Journal of the American Heart Association

ORIGINAL RESEARCH

Geographical Requirements for the Applicability of the Results of the RACECAT Study to Other Stroke Networks

Florian A. F. Schuler, MD, PhD; Marc Ribó, MD; Nelly Dequatre-Ponchelle, MD; Jan Rémi, MD; Tomas Dobrocky, MD; Martina B. Goeldlin, MD; Jan Gralla, MD, MSc; Johannes Kaesmacher, MD; Thomas R. Meinel, MD; Pasquale Mordasini, MD; David J. Seiffge, MD; Urs Fischer, MD, MSc; Marcel Arnold, MD; Georg Kägi, MD; Simon Jung, MD

BACKGROUND: The RACECAT (Transfer to the Closest Local Stroke Center vs Direct Transfer to Endovascular Stroke Center of Acute Stroke Patients With Suspected Large Vessel Occlusion in the Catalan Territory) trial was the first randomized trial addressing the prehospital triage of acute stroke patients based on the distribution of thrombolysis centers and intervention centers in Catalonia, Spain. The study compared the drip-and-ship with the mothership paradigm in regions where a local thrombolysis center can be reached faster than the nearest intervention center (equipoise region). The present study aims to determine the population-based applicability of the results of the RACECAT study to 4 stroke networks with a different degree of clustering of the intervention centers (clustered, dispersed).

METHODS AND RESULTS: Stroke networks were compared with regard to transport time saved for thrombolysis (under the drip-and-ship approach) and transport time saved for endovascular therapy (under the mothership approach). Population-based transport times were modeled with a local instance of an openrouteservice server using open data from OpenStreetMap.The fraction of the population in the equipoise region differed substantially between clustered networks (Catalonia, 63.4%; France North, 87.7%) and dispersed networks (Southwest Bavaria, 40.1%; Switzerland, 40.0%). Transport time savings for thrombolysis under the drip-and-ship approach were more marked in clustered networks (Catalonia, 29 minutes; France North, 27 minutes) than in dispersed networks (Southwest Bavaria and Switzerland, both 18 minutes).

CONCLUSIONS: Infrastructure differences between stroke networks may hamper the applicability of the results of the RACECAT study to other stroke networks with a different distribution of intervention centers. Stroke networks should assess the population densities and hospital type/distribution in the temporal domain before applying prehospital triage algorithms to their specific setting.

Key Words: drip-and-ship ■ mothership ■ population-based ■ prehospital stroke triage ■ reperfusion therapy ■ stroke networks

See Editorial by Royan and Meurer.

With the introduction of time-critical reperfusion therapies for acute ischemic stroke, the prehospital phase of the treatment workflow with the organization of stroke care networks has become more important.[1] In the region around a thrombolysis center (TC) where transport times to TC are shorter than those to the nearest intervention center (IC, equipoise region), a prehospital triage policy is needed to

Correspondence to: Florian A. F. Schuler, MD, PhD, Department of Neurology, Inselspital, Bern University Hospital, University of Bern, CH-3010 Bern, Switzerland. Email: florianschuler@gmx.ch

This article was sent to Luciano A. Sposato, MD, MBA, FRCPC, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.123.029965

For Sources of Funding and Disclosures, see page 10.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Prehospital and interhospital modeled transport times are different in stroke networks depending on the degree of clustering of the intervention centers.

What Are the Clinical Implications?

- Stroke networks should assess the population densities and hospital type/distribution in the temporal domain before applying prehospital triage algorithms to their specific setting.
- The methods can be transferred to networks of treating cardiac infarction.

Nonstandard Abbreviations and Acronyms

EVT	endovascular therapy
IC	intervention center
TC	thrombolysis center

guide the patients to the right hospital without unnecessary delays if a large-vessel occlusion is suspected.[2] In this equipoise region, it is not clear whether the mothership paradigm with the shorter time delay to endovascular therapy (EVT) is better or the drip-and-ship paradigm[3] with the shorter time delay to intravenous thrombolysis.

Several modeling studies aiming to improve the prehospital triage of patients with a suspected acute stroke were either performed in an abstracted scenario[4–9] or with actual transport times, either from coordinates or from actual stroke patients.[10–20] Some studies employ a population-based strategy incorporating also detailed population census.[21–26] However, these studies are restricted to the additional time to an IC as compared with the TC. These time differences are the transport time savings for intravenous thrombolysis, whereas the transport time savings for EVT, which incorporates also the time of the secondary transfer from the TC to the IC, are underrepresented in these studies. In addition, these heterogeneous modeling studies were not able to answer the question of ideal triage in the equipoise region due to their study designs.

The first randomized controlled trial comparing the mothership with the drip-and-ship approach in patients in the equipoise region and with suspected large vessel occlusion (Rapid Arterial Occlusion Evaluation score >4) has been conducted in the stroke network of Catalonia (RACECAT [Transfer to the Closest Local Stroke Center vs Direct Transfer to Endovascular Stroke Center of Acute Stroke Patients With Suspected Large Vessel Occlusion in the Catalan Territory] study).[27] In the RACECAT study, no differences were found in the outcome between the mothership and drip-and-ship approach.[28]

Because the results of the RACECAT study are based on the individual regional distribution of TCs and ICs in Catalonia and because of different arrangements/layout of the ICs and TCs, it remains unknown whether the triage of patients with suspected large vessel occlusion by the Rapid Arterial Occlusion Evaluation score can be directly applied to other stroke networks or whether the same randomized controlled trial would have had positive results in other networks where ICs are geographically more distributed. Indeed, the clustering of ICs has been discussed before in King County in the state of Washington, where all ICs are clustered near Seattle.[22] In the assumption that with appropriate measures, the variables of in-hospital workflow (Figure 1) can potentially be harmonized, the transport times remain a critical time variable due to the different road infrastructure that cannot easily be modified.

Therefore, the aim of this study was to analyze the potential impact of different regional network distributions of TCs and ICs on the population-based transportation times in 4 well-known stroke networks. The critical measures for the transferability of the results are the fraction of the population in the equipoise region and the population density distribution in the temporal domain.

