Optimizing emergency stroke transport strategies using physiological models

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Non-Standard Abbreviations and Acronyms

CSC: Comprehensive Stroke Center
DNS: Drip and Ship
EMS: Emergency Medical Services
EVT: Endovascular Thrombectomy
LVO: Large Vessel Occlusion
mRS: modified Rankin Score
MS: Mothership
PSC: Primary Stroke Center
tPA: Tissue Plasminogen Activator
Table of Contents:

Abstract … 4 – 5

Introduction … 6 – 7

Methods … 7 – 16

Results … 17 – 18

Discussion … 18 – 22

Conclusion … 22 – 23

References … 24 – 28

Figure Legends … 29 – 31

Figures … 32 – 37

Appendix … 38 – 53
Abstract

**Background and Purpose:** The criteria for choosing between Drip and Ship (DNS) and Mothership (MS) transport strategies in emergency stroke care is widely debated. While existing data-driven probability models can inform transport decision-making at an epidemiological level, we propose a novel mathematical, physiologically derived framework that provides insight into how patient characteristics underlying infarct core growth influence these decisions.

**Methods:** We represent the physiology of time-dependent infarct core growth within an ischemic penumbra as an exponential function with consideration to rate-determining collateral blood flow. Monte Carlo methods generate distributions of infarct core volumes, which are translated to distributions of 90-day modified Rankin Scores. We apply the model to a stroke network that serves the rural Bastrop County and urban Travis County by simulating transport strategies from thousands of potential patient pickup locations. In every pickup location, the simulation yields a distribution of outcomes corresponding to each transport strategy. A two-sample Kolmogorov-Smirnov test and student t-test determine which transport strategy provides a significantly better probability of a good outcome for a given pickup location in each respective county ($P < 0.01$).

**Results:** In Travis County, DNS provides significantly better probabilities of a good outcome in 24.0% of the pickup locations, while 59.8% favor MS. In Bastrop County, 11.3% of the pickup locations favor DNS, while only 7.1% favor MS. The remaining pickup locations in each county are not statistically significant in either direction. We also reveal how differing rates of infarct core growth, the application of bypass policies, and the use of large vessel occlusion field tests impact these results.

**Conclusions:** Modeling stroke physiology enables the use of clinically relevant metrics for determining comparative significance between DNS and MS in a given geography. This formalism can help
understand and inform emergency medical service transport decision-making, as well as regional bypass policies.
**Introduction**

Rapid neuronal loss from acute ischemic stroke occurs as the infarct core grows within its ischemic penumbra. The duration of ischemic stroke evolution is highly variable, ranging between 6 to 18 hours for large vessel occlusions,¹ and the degree of collateral blood flow is a major determinant of the rate at which an infarct core achieves full ischemic volume.² Large vessel occlusions (LVO) are the most severe stroke-type, with an incidence rate of 25% of ischemic stroke cases.³ Endovascular thrombectomy (EVT) is the primary treatment method for LVOs and can be administered at a comprehensive stroke center (CSC).⁴ Non-LVOs, comprising of lacunar strokes related to small vessel disease as well as small emboli, comprise 75% of ischemic stroke cases,³ and thrombolysis with intravenous tissue plasminogen activator (tPA) is the standard treatment for qualifying patients who present symptoms up to 4.5 hours prior at either a primary stroke center (PSC) or a CSC.⁵,⁶ Stroke outcomes are time-dependent, so it is pertinent for a suspected stroke patient to receive suitable treatment quickly.⁷-⁹

If a CSC is the closest stroke center to the patient pickup location in terms of transport time, then the patient is taken directly there as the best treatment options for any stroke type are available. When a PSC is closer to the patient pickup location than a CSC, emergency medical services (EMS) must decide between two strategies of emergency stroke transport. The first is Drip and Ship (DNS). This transport strategy takes the patient directly to the closer PSC where they are able to receive cerebrovascular imaging and tPA, then proceeds to the CSC if an LVO is identified. The second transport strategy is Mothership (MS), which bypasses the closer PSC for a more distant but EVT-capable CSC. While there are cases in which the optimal emergency transport strategy is clear (e.g. a patient with unequivocal signs and symptoms of a non-LVO),
EMS is often unable to ascertain a patient’s stroke type with certainty given current field-testing capabilities. For these patients, the optimal transport strategy is ambiguous.\textsuperscript{10}

We propose a novel framework that uses a physiological model of time-dependent infarct core growth and represents key, patient-specific parameters as population-based distributions. We then implement this framework in two case studies to provide insight into how physiology can influence and potentially inform emergency stroke transport decisions. These applications focus on the optimization of EMS transport decisions and regional bypass policies in the Bastrop and Travis Counties in Texas. A detailed description of Texas stroke center capabilities and resources can be found in the Texas Department of State Health Services report.\textsuperscript{11}

**Methods**

The materials that support the findings of this study are available from the corresponding author upon reasonable request.

**Mathematical Model of Infarct Core Growth**

If a stroke patient’s ischemic region does not reperfuse, their infarct core will eventually attain the total ischemic penumbra volume. Mathematically, the physiology of a growing infarct core within the spatial constraint of its ischemic penumbra can be modeled as an exponential function.

Let $v(t)$ be the infarct core volume in mL at time $t$ minutes after stroke onset, $v_p$ be the constant, total volume of at-risk tissue encompassed by the ischemic penumbra, and $\tau$ be the collateral-dependent time constant in minutes. The dynamics of infarct core growth with respect to time are modeled as
\[ v(t) = v_p \cdot \left(1 - e^{-t/\tau}\right) \]  \hspace{1cm} \text{Eqn. 1}

where the time constant \( \tau \) determines the rate at which the infarct core volume \( v(t) \) achieves the ischemic penumbra volume \( v_p \). In the case of a patient with an LVO, an infarct core with poor collateral blood flow tends to grow faster and to a larger ischemic penumbra volume, while stronger collateral blood flow tends to slow infarct core growth and decrease the maximum ischemic penumbra volume.\(^2\) We constructed the time constant \( \tau \) to be parameterized by a 12-point pial collateral score (0-11),\(^12\) which is linearly dependent on large vessel ischemic penumbra volume.\(^12,13\) \textbf{Figure 1} provides a visualization of our exponential model of infarct core volume, which is consistent with existing experimentally and theoretically derived models.\(^12,13\)

The Mathematical Model of Infarct Core Growth and the Time Constant Parameterization sections of the Supplemental Materials provide further details of the model and its time constant.

