1. Title Page

Project Title	**Enhancing Stroke Prehospital and Emergency Evaluation and Delivery**
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Organization	**University of Chicago**
Dates of the Project	**07/01/2018 - 04/30/2023**
Federal Project Officer	**Darryl T. Gray, MD, ScD**
Agency Grant #	**R18 HS025359**

2. Structured Abstract

Purpose
Some acute ischemic stroke (AIS) patients require transfer from a Primary Stroke Center (PSC) to a Comprehensive Stroke Center (CSC) for advanced time-sensitive AIS treatments. Reducing PSC Door-In-Door-Out (DIDO) time could improve quality of care and outcomes.
Scope
Focus on systems and processes of emergency department (ED) care from PSC arrival to departure for CSC.
Methods
Natural language processing (NLP) retrospective analysis of Emergency Medical Services (EMS) reports of AIS patients with large vessel occlusion (LVO) analyzed using machine learning (ML) (**Aim 1**) and creation of a Learning Collaborative (LC) of clinicians involved in the DIDO process at two Chicago-area PSCs and their affiliated CSCs to (1) conduct a Failures Modes, Effects, and Criticality Analysis (FMECA), (2) engage in user-centered design of solutions, and **(3)** apply principles of implementation science to implement and then pilot test the solutions (**Aim 2**).
Results
Analysis of 965 reports showed that a text-based model predicted LVO better than the Cincinnati Prehospital Stroke Scale (CPSS) ($p = 0.165$) and the 3-Item Stroke Scale (3 I-SS) ($p < 0.001$) scores. High-criticality failures (e.g., failure to detect LVO, failure to use screening tools) led to the design of a seven-solution intervention, with six of the seven being implemented at the two PSCs. Pre-implementation and post-implementation operational data were collected from February 2018 through December 2022 and showed a 71-minute decrease in mean DIDO time, with high levels of clinician satisfaction.

Key Words: Acute Stroke, Door-In-Door-Out

3. Purpose (Objectives of the Study)

This study addresses two important areas in need of improvement in the delivery of high-quality, advanced care for acute ischemic stroke (AIS) patients: optimal screening for acute stroke and efficient inter-hospital transfer for patients who present at a Primary Stroke Center (PSC) and require transfer to a Comprehensive Stroke Center (CSC) for advanced stroke treatments. The specific aims are to:

Aim 1: Identify items from existing large vessel occlusion (LVO) scales that best predict LVO (**Aim 1a**), assess whether machine learning (ML) and natural language processing (NLP) of emergency medical services (EMS) (prehospital) electronic medical records improve LVO prediction (**Aim 1b**), and evaluate an Enhanced LVO screening tool (**Aim 1c**);

Hypothesis 1: Gaze preference, unilateral weakness, and aphasia will best predict LVO (*H1a*); machine learning approaches will identify the optimal combination and additional features that improve LVO prediction (*H1b*); and an enhanced LVO screening tool will perform better than published scales (*H1c*).

Aim 2: Design, develop, implement, and pilot test a new stroke door-in-door-out (DIDO) protocol, using a learning collaborative, data simulation, and iterative, user-centered design and implementation approaches to reduce door-in-door-out (DIDO) times in stroke patients requiring transfer from PSCs to CSCs.

Hypothesis 2: Application of collaborative, iterative design and data simulation for protocol development and implementation will reduce DIDO time.

4. Scope

Nearly 800,000 people in the United States (US) each year are affected by acute stroke, with acute ischemic stroke (AIS) being the most common, and stroke remains a leading cause of adult disability and the fifth leading cause of death. Despite the proliferation of stroke centers nationwide, access to timely stroke care and evidence-based therapies is still poor, with multiple inefficiencies, redundancies, errors, and system-based barriers that lead to care fragmentation. A stroke system of care that integrates and coordinates care between non-Stroke Center hospitals, PSCs, and CSCs is highly recommended and has been estimated to potentially reduce stroke-related deaths by 20,000 annually in the US and by nearly 400,000 worldwide.

