*Introduction*

Sepsis survivors represent a vulnerable population with high morbidity, mortality, and hospital readmissions, and strategies to improve transition and recovery are urgently needed. Post-sepsis care recommendations target specific deficits experienced by sepsis survivors; however, these recommendations are infrequently applied. Our STAR program implements evidence-based post-sepsis care recommendations, directed to high-risk sepsis survivors, and delivered using a proactive, nurse navigation process demonstrated to reduce readmissions and costs. This project will evaluate if implementation of the STAR program within a large healthcare system will improve outcomes for high-risk sepsis patients and will generate knowledge of best practices for implementation and dissemination of post-sepsis transitions of care.

The proposed research consists of 1) a pragmatic, stepped-wedge, cluster randomized controlled trial, 2) prospective economic evaluation, and 3) concurrent analyses of the implementation process.

1) We will conduct a two-arm, pragmatic, stepped-wedge, cluster randomized controlled trial to test the effects of two post-sepsis care implementation strategies on clinical outcomes. At each four-month interval, one of eight hospitals will be randomly assigned to transition from ARM 1) usual care (UC) consisting of current, standard peri- and post-discharge activities, to ARM 2) STAR program beginning during index hospitalization for sepsis and extending 90 days after hospital discharge.

2) Cost analysis will occur through a prospective economic evaluation that uses empirical trial data on healthcare costs, health utilization, and clinical outcomes from the hospital system's data warehouse as inputs to a Markov state transition model for formal cost-effectiveness analysis.

3) The study's implementation will be guided by the Consolidated Framework for Implementation Research. A mixed methods evaluation framework will be used to inform future implementation and dissemination activities.

*Primary Objective*

The primary objective is to evaluate composite 90-day hospital readmissions and mortality between usual care and the STAR program.

*Hypothesis*

Patients allocated to receive the STAR program intervention will have lower combined hospital readmission and mortality rates at 90 days post hospital discharge, compared to patients allocated to receive usual care.

*Primary Outcome Variable*

Composite, dichotomous endpoint of all-cause mortality or unplanned hospital readmission assessed 90 days post index hospital discharge. Both inpatient and observation status hospitalizations will count towards the readmission outcome because either status represents an adverse event important to patients and healthcare systems. For the composite primary outcome, we will capture all patients with either date of death or eligible hospital readmission prior to 90 days post discharge as event-positive.

*Secondary Outcome Variables*

1. 90-day all-cause mortality

2. 90-day all-cause hospital readmission

3. 90-day all-cause emergency department visits

4. 90-day outpatient provider visits

5. 90-days cause-specific hospital readmissions for a) infection, b) chronic lung disease, c) heart failure, and d) acute kidney injury

6. 90-day acute care-free days alive, defined as the sum of days alive without inpatient, observation, and emergency department encounters during the 90 days after discharge

7. Percentage of patients with documented inpatient functional assessment or physical therapy consult

8. Percentage of patients with documented inpatient mental health assessment

9. Percentage of patients with documented referrals to a) rehabilitation services, b) speech therapy, and c) behavioral health

10. Percentage with outpatient follow-up within 7 days of hospital discharge

11. Percentage with designated medication reconciliation form in the electronic health record during the 90 days post hospital discharge

12. Percentage with palliative care consult

13. Percentage with completed care preferences documentation

14. Percentage discharged to hospice care from initial sepsis hospitalization

15. Place of death

*Subject Selection*

Consistent with our pragmatic study design concept, eligibility criteria are broad, the sample size is large, and study procedures are embedded into the context of routine care. Patients are eligible if they present to the emergency department and are subsequently admitted under inpatient or observation status to a participating hospital. Specific inclusion and exclusion criteria are described.

Inclusion Criteria:

1. At least 18 years of age upon admission

2. Oral/parenteral antibiotic or bacterial culture order within 24 hours of emergency department presentation

a) culture drawn first, antibiotics ordered within 48 hours or

b) antibiotics ordered first, culture ordered within 48 hours (adapted from criteria applied in development of the Third International Consensus Definitions for Sepsis and Septic Shock)

3. Deemed as high-risk for death or 90-day readmission using risk-scoring models

4. Not discharged at the time of patient list generation

Exclusion Criteria:

1. Antibiotic doses administered in the operating room will be excluded from eligibility determination as these administrations are likely to represent pre-operative infection prophylaxis and not presumed infection

2. Patients transferred from other acute care hospitals due to lack of data on disease course prior to transfer receipt

3. Patients with a change in code status (i.e., do not resuscitate, do not intubate) within 24 hours after infection onset due to presumed limitation of aggressive treatment.

4. Patient has not been randomized previously.

Risk models include clinical and administrative data to produce a near-real time risk score that identifies cohorts at high risk for death and 90-day readmission, delivering the information at the point of care. Risk models will run each morning and automatically generate lists of eligible, high-risk patients admitted over the prior 72 hours. During the intervention phase at each facility

(i.e., after transition from UC to STAR), the navigator will receive the list of admitted, high risk patients via secure email. Patients will only be identified as eligible for randomization once during the index hospital stay and will not be eligible for study inclusion during subsequent admissions. Patients assigned to the intervention will be contacted and introduced to the navigation process before hospital discharge.

*Randomization*

Eight participating hospitals will be randomized to a staggered sequence (i.e., steps 1 to 8) of transitioning from UC to STAR group assignments using SAS Enterprise Guide v7.1 (Cary, NC). All eight hospitals will start with a control period of varying length, dependent on timing of transition to the intervention arm. Every four months, one randomly assigned hospital will cross over to initiate the STAR program and remain in the intervention arm through study completion. All patients identified as eligible using the risk model will be allocated to the study ARM that matches the admitting hospital's assignment (STAR or UC). During the intervention phase at each facility (i.e., after transition from UC to STAR), the navigator will receive the list of admitted, high risk patients via secure email.

*Study Procedures*

Patient identification: Each morning, the list of eligible, high-risk patients is automatically securely transmitted to the study database within REDCap and the study PIs are notified of completed transmission. The list of eligible, high risk patients at hospitals allocated to receive the STAR program (based on randomly assigned months) will also be automatically emailed via secure transmission to the STAR navigators.

Initial contact with the STAR program: After the patient list is generated, the STAR navigator will contact the care team (e.g., bedside nurse, hospitalist) to obtain permission to discuss the STAR program with patients assigned to STAR. At any time, the hospitalist, bedside nurse, or

patient may decline for the patient to participate in the STAR program or any components of usual care.

Summary of STAR services duration: The STAR navigator will provide telephone- and EHR-based support within the hospitalization and to patients across all discharge settings with remote monitoring at specified intervals following hospital discharge. Within 48 hours of discharge, patients allocated to STAR will have their first post-discharge follow-up. They will continue to receive STAR directed services for 90 days following their discharge. Subsequently, they will be transitioned back to the next appropriate care location.

Detailed description of STAR services: At the initial contact with the patient or caregiver during hospitalization, the STAR navigator will introduce the STAR program and conduct health literacy screening and mental health screening using the Patient Health Questionnaire (PHQ)-2, with reflex administration of PHQ-9 for positive PHQ-2 (i.e., > or = 3).130 The STAR navigator will convey results to the care team for appropriate behavioral health referrals. The STAR navigator will also confirm consultations with physical therapy (recommendations delivered to care team), antibiotic stewardship (i.e., a coordinated program that promotes appropriate antibiotic use) with additional infectious disease consult if ongoing Systemic Inflammatory Response Syndrome criteria more than 48 hours after infection onset (i.e., abnormal body temperature, heart rate, respiratory rate, white blood cell count), and palliative care team. For discharge, the STAR navigator will provide disease-specific education to the patient and caregiver and discharge education including what to expect during transition and a "playbook" with information on planned follow-ups. The navigator will also record all in-person and phone follow-up and all disciplines with post-acute touchpoints in the provider discharge plan. Because communication of care gaps and recommendations can be difficult in the complex acute care environment, our group has conducted a pilot with 15 patients to define communication strategies and contact points. Important elements include connecting to: patient and caregiver personal phones while

admitted; inpatient case managers for estimated discharge date, primary care provider information, and regular 24-48-hour contact until discharge; EHR-based messaging to providers; and post-acute care team within 24 hours of discharge (e.g., home health clinical supervisor) to initiate two-way communication.

Irrespective of discharge location (e.g., home versus skilled nursing facility), the STAR navigator will provide monitoring through phone contact with patient, caregiver, or provider (as appropriate for post-acute care location) at <48 hours, 72-96 hours, and 7-10 days post-discharge. These touchpoints will include medication reconciliation, infection and respiratory symptom monitoring, vitals and weight checks, and confirmation that the patient can make scheduled outpatient appointments. Concerns identified through proactive monitoring will prompt a primary care provider contact for follow-up. If the primary care provider cannot be reached after one attempt, the navigator will contact the hospitalist back-up provider. Following the immediate post-acute interval, the STAR navigator will maintain weekly telehealth touchpoints with patients who remain at high-risk for poor outcome (i.e., any previous positive screen, high-risk comorbid condition [e.g., chronic lung disease, heart failure], or low health literacy) and every third week touchpoints with patients considered low-risk after the immediate post-acute interval. These 90-day post-acute touchpoints will include infection and respiratory symptom check, vitals and weight monitoring, and consideration for repeat outpatient provider visit. Identified concerns will prompt attempts to contact the primary care provider followed by hospitalist back-up provider. The STAR support service will complete 90 days post hospital discharge.

*Statistical Analysis*

Sample Size Determination: This study is designed to detect a 20% relative reduction in composite 90-day mortality and hospital readmission. The usual care group is indicated to have

roughly 40% combined 90-day mortality and readmission rate. With a total sample size of 4392 patients enrolled over 36 unit-months, we will have 90% power (α=0.05) to detect a 20% relative reduction in composite 90-day mortality and hospital readmission.

Statistical Methods

**Aim 1: Evaluate the effectiveness of an innovative, virtual nurse navigator implementation strategy to improve post-sepsis care**.

All primary and secondary analyses will follow intention to treat approach, such that all patients meeting identical criteria and randomized will be analyzed, regardless of adherence to intervention assignment. This real-world approach will assess intervention effectiveness while limiting selection biases associated with adherence. We will compare the two groups (STAR versus usual care) at baseline for age, sex, race, and comorbidities to assess for balance inferred randomization. The primary outcome is the composite of hospital readmission and mortality at 90 days post hospital discharge. Because hospitals are randomized to STAR in a staggered sequence and the outcome varies at the patient level, we will use a generalized linear mixed-effects model to compare the composite 90-day mortality and readmission primary outcome measure between the intervention conditions, adjusting for clustering effects across multiple levels (e.g., admitting hospital, implementation timing) to include hierarchical data structures. The intervention fixed-effect coefficient will compare STAR versus UC conditions (i.e., UC as reference). We will evaluate covariates for patient (e.g., sex, race, comorbidities, length of stay, discharge disposition [skilled nursing facility, rehabilitation, home]) and organizational factors (e.g., admitting hospital, guideline adherence, urban versus rural setting, implementation timing) to identify any potential differences between study arms. We will include covariates in model if unbalanced between STAR and UC groups. We will also evaluate effect

modification by conducting analyses stratified by these characteristics (e.g., discharge disposition) and by process measures with potential to effect outcomes (e.g., referrals).

Secondary outcomes are described below and will be assessed using the same approach. That is, we will construct generalized linear mixed-effects models, like for the primary outcome analysis, for individual assessments of secondary outcomes and process measures. We will test different distribution parameters to determine the optimal distribution family for each model and outcome variable (e.g., binomial, gamma distributions).

1. All-cause mortality. We will assess the individual mortality component of the primary composite endpoint separately. We will construct generalized linear mixed-effects models with all-cause mortality as the dependent variable, assessed as a binary outcome at 90 days post discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

2. All-cause hospital readmission. We will assess the individual hospital readmission component of the primary composite endpoint separately. We will construct generalized linear mixed-effects models with all-cause hospital readmission, including inpatient and observation status, as the dependent variable, assessed as a binary outcome at 90 days post discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

3. All-cause emergency department visits. We will assess the number of emergency department visits. We will construct generalized linear mixed-effects models with the number of emergency departments visits as the dependent variable assessed at 90 days post discharge. We will use the Poisson distribution to model the outcome due to the expected distribution of the

counts of emergency department visits. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

4. Outpatient provider visits. We will assess the number of outpatient provider office visits. We will construct generalized linear mixed-effects models with the number of outpatient provider office visits as the dependent variable assessed at 90 days post discharge. We will use the Poisson distribution to model the outcome due to the expected distribution of the counts of outpatient provider office visits. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

5. Cause-specific hospital readmission. We will assess the cause-specific hospital readmissions related to a) infection, b) chronic lung disease, c) heart failure, and d) acute kidney injury. We will construct separate generalized linear mixed-effects models for each of the four cause-specific hospital readmission conditions. The dependent variable for each model will be infection-, chronic lung disease-, heart failure-, and acute kidney injury-related hospital readmissions, respectively, assessed as a binary outcome at 90 days post discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intentto-treat approach.

6. Acute care-free days alive. We will assess the total sum of days alive without inpatient, observation, and emergency department care utilization. The number of acute-care free days will be calculated from the date of index hospital admission through 90 days after discharge or date of death if prior to 90 days. We will construct generalized linear mixed-effects models testing different distribution patterns to determine the optimal distribution family for the count of acute care-free days. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

7. Inpatient functional assessment or physical therapy consult. We will compare the receipt of inpatient functional assessment or physical therapy consult, captured from the electronic health record. We will construct generalized linear mixed-effects models with documented functional assessment or physical therapy consult as the dependent variable, assessed as a binary outcome at the time of hospital discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

8. Inpatient mental health assessment. We will compare the receipt of inpatient mental health assessment, captured from the electronic health record. We will construct generalized linear mixed-effects models with documented mental health assessment as the dependent variable, assessed as a binary outcome at the time of hospital discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

9. Support service referrals. We will compare the receipt of support service referrals. Documented referrals to a) rehabilitation services, b) speech therapy, and c) behavioral health will each be captured separately from the electronic health record. We will construct separate generalized linear mixed-effects models with documented referral to rehabilitation services, speech therapy, and behavioral health each as the dependent variable of one model. Each variable will be assessed as a binary outcome at 90 days after hospital discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intentto-treat approach.

10. Early outpatient provider follow-up. We will compare the receipt of early outpatient provider followup, defined as an outpatient provider encounter within 7 days of hospital discharge and captured from the electronic health record. We will construct generalized linear mixed-effects models with documented early outpatient provider follow-up as the dependent variable, assessed as a binary outcome at 7 days after hospital discharge. The intervention

fixed-effect coefficient will compare STAR versus UC conditions, using an intent-totreat approach.

11. Outpatient medication reconciliation. We will compare the receipt of outpatient medication reconciliation, captured from the electronic health record. We will construct generalized linear mixed-effects models with designated outpatient medication reconciliation form completion as the dependent variable, assessed as a binary outcome at 90 days after hospital discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

12. Palliative care consult. We will compare the receipt of palliative care consult, captured from the electronic health record. We will construct generalized linear mixed-effects models with documented palliative care consult completion as the dependent variable, assessed as a binary outcome at index hospital discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

13. Completed care preferences. We will compare the completion of care preferences documents, captured from the electronic health record. We will construct generalized linear mixed-effects models with care preferences document completion as the dependent variable, assessed as a binary outcome at index hospital discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

14. Discharged to hospice care. We will compare the discharged to hospice care from the index hospitalization for sepsis, captured from the electronic health record and hospital discharge records in the enterprise data warehouse. We will construct generalized linear mixed-effects models with discharged to hospice care as the dependent variable, assessed as a binary outcome at index hospital discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach.

15. Place of death. We will compare the place of death for individuals who die over the 90-day trial interval, captured from the electronic health record and hospital discharge records. We will construct generalized linear mixed-effects models with place of death as the dependent variable, assessed as a categorical outcome at 90 days after hospital discharge. The intervention fixed-effect coefficient will compare STAR versus UC conditions, using an intent-to-treat approach. In addition to primary intent-to-treat analyses, we will conduct modified intent-to-treat analyses excluding sepsis patients 1) who do not survive index hospitalization since STAR is designed to support patients during their transition out of the hospital; and 2) discharged against medical advice since providers do not have the opportunity to deliver full care and prepare the patient for discharge. Based on published data and internal estimates, we expect less than 10% of study patients will die during index hospitalization and fewer than 2% will be discharged against medical advice. We will present results from group comparisons as odds ratios and 95% confidence intervals.

We do not anticipate substantial missing data because all outcomes are routinely collected variables and utilization is broadly captured within the large integrated system. While utilization may occur outside of CHS, this is not expected to be a major limitation because of CHS market share and accessibility. Specifically, CHS operates three large hospitals in Mecklenburg County, the only acute care hospitals in Anson, Burke, Cleveland, Lincoln, Stanly, and Union counties, where most of this study will be conducted, and more than 40 hospitals in the region overall. Additionally, any utilization that occurs outside the system is anticipated to be non-differentially distributed between groups and thus impact treatment groups equally. Further, internal data indicates nearly 75% of high-risk patients are Medicare-insured and have complete healthcare claims within and outside CHS facilities captured through participation in the ACO managed by CHS. We will leverage this data for subgroup analyses and to explore missing data patterns that can be adjusted using pattern-mixture methods in sensitivity analyses.

All hypothesis tests will be two sided and data will be analyzed using SAS Enterprise Guide v7.1 (Cary, NC) or R v3.5 (Vienna, Austria).

Interim Analysis

Interim analyses will be conducted when 50% of enrollment targets are met and 90-day patient outcomes are obtained. All interim analyses will be presented to the Data and Safety Monitoring Board (a Steering Committee representative, an independent clinician investigator, and an independent biostatistician), who will make a recommendation on continuing the trial as planned or modified. The following analyses will be conducted by the study statistician and provided to the Data and Safety Monitoring Board:

1. Sample size re-estimation

a. Drop-out rate for STAR: We define the drop-out rate for the STAR program to be the rate of nonadherence to the intervention. Non-adherence is defined by those patients who declined, were discharged before contact by STAR staff, and were not able to be contacted after hospital discharge. The population is defined as all patients who were deemed eligible and identified as high risk for readmission or mortality. We propose to assess the drop-out rate in the STAR intervention arm when half of patients have 90-day follow up information available (n=2196). At that time, we will re-estimate the sample size needed for the study using drop-out rates.

b. Event rate: We propose to re-estimate the sample size based on the combined 90-day hospital readmission and mortality rates for both patients randomly assigned to STAR and usual care when half of the information is available for the trial (n=2196). We will base the re-estimation on the original 20% relative reduction to determine if more patients are needed to maintain 90% power. We will measure the composite outcome as defined for the primary effectiveness analysis, i.e., we will capture all patients with either

date of death or eligible hospital readmission prior to 90 days post discharge as event-positive.

2. Interim efficacy analysis with 50% information (i.e., 50% of target accrual with 90-day follow up data).

We propose to conduct an interim effectiveness analysis of the primary outcome of composite 90-day hospital readmission and mortality rates once 50% of patients have been accrued and have 90-day outcomes. We will use the Haybittle-Peto procedure with boundary of less than 0.001. No additional interim analyses will be planned until the sample size re-estimation and futility analyses are reviewed and a recommendation is made to continue, stop, or modify the study.

3. Futility analysis/conditional power at 50% complete data information (50% of target accrual with 90-day follow-up data. We propose to conduct a futility analysis at 50% information accrual for the trial. The first futility analysis will be conducted at the same time as the sample size re-estimation based on the drop-out rate. Conditional power is the probability of detecting a difference at the end of the study ($p<0.05$) given the current data trend. We will estimate conditional power under the null hypothesis of no difference, the designed alternative of 20% relative reduction, and the current observed trend. A recommendation would be made to stop the study for futility if the conditional power is less than 0.10 for the designed alternative.

**Aim 2: To assess the cost-effectiveness of virtual nurse navigator-driven STAR program Within-trial Incremental Cost Effectiveness Ratio.**

We will estimate Incremental Cost Effectiveness Ratio (ICER) of STAR versus UC using data derived during the study interval as a measure of benefit to the hospital system. We will estimate ICER as incremental costs divided by incremental QALYs. The intervention group beta weight from cost model will be divided by the intervention group beta weight from QALYs model.

We will perform a one-way probabilistic sensitivity analysis to address uncertainty by varying inputs within 10-15%.

Subgroup Analyses: Reliance on CHS data warehouse for measuring healthcare use may miss costs incurred in other health systems. We expect cross-system healthcare utilization to be similar between groups and low overall due to the size and accessibility of CHS in the study region. However, we will repeat analyses within the subgroup of patients enrolled in the ACO managed by CHS (more than 140,000 lives covered in 2018). Within this subset, we will have complete visibility of all healthcare claims within and outside of CHS during the study interval. Data from this group will be informative to health policy given the introduction of the CMS BPCI, a value-based alternative payment model to improve post-acute care for specific hospital diagnoses, including sepsis. Subgroup analyses will also be performed by hospital and patient factors (e.g., hospital length of stay, discharge disposition, comorbidities).

Extrapolated Incremental Cost Effectiveness Ratio. We will build a Markov-type state-transition simulation model using TreeAge (TreeAge Software Inc.) to estimate ICER of receiving STAR. We will use data derived during the study interval and other evidence-based sources to extrapolate cost-effectiveness analyses to 12 months after discharge. This analysis will be conducted to assess benefit from a societal perspective and determine if the intervention costs associated with STAR are offset by any subsequent reduction in morbidity costs (e.g., reduced hospital readmissions) and improvements in mortality. We will estimate the ICER as the incremental costs divided by the incremental QALYs, including a 3% standard discount for costs and outcomes. The intervention group beta weight from the cost model will be divided by the intervention group beta weight from the QALYs model. Sensitivity Analyses and Uncertainty: Model parameters will be sampled from their appropriate distributions over 1000 runs. We will vary key costs and effectiveness estimates across the range of plausible values to determine whether cost-effectiveness of STAR is sensitive to changes in specific assumptions made to

inform the baseline analysis. We will also estimate 95% confidence intervals around ICER point estimates using probabilistic analyses and create acceptability curves comparing STAR favorability at various willingness to pay thresholds.

The data analyses for Aim 2 will be supported by a health economist consultant. The health economist consultant will support the cost and cost-effectiveness analysis of the intervention and will securely maintain the data files on a secure server with encryption. Data will be shared using a secure file transfer protocol, and will be facilitated through the Atrium Health Information and Analytics Services division. A consulting agreement is in place which specifies the sharing of data under a limited data set.

**Aim 3: To determine the key enablers, barriers, and contextual factors that contribute to the successful implementation of the STAR program**

The goal of this mixed methods assessment is to identify perceived barriers to, and enablers of, implementing the STAR program into the peri-discharge setting and feedback results to improve process. The Consolidated Framework for Implementation Research will guide discovery and evaluation of implementation barriers and enablers. Other outcomes will be assessed based on elements from the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) model to quantify the reach and effectiveness of the STAR program and its potential for dissemination and scalability.

Our mixed-methods approach includes: a) semi-structured interviews conducted with administrative leaders and providers during Pre-Implementation to assess organizational support, culture, and recommendations for STAR implementation and then Post-implementation to plan future dissemination; b) navigator/provider interviews and surveys during Implementation to assess inner setting, intervention, and individual factors; c) patient/caregiver interviews and surveys during implementation phase (recruited from the intervention arms) to learn about their

experiences with the STAR program and perceived barriers and facilitators to act on STAR recommendations; and d) focused ethnography of the navigator role in the program conducted on four work days (two days for each navigator) at the three 8-month intervals during implementation. Focused ethnography is an innovative component of our study, selected to obtain a holistic and nuanced understanding of the navigator's role in the intervention. Interview recordings and ethnographic observation fieldnotes will be transcribed for coding and qualitative analysis using ATLAS.ti v8.0. We will perform content analysis using the constant comparison method, an inductive grounded theory approach for developing code structure through iterative comparison of newly coded text with previously coded text of the same theme until final thematic refinement is achieved. We will finalize the code list and repeat data review using the finalized code structure for coding reliability. Participant recruitment will be primarily facilitated through email survey invitation in REDCap. Subject identifiers, including email address, will also be tracked and captured in REDCap.

## RECRUITMENT AND RETENTION PLAN

### *Recruitment Plan*

#### Pragmatic Clinical Trial

Eligible patients at any of the (8) selected hospitals will be included in the study. Risk models will run each morning and automatically generate lists of eligible patients admitted over the prior 72 hours identified to be high-risk for readmission or mortality. During months allocated to the intervention, the navigator will receive the list of actively admitted, high risk patients via secure email. Assignment to a study arm will be based on the date the eligible patient is identified by the risk model. Patients will only be identified as eligible for randomization once during the index hospital stay, regardless of hospital length of stay. Patients with repeat hospitalization will be eligible for repeat study inclusion during admissions that begin more than

90 days after discharge from index hospitalization. Patients assigned to the intervention will be contacted by telephone via the bedside nurse (or other member of the care team) and introduced to the Sepsis Transition and Recovery program and navigation process prior to hospital discharge.

Mixed-methods process analyses

A subset of patients randomized to receive the STAR program and providers and administrative leaders will be recruited to provide interviews for analyses of STAR program implementation processes. For pre- and postimplementation data collection, we will recruit and interview 8 administrative leaders and 8 providers regarding organizational support and recommendations for STAR implementation. During the implementation phase, the study team will gather data from providers, navigators, and patients at 12-, 20-, and 28-month implementation time points to inform and adapt the implementation process. We will recruit administrative leaders and providers via email with three attempts made to contact and enroll each person. For patient recruitment, we will identify patients or their caregivers prior to hospital discharge. The STAR navigator will ask about interest in participating in the research interview. Research staff will contact interested individuals for written informed consent, and Dr. Eaton or other qualitatively trained research staff will conduct the interviews.

Duration of Human Subjects Involvement

It is expected that participant enrollment will begin by July 2020 and that human subjects' activity will be completed by December 2023.

Length of Active Enrollment

It is expected that participant enrollment and randomization for the stepped-wedge randomized trial will take place from July 2020 through June 2023.