We extended Eqn. 1 to relate infarct core volume to 90-day modified Rankin Score (mRS), a measure of patient outcomes,\(^14\) via the following linear function derived from Ernst et al’s clinical study of outcome-volume association,\(^15\)

\[ mRS(t) = 0.0376 \cdot v(t) \]  \hspace{1cm} \text{Eqn. 2}

and imposed the constraint that 90-day mRS cannot exceed an upper limit of 6, which represents patient death on the scale. Thus, Eqn. 2 allowed us to compute a 90-day mRS outcome for any patient at time \( t \) after acute ischemic stroke onset. It is important to note that our framework uses a continuous scale of 90-day mRS outcomes because it provides a more mathematically sound basis for statistical testing and improves the accuracy of probability estimates.\(^16\)
EMS Transport Times

The adjacent Travis and Bastrop Counties, Texas, are defined by the United States Census Bureau as urban and rural geographies, respectively. Their shared stroke network consists of three PSCs and three CSCs within Travis County, zero stroke centers within Bastrop County, and seven PSCs outside of both counties (Figure 2). We assumed the following non-transport time intervals for this stroke network: stroke onset to departure from pickup location with EMS = 60 minutes; door-to-needle (tPA) = 30 minutes; needle-to-door-out = 20 minutes; door-to-puncture (EVT) = 30 minutes. Time intervals specific to a stroke center type were kept constant across the network, but hospital-level variation can be integrated easily with the provision of relevant data.

In order to compute EMS transport times in Travis County, Texas, we created a coordinate grid with 10,562 nodes spaced 500-meters apart, representing hypothetical patient pickup locations within the county. Of these nodes, 2,872 (27.2%) have a CSC as the nearest stroke center, so the optimal decision is clear. The focus of our analysis was on the remaining 7,690 (72.8%) locations for which the optimal transport strategy is uncertain. We overlaid an equivalently resolved coordinate grid onto Bastrop County with 14,555 nodes, of which 11,959 (82.0%) were of interest in this analysis. Node-specific EMS transport times to the nearest PSC, nearest CSC, and transfer from the PSC to its nearest CSC were calculated with ArcGIS SDK (Esri, v10.8), utilizing average speed limits. Table I in the Supplemental Materials provides transport time data averaged across the nodes of interest in each respective county.

The total time for a DNS transport strategy is the sum of the time from stroke onset to departure from the pickup location, EMS transport time to the PSC, door-to-needle time, needle-to-door-
out time, transport time to transfer from the PSC to its nearest CSC, and door-to-puncture time. A non-LVO patient on the DNS strategy does not proceed past the PSC. The total time for a MS transport strategy is the sum of the time from stroke onset to departure from the pickup location, EMS transport time to the CSC, and door-to-needle or door-to-puncture time depending on the stroke type.

**Monte Carlo Patient Volume Generation**

In lieu of a clinical dataset, we used Monte Carlo methods to generate synthetic data in order to model infarct core growth for a population of acute ischemic stroke patients. For every node of interest in the Travis and Bastrop Counties, we simulated 13,000 patients each with a randomly generated ischemic penumbra volume $v_p$. Of the total patients in each location, there were 3,900 LVO patients (25% incidence rate) with their $v_p$ sampled from a skew-left beta distribution, and 9,100 non-LVO patients (75% incidence rate) with their $v_p$ sampled from a skew-right beta distribution (see Figure I in the Supplemental Materials for example distributions). The total number of patients we simulated at each node of interest was chosen to maximize statistical power, thereby reducing Type II error, and to avoid unreliable significance testing that may result from oversampling or undersampling volumes.

The respective skewness of the generated LVO and non-LVO $v_p$ beta distributions were derived from published 90-day mRS outcome distributions for LVO and non-LVO patient subpopulations.\textsuperscript{17} The mean, range, and standard deviation of the LVO distribution resembles that of a sample of clinically measured LVO penumbra volumes.\textsuperscript{18,19} Moreover, while non-LVO volumes include a similar range of volumes related to LVO cases that spontaneously recanalize,
there is a preponderance of smaller stroke volumes of lacunar infarcts caused by small vessel
disease,\textsuperscript{20,21} further supporting the notion that non-LVO volumes tend to be skew-right.

Because we expanded Eqn. 1 to accommodate a distribution of ischemic penumbra volumes
representative of a population of acute ischemic stroke patients, the collateral-dependent time
constant $\tau$ also became a distribution for the LVO subpopulation. However, we have not
identified literature that addresses the time constant $\tau$ parameterization with respect to non-LVO
collateral blood flow. Therefore, for the non-LVO subpopulation, we varied $\tau$ and present our
results using two extreme time constant parameterizations for non-LVO infarct core growth. In
one case, we assumed $\tau$ to be the largest time constant (slowest rate of infarct core growth) from
the distribution of LVO time constants, and in the second case we assumed $\tau$ to be the smallest
(fastest rate of infarct core growth). The generation of synthetic patient data and the following
simulations were performed in MATLAB (MathWorks, version r2017b). The Monte Carlo
Patient Volume Generation section in the Supplemental Materials provides further details of the
volume and time constant distributions.

\textit{Emergency Stroke Transport Simulations}

Timely acute stroke interventions can lead to successful reperfusion of the ischemic region,
preventing the infarct core from expanding to the full ischemic penumbra volume. For patients
that successfully reperfuse, their infarct core volume at the time of treatment is defined as the
final infarct core volume. Those that do not successfully reperfuse from any treatment have a
final infarct core volume that is equal to their ischemic penumbra volume. In our simulations, we
assumed that (1) administering tPA prior to EVT did not improve the probability of successful
reperfusion with EVT for an LVO patient (i.e. the probabilities of successful reperfusion with tPA and EVT for an LVO patient are independent);\textsuperscript{22-24} and (2) the probability of successful reperfusion for non-LVO patients given tPA was time-dependent.\textsuperscript{25} \textbf{Table II} in the Supplemental Materials presents framework reperfusion parameters.\textsuperscript{25-27}

For each node of interest in both counties, we simulated an emergency stroke transport scenario where the Monte Carlo generated stroke population (composed of 25\% LVO patients and 75\% non-LVO patients) followed the DNS strategy, and then re-ran the simulation with the MS strategy. The resultant distributions of the population’s final infarct core volumes corresponding to each transport strategy were translated to distributions of 90-day mRS outcomes via Eqn. 2. We then constructed cumulative distribution functions of 90-day mRS respective to DNS and MS in each node. \textbf{Figure 3} visualizes the simulation framework, and the Emergency Stroke Transport Simulations section in the Appendix provides further details of its methodology.

\textit{Framework Assumptions}

As with any model, we made a few assumptions in order to focus the scope of the study. First, all patients in the simulated population had a prehospital mRS of 0, as future studies are necessary to better understand stroke growth mechanisms in nonzero pre-hospital mRS subgroups. Secondly, all non-LVO and LVO patients were eligible for tPA and all LVO patients were eligible for EVT. The inclusion of those who do not meet treatment eligibility criteria would likely create negligible and inconsequential differences in the cumulative distribution functions of 90-day mRS and therefore simulation results. Thirdly, our population of stroke patients did not include stroke mimic cases, or intracerebral hemorrhage cases. An extensive review of the
literature by a previously published simulation study concluded that mimic and hemorrhage cases can be considered to have a time invariant probability of a good outcome. Clinical trials show that interventions of hemorrhagic stroke in the hyperacute window post-onset do not improve outcomes relative to standard of care. Because bypass times in the Travis and Bastrop Counties are < 1 hour, including this subgroup would not affect simulation results.

From a clinical perspective, we assumed that for patients who respond to treatment, successful reperfusion occurred with negligible delay and infarct core growth was halted. It is possible that treatment-to-reperfusion time intervals are not negligible, and if so, our framework results likely underestimate MS favorability. Additionally, the probabilities of successful reperfusion given EVT or tPA for LVO patients were independent of time from onset of acute ischemic stroke. If these probabilities decrease with time in actuality, then our simulation results likely underestimate DNS favorability. While Menon et al show that the probability of successful reperfusion for LVO patients has a dependency on time from treatment with tPA, their model does not discuss the likely dependence of these results on patient-specific onset-to-treatment times. In order to integrate their model with our framework, data that relates the stroke onset-to-treatment and treatment-to-reperfusion windows is necessary.

Finally, we assumed that the transport decision made by EMS at the pickup location was carried through completely and there was no switch to another method of transportation at any point thereafter.
**Case Study I: Optimal Transport Decisions Analysis**

In order to determine which transport strategy provides significantly better probabilities of a good outcome (90-day mRS 0-2) for each node of interest in a given county, we extracted the probability of a good outcome respective to DNS and MS from their cumulative distribution functions outputted by the emergency stroke transport simulations. We repeated these simulations and extractions twenty times, yielding a distribution of twenty distinct probabilities of a good outcome given DNS and twenty distinct probabilities of a good outcome given MS for every node of interest. A 2-sample, one-sided Kolmogorov-Smirnov test compared the shape of these two distributions within each node and determined which transport strategy provides significantly better probabilities of a good outcome ($\alpha = 0.01$ level). In addition to the Kolmogorov-Smirnov test, we performed a 2-sample student t-test to determine statistical significance between the means of the DNS and MS distributions of a probability of a good outcome in each node ($\alpha = 0.01$ level). These two statistical tests provided a useful combination that can detect, respectively, significant differences between the variances and means of the distributions in question. Furthermore, we used the Cohen’s $d$ statistic for effect size to quantify the magnitude of statistical significance in the nodes that favor DNS or MS. Cohen’s $d$ is a metric of practical significance that measures the standardized difference in means (extent of overlap or separation between distributions), in units of standard deviations, between the DNS and MS distributions of 90-day mRS good outcomes. QGIS mapping software (QGIS Development Team, v3.12) was used for visualizing statistical results. The Cohen’s $d$ Effect Size section in the Appendix provides further detail on the statistical methods, and a sensitivity analysis of select model parameters is included in the Appendix.
**Case Study II: Optimal Bypass Policy Analysis**

Bypass time is defined as the added transport time taken to reach the more distant CSC from the pickup location compared to going directly to the closer PSC. There are bypass policy recommendations provided by the American Heart Association and by regional health care networks establishing that if the bypass time from a given pickup location exceeds the policy recommended threshold, then a patient suspected to have an LVO should be transported directly to the PSC.\(^{36}\)

The Tiger/Line Shapefiles published online annually by the United States Census Bureau provide population data for the 580 geographic census block-groups in Travis County (2010 census total county population ~ 1.03 million).\(^{37}\) We uniformly distributed each block-group’s population amongst the nodes in its geographic boundaries. For example, if a census block-group with a population of 1000 enclosed 100 nodes, then each node in that block-group would be assigned a population of 10. Using this census data and the node-specific probabilities of a good outcome outputted by the simulation, we assessed the number of people with a good outcome per 1000 stroke cases in Travis County under a range of bypass policies, without LVO field testing. These results were compared to an ideal threshold of stroke care, defined as the number of people with a good outcome per 1000 stroke cases if EMS utilized an LVO field test with 100% sensitivity and specificity, and always transported the patient to the center that provides the highest probability of a good outcome for their stroke type. The bypass policy that yields the smallest deviation in the number of people with a good outcome per 1000 stroke cases from the ideal threshold is considered the optimal county-wide bypass policy without LVO field testing.
We also extended this methodology to incorporate common LVO field tests,\textsuperscript{38} such as the Los Angeles Motor Scale (LAMS \( \geq 4 \); sensitivity = 0.66, specificity = 0.86), Cincinnati Prehospital Stroke Severity Scale (CPSSS \( \geq 2 \); sensitivity = 0.56, specificity = 0.86), and the Prehospital Acute Stroke Severity scale (PASS \( \geq 2 \); sensitivity = 0.71, specificity = 0.84). For each field test, we employed a range of bypass policies for suspected LVO patients only, while always sending those with a negative test to the PSC. Assessing the number of people with a good outcome per 1000 stroke cases in Travis County, we used the same ideal threshold as before to determine the optimal county-wide bypass policy. We repeated these analyses for Bastrop County (39 block-groups, 2010 census total county population \( \sim 74.17 \) thousand).

**Results**

**Optimal Transport Decisions**

Of the 7,690 nodes of interest in Travis County, we find that DNS provides significantly better probabilities of a good outcome in 13.3\% and MS provides significantly better probabilities of a good outcome in 74.2\%, assuming a fast rate of non-LVO infarct core growth (KS-test, student t-test: \( P < 0.01 \); Figure 4A). The remaining 12.5\% are not statistically significant in either direction.

Assuming a slow rate of non-LVO infarct core growth, DNS provides significantly better probabilities of a good outcome in 24.0\% of the nodes of interest and MS provides significantly better probabilities of a good outcome in 59.8\% (KS-test, student t-test: \( P < 0.01 \); Figure 4B). The remaining 16.2\% are not statistically significant in either direction.
Figure 5 presents heatmaps of Travis County colored by Cohen’s d effect size statistic, showing dissipation of the effective significance of the MS transport strategy over DNS when considering pickup locations that are increasingly distant from CSCs.

The northwest corner of Travis County is one of the most isolated locations from road and highway access in Travis County because the Colorado River encompasses it (the river is most easily discernible on Figure 2). We see that the regions of insignificance in this corner under the assumption of a fast rate of non-LVO infarct core growth (Figure 4A or Figure 5A) convert to DNS significant when assuming a slow rate instead (Figure 4B or Figure 5B).