For **Aim 1**, we analyzed de-identified EMS text notes for AIS patients with LVO (adjudicated), transferred from a PSC to a CSC for advanced stroke care. The EMS de-identified data were highly diverse, with substantial proportions of minority subpopulations, reflecting Chicago's diverse demographics, and included AHRQ priority populations (elderly, those who live in the inner city, low-income patients, those who are disabled or have chronic conditions, or those who may be at the end of life) because the study focuses on AIS, which is highly prevalent among the elderly, poor, and urban populations with chronic diseases. For **Aim 2**, to gain an in-depth understanding of the systems and processes involved in AIS, we created a Learning Collaborative by recruiting a wide range of clinicians involved in the PSC to CSC transfer process, including AIS patients and caregivers of patients who had undergone a transfer from a PSC to a CSC for stroke care, emergency department (ED) MDs, ED nurses, EMS leadership and technicians, Stroke Neurology MDs, Stroke Coordinators, and Hospital Transfer Coordinators. All clinicians interested in participating, regardless of gender, race, or ethnicity were invited to participate in the study.

The Research Team was composed of acute stroke researchers, bioinformatics experts, Emergency Medicine researchers, systems engineers, and health service and outcomes researchers to produce generalizable knowledge that can be widely applied to other urban regions of the country and can provide preliminary data and demonstration of novel approaches that could be evaluated in future large-scale comparative effectiveness studies.

5. Methods

Aim 1

- **Retrospective Secondary Data Analysis:** We used NLP to extract textual and discrete (structures) data from the EMS electronic medical record (EMR), SafetyPad, provided by the Chicago Fire Department (CFD). The SafetyPad is a tablet-based EMR used by the CFD EMS paramedics and includes standardized categorical or numerical demographic data (e.g., age, sex, race, insurance, address), operational data (e.g., ambulance number, times for dispatch, drive, scene arrival and departure, and hospital arrival times), and discrete clinical data (e.g., electrocardiogram, blood sugar, vital signs, LVO and CPSS scores) and textual descriptions of cause, complaint, symptoms, and examination findings (e.g., level of consciousness as measured by the Glasgow Coma Scale), disposition, reason for destination (e.g., nearest stroke center), and name of destination hospital. The Get-With-The Guideline-Stroke (GWTG-Stroke) registry is a quality improvement program for stroke care in the US that promotes consistent adherence to the latest scientific management guidelines. Hospitals enter de-identified clinical and outcomes data via a web-based Patient Management Tool (PMT; IQVIA, Cambridge, MA). Outcome data for patients in the EMS dataset were captured in a de-identified csv format and then entered into a REDCap database for analysis.
    - All patients between November 28, 2018, and May 31, 2019, suspected of having AIS by EMS, with an abnormal prehospital stroke screening, or with a hospital-diagnosed AIS at the ED encounter were initially included in the study cohort; only records of patients with a hospital-confirmed acute stroke were retained in the analytic cohort. The primary outcome was acute stroke diagnosis; secondary outcomes were severe stroke (National Institutes of Health Stroke Scale score >5, and AIS with LVO, and CSC-eligible stroke, defined as having either AIS LVO or intracerebral/subarachnoid hemorrhage). Text within the EMS reports, extracted by NLP, was converted to unigram features, which were given as input to a support-vector machine classifier that was trained on 70% of the cohort and tested on the remaining 30%. Logistic regression was used to develop baseline models for the CPSS and 3 I-SS categorical scores. Model discrimination was assessed using area under the receiver operating characteristic curve (AUROC) and corresponding 95% confidence intervals (CIs).

