Official Title: Effect of Emergency Department Care Reorganization on Door-to-antibiotic Times for Sepsis (LDS SWARM)

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Protocol

Title: **Effect of emergency department care reorganization on door-to-antibiotic times for sepsis (LDS SWARM)**

Facilities involved: Alta View Medical Center, LDS Hospital, Riverton Hospital

Principal Investigator: Ithan Peltan, MD, MSc

Sponsor: This study has no direct funding. Indirect funding from NIH.

Co-investigators: Samuel Brown, MD, MPH
Joseph Bledsoe, MD
David Brems, RN

Purpose of the Study:
Our long-term goal is to improve outcomes from septic shock by speeding delivery of appropriate antibiotic therapy and resuscitation. In other conditions for which treatment time affects outcomes -- including trauma, stroke, and myocardial infarction -- system- and provider-level influences are important and well studied. By contrast, only limited data exist to guide early resource allocation in sepsis. The potential effect of reorganization of very early care for sepsis is unknown. The overall objective of the proposed project is therefore to improve our understanding of how emergency department (ED) care reorganization influences time from hospital arrival to antibiotic delivery in patients presenting with sepsis or septic shock. We propose to accomplish this goal by pursuing the following specific aim:

Hypothesis/Research Questions:

Aim: **Determine whether multidisciplinary coordination of the initial patient evaluation in the emergency department influences door-to-antibiotic time for septic patients.**
Hypothesis: ED care reorganization (the "swarming" intervention implemented in the intervention ED beginning May 1, 2016) resulted in faster door-to-antibiotic times for patients with sepsis or septic shock present on ED arrival.

Background and Significance:
Sepsis, the combination of infection, systemic inflammation, and acute organ dysfunction, is an increasingly common and highly morbid syndrome.[1-3] Severe sepsis and septic shock kill 20% of the 700,000 patients hospitalized with this diagnosis each year and cost the U.S. medical system $24.3 billion in 2007.[4,5] Although specific protocols have not been confirmed to improve sepsis outcomes, early identification and aggressive management is now the standard of care for sepsis.[6-8] Timely administration of effective antibiotics is particularly important: survival suffers for every hour's delay.[9-11] However, while recommending antibiotics within an hour of patient recognition, the Surviving Sepsis Campaign acknowledged a lack of data supporting the feasibility and acceptability of this target.[12]

Upon arrival to the ED, patients perceived to need "immediate life-saving intervention" are assigned the highest triage acuity score[13] and receive immediate evaluation by a multidisciplinary team. However, even among sepsis patients ultimately admitted to an Intermountain ICU, only about 5% are assigned a level 1 acuity score. Most sepsis patients are assigned a lower triage priority and therefore receive sequential evaluation by ED clinicians. To help expedite care for the patients in this latter group, the ED at the

intervention hospitall reorganized care in May 2016 to facilitate simultaneous initial evaluation by the ED physician, nurse and patient care associate for patients with triage. This approach, termed "swarming," has been associated with shorter ED length of stay and shorter time between ED arrival and physician evaluation. The impact of this care reorganization on other important care processes, however, has not yet been evaluated.

Data set: Retrospective cohort study

- Inclusion criteria (expected N=1800, maximum expected N=3500): Adult patients age ≥18 years presenting to the ED of a study hospital with sepsis or septic shock between May 16, 2015 and April 15, 2016 (pre-implementation cohort) or May 16, 2016 and February 15, 2017 (post-implementation cohort). Sepsis is defined as Sequential Organ Failure Assessment (SOFA) score ≥2 points above baseline in the ED plus antibiotics initiation within 24 hours of ED arrival.
    - Institutions: Alta View Medical Center, LDS Hospital, Riverton Hospital
    - Timeframe: Patients admitted in the months before and after implementation with a 2 week window before and after implementation for effect "wash-in"
        - Preimplementation cohort: May 16, 2015 through April 15, 2016 (11 months)
        - "Wash-in" period: April 16-May 15, 2016
        - Post-implementation cohort for potential sensitivity analysis: May 16-November 15, 2017 (6 months post-implementation)
        - Post-implementation cohort for potential sensitivity analysis: May 16-February 15, 2017 (9 months, end date due to iCentra activation at control hospitals)
- Exclusion criteria: Age <18 years, no antibiotics within 24 hours of ED arrival

Outcomes:

- Primary: Time from ED arrival to administration of first dose of antibiotics
- Secondary: Hospital mortality, ED length of stay, door-to-physician evaluation time, door-to-diagnostic testing time, door-to-lactate time

Primary exposure: Arrival to intervention ED after implementation of "swarming" protocol

Data collection: All patients arriving to an eligible Intermountain ED during the study timeframe will be evaluated electronically for meeting Sepsis III criteria (initial SOFA ≥2 above baseline and antibiotics started within 24 hours). Identified subjects will have ED data stored in the EMR and Intermountain Electronic Data Warehouse merged with additional data obtained by electronic abstraction of the electronic health record including laboratory data and vital signs. Manual review of the electronic health record will be used to fill in missing data as needed. The patient information in the dataset will be linked to ED census, hospital characteristics, and staffing data and to long-term mortality data provided from Utah state and the federal Social Security Death Index.

Methods/Procedures:

- Study design: Retrospective cohort study
- Interventions: None
- Interaction with subjects: None
- Procedures: Eligible subjects will be identified by project data managers, who will generate a dataset specific to the proposed study by linking EDW data to additional data abstracted from the electronic health record. Manual chart review will be employed as needed to supplement

electronically-available data. This encounter level data will be linked to additional data on hospital characteristics, physician and nurse staffing. Long-term mortality data will be obtained through linkage to Utah state death records and/or the federal Social Security Death Index.

- Outcomes:
    - Primary: Time from ED arrival to administration of first dose of antibiotics
    - Secondary: Hospital mortality, ED length of stay, door-to-physician evaluation time, door-to-diagnostic testing time
- Analysis:
    - Primary analysis: Among patients with sepsis present on arrival to the ED (defined by antibiotics initiated in the ED plus SOFA score ≥2 above baseline), a triage acuity score of 2-5, and ED arrival from May 16, 2015 to April 15, 2016 (pre-implementation cohort) or May 16 to November 15, 2016 (post-implementation cohort), assess change in door-to-antibiotic time for septic ED patients at the intervention hospital before versus after implementation of "swarming" protocol in May 2016 using a differences-in-differences linear regression model, adjusted for confounding factors, comparing the change in door-to-antibiotic time before/after swarming intervention at the intervention ED to the change in door-to-antibiotic time before/after swarming intervention at other nearby hospital EDs.
        - Difference-in-differences model: The multivariable linear regression models will compare the *difference* between intervention and non-intervention hospitals' *differences* in outcome before/after swarming intervention
        $$Y_i = \beta_0 + \beta_1 \mathrm{ERA}_i + \beta_2 \mathrm{SITE}_i + \beta_3 \mathrm{ERA}_i \times \mathrm{SITE}_i + \beta_8(\mathrm{Z}_i) + \varepsilon$$
        where Y_i was the door-to-antibiotic time for patient *i*, SITE is an indicator variable for care at the intervention hospital vs. other site, ERA is a binary indicator variable for ED arrival date before/after institution of swarming intervention, Z is a vector of covariates and ε is the error term. The $ß_3$ parameter — with its associated 95% interval and p value — provides the difference-in-difference estimate and significance tests for swarming's influence on the outcome of interest.
        - Adjustment variables: mode of arrival (ambulance vs walk-in), initial systolic blood pressure, initial GCS, initial temperature, triage acuity score, Charlson comorbidity score,[15,16] sex, age
    - Secondary analyses: Using a similar confounder-adjusted model (substituting logistic regression for binary outcomes as needed), assess change in hospital mortality, ED length of stay, door-to-physician evaluation time, door-to-diagnostic testing time
- Sample size/power analysis: Based on a conservative estimate of 200 eligible patients in both the pre- and post-intervention groups at the study hospital and 350 total eligible patients in both groups at the control hospitals (total N=1100 patients), a 10 minute baseline difference between the control and study hospital, and a 15 minute decrease in door-to-antibiotic time between the pre- and post-intervention period at the control hospitals, a type I error rate of 5%, and 80% power, the minimum detectable difference due to the intervention will be approximately 26 minutes.

Privacy, Confidentiality and Data Management

All patient names, contact information, and data will be kept in a protected database on a protected computer. All names will be linked to a study identification number, and we will maintain minimal patient identifiers. Any hard copy case report forms will only include study identification numbers, and will be stored in a locked file cabinet.

Waiver of Informed Consent and HIPAA Authorization:
We are requesting a waiver of informed consent and HIPAA authorization for this study. The proposed study involves retrospective review only of data previously recorded in existing medical records and institutional data on patient census and hospital/ED resources and staffing. The research involves no more than minimal risk to the subjects; the only potential risk is a breach of confidentiality, and protections are in place to safeguard the data.

Retrospective analysis of previously-collected and previously-recorded data should have no influence on the welfare of study subjects. Because risk is minimal given this design, the waiver of consent and authorization will not adversely affect the rights or welfare of subjects.

The research could not practicably be carried out without the waiver of consent and authorization. We anticipate we will include up to 2000 charts/records in the dataset. The sample size for this retrospective chart review is large enough that including only those data for which consent could be obtained would prohibit conclusions to be drawn and would compromise the scientific validity of the study, as a large proportion of the data would be eliminated if obtaining consent were a requirement. The subjects whose records will be reviewed are no longer followed and may be lost to follow up. The proportion of subjects who have relocated or have passed away may be a significant percentage of the subject population, and so the research results may not be meaningful and would lose statistical power if obtaining consent were a requirement. We feel that for these reasons, the research could not practicably be carried out without the waiver. Since in the current protocol there will be no contact with study subjects, the risk for breach of confidentiality would be substantially greater in order to make contact with each provider of each patient.

Only data necessary for the completion of the study will be collected. Safeguards will be in place to protect subject identity. The data will only be accessible to members of the research team, and all members of the research team have completed Human Subjects Protections and understand the importance of protecting subject privacy and confidentiality. No PHI will be recorded on the CRFs for the study dataset.

It is not possible to provide subjects with information about the study as there is no feasible mechanism by which to notify subjects, attempting to do so would substantially increase the risk of a confidentiality breach, and because the information that is found will have no impact on subjects' clinical care.

Only data necessary for the completion of the study will be collected. The patient name, subject ID and encounter ID are necessary to allow identification of the specific patient encounter for supplemental data abstraction. The elapsed time related to various patient management actions include the primary outcome and otherwise represent potential important factors influencing our outcomes of interest.

Safeguards will be in place to protect subject identity. The data will be protected from improper use or disclosure. The study data will be kept on encrypted, password-protected computers. These computers are Intermountain Healthcare devices, which are routinely used for storage of patient data and research data including subject identifiers. No PHI will be recorded on the CRFs for the study dataset. Minimal identifiers will be maintained linked to the data. Maintaining minimal identifiers linked to the data is necessary to allow (1) manual abstraction of additional data from the electronic medical record and (2) potential future linkage – with IRB approval -- of the data to additional datasets. No individual subject data will be presented in any presentation, publication or report related to this research. Data will be

presented only in aggregate or as results of statistical analyses and will not include any individual-level data that could be traced to a particular subject.

Risks: The only risk involved with this retrospective data study is a potential breach of confidentiality. There is a minimal risk of a privacy and confidentiality breach; however, this risk is low given the secured databases and computers that will be employed for data storage.

Benefits: There are no foreseeable direct benefits for the individual patient or provider subjects. Improved understanding of factors affecting early detection and management of sepsis could improve treatment of this syndrome thereby improving outcomes for all patients with sepsis, severe sepsis, and septic shock.

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