Optimal Bypass Policies

In Travis County, bypass policies from 10- through 21-minutes without LVO field testing yield the optimal number of people with a good outcome per 1000 strokes, assuming a fast rate of non-LVO infarct core growth (Figure 6A). Furthermore, Figure 6A shows that implementing any LVO field test in conjunction with bypass policies only for suspected LVO patients decreases the number of people with a good outcome per 1000 strokes.

Under the assumption of a slow rate of non-LVO infarct core growth, administering LAMS or PASS and always sending suspected LVO patients directly to the CSC is optimal (Figure 6B). However, utilizing the CPSSS LVO field test with bypass policies only for suspected LVO patients yields fewer people with a good outcome per 1000 strokes than implementing bypass policies without LVO field testing.
The Bastrop County statistical significance analysis yields a great deal of variation in transport strategy favorability depending on the rate of non-LVO infarct core growth, and its optimal bypass policies are similar to Travis County. The Appendix presents the results of the Bastrop County simulation.

Discussion

Herein, we propose a framework with a physiology-based, mathematical model of infarct core growth. Monte Carlo methods allowed us to generate synthetic patient data, and emergency stroke transport simulations outputted distributions of 90-day mRS outcomes corresponding to DNS and MS in every node. Although the probability of a good outcome was deemed the most clinically relevant metric, this framework has the capability to also make statistical comparisons between the transport strategies with respect to all outcomes 0-6 on the 90-day mRS scale. An analysis of the comprehensive outcome scale would be particularly useful in studying burdens of cost or other healthcare value metrics, such as cost-effectiveness models that seek to optimally place new stroke centers or upgrade existing centers by equilibrating healthcare costs and patient outcomes.

This work builds on previous, foundational studies of emergency stroke transportation. Some of these studies compare the two emergency stroke transport strategies using conditional probability models derived from large clinical datasets, and are able to compute probabilities of a good outcome on the 90-day mRS scale, dependent on the time from stroke onset to treatment, the type of stroke and corresponding treatment, and the particular transport strategy. This data-driven approach of emergency stroke transportation modeling offers validity and accuracy
only within the bounds of the dataset (i.e. the patients and geographic times the model is derived from), and cannot identify underlying patient-specific, physiological mechanisms that account for trends in the data. The proposed framework serves as a foundation to resolve these issues by providing a ground-up model that accounts for inherent, population-level variability, or stochasticity, of physiology-based independent variables. As a result, the framework can be applied to any geography, and cause-effect relationships motivating the results of the study are easily identifiable. Furthermore, it can determine statistically significant differences in outcomes between emergency stroke transportation strategies contingent on the stochasticity of these clinically relevant independent variables, whereas the data-driven models are deterministic in their current form and do not compute statistical significance.

In our first case study, optimizing transport decisions, we show that in both counties a fast rate of non-LVO infarct core growth decreases the number of nodes that favor DNS and increases the number of nodes that favor MS compared to when a slow rate is assumed. From a physiological perspective, if a non-LVO patient’s infarct core growth rate is fast and their pickup location is sufficiently remote from any stroke center, then their infarct core will quickly achieve a significant proportion of the ischemic penumbra volume before time of treatment, regardless of transport strategy. By extension, the non-LVO subpopulation’s distribution of final infarct core volumes will differ marginally between strategies, so DNS will not provide significantly better good outcomes as often for a mixed stroke population transported from these locations. This case study also reveals that geographies with long onset-to-treatment times (e.g. Bastrop County) are likely to have a greater proportion of nodes that do not significantly favor any strategy relative to geographies closer to stroke centers (e.g. Travis County), irrespective of infarct core growth
rates. As onset-to-treatment time increases, the likelihood that any stroke patient’s infarct core will achieve a significant proportion of the penumbra volume before treatment also increases. When transport times are exceptionally long, final infarct core volumes are approximately equal, translating to a lack of statistical favorability towards either transport strategy.

The physiological rationale for cases in which there is no statistical significance between DNS and MS may lend some insight into the recent, preliminary results of the RACECAT study. In particular, they report that there was no benefit in outcomes due to the choice of emergency stroke transport in Catalonia, Spain. Catalonia’s mean transport times to the nearest PSC and nearest CSC exceed the rural Bastrop County’s by approximately 42 minutes and 110 minutes respectively. Although more information is needed, we postulate that Catalonia’s exceptionally long transport times led to considerable growth of patient infarct core volumes with either transport strategy. Consequently, there were negligible differences between the distributions of final infarct core volumes, and therefore outcomes, corresponding to patients randomly assigned to DNS or MS.

In addition, our analysis of optimal bypass policies in the second case study revealed counterintuitive results. We found that under the assumption of a fast rate of non-LVO infarct core growth in either county, implementing any LVO field test in conjunction with bypass policies only for suspected LVO patients performs worse than implementing bypass policies without LVO field testing. This result follows from our first case study, showing that under the same rate assumption, MS provides significantly better probabilities of a good outcome than DNS in a majority of Travis County (Figure 4). These MS-favored regions cover the densely
populated areas of Travis County (e.g. Austin proper and its suburbs), so a county-wide bypass policy completely washes out the DNS preference of the few, less-populated regions. By implementing LVO field tests, we introduce rates of misclassification inherent to these tests. Evidently, a majority of the county significantly favors MS, so misclassifying LVO patients as non-LVO and transporting them to the PSC causes substantial harm (false-negatives). The implementation of a bypass policy without LVO field testing eliminates this harm by transporting all patients directly to the CSC. Importantly, the outcomes of non-LVO patients transported from remote pickup locations do not differ significantly between DNS or MS under this rate assumption. Field testing therefore negligibly benefits the non-LVO subpopulation, and does not offset the harm done to the misclassified LVO patients taken to the PSC.

Conversely, assuming a slow rate of non-LVO infarct core growth, we found that implementing LVO field tests in conjunction with bypass policies only for suspected LVO patients performed better than implementing bypass policies without LVO field testing (with the exception of CPSSS in Travis County). Under this rate assumption, the non-LVO’s in remote pickup locations benefit significantly more from transport to the PSC. As a result, implementing bypass policies without LVO field testing harms the entire non-LVO subpopulation (false-positives and true-negatives alike), whereas field testing mitigates this harm by accurately classifying a proportion of the non-LVO patients for optimal transport to the PSC (true-negatives). The drastic differences in optimal emergency stroke transport policy stemming from the rate of non-LVO infarct core growth underscores the critical importance of gaining empiric data of the physiological kinetics of this stroke type’s growth rate.
It is important to note the potential resource constraints associated with emergency stroke transport decision making. This analysis did not consider the common resource burdens or triage difficulties that often plague stroke centers. For instance, under the assumption of a slow rate of non-LVO infarct core growth, our simulation suggests always sending suspected LVO patients (LAMS or PASS) directly to the nearest endovascular capable center, yet a consequence of this directive may be a large buildup of patients in triage. This inefficiency would directly translate to worsened patient outcomes. Furthermore, Bastrop County is relatively close to a metropolitan center and extensive stroke network, so it would be important to analyze other rural geographies that do not have the same level of access to emergency stroke care resources.

**Conclusions and Opportunities for Model Improvement**

We hope to bring a new perspective to the discussion of emergency stroke transport by elucidating the relevance of physiology in decision-making. As noted previously, data-driven models map time from stroke onset to reperfusion directly to a probability of a good outcome. Our model generalizes this relationship by explicitly considering the underlying patient-specific, physiological variables that are fundamental determinants of stroke outcomes. By doing so, we are able to expand these clinically relevant factors to account for variation in a patient population, thereby gaining insight into the physiology that substantially influences optimal decisions.

Future work will modify the Eqn. 1 time constant to accommodate age, hypertension, or other patient comorbidities that may also affect infarct core growth rates. Early knowledge of a patient’s stroke type and degree of collateral blood flow with CT-capable ambulances would
allow for personalized emergency transport decisions with our framework. In addition, the time from stroke onset to reperfusion can be expanded into a statistical distribution to account for the inherent stochasticity of pre-hospital, transport and hospital time intervals found in a given geography and stroke center network (e.g. traffic, triage delays, etc.). These model capabilities pose valuable opportunities to tailor our estimates with region-specific data that encapsulates as much realistically-occurring variability as possible.

As our mathematical understanding of stroke physiology improves, our framework can provide more reliable estimates to inform transport decisions and policies. Our case studies highlight the importance for clinical studies that empirically measure infarct core growth rates in humans. The non-LVO infarct core growth rate is not currently defined by clinical data, but evidently has a large influence on optimal decisions and policies. In the same regard, the parameterization of the LVO time constant utilizes data from non-human experiments, which may affect the accuracy of our estimates. Moreover, while it remains to be seen if the 90-day mRS-volume relationship (Eqn. 2) varies by population, Ernst et al reports uncertainty in this association which directly translates to uncertainty in our modeling results (see Sensitivity Analysis in the Appendix). The precision of our estimates would improve with data that reports a 90-day mRS-volume relationship to a greater degree of confidence. Additionally, all probabilities of successful reperfusion are taken from clinical trials that define successful reperfusion as a Thrombolysis in Cerebral Infarction score $\geq 2b$, but scores $\geq 2a$ will be considered in future work given clinical studies that provide such data, as partial reperfusion can affect final infarct volume.
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Disclosures: None

Appendix

• Expanded Materials, Methods, & Results
• Online Tables I – II
• Online Figures I – VII
• Reference 44

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Figure Legends

Figure 1. Visualization of Eqn. 1, the exponential function of infarct core volume. Each example curve corresponds to a single patient’s infarct core volume over time, eventually reaching their ischemic penumbra volume $v_p$ if successful reperfusion is not achieved prior to full saturation. The time constant $\tau$, parameterized by patient-specific collateral blood flow, determines the rate at which the infarct core achieves its maximum value $v_p$. Because $\tau_1$ is steeper than $\tau_2$ (i.e. has a faster rate of growth), the red curve reaches $v_{p_1}$ sooner than the green curve reaches $v_{p_2}$.

Figure 2. Map of Travis County (A) and Bastrop County (B). A coordinate grid consisting of hypothetical patient pickup locations is generated within the boundaries of each respective county. Stroke centers outside of these boundaries are still considered for emergency medical service (EMS) transport in the simulations.

Figure 3. Emergency stroke transport simulations run in each node of interest. Monte Carlo methods generate a population of patients with LVOs and non-LVOs. The time taken from stroke onset to successful reperfusion from treatment determines how much of a patient’s penumbra volume their infarct core achieves (Eqn. 1). An LVO patient has a probability of successful reperfusion from EVT (green) at the CSC, or from tPA (purple) at the PSC. A non-LVO patient has a probability of successful reperfusion from tPA (purple) at either stroke center. Those that do not successfully reperfuse from any treatment (grey) have a final infarct core volume that is equal to their ischemic penumbra. For nodes with exceptionally long transport times, the final infarct core volume could be approximately equal to the penumbra volume despite successful reperfusion from treatment. For a given transport strategy simulation, the
distributions of final infarct core volumes of non-LVO and LVO patients were aggregated and then translated to a distribution of 90-day mRS via Eqn. 2. For visualization purposes, the proportions of green, purple, and grey are not exactly to scale with the values presented in Table II of the Appendix. The illustrated patient populations on the left-hand side are not representative of the 25/75 stroke type distribution for the same reason.

Figure 4. DNS provides a significantly better probability of a good outcome (90-day mRS 0-2) in fewer nodes assuming a fast rate of non-LVO infarct core growth (4A) compared to when slow rate is assumed (4B). MS provides significantly better probabilities of a good outcome in fewer nodes if the non-LVO infarct core growth rate is slow (4B) compared to when a fast rate is assumed (4A). Access to transportation routes can account for the difference between DNS and MS favorability, as seen in the northwest region of Travis County. Note that the colorless area in the northwest region is occupied by the Balcones Canyonlands National Wildlife Refuge and does not contain any nodes.

Figure 5. A heatmap showing Cohen’s d effect size. Assuming a fast rate of non-LVO infarct core growth (5A), DNS yields more relative benefit in the northwest region bounded by the Colorado River compared to when a slow rate of non-LVO infarct core growth is assumed (5B). With either choice of non-LVO infarct core growth rate, the magnitude of MS statistical significance decreases as the transport time to the CSCs in the city-center increases (relative to the transport time to the nearest PSC).
Figure 6. Assuming a fast rate of non-LVO infarct core growth, bypass policies 10- through 21-minutes are optimal without LVO field testing (6A). Under the assumption of a slow rate of non-LVO infarct core growth, employing the LAMS or PASS field tests and always sending suspected LVO patients directly to the CSC is optimal (6B).
Figures

Figure 1.

\[ v(t) = v_p \cdot (1 - e^{-t/\tau}) \]
Figure 2.
Figure 3.

A. Mothership Simulation

LVO Patients

Non-LVO Patients

Treatment Success Rate

Final Infarct Core Volumes

Eqn. 1
onset-to-treatment time

Eqn. 2

B. Drip and Ship Simulation

LVO Patients

Non-LVO Patients

Treatment Success Rate

Final Infarct Core Volumes

Eqn. 1
onset-to-treatment time

Eqn. 2

Population 90-day mRS
Figure 5.
Figure 6.
Appendix

Table of Contents:

Supplemental Methods

Mathematical Model of Infarct Core Growth … 39
Time Constant Parameterization … 39 – 40
Monte Carlo Patient Volume Generation … 40
Emergency Stroke Transport Simulations … 41 – 42
Cohen’s d Effect Size … 42

Supplemental Results

Optimal Transport Decisions (Bastrop County) … 43
Optimal Bypass Policies (Bastrop County) … 43
Sensitivity Analysis … 43 – 44

Supplemental Tables

Tables I – II … 45

Supplemental Figures and Figure Legends

Figures I – VII … 46 – 53
Supplemental Methods

Mathematical Model of Infarct Core Growth

As the volume of the infarct core grows within the ischemic penumbra, the instantaneous rate of change of infarct core volume with respect to time converges to zero. In the limit of a “long time” elapsing without reperfusion, the volume of the infarct core will achieve the total ischemic penumbra volume. Given these conditions, the physiology of a growing infarct core within the spatial constraint of its ischemic penumbra can be modeled as a first-order ordinary differential equation. Let $v(t)$ be the infarct core volume in mL at time $t$ minutes after stroke onset, $v_p$ be the constant, total volume of at-risk tissue encompassed by the ischemic penumbra, and $\tau$ be the collateral-dependent time constant in minutes. We can represent the dynamics of the infarct core growth as the following differential equation,

$$v_p = \tau \frac{dv(t)}{dt} + v(t)$$

which has the desired behavior for the instantaneous rate of change of infract core volume with respect to time,

$$\lim_{v(t) \to v_p} \frac{dv(t)}{dt} = 0$$

Suppose that there is no infarct volume at $t_0 = 0$ minutes after stroke onset, then we have $v(t_0) = 0$. The solution to the given initial-value problem is then

$$v(t) = v_p \cdot \left(1 - e^{-t/\tau}\right) \quad \text{Eqn. 1}$$

Eqn. 1 has the desired behavior over a long time-scale,

$$\lim_{t \to \infty} v(t) = v_p$$

Time Constant Parameterization

The time constant $\tau$ is parameterizable by a 12-point pial collateral score (0-11) dependent on large vessel ischemic penumbra volume in canines. We rescaled the linear collateral-volume relationship in canines to the scale of ischemic penumbra volumes found in human physiology using the two edge conditions: the mapping of the best collateral score with a minimum $v_p$ (pial = 11, $v_p = 0$ mL) and the worst collateral score with a maximum $v_p$ (pial = 0, $v_p = 220$ mL). Given these two points, we constructed the linear function $p(v_p)$ to relate pial collaterals and large vessel ischemic penumbra volumes in humans:

$$p(v_p) = (220 - v_p) \cdot \frac{11}{220}$$
The experimentally derived linear relationship between the rate-determining time constant $\tau$ and the pial collateral score $p$ is then given by

$$\tau(p) = (-0.0013 \cdot p + 0.0179) \cdot 60$$

Eqn. 3

A theoretical modeling paper corroborates the linearity of the relationship between the time constant $\tau$ and collateral blood flow.\textsuperscript{13}

It is important to note that the linear collateral-volume relationship should have associated uncertainty. Christiforidis et al provide the experimentally derived linear collateral-volume relationship,\textsuperscript{12} but do not provide confidence bounds. Future studies will expand this linear relationship to account for stochasticity in the random variables (i.e. a score of 11 is mapped to a distribution of possible ischemic penumbra volumes), contingent on the availability of relevant data. Nonetheless, this model allows us to expand these clinical variables to account for natural variation in patient-specific attributes.

**Monte Carlo Patient Volume Generation**

We added a notion of stochasticity to Eqn. 1 by letting $v_p$ be a beta($\alpha$, $\beta$) distributed random variable. Beta($\alpha$, $\beta$) distributions allowed us to sample $n_{LVO} = 3,900$ LVO and $n_{non-LVO} = 9,100$ non-LVO $v_p$ values on a closed interval of realistically occurring ischemic penumbra volumes, [10 mL, 220 mL], unlike Gaussian distributions, for example. Furthermore, beta skewness was adjustable via the two shape parameters $\alpha$ and $\beta$, allowing us to characterize two independently generated distributions, one corresponding to a distribution of $v_p$ values representative of LVOs, and one corresponding to a distribution of $v_p$ values representative of non-LVOs. The LVO ischemic penumbra volume beta distribution has skew-left shape conditions ($\alpha = 2$, $\beta = 2$, generating the example distribution in Figure I-A), and the non-LVO ischemic penumbra volume beta distribution has skew-right shape conditions ($\alpha = 2$, $\beta = 6$, giving Figure I-B).

Administering EVT to an LVO patient with an onset-to-treatment time exceeding six hours is often ineffective.\textsuperscript{44} We suppose that at this point in time, the infarct core is essentially evolved to its asymptotic value $v_p$ and treatment administered thereafter would negligibly improve outcomes. Although the asymptote of the exponential growth model is never reached in finite time (a property of asymptotic models), we know that at $t = 5\tau$, $v(t) = 0.9933 \cdot v_p$, and it is at this point in time that we consider the asymptotic value of the model to be achieved. Accordingly, we set the median of the distribution of time constants outputted from Eqn. 3 corresponding to the beta distribution of $n_{LVO}$ penumbra volumes to be 1.2 hours.
Emergency Stroke Transport Simulations

Final infarct core volume depends on the total elapsed time from stroke onset to successful reperfusion (Eqn. 1). A stroke patient can follow one of four possible onset-to-reperfusion time pathways, depending on their ischemic stroke type, transport strategy, and treatment (Figure II). Each pathway consists of non-transport time intervals and node-specific EMS transport times (transport time to the nearest PSC, nearest CSC, and transfer from the PSC to its nearest CSC).

We assumed in our simulations that administering tPA prior to EVT did not improve the probability of successful reperfusion with EVT for an LVO patient (i.e. the probabilities of successful reperfusion with tPA and EVT for an LVO patient are independent), and that an LVO patient has a 74% chance of successful reperfusion given EVT. For the MS simulation, we first apportioned $v_p$ values from the distribution of $n_{LVO}$ into two groups – those that will reperfuse given EVT and those that will not. Each node’s respective $treatment \mid LVO, MS, EVT$ and the proportion of $v_p$ values that will reperfuse from EVT were inputted into Eqn. 1 to yield time-evolved LVO infarct core volumes (i.e. final infarct core volumes). The remaining $v_p$ values maintained non-evolved LVO penumbra volume because we assumed that a patient who does not reperfuse from any treatment will eventually have an infarct core that achieves the total ischemic penumbra volume $v_p$.