Aim 2

- **Learning Collaborative:** We created a Learning Collaborative (LC), as recommended by the Institute for Healthcare Improvement's (IHI) collaborative model, by recruiting an interdisciplinary team of relevant clinicians and individuals (e.g., patients, paramedics, nurses, physicians, and ED and stroke experts, operations and data simulation engineers, design experts, and process improvement experts) from across multiple institutions, involved in the DIDO transfer process of AIS patients. The LC included 19 clinicians, four patients, and two family members/caregivers of patients who underwent a transfer from a PSC to a CSC.
- **Failure Mode Effects and Criticality Analysis (FMECA):** The LC was asked to identify failures (weaknesses) in the systems and process of the DIDO process, understand the underlying causes of the failures, and then score the frequency, harm to the DIDO process, and any existing safeguards of the identified failures. The scores were then used to calculate a Risk Prediction Number (RPN) and Criticality Number (CN) for each failure. These numbers were then rank ordered to identify the most critical failures for solution and intervention design.
    - During the LC Session #1, participants were asked to describe, in his/her own words, the steps and tasks that he/she performs or plays in the DIDO process. The session, lasting 1.5 hours, was audio recorded, and field notes will be taken. Each identified step or task was written on a Post-it™ note and was placed in the appropriate sequence, as described by the participants. Following identification of all steps and tasks in the DIDO process, LC participants were asked to identify steps that are problematic, duplicative, unnecessary, or potentially harmful. This information, captured in field notes and on the audiotape, was subsequently added to the Process Diagram.
    - During LC Session #2, participants collectively suggested and reached consensus about key metrics in the DIDO process, such as times from ED arrival to ED physician exam, CT imaging, CSC contact, and private ambulance arrival, to be collected as part of GWTG-Stroke data collection. The research team reviewed and refined the metrics and then created these fields in the data collection form. The stroke coordinator at each site abstracted records for 6 months for all patients with stroke, ischemic and hemorrhagic, who are transferred from the PSC to a CSC. The research team compiled descriptive statistics (e.g., mean, median, variance) by site and across all sites.
    - Following these sessions, a process map of the DIDO process was created by the LC session facilitators (Prabhakaran, Khorzad, and Holl). The map was sent electronically to all LC participants with instructions to document revisions on the diagram, scan it, and return it to the research team. Follow-up virtual sessions were held with individual LC members to clarify and refine the process map. Co-I Khorzad and a design student observed ED workflows of the DIDO processes, as external auditors, to assess variations. A final Process Diagram was distributed to all participants for approval and approved.
- **Intervention Design:** The LC then participated in a series of design sessions. A design process, used by Design for America (designforamerica.com), guided the design and development of the solutions of the intervention, the Acute Stroke DIDO Protocol. The process involved a user-centered approach in which frontline "users" (LC members) provided their perspectives and feedback throughout the design process. To address human factors into the design, the research and design team focused on identifying cognitive, emotional, physical, organizational, and environmental capabilities and limitations and system weaknesses and deficits from the FMECA.
    - In the summer of Year 2, a student design team from the Northwestern University Segal Design Institute, taking part in a 12-week design workshop, under the guidance of Co-Is B. Ankenman, PhD, and R. Khorzad, MEM, worked with the research team and frontline users to design potential solutions and conduct usability testing, taking into account data from the simulation modeling (see below).
    - During LC Session #4 (fall Year 2), the LC split into interdisciplinary teams (N~5) inclusive of facilitators, design students, and LC participants to create "out of the box" solutions to reduce DIDO times, based on the most impactful targets identified from the FMECA and simulations. Potential solutions were grouped by theme and ranked by the participants using specific sets of criteria. A list of the top-ranked potential solutions was created.

- The teams then generated a list of needs (e.g., standardized order sets) for more complex solutions to be considered by the design team to further scope solutions for feasibility.
  The design team then examined the top-ranked proposed solutions, reviewed current solutions to related problems (e.g., DIDO for AMI), and selected several solutions for further simulation to assess impact on DIDO times, treatment rates, and unintended consequences.
- For more complex solutions, the design team built lo- fidelity prototypes. The prototypes were evaluated against the predetermined system attributes and requirements. Additional data simulations were performed by the McCormick engineering students to evaluate which prototype would have maximum impact on reducing DIDO times. Based on feasibility and simulation data, a single prototype was selected for further development. The prototype was then refined through iterative interviews of end users (members of the LC) and by conducting small tests of change in simulation. Similarly, selected LC participants, facilitated by Drs. Prabhakaran and Holl and Ms. Khorzad, provided feedback on prototypes of less complex solutions through similar iterative user sessions and small tests of change.
- The final Acute Stroke DIDO Protocol (Table 1) consists of seven solutions that were combined into a "bundle." A "new DIDO Process Map" was created, which integrated the "bundle" into the ED workflow of AIS patients needing PSC to CSC transfer.

- **Mathematical Simulation Modeling**: The purpose was to assess the potential impact of LC proposed solutions on DIDO time. Data collection for this aim consisted of (1) data with the frontline clinicians/staff and patients/caregivers from the LC sessions and (2) de-identified operational data on DIDO time and other metrics (e.g., time to alteplase), from the Chicago GWTG-Stroke registry.
  - Co-Investigator Ohad Perry, PhD, Associate Professor of Industrial Engineering & Management Sciences at Northwestern's McCormick School of Engineering, and a team of industrial engineering students (N=4-6), as part of their Senior Design class, conducted the simulation modeling of the DIDO process. The baseline data, collected by PSCs, was the prime source of data for the simulation modeling. Prior to any modeling, the research team presented and reviewed, in detail, the DIDO Process Map Diagram and the descriptive statistics of the baseline data with the simulation team. Identified potential changes in the process were discussed and assessed for (1) impact on DIDO time; (2) impact on AIS treatment rates; and (3) unintended consequences, such as patient harm.
  - During LC Session #3, the Simulation Team presented final results to LC participants, the research team, and the design team. The simulation modeling resulted in the identification of the most impactful step(s) for reducing DIDO to <30 minutes and guided the scope for redesign of the DIDO process. Team members reviewed process diagrams and observations were conducted to show how users overcome challenges and provide critical information for design.

