examine whether interventions can cause individuals to switch or change trajectory. This can be done using a combination propensity score matching and group-based trajectory analysis, described by Haviland et. Al. [142] Moreover, such investigations are needed as they will give us the evidence we need in finding effective interventions to attempt to help those who were more likely to be in the worst trajectories. Future methodological work should also be undertaken to allow trajectory models to be utilized in real time in a clinical setting. Specifically, it is not currently possible to apply a trajectory model reported in the literature to a patient not in the original sample that the trajectory model was built with and determine posterior probabilities of trajectory membership. Future methodological work will have to enable this capability before trajectory models can be incorporated into medical records and used real time for targeting interventions.

Conclusions

This dissertation has examined how two techniques, measuring NSES from patient addresses and group-based trajectory modeling, can provide us with deeper insights and understanding into patient's health status after an ACS. In doing so, we have attempted to not only answer the AHA's call for additional research into patient health status among patients with cardiovascular disease, but also provide a fresh perspective on what predicts recovery after an ACS and what the consequences of that recovery may be for future mortality and morbidity.

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