The probability of successful reperfusion with tPA for non-LVO patients was time-dependent. We apportioned $v_p$ from the distribution of $n_{non-LVO}$ into two groups – those that will reperfuse given tPA and those that will not. Each node’s respective $treatment \mid non-LVO, MS, tPA$ and the proportion of $v_p$ values that will reperfuse from tPA were inputted into Eqn. 1 to yield time-evolved non-LVO infarct core volumes, and the remaining $v_p$ values maintained non-evolved non-LVO penumbra volume. The set of time-evolved non-LVO infarct core volumes and the set of non-evolved penumbra volumes were aggregated with the time-evolved and non-evolved LVO volumes computed previously. The combined set consisting of 75% non-LVO and 25% LVO volumes was mapped to 90-day mRS outcomes via Eqn. 2, yielding a cumulative distribution function of continuous 90-day mRS outcomes on the interval $[0,6]$ for a general population of stroke patients that follow the MS transportation strategy for each of 7,690 nodes of interest in Travis County and each of 11,959 nodes of interest in Bastrop County.

For the DNS simulation, we apportioned $v_p$ values from the distribution of $n_{LVO}$ into three groups - those that will successfully reperfuse given tPA at the PSC (20%), those that will reperfuse given EVT at the CSC (74% of the remaining $n_{LVO}$), and those that will not reperfuse from either treatment. Each node’s respective $treatment \mid LVO/non-LVO, DNS, tPA$ and the proportion of $v_p$ values that will reperfuse from tPA, as well as $treatment \mid LVO, DNS, EVT$ and the proportion of $v_p$ values that will reperfuse from EVT, were separately inputted into Eqn. 1 to yield two sets of respectively time-evolved LVO infarct core volumes. The remaining $v_p$ values in each pickup location where there was no reperfusion from either treatment maintained non-evolved LVO penumbra volume as in the MS simulation.

Non-LVO patients in the DNS simulation did not proceed past the PSC, as the provision of tPA is sufficient. Thus, the same stratifications of $n_{non-LVO}$ in the MS simulation were used, but now
each node’s respective treatment\textsubscript{LVO/non-LVO, DNS, tPA} was inputted into Eqn. 1 to yield a set of time-evolved non-LVO infarct core volumes. The set of time-evolved non-LVO infarct core volumes and the set of non-evolved non-LVO penumbra volumes were aggregated with the DNS time-evolved and non-evolved LVO volumes computed previously. The final set consisting of 75% non-LVO and 25% LVO volumes was mapped to 90-day mRS outcomes via Eqn. 2, yielding a cumulative distribution function of continuous 90-day mRS outcomes on [0,6] for a general population of stroke patients that follow the DNS transportation strategy for each of 7,690 nodes of interest in Travis County and each of 11,959 nodes of interest in Bastrop County.

All probabilities of successful reperfusion were taken from clinical studies, and Table II summarizes the reperfusion parameters. Furthermore, a 4.5-hour onset-to-treatment time window was taken as the acceptable window for tPA administration.\textsuperscript{5,6} All non-LVO patients that took longer than 4.5 hours to receive tPA mapped their non-evolved \(v_p\) directly to 90-day mRS, and LVO patients on the DNS track that arrived at the PSC after the time window were not considered for tPA treatment.

### Cohen’s d Effect Size

Effect size is often reported along with tests of statistical significance to quantify the magnitude of significance (cf. rejecting the null hypothesis of no effect). Cohen’s d measures the effect size as the standardized difference between the means of two distributions, which relies on a pooled standard deviation computation. In our simulation, the pooled standard deviation considers the respective variances of the DNS and MS distributions of a probability of a good outcome in each node. Figure 5 of the main text presents the Cohen’s d results for Travis County using the empirically calculated standard deviations for the probability of a good outcome measured across each node’s Monte Carlo simulations.

We would also like to consider an alternative Cohen’s d effect size calculation in terms of the variance of a Bernoulli distributed random variable with the specified value of the probability of a good outcome when computing the pooled standard deviation. This alternative variance calculation considers the respective means of the DNS and MS distributions of a probability of a good outcome in each node. As a result, this adapted effect size metric can be interpreted as the effect on a single individual who is transported with a particular strategy given the two probabilities, whereas using the pooled standard deviation on the probability of a good outcome from the simulations calculates an effect size that can be interpreted as the collective effect on many individuals. Figure III presents the results of the simulation with consideration to this adapted Cohen’s d metric. We find that the coloring of Figure 5 and Figure III is largely equivalent because the relative magnitudes of effect size amongst the non-adapted and adapted Cohen’s d measurements are the same, though the quantities themselves differ in scale. Variations in the number of nodes that favor a certain transport strategy or that are non-significant between Figure 5 and Figure III is attributable to modeling stochasticity that results from running independent simulations (i.e. volume distributions are re-generated between independent runs, creating slight differences in simulation results).
Supplemental Results

Optimal Transport Decisions

Of the 11,959 nodes of interest in Bastrop County, we find that DNS never provides significantly better probabilities of a good outcome and MS provides significantly better probabilities of a good outcome in 57.6%, assuming a fast rate of non-LVO infarct core growth (KS-test, student t-test: \( P < 0.01 \)). The remaining 42.4% are not statistically significant in either direction.

Assuming a slow rate of non-LVO infarct core growth, DNS provides significantly better probabilities of a good outcome in 11.3% of the nodes of interest and MS provides significantly better probabilities of a good outcome in 7.1% (KS-test, student t-test: \( P < 0.01 \); Figure IV-A). Figure IV-B is the heatmap of Bastrop County colored by non-adapted Cohen’s d effect size statistic under the assumption of a slow rate of non-LVO infarct core growth. The remaining 81.6% are not statistically significant in either direction.

Optimal Bypass Policies

In Bastrop County, always bypassing the PSC without field testing yields the optimal number of people with a good outcome per 1000 strokes, assuming a fast rate of non-LVO infarct core growth (Figure V-A). Furthermore, Figure V-A shows that implementing any LVO field test in conjunction with bypass policies only for suspected LVO patients decreases the number of people with a good outcome per 1000 strokes.

Conversely, under the assumption of a slow rate of non-LVO infarct core growth, administering any field test and always sending suspected LVO patients to the CSC is optimal and yields a greater number of people with a good outcome per 1000 strokes than if bypass policies were implemented without LVO field testing (Figure V-B).

Sensitivity Analysis

Figure VI visualizes the percentage of the total nodes of interest that significantly favor a given transport strategy in Travis County (KS-test, student t-test: \( P < 0.01 \)) under four different combinations of door-to-needle (DTN), door-to-puncture (DTP), and expedited-door-to-puncture (EDTP; for LVO’s identified at the PSC that are then transported to the CSC) time interval model parameters, including the combination of parameters considered in the main text (DTN = 30 minutes, DTP = 30 minutes, EDTP = 30 minutes). Assuming a fast rate of non-LVO infarct core growth, MS is significantly favored by a greater percentage of nodes than DNS in each of the scenarios considered except when the DTP time at the CSC is greater than the DTN at the PSC (Figure VI-A).

Figure VII presents the same sensitivity analysis for Bastrop County, with Figure VII-A showing that DNS is essentially never favored by any nodes of interest in the county, under the assumption of a fast rate of non-LVO infarct core growth.
The error bars in both sensitivity analyses represent the variation in results due to uncertainty in the outcome-volume relationship (the multiplier in Eqn. 2 of the main text).¹⁵ Though the uncertainty in the relationship itself is small, it amplifies the uncertainty in the simulation study results. This phenomenon can be explained by the sensitivity of the statistical significance tests to ‘boundary cases,’ which are the nodes of interest that significantly favor a transport strategy given small changes in model parameters but that do not actually favor the transport strategy in any practical sense (small effect size). We see that the Bastrop County results are quite variable compared to Travis County because nodes in Bastrop County tend to be further from any stroke center, leading to nodes that are highly sensitive to slight adjustments in model parameters. In future studies, it would be useful to determine the most clinically relevant effect size cutoff in order to eliminate these negligible, practically insignificant nodes and consequentially reduce the variation between and within (error bars) each scenario.
Supplemental Tables

Table I. Mean transport time in minutes to the nearest PSC, nearest CSC, and transfer from the PSC to its nearest CSC.

| County  | Time to nearest PSC | Time to nearest CSC | Transfer Time |
|---------|---------------------|---------------------|---------------|
| Travis  | 21.5 (SD = 11.3)    | 29.5 (SD = 15.5)    | 18.1 (SD = 10.1) |
| Bastrop | 39.8 (SD = 8.0)     | 46.5 (SD = 8.8)     | 30.8 (SD = 26.8) |

Table II. Percentage of the 13,000 simulated patients in each node that successfully reperfuse or do not reperfuse based on stroke type, transport strategy and treatment type. An LVO patient has a 74% chance of successful reperfusion with EVT, and a 20% chance of successful reperfusion with tPA.27

| LVO (n = 3900 patients), Mothership | Reperfuses with tPA | 0%     |
|------------------------------------|---------------------|--------|
|                                    | Reperfuses with EVT | 74.0%  |
|                                    | Does not reperfuse  | 26.0%  |

| LVO (n = 3900 patients), Drip and Ship | Reperfuses with tPA | 20.0%  |
|---------------------------------------|---------------------|--------|
|                                       | Reperfuses with EVT | 59.2%  |
|                                       | Does not reperfuse  | 20.8%  |

| Non-LVO (n = 9100), Mothership or Drip and Ship | Reperfuses with tPA | ‡ |
|--------------------------------------------------|---------------------|---|
|                                                 | Does not reperfuse  | ‡ |

‡ The probability of successful reperfusion with tPA for non-LVO patients is time-dependent.25
Figure I. Example distributions of Monte Carlo generated LVO ischemic penumbra volumes (I-A: $n_{LVO} = 3900$, mean: 115.2 mL, SD: 46.9 mL) and non-LVO ischemic penumbra volumes (I-B: $n_{non-LVO} = 9100$, mean: 69.9 mL, SD: 33.5 mL), sampled on the closed interval [10 mL, 220 mL]. These distributions are inputted into the time-dependent model of infarct core growth (Eqn. 1).
Figure II. There are four possible onset-to-treatment time pathways each consisting of pre-hospital, transport, and hospital time intervals. **II-A** shows the DNS pathway for a patient with an LVO that will reperfuse with EVT at the CSC. **II-B** shows the DNS pathway for non-LVO and LVO patients that will reperfuse with tPA at the PSC. **II-C** shows the MS pathway for LVO patients that will reperfuse with EVT at the CSC. **II-D** shows the MS pathway for non-LVO patients that will reperfuse with tPA at the CSC. The non-transport time intervals are defined in the presented model as: onset to departure from pickup location with EMS (t_{OTD}) = 60 minutes; door-to-needle (t_{DTN}) = 30 minutes; needle-to-door-out (t_{NTDO}) = 20 minutes; expedited door-to-puncture (t_{EDTP}) = 30 minutes; door-to-puncture (t_{DTP}) = 30 minutes. Transport times vary by node: transport time to PSC (t_{PSC}); transport time to CSC (t_{CSC}); transfer time from PSC to CSC (t_{PSC-CSC}). Total time for each pathway: **II-A** (t_{Treatment | LVO, DNS, EVT}) = 140 minutes + t_{PSC} + t_{PSC-CSC}.
CSC; **II-B** (Treatment | LVO/non-LVO, DNS, tPA) = 90 minutes + t\textsubscript{SC}; **II-C** (Treatment | LVO, MS, EVT) = 120 minutes + t\textsubscript{SC}; **II-D** (Treatment | non-LVO, MS, tPA) = 90 minutes + t\textsubscript{SC}. The DTN, DTP, and EDTP times are varied in the Sensitivity Analysis section.
Figure III. Figure 5 re-colored by the adapted, single-individual-based Cohen’s d effect size for Travis County. III-A assumes a fast rate of non-LVO infarct core growth, and III-B assumes a slow rate. This colormap has subtle differences from Figure 5 (mostly due to the inherent stochasticity of the simulations), but the relative magnitudes of effect size amongst each set of measurements are largely equivalent. As such, the figures yield similar interpretations – the MS transport strategy’s effective significance dissipates as the patient pickup locations become increasingly far from the CSCs.
Figure IV. In Bastrop County, under the assumption of a slow rate of non-LVO infarct core growth, the DNS transport strategy provides significantly better probabilities of a good outcome in more nodes of interest than MS (IV-A). However, a majority of the region does not statistically favor either transport strategy. IV-B is the corresponding effect size plot colored by the non-adapted Cohen’s d.
Figure V. Efficacy of Bastrop County bypass policies relative to the ideal threshold. Under the assumption of a fast rate of non-LVO infarct core growth \( (V-A) \), always going directly to the more distant CSC is optimal without LVO field testing. If a slow rate is assumed \( (V-B) \), then implementing any of the three field tests and always sending suspected LVO patients to the CSC is optimal.
Figure VI. Sensitivity analysis of hospital time interval parameters in Travis County, under the assumption of a fast (VI-A) or slow (VI-B) rate of non-LVO infarct core growth. The error bars reflect variation in simulation results due to the uncertainty in the outcome-volume relationship (Eqn. 2).
Figure VII. Sensitivity analysis of non-transport time interval parameters in Bastrop County, under the assumption of a fast (VII-A) or slow (VII-B) rate of non-LVO infarct core growth. The error bars reflect variation in simulation results due to the uncertainty in the outcome-volume relationship (Eqn. 2).