Table 1. Acute Stroke DIDO Protocol		
Solution	**Problem(s) To Be Solved**	**Solution**

1 & 2	• Optimize early recognition of acute stroke
	• Optimize detection of Severe Stroke or Large Vessel Occlusion (LVO)
		• EHR template to document the BEFAST Stroke Screening Tool
		  ○ For BEFAST ≥ 1, automate pop up of a Severe Stroke/LVO Scale
		  ○ For + Severe Stroke/LVO Scale, automate pop up “Direct to CT/CTA”

3	• Reduce the need for monitoring creatinine/BUN prior to obtaining a CTA to reduce CTA delays. • Reduce delay in accessing CT scanner for a potential stroke patient	• Decision support for CTA order that establishes that creatinine/BUN ARE GENERALLY NOT REQUIRED with some exceptions • Protocol for CT scanner prioritization for stroke patients from the ED who require a CT and/or CTA”
4	• Eliminate delay in obtaining CT and/or CTA for a potential stroke patient	• Implement "Direct to CT/CTA" protocol and process, based on Stroke Screening Tool Score + Severe Stroke/LVO Tool Score (Bundle #1)
5	• Ensure that Telestroke video conference machine is always charged and functioning • Ensure that Telestroke video conference machine can always be located	• Process for "verifying" and "testing" that Telestroke machine is charged and functioning every • Locate Telestroke machine in a standardized location and create a process for identifying ED room when in use.
6	• Delays in being able to reach a Telestroke MD by telephone occur occasionally.	• List 1st Call Telestroke MD AND a "back-up" Telestroke MD

- **Implementation:** During LC #4, implementation barriers and facilitators were reviewed. The Protocol was also further tested to detect and remediate any unintended consequences by applying data simulation techniques, adjusting for changes (e.g., new ED staff assignments and timing of CSC contact) in the new Process Diagram. Simulation modeling was performed by the engineering students with faculty advisor, O. Perry, PhD. The final results were presented during LC Session #5 to the research team and LC participants for final modifications.
  - The implementation was led at the two PSCs [Lake Forest Hospital (LFH) and Rush Oak Park Hospital (ROPH)] by the PSC Stroke Coordinator and ED and Stroke leadership, using a Plan Do Study Act model, to engage ED nursing and directors to train physicians, nurses, technologists, clerks, and paramedics. The Stroke Coordinators led the training sessions at their sites. The research team assisted by creating training slides and materials. Just before “official” implementation, the PSCs conducted a low-fidelity “walk through” of the new protocol with their ED teams and assessed whether additional training was required.
  - The two PSCs, LFH and ROPH implemented six of the seven solutions on 9/14/22 and 1/25/22, respectively. Both sites opted not to implement solution 7 because of the significant EPIC modifications that would be required and concerns about ability to implement this solution in a timely manner.
- **Evaluation:** In May 2023, the research team completed site visits at LFH and ROPH. Clinicians (e.g., ED nurses, ED physicians, ED techs, radiology techs) participated in a 10-minute “clinician experience” interview, which included questions about their experience with learning about the new Stroke DIDO Protocol (e.g., How were they informed about the new protocol? What teaching did they receive?). Interviews were audio recorded and transcribed for analysis. In September/October 2023, clinicians at both sites were invited to participate in an anonymous, REDCap survey, asking about the process of a recent acute stroke patient transfer from their PSC to the CSC. The survey assessed Stroke DIDO Protocol adherence.

Data were collected and analyzed by the research team. In the Evaluation Phase, 14 clinicians participated in clinician experience interviews about the DIDO Protocol, and seven clinicians participated in implementation adherence surveys.