METHODS

In this study, we compared transport metrics in communes of 4 different stroke networks based on transport time measurements to the nearest TC and IC in different logistic strategies. Transport metrics were weighted by the proportion of the inhabitants living in the respective commune. Primary outcome measure was the fraction of the population in the equipoise region. Secondary outcome measures were the transport time savings in the drip-and-ship and in the mothership approach.

The authors declare that all supporting geographical and demographic data are available as open data in the following sources and that all further information is available within the article and its online supplementary files. Cartographic information and population statistics were downloaded from publicly available databases from official institutions (Institut Cartogràfic i Geològic de Catalunya, Dades obertes, Generalitat de Catalunya, Spain; statistical office of the European Union Eurostat, Institut national de la statistique et des études économiques, France; Landesamt für Digitalisierung,

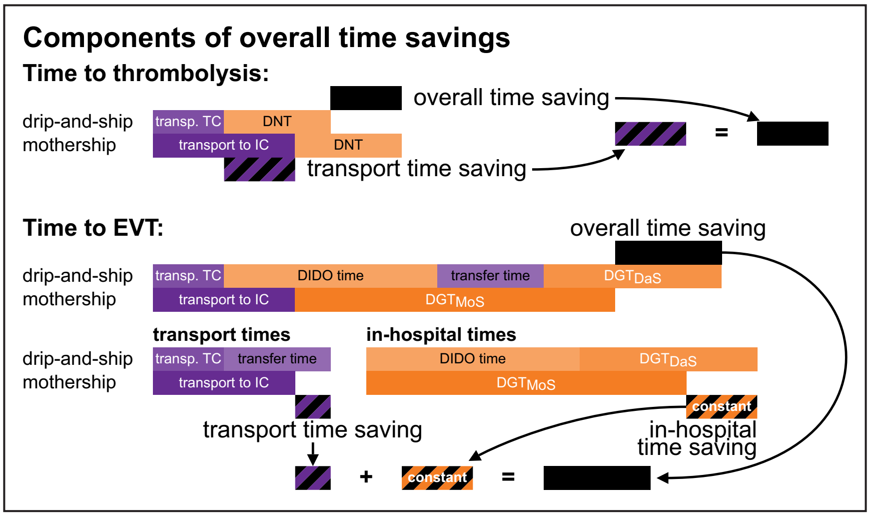

Figure 1. Components of the overall time savings.

For thrombolysis, the overall time saving (black) is the same as the transport time saving (hatched purple). For EVT, the overall time saving can be split into the transport time saving (hatched purple) and the in-hospital time saving (hatched orange). Note that the door-to-groin time in the drip-and-ship approach is shorter than in the mothership approach because of the preannouncement and the potential withholding from a repeat imaging.[3,34] In this study, we assessed the transport time saving in detail and assumed a constant in-hospital time saving. DaS indicates drip-and-ship; DGT, door-to-groin time; DIDO time, door-in-door-out time; DNT, door-to-needle time (assumed to be the same in TC and in IC); EVT, endovascular therapy; IC, intervention center; MoS, mothership; and TC, thrombolysis center. In stroke networks where the DNT in ICs differs from the DNT in TCs, an analog hatched orange bar can be defined for the time to thrombolysis.

Breitband und Vermessung, Bavaria, Bayerisches Landesamt für Statistik, Germany; Federal Statistical Office, ThemaKart 2020, Switzerland). To determine transport times, a local instance of an openrouteservice server (HeiGIT gGmbH at Heidelberg University, Germany) was run based on data from OpenStreetMap downloaded from geofabrik.de. The assumed velocities can be found in Table S1. The 2 referral paradigms drip-and-ship and mothership approach were assessed.

The entire population of 4 stroke networks was assessed. In 2 stroke networks (Catalonia, Spain; France North, France), ICs are geographically clustered (clustered stroke network), whereas in the other 2 stroke networks (Southwest Bavaria, Germany[29]; Switzerland), ICs are geographically distributed (dispersed stroke network). The limits of the stroke networks (Data S1) were defined restrictively to avoid a scenario in which a part of the population has a faster transport time to an external TC or IC.

Hospitals with round-the-clock availability of imaging and thrombolysis were classified as TCs, irrespective of the fact whether there is a certified stroke unit in the same hospital or not. Some of them provide acute neurological care in a telemedicine setting. Hospitals with additional round-the-clock availability of EVT were classified as ICs, irrespective of the certification status. To allow a conclusion about the applicability of the RACECAT study results, other factors such as the certification status of a hospital or triage protocols/hospital alliances were not accounted for.

The degree of clustering in the stroke networks was assessed with the average nearest neighbor (ANN) index.[30] For compatibility with the area in km^2, the distance of the nearest neighbor was determined in airline distance. The ANN index is the ratio between the ANN and the expected mean distance in a random pattern, $\frac{0.5}{\sqrt{\frac{n}{A}}}$, where n is the number of ICs, and A is the area of the stroke network, neglecting border effects of the irregular shaped regions.[30] The cutoff of the ANN index is 1 (complete spatial randomness). An ANN index of 0 to 1 indicates a clustered pattern, whereas an ANN>1 indicates a more dispersed pattern than complete spatial randomness. If there is only 1 IC (France North), the ANN index is undefined.

Transport times were determined on road from each commune (centroid, provided in the publicly available database) to each TC and each IC in the stroke network to determine the nearest TC and the nearest IC. In this article, the terms nearest TC and nearest IC are used for the shortest transportation time, not for the spatial distance. Furthermore, for each TC, the corresponding IC was defined as the one with the shortest secondary (interfacility) transport time. The nearest IC of a commune did not need to be the same as the one corresponding to the nearest TC, as depicted in the example in Figure 2 on the right side of panel A. Air transportation was not considered because it depends on availability and weather conditions (for discussion of the drip-and-drive paradigm see Discussion).

Statistical Analysis

As a sensitivity analysis and to assess the error introduced by the assumption that the population resides in the centroid of each commune, all 145 private addresses in the Swiss telephone directory of all 12 combinations of the 4 common first names Eva, Ines, Francesco, and Mauro with the 3 common last names Müller, Schmid, and da Silva were retrieved. The 3 last names were selected because they are the only ones in the top 100 in each of the 4 language region of Switzerland to ensure coverage of all language regions. For selecting the 4 first names the normalized dot-product of the name frequency per age (resolution 1 year) with the whole population per age (resolution 1 year) was assessed to ensure coverage of all age classes. The 2 selected female names and the 2 selected male names had the highest normalized dot-product, respectively, all >0.95. Hence,

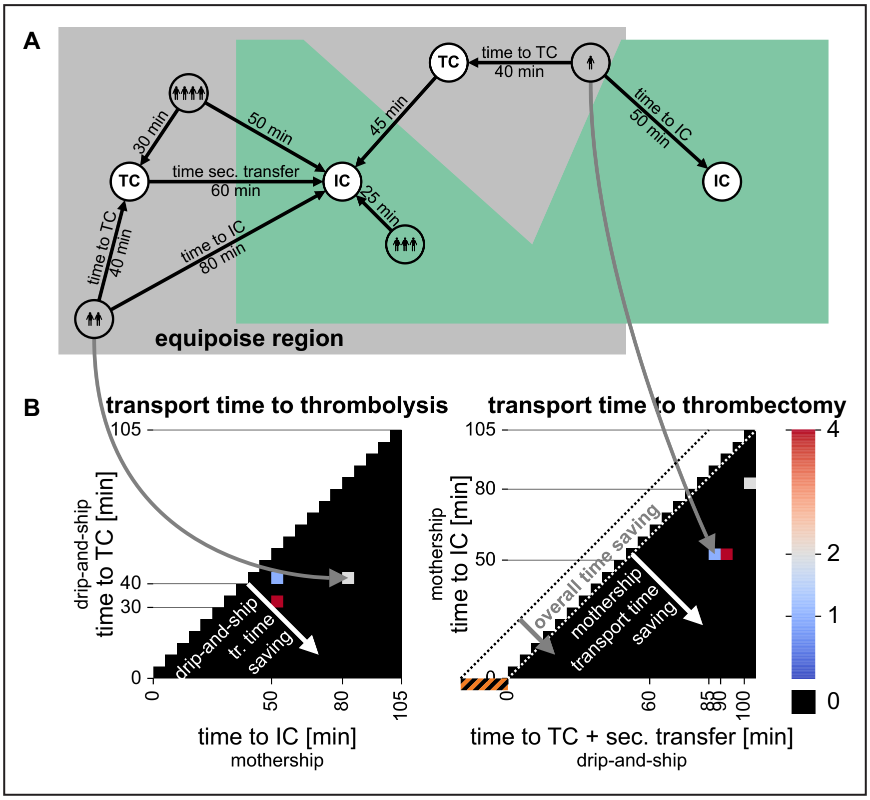

Figure 2. Explanation of the approach of the population-based transport time assessment and the population density in the temporal domain through a schematic imaginary stroke network with 2 TCs, 2 ICs, and 10 individuals living distributed across 4 communes of 1, 2, 3, and 4 inhabitants.

A, Temporospatial plane with schematic layout of the simplified imaginary stroke network of 2 TCs and 2 ICs, with 4 communes. Transport times are plotted as distance in the figure. Gray shading, equipoise region where a TC can be reached faster than the nearest IC. Green shading, region where an IC can be reached faster than any TC. Arrows, routing for reperfusion therapies. Note that the drip-and-ship approach and the mothership approach can end in 2 different ICs, as in the right part of the panel. **B**, Population densities in the temporal domain for the population in panel A. Left, transport time to thrombolysis with time to IC (mothership approach) vs time to TC (drip-and-ship approach). Right, transport time to EVT with time to TC+time of the secondary transfer (drip-and-ship approach) vs time to IC (mothership approach). Note that the commune with a population of 3 is not represented in panel B because it is not located in the equipoise region. The hatched orange bar is the in-hospital time saving, same as in Figure 1. The plots in panel B can also be read along the diagonal depicted with the gray and white arrows. When reading along the diagonal depicted with the white arrow, it becomes clear that for the population of 2 (white), the transport time saving for thrombolysis under the drip-and-ship approach (left subpanel) is larger than the transport time saving for EVT under the mothership approach (right subpanel). This asymmetry in time saving is inverse for the population of 4 (red). EVT indicates endovascular therapy; IC, intervention center; and TC, thrombolysis center.

these first names are popular across all age categories. Of the 145 addresses in the telephone directory, 62 were in the equipoise region. Median driving time from these 62 addresses to the centroid of the respective commune was 2.9 minutes (2.1–4.2 minutes, interquartile range) as determined with GraphHopper Routing Engine.

Time definitions are depicted in Figure 1. Time saving for thrombolysis under the drip-and-ship approach was defined as the time to the IC—time to the TC. Time saving for EVT under the mothership approach was defined as the time to the TC+transport time of the secondary transfer—time to the IC. For the population-based assessments, all transport times and time savings were weighted with the number of the population with residence in the considered commune. Time bins for histograms were 5 minutes. Analyses were carried out in Python.

The study did not use individual patient data and, therefore, there was no need for approval by an ethics committee or informed consent.

RESULTS

The main results are listed in the Table. In the 4 stroke networks, a total of 28 ICs and 70 TCs were identified. The stroke networks displayed a broad range of geographical clustering of ICs. In the dispersed stroke networks (Southwest Bavaria, Switzerland), the ANN index was above the cutoff value of 1, in contrast to clustered stroke networks (Catalonia, ANN index <1; France North, only 1 IC). The fraction of the population in the equipoise region was higher in the clustered stroke networks than in the dispersed stroke networks. The stroke network maps and the population densities in the temporal domain can be found in Figure 3 (Catalonia), Figure S1 (France North), Figure S2 (Southwest Bavaria), and Figure 4 (Switzerland).

When comparing the population-based transport times in all 4 stroke networks (Figure 5), the stroke network of Catalonia had the largest transport times to an IC, whereas Switzerland had the largest transport times to a TC. In the analysis of transport time savings, the clustered stroke networks (Catalonia, France North) had larger time savings for thrombolysis under the drip-and-ship approach than the dispersed stroke networks (Southwest Bavaria, Switzerland). This difference was evident over a wide range of transport times in the population density in the temporal domain (Figures 3C and 4C). In contrast, transport time savings for EVT under the mothership approach were similar in all assessed stroke networks (Figure 5).

DISCUSSION

In the population-based assessment of transport times at commune resolution, the comparison of clustered stroke networks (Catalonia, France North) and dispersed stroke networks (Southwest Bavaria, Switzerland) revealed marked differences with regard to time delays or time savings until treatment. First, the percentage of the population living in the equipoise region was higher in clustered stroke networks; thus the results of the RACECAT study are applicable to a larger part of the population in these networks. Second, transport time savings for thrombolysis under the drip-and-ship approach were more marked in clustered stroke networks. In contrast, transport time savings for EVT under the mothership approach were similar in all assessed stroke networks.

The larger transport time savings for thrombolysis due to the clustering of ICs may have a major effect on a randomized trial between the mothership and the drip-and-ship approach or even may be the main reason why the superiority end point in the RACECAT study was not met. Hence, it is uncertain whether the results of the RACECAT trial are applicable to stroke networks with geographically distributed ICs, where the benefits of the mothership approach would be arguably more pronounced. In the stroke network of Denmark, where another randomized trial is being performed (TRIAGE-STROKE [Treatment Strategy in Acute Large Vessel Occlusion: Prioritize IV or Endovascular Treatment]), ICs are indeed geographically more distributed.[31]

In previous population-based studies with actual transport times[21–26] the assessment of the transport time savings was often limited to the additional time to an IC as compared with the TC. This time saving represents the time saving for thrombolysis under the drip-and-ship approach. Our study includes the calculation of transport time savings for EVT under the mothership approach, which takes into account also the transport time of the secondary (interfacility) transfer, because the effect of the time savings for EVT on stroke outcome is large.[32,33] In addition, we decided to weight all transport times with the actual population living there (population-based analysis) because it reflects timely access to acute stroke therapies most accurately. Because the elapsed time before the reperfusion therapy is the critical measure, not the geographical/spatial domain, we chose the temporal domain for the assessment of the population density. This temporal domain is relevant for the applicability of the results of the randomized study RACECAT to other stroke networks. The time savings for thrombolysis were similar in our study and in the RACECAT study.[28]

The clustering of IC should not be viewed as a dichotomized feature but as a continuum based on the temporal population densities, quantified by the ANN index. Hence, our study results are relevant for all stroke networks.

For the interpretation of our results and comparison with observational data it has to be kept in mind that

Table. Comparative Features of 4 Stroke Networks

Stroke network	Catalonia	France North	Southwest Bavaria	Switzerland
Area	32 100 km^2	12 400 km^2	21 800 km^2*	40 200 km^2†
Number of communes	947	1539	688*	2202
Number of ICs	6	1	11	10
Number of TCs	22	15	18	15
Figure number	3	S1	S2	4
Number of ICs in a cluster	6 (Barcelona/Badalona)	Only IC located in Lille	5 (Munich)	2 (Zurich)
Average nearest neighbor between ICs	4.8 km	Undefined	26.7 km	48.5 km
Average nearest neighbor ratio (index, spatial clustering)	0.13	Undefined	1.20	1.53
Population-based transport time analysis				
Total population	7 675 217	4 072 977	5 587 693	8 606 033
Population in the equipoise region	4 862 801 (63.4%)	3 573 106 (87.7%)	2 241 106 (40.1%)	3 442 482 (40.0%)
Equipoise region				
Maximum population density for thrombolysis time saving (panel C of Figures 3 and 4, Figures S1 and S2)	20–24.9 min to IC and 10–14.9 min to TC	20–24.9 min to IC and 5–9.9 min to TC	30–34.9 min to IC and 20–24.9 min to TC	25–29.9 min to IC and 0–4.9 min to TC
Maximum population density for EVT time saving (panel D of Figures 3 and 4; Figures S1 and S2)	25–29.9 min total transport to IC and 20–24.9 min direct transport to IC	45–49.9 min total transport to IC and 40–44.9 min direct transport to IC	40–44.9 min total transport to IC and 35–39.9 min direct transport to IC	30–34.9 min total transport to IC and 25–29.9 min direct transport to IC
Median time to the nearest IC (column 1 of Figure 5)	46.2 min (25.6–71.9 min, IQR)	41.1 min (28.1–56.8 min, IQR)	35.0 min (27.5–42.7 min, IQR)	39.2 min (29.8–53.6 min, IQR)
Median time to the nearest TC (column 2 of Figure 5)	15.3 min (5.9–21.5 min, IQR)	13.6 min (9.1–19.9 min, IQR)	18.9 min (12.0–23.3 min, IQR)	21.0 min (13.4–30.5 min, IQR)
Median total transport time to the corresponding IC of the nearest TC (column 3 of Figure 5)	55.0 min (39.0–87.4 min, IQR)	52.7 min (41.3–72.8 min, IQR)	51.9 min (43.4–59.6 min, IQR)	57.6 min (45.9–74.4 min, IQR)
Median saved time for thrombolysis under the drip-and-ship approach (column 4 of Figure 5)	29.0 min (13.7–55.1 min, IQR)	26.7 min (15.7–38.8 min, IQR)	17.5 min (9.1–25.6 min, IQR)	17.6 min (8.7–31.7 min, IQR)
Median saved time for EVT under the mothership approach (column 5 of Figure 5)	9.8 min (5.7–18.6 min, IQR)	10.4 min (6.0–17.8 min, IQR)	13.3 min (7.7–22.3 min, IQR)	13.1 min (8.0–23.2 min, IQR)

Comparative features of 4 stroke networks: Catalonia, France North, Southwest Bavaria, and Switzerland. See also Data S1 for definitions. EVT indicates endovascular therapy; IC, intervention center; IQR, interquartile range; and TC, thrombolysis center.

*Including 359 km^2 in 20 backcountry areas ("gemeindefreie Gebiete").

†Excluding major lakes.

the overall transport time saving for EVT also has an in-hospital component (Figure 1). This may be a reason for the time saving for EVT of 91 minutes in the multicenter observational study STRATIS (Systematic Evaluation of Patients Treated With Stroke Devices for Acute Ischemic Stroke).[34] Differences in time savings may also be due to different geographical settings and to different means of transport. In particular, time delays due to long door-in-door-out times may hamper the benefit of the drip-and-ship approach in networks with geographically distributed ICs. Also, the heterogeneity of the equipoise regions in our study challenges a fixed triage according to the drip-and-ship or the mothership approach and favors an individual approach according to the saved transport times in consideration also of individual clinical characteristics. Here, it also has to be considered that the population in the equipoise region is potentially vulnerable to mistakes in triage choice and that this population is larger in the clustered scenario of ICs.

Several modeling studies aiming to improve the prehospital triage of patients with a suspected acute stroke were performed in an abstract spatiotemporal scenario.[4–9] To make these abstract models more realistic, our data of the transport times can be taken as a source of population-based data to improve the validity of the modeling studies in an abstract spatiotemporal scenario.

Our study assessed the referral paradigms of the drip-and-ship and the mothership approach in the

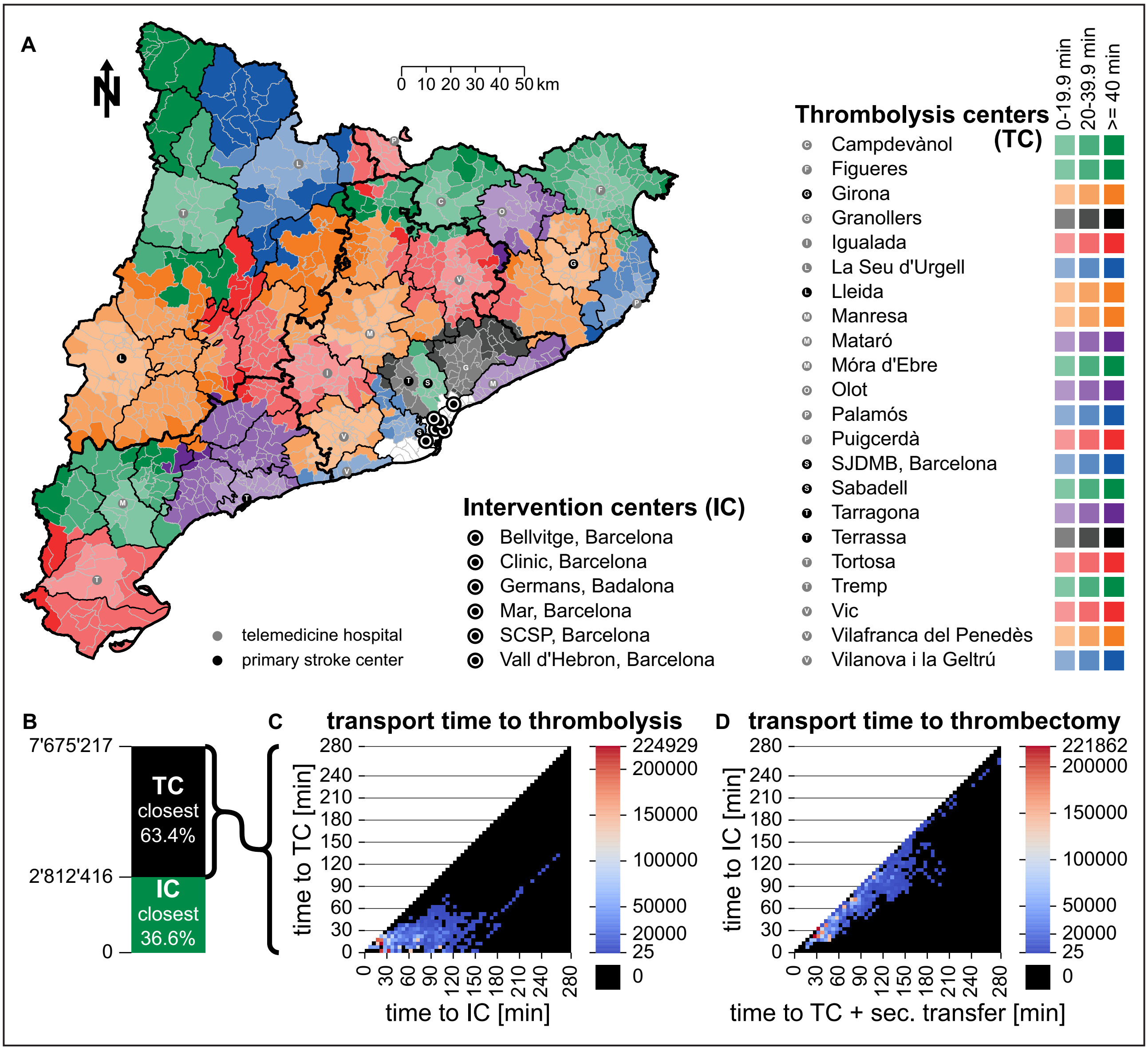

Figure 3. Population-based analysis of transport times in the stroke network of Catalonia, Spain.
A, Map of the municipalities (communes) in the stroke network. The 6 ICs are clustered in Barcelona/Badalona, whereas the 22 TCs are geographically distributed. The transport times to the nearest TC are indicated with colors for the equipoise region only (region where transport to a TC is shorter than to an IC). **B**, Proportion of the population in the equipoise region. **C**, Population density in the temporal domain for the transport time to thrombolysis (time to IC for the mothership approach vs time to TC for the drip-and-ship approach). **D**, Population density in the temporal domain for the transport time to EVT (time to TC+secondary transfer for the drip-and-ship approach vs time to IC for the mothership approach). For panels (**C** and **D**), only the equipoise region was analyzed. EVT indicates endovascular therapy; IC, intervention center; and TC thrombolysis center. Map derived from Cartographic and Geological Institute of Catalonia (ICGC), Spain.

same way as in the RACECAT study. However, the calculated transport times can be used also for the mobile stroke unit[35] and for the drip-and-drive paradigm, where the transport directions simply are in opposite direction (from the IC to the TC).

Several limitations of our study need to be considered. First, the analysis is limited to ground transportation. Also in several other studies, only ground transportation is accounted for.[25] Particularly for the areas with the longest time to TC in Switzerland, helicopter is often the preferred option, as long as environmental conditions allow it. Second, time from ambulance dispatch until arrival at scene is not considered. Third, our analysis is not valid for urban regions where TCs and ICs are mixed because in the large cities in our study, there are only ICs. Fourth, the results may not be valid for stroke networks in other countries. For instance, in the United States transport times are

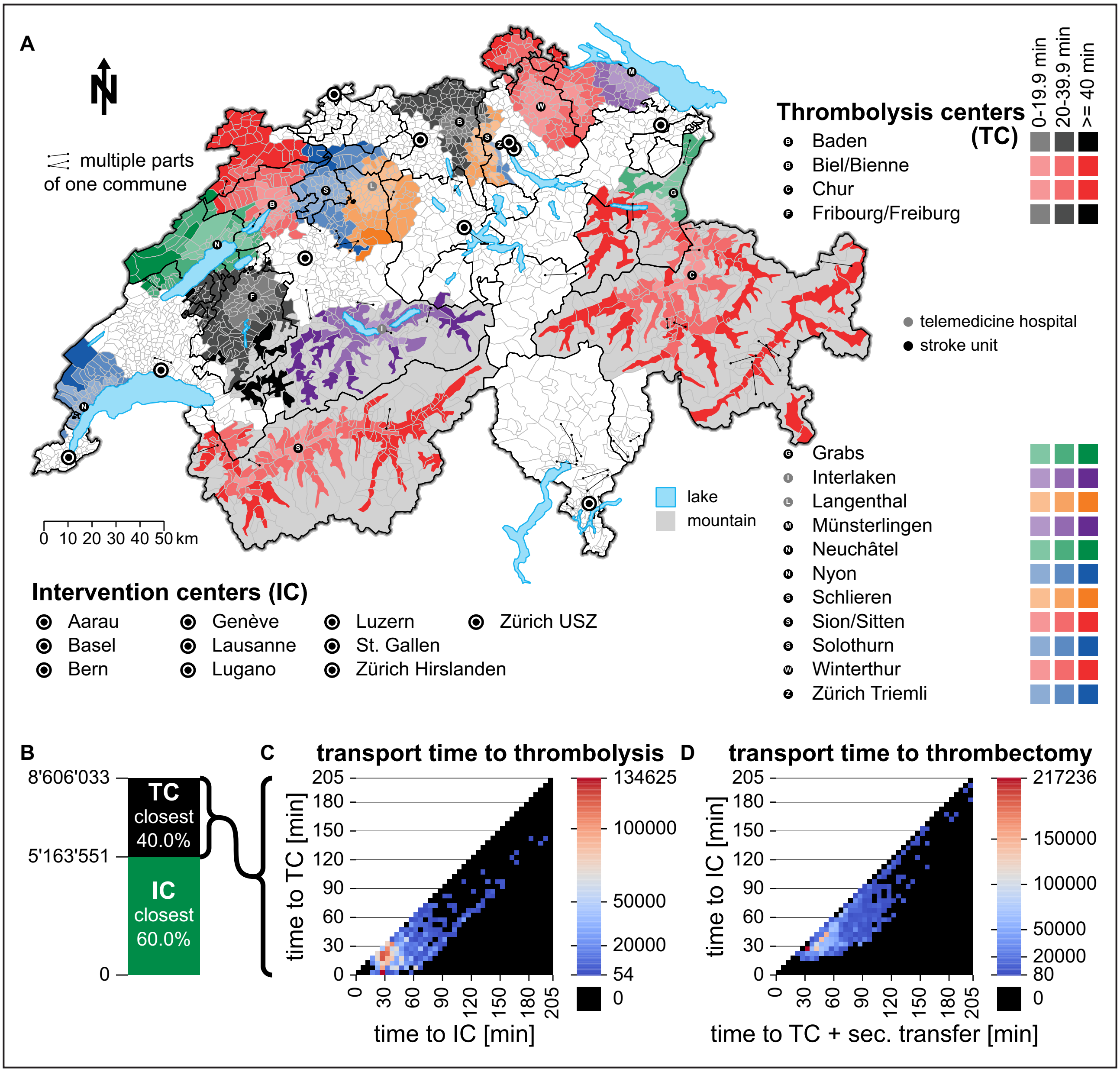

Figure 4. Population-based analysis of transport times in the stroke network of Switzerland.
A, Map of the communes in the stroke network. The 10 ICs and the 15 TCs are geographically distributed with the exception of a cluster in Zurich. Rest (**B–D**) as in Figure 3. Note different time scales in panels (**C** and **D**) than in Figure 3. Map derived from Federal Statistical Office, Switzerland. IC indicates intervention center; and TC thrombolysis center.

outside the range of transport times we assessed in our analysis.[26] Fifth, situational traffic delays[11] were not accounted for in our study. Sixth, only the number of the population in general is considered, not the population at high risk of stroke and nonresidents suffering a stroke in the region of the stroke network. Seventh, we did not assess overcrowding at the IC due to overtriage. However, our data serve as a foundation for well-designed triage policies.

Our study has several strengths. First, it is a population-based study. Second, it is independent of assumptions on delays of in-hospital workflow. Third, it is independent of time windows for time-critical reperfusion therapies, a changing concept. Fourth, the population densities in the temporal domain can also be used for the drip-and-drive paradigm (discussed previously). Fifth, commune resolution in our study was important to make sure that granularity is fine enough to match with the population statistics. Sixth, it is independent of a prehospital clinical score to predict large-vessel occlusion, although prehospital scores can help triage decisions. Seventh,

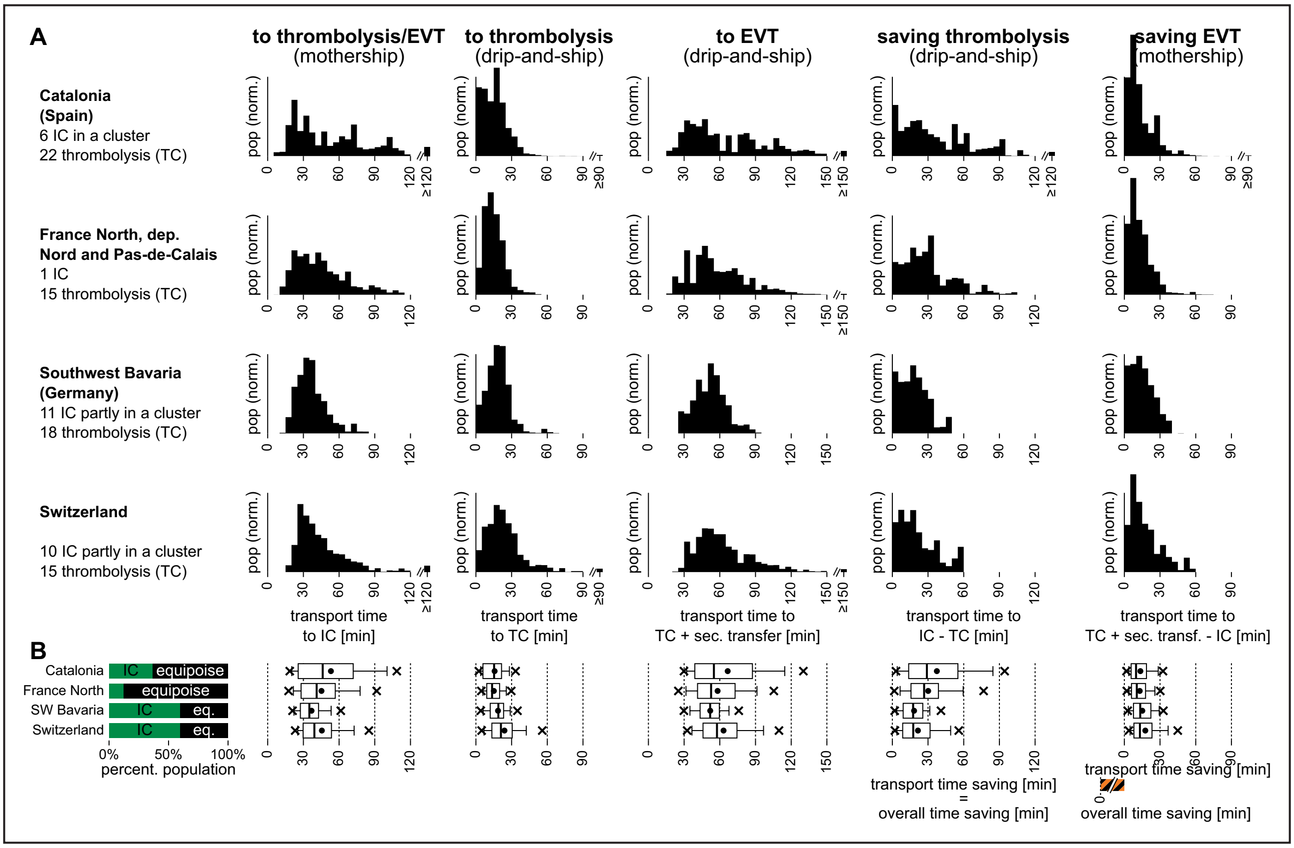

Figure 5. Direct comparison of the transport times and transport time savings in 4 stroke networks.
A, Normalized histograms of the population in the equipoise region. In columns 1 to 3, transport times are assessed. In columns 4 and 5, the transport time savings of the drip-and-ship or the mothership approach are depicted. In addition to the transport time savings, the overall time saving for EVT under the mothership approach also incorporates the door-in-door-out time, but the time difference in the door-to-groin time for the drip-and-ship vs mothership approach must be subtracted (hatched orange bar). **B**, Percentage of the population living in the equipoise region (same data as in panel B of Figures 3 and 4; Figures S1 and S2). Boxplots of the population in the equipoise region in the same column and scale as in **A**. Boxes denote median and interquartile range. Whiskers denote the 10th and 90th percentiles. Crosses denote the 5th and 95th percentiles. Dots denote the mean. Transport times to ICs are longest in the stroke network Catalonia, whereas transport times to TCs are longest in Switzerland. The time savings for thrombolysis under the drip-and-ship approach are largest in the stroke networks Catalonia and France North (clustered stroke networks), compared with the stroke networks Southwest Bavaria and Switzerland (dispersed stroke networks). In contrast, the time savings for EVT were similar in all 4 stroke networks. Hatched bar, the in-hospital time saving as defined in Figure 1, must be added to the transport time saving to obtain the overall time saving. EVT indicates endovascular therapy; IC, intervention center; and TC thrombolysis center.

the study is based on the open-source software OpenStreepMap and independent of proprietary software.

CONCLUSIONS

Our quantitative population-based data show that the infrastructure differences in the stroke networks may hamper the applicability/generalizability of the results of the RACECAT study to stroke networks without a marked clustering of ICs. We suggest that stroke networks assess the population densities and hospital type/distribution in the temporal domain before implementing the results of the RACECAT study in their territory. In addition, the results of another randomized trial (TRIAGE-STROKE), which is performed in Denmark,[31] will deliver further evidence for optimal patient triage.

ARTICLE INFORMATION

Received February 23, 2023; accepted August 11, 2023.

Affiliations

Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Switzerland (F.A.F.S., M.B.G., T.R.M., D.J.S., U.F., M.A., G.K., S.J.); Stroke Unit, Department of Neurology, Vall d'Hebron University Hospital, Barcelona, Spain (M.R.); LilNCog—Lille Neuroscience & Cognition, Univ. Lille, CHU Lille, INSERM, U1172, Lille, France (N.D.-P.); Department of Neurology, University Hospital, Ludwig-Maximilians-University, Munich, Germany (J.R.); Institute of Diagnostic and Interventional Neuroradiology, Inselspital, Bern University Hospital, University of Bern, Switzerland (T.D., J.G., J.K., P.M.); Network Radiology, Kantonsspital St. Gallen, St. Gallen, Switzerland (P.M.); Department of Neurology, University Hospital Basel, University of Basel, Switzerland (U.F.); and Department of Neurology, Kantonsspital St. Gallen, St. Gallen, Switzerland (G.K.).

Sources of Funding

None.

Disclosures

M.G. has received grants from the Swiss Academy of Medical Sciences/Bangerter-Rhyner-Foundation, Swiss Stroke Society, and Mittelbauvereinigung der Universität Bern as well as a congress grant from Pfizer, not related to this project. J.G. reports being global co-principal investigator of the STAR Study, NCT01327989; consultancy Medtronic; global co-principal investigator of SWIFT DIRECT, NCT03192332; consultancy Medtronic; principal investigator: Stroke treatment goes personalized: Gaining added diagnostic yield by computer-assisted treatment selection (the STRAY-CATS project), Swiss National Funds 170060. J.K. reports grants from the Swiss Academy of Medical Sciences/Bangerter Foundation, Swiss Stroke Society, and Clinical Trials Unit Bern during the conduct of the study. T.R.M. reports grants from the Swiss Academy of Medical Sciences/Bangerter Foundation, Swiss National Science Society, and Swiss Heart Foundation during the conduct of the study. U.F. reports research grants from Medtronic for the SWIFT DIRECT trial and BEYOND SWIFT registry, Swiss National Science Foundation, Swiss Heart Foundation; consulting fees from Medtronic, Stryker, and CSL Behring (fees paid to institution); membership of a Data Safety Monitoring Board for the IN EXTREMIS trial and TITAN trial and Portola (Alexion), advisory board (fees paid to institution); and vice presidency of the Swiss Neurological Society. The remaining authors have no disclosures to report.

Supplemental Material

Data S1
Table S1
Figures S1–S2

REFERENCES

1. Fassbender K, Walter S, Grunwald IQ, Merzou F, Mathur S, Lesmeister M, Liu Y, Bertsch T, Grotta JC. Prehospital stroke management in the thrombectomy era. *Lancet Neurol*. 2020;19:601–610. doi: 10.1016/S1474-4422(20)30102-2
2. Jauch EC, Schwamm LH, Panagos PD, Barbazzeni J, Dickson R, Dunne R, Foley J, Fraser JF, Lassers G, Martin-Gill C, et al. Recommendations for regional stroke destination plans in rural, suburban, and urban communities from the Prehospital Stroke System of Care Consensus Conference: a consensus statement from the American Academy of Neurology, American Heart Association/American Stroke Association, American Society of Neuroradiology, National Association of EMS Physicians, National Association of State EMS Officials, Society of NeuroInterventional Surgery, and Society of Vascular and Interventional Neurology: endorsed by the Neurocritical Care Society. *Stroke*. 2021;52:e133–e152. doi: 10.1161/STROKEAHA.120.033228
3. Shah S, Xian Y, Sheng S, Zachrison KS, Saver JL, Sheth KN, Fonarow GC, Schwamm LH, Smith EE. Use, temporal trends, and outcomes of endovascular therapy after interhospital transfer in the United States. *Circulation*. 2019;139:1568–1577. doi: 10.1161/CIRCULATIONAHA.118.036509
4. Holodinsky JK, Williamson TS, Kamal N, Mayank D, Hill MD, Goyal M. Drip and ship versus direct to comprehensive stroke center: conditional probability modeling. *Stroke*. 2017;48:233–238. doi: 10.1161/STROKEAHA.116.014306
5. Schlemm E, Ebinger M, Nolte CH, Endres M, Schlemm L. Optimal transport destination for ischemic stroke patients with unknown vessel status: use of prehospital triage scores. *Stroke*. 2017;48:2184–2191. doi: 10.1161/STROKEAHA.117.017281
6. Benoit JL, Khatri P, Adeoye OM, Broderick JP, McMullan JT, Scheitz JF, Vagal AS, Eckman MH. Prehospital triage of acute ischemic stroke patients to an intravenous tPA-ready versus endovascular-ready hospital: a decision analysis. *Prehosp Emerg Care*. 2018;22:722–733. doi: 10.1080/10903127.2018.1465500
7. Venema E, Lingsma HF, Chalos V, Mulder M, Lahr MMH, van der Lugt A, van Es A, Steyerberg EW, Hunink MGM, Dippel DWJ, et al. Personalized prehospital triage in acute ischemic stroke. *Stroke*. 2019;50:313–320. doi: 10.1161/STROKEAHA.118.022562
8. Xu Y, Parikh NS, Jiao B, Willey JZ, Boehme AK, Elkind MSV. Decision analysis model for prehospital triage of patients with acute stroke. *Stroke*. 2019;50:970–977. doi: 10.1161/STROKEAHA.118.023272
9. Schlemm L, Endres M, Nolte CH. Bypassing the closest stroke center for thrombectomy candidates: what additional delay to thrombolysis is acceptable? *Stroke*. 2020;51:867–875. doi: 10.1161/STROKEAHA.119.027512
10. Milne MS, Holodinsky JK, Hill MD, Nygren A, Qiu C, Goyal M, Kamal N. Drip 'n ship versus mothership for endovascular treatment: modeling the best transportation options for optimal outcomes. *Stroke*. 2017;48:791–794. doi: 10.1161/STROKEAHA.116.015321
11. Phan TG, Beare R, Chen J, Clissold B, Ly J, Singhal S, Ma H, Srikanth V. Googling service boundaries for endovascular clot retrieval hub hospitals in a metropolitan setting: proof-of-concept study. *Stroke*. 2017;48:1353–1361. doi: 10.1161/STROKEAHA.116.015323
12. Katz BS, Adeoye O, Sucharew H, Broderick JP, McMullan J, Khatri P, Widener M, Alwell KS, Moomaw CJ, Kissela BM, et al. Estimated impact of emergency medical service triage of stroke patients on comprehensive stroke centers: an urban population-based study. *Stroke*. 2017;48:2164–2170. doi: 10.1161/STROKEAHA.116.015971
13. Allen M, Pearn K, Villeneuve E, Monks T, Stein K, James M. Feasibility of a hyper-acute stroke unit model of care across England: a modelling analysis. *BMJ Open*. 2017;7:e018143. doi: 10.1136/bmjopen-2017-018143
14. Parikh NS, Chatterjee A, Diaz I, Pandya A, Merkler AE, Gialdini G, Kummer BR, Mir SA, Lerario MP, Fink ME, et al. Modeling the impact of interhospital transfer network design on stroke outcomes in a large city. *Stroke*. 2018;49:370–376. doi: 10.1161/STROKEAHA.117.018166
15. Mullen MT, Pajerowski W, Messe SR, Mechem CC, Jia J, Abboud M, David G, Carr BG, Band R. Geographic modeling to quantify the impact of primary and comprehensive stroke center destination policies. *Stroke*. 2018;49:1021–1023. doi: 10.1161/STROKEAHA.118.020691
16. Holodinsky JK, Patel AB, Thornton J, Kamal N, Jewett LR, Kelly PJ, Murphy S, Collins R, Walsh T, Cronin S, et al. Drip and ship versus direct to endovascular thrombectomy: the impact of treatment times on transport decision-making. *Eur Stroke J*. 2018;3:126–135. doi: 10.1177/2396987318759362
17. Ali A, Zachrison KS, