A- SPECIFIC AIMS

Despite remarkable progress, cardiovascular disease (CVD) remains a major cause of morbidity, mortality, and impaired quality of life, with unrealized health gains from underuse of available evidence. Our Transitions, Risks, and Actions in Coronary Events Center for Outcomes Research and Education (**TRACE-CORE**) will:

(A) **Advance the science** of improving CVD outcomes by providing critical new knowledge about quality measurement and health disparities; and by developing novel Action Scores that emphasize modifiable factors under patient and clinician control.

(B) **Train a next generation** of CVD outcomes researchers.

Nearly 1.5 million Americans are hospitalized yearly for acute coronary syndromes (ACS) and re-hospitalizations are frequent[1] and often avoidable.[2-4] In-hospital and 30-day mortality for ACS have declined markedly over the years,[5-7] partly due to improved treatment and risk factor control. Still, evidence-based interventions for ACS patients are often under-prescribed or not followed by patients. This gap between best and routine peri- and post-ACS practice is exacerbated by poor transitional care, as patients return from the hospital to the community. Research from the geriatrics, generalist, and hospitalist communities demonstrates that global interventions improve transition care, and the American College of Cardiology has launched the Hospital-to-Home (H2H) program, a national effort to promote excellence in transition care.[8]

However, many insights from the transition literature have yet to be specifically adapted for ACS patients. Few interventions have focused on quality of life. We currently lack the necessary tools to comprehensively measure ACS transition quality, and we also do not understand the complex relationship between transition quality and ACS health disparities, which have been repeatedly documented.[9-15] Therefore, the Transitions Project will develop the tools to characterize the ACS transition process and identify modifiable factors to improve ACS care and reduce observed health disparities.

ACS clinical decisions depend upon accurate risk assessment. Predictive indices such as the Framingham Risk Score for general populations,[16] and the Global Registry of Acute Coronary Events (GRACE) Risk Score for hospitalized ACS patients,[17] are widely used in research, but less so in routine care. Use is limited because these scores 1) place limited emphasis on modifiable factors; 2) exclude patient-centered factors such as symptoms; 3) exclude patient complexity, such as cognitive impairment; and 4) focus mostly on clinical endpoints (e.g., mortality, re-admission) without considering quality of life (QoL). Thus, a new approach that builds on the Framingham score tradition but separates modifiable from non-modifiable risk and also considers patient-centered measures such as QoL is in order. Drawing upon item response theory (IRT) and computer adaptive testing (CAT) the Action Scores Project will advance the science of cardiovascular risk assessment.

Our two research projects (Transitions, Action Scores) will use data from a single new large and diverse cohort of adults hospitalized for ACS that we will enroll and follow into the community. Importantly, this cohort will serve as a laboratory to train CVD outcomes researchers and to develop new approaches to improving patient outcomes. Over 4 years, we will accomplish the following **Specific Aims:**

Aim 1 – **Recruit and follow for 2 years a multi-racial Transitions, Risk, and Actions in Coronary Events (TRACE) cohort** of 2,500 eligible and consenting adults residing in urban, suburban, and rural areas of Massachusetts and Georgia, hospitalized with ACS at 7 community teaching and non-teaching hospitals.

Aim 1A: Enroll patients, review the inpatient medical records of the index ACS hospitalization, and conduct baseline in-person interviews.

Aim 1B: Follow patients for 2 years, reviewing re-hospitalization records and electronically-available outpatient medical records.

Aim 1C: Conduct follow-up interviews at 1, 3, 6, 12, and 24 months after discharge from the index hospitalization. All interviews will collect QoL, cognitive impairment, medication adherence, and health behavior, among other data; and use novel approaches to parsimoniously yet precisely collect patient-reported outcomes such as shortness of breath.

Aim 2 - **Transitions Project.**

Aim 2A: Characterize transition from hospital to community for ACS patients with TRACE data

Aim 2B: Engage a technical advisory group in consensus building to develop an ACS Transition Measurement Set focused on quality during the first 90 days after discharge, extending beyond existing systems limited to the discharge process.

Aim 2C: Examine the determinants and outcomes of transitional care quality, testing the following hypotheses (with adjustment for differences in case mix):

H1: Better transition quality is associated with improved post-discharge QoL.

H2: Better transition quality is associated with longer time to first ED visit or readmission.

H3: Patients who are potentially vulnerable due to (a) race/ethnicity, (b) socioeconomic status, (c) total morbidity burden, or (d) cognitive status have worse transition quality.

H4: Transition quality partially mediates observed disparities in outcomes for vulnerable patients.

Aim3 – Actions Scores Project

Aim 3A: Develop and validate two kinds of "CVD Action Scores" to predict 1) recurrent cardiac events or death and 2) QoL. Patients and clinicians may calculate the Action Scores at the point of ACS discharge or "on

demand" after the patient has transitioned to the community. Action Scores will be based on statistical models that include both non-modifiable (e.g., age) and modifiable (e.g., medication adherence) factors, but will emphasize the characterization of modifiable factors.

Aim 3B: Describe longitudinal variation (if any) in the Action Scores over 2 years and test the hypothesis:

H5: Observed health disparities for vulnerable populations (as in H3) would be reduced if actions identified by the Action Scores were taken by patients and providers.

Aim 3C: Develop a dashboard (control panel) for CVD action as a blueprint for a tailored measurement system for CVD action. Calculations based on the final regression models (Aim 3A) will populate the dashboard and produce the Action Scores. The tailored system (as refined in future research using IRT and CAT) will populate the dashboard's elements with good precision and reduced respondent burden.

Aim 4 – Develop a nucleus of early stage investigators (ESIs)

We have recruited two epidemiologists, a cardiologist and a psychometrician with a strong interest in CVD outcomes research at the Assistant Professor level. The 4 ESIs commit to research careers in CVD outcomes through their participation in TRACE-CORE; senior TRACE-CORE investigators, highly experienced mentors and active researchers themselves, commit to nurturing those careers.

Aim 4A: Implement structured mentoring for the ESIs.

Aim 4B: Engage the ESIs as investigators in TRACE-CORE and as co-PIs in the two Research Projects. Also, in the early years, ESIs will develop manuscripts using existing GRACE data.

Aim 4C: Assist the ESIs in preparing both K and R-type applications, as appropriate. These applications will build on TRACE-CORE data and findings. In particular, findings from Aims 2 and 3 will yield intervention prototypes to be developed and evaluated in future projects.

Our team involves prominent CVD outcomes researchers, epidemiologists, methods experts such as those at the forefront of IRT and CAT, experienced cardiologists, and other clinicians, including leaders from the multinational GRACE study. We will build on an existing recruitment and data infrastructure to advance the science of CVD outcomes research and build research capacity. Our innovative CVD Action Scores should help activate patients and their health care providers to improve CVD outcomes; our Transitions Project will fill important knowledge gaps in the high-risk period following an ACS hospitalization. Future interventional studies will benefit from our database, research infrastructure, Action Scores, and transition process measures to build on findings from the TRACE cohort and underpin the careers of future CVD outcomes researchers.