6. Results

Aim 1

- We derived and tested an Enhanced LVO Screening Tool (text-based model) on a cohort of 965 patients, of which 580 had confirmed stroke diagnosis. On a test cohort of 289 patients, the text-based model predicted AIS better than the Cincinnati Prehospital Stroke Scale (CPSS) (c-statistic: 0.73 vs. 0.67, P=0.165) and the 3-Item Stroke Scale (3 I-SS) (c-statistic: 0.73 vs. 0.53, P <0.001) scores. In a test cohort of 267 patients with and without severe stroke (National Institutes of Health Stroke Scale score >5), the text-based model predicted LVO/severe stroke better than the CPSS (AUROC, 0.82 versus 0.70, *P*=0.006) and 3 I-SS (AUROC, 0.82 versus 0.57, *P*<0.001) models. In 232-patient cohort with and without AIS-LVO, the test-based model's performance in identifying AIS-LVO was not statistically significant (text-based model AUROC 0.76 versus CPSS AUROC 0.65, P=0.133; text-based model AUROC 0.76 versus 3 I-SS AUROC 0.64, P=0.074) in a test set of 232 patients with and without AIS-LVO.
- The Enhanced LVO Screening Tool performed better in predicting CSC-eligible stroke patients. The text-based model for predicting CSC-eligible stroke performed better in identifying patients eligible for CSC transfer compared to both CPSS and 3 I-SS stroke-related phenotypes, compared with non-stroke patients, therefore showing that the model has good face validity.
- Aim 1 results show that NLP and ML can be used to extract information from EMS reports to accurately identify acute stroke in a pre-hospital setting.
    - Future study needs to validate the text-based model, prospectively, and in larger populations to assess generalizability.
    - If validated, a text-based model could potentially improve stroke care in the pre-hospital setting by identifying stroke patients who are likely to require CSC care. Such patients could be transferred directly to a CSC, assuming the travel time would not be significantly longer, or could be assessed and transferred more expeditiously by PSCs to CSCs, if distance to CSC is significant. Other models have derived and validated stroke scales (e.g., CPSS and 3 I-SS); however, these models depend on accurate assessment and documentation of the stroke characteristics, which may be difficult to acquire and document in a pre-hospital setting.

Aim 2

- Pre-implementation: We simulated implementation of the Acute Stroke DIDO Protocol and found that, combined, the solutions could achieve a 37% (67-minute) reduction in DIDO times.
- Pre-Post Implementation Change in DIDO Time: We used actual DIDO data from LFH and ROPH, respectively, and showed a 71-minute decrease (change) in mean DIDO time (pre-implementation N=382 and post-implementation N=254). Data collection continued until 12/22, and the final results are being analyzed. Additionally, we collected implementation adherence and clinician satisfaction data from clinicians at both PSCs. We found that ROPH had high adherence levels, but LFH had lower adherence levels. The implementation teams at LFH were then able to address protocol re-training. However, surveys showed high levels of clinician satisfaction at both sites.
- Limitations: The Acute Stroke DIDO Protocol was only implemented at two PSCs in urban Chicago, and the results may not be applicable to other settings. Furthermore, the results are based on a relatively modest sample and, therefore, are not likely generalizable. However, we have been notified that we will receive funding for a new study: "Hospital Implementation of a Stroke Protocol for Emergency Evaluation and Disposition (HI-SPEED) (R01 NS131797, MPIs Prabhakaran and Holl), most likely as a U01 award. This study will be able to address many of the limitations of E-SPEED, as we will be implementing the E-SPEED protocol at eight large health systems in the US, with CSCs and multiple PSCs.

7. List of Publications and Products

Holl JL, Khorzad R, Zobel R, Barnard A, Hillman M, Vargas A, Richards C, Mendelson S, Prabhakaran S. Risk Assessment of the Door-In-Door-Out Process at Primary Stroke Centers for Patients With Acute Stroke Requiring Transfer to Comprehensive Stroke Centers. J Am Heart Assoc. 2021 Sep 21;10(18):e021803. doi: 10.1161/JAHA.121.021803. Epub 2021 Sep 17. PMID: 34533049; PMCID: PMC8649509.

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Prabhakaran S, Khorzad R, Parimpour Z, Richards C, Meurer W, Barnard A, Bader E, Hillman M, Zobel R, Lee J, Mendelson S, Holl JL. Door-In-Door-Out Process Times at 5 Primary Stroke Centers in Chicago. International Stroke Conference, March 17–19, 2021; **March 2021 - Volume 52, Issue Suppl_1: Abstracts From the American Stroke Association 2021 International Stroke Conference.**

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Abughoush K, Parimpour Z, Holl JL, Ankenman B, Khozard R, Perry O, Barnard A, Brenna J, Zobel R, Bader E, Hillmann M, Vargas A, Lynch D, Maymapurath A, Lee J, Richards C, Peacock N, Meurer W, Prabhakaran S. Simulating The Effects of Door-In-Door-Out (Dido) Interventions. International Stroke Conference, February 8-11, 2022; February 2022 - Volume 53, Issue Suppl_1: Abstracts From the American Stroke Association 2022 International Stroke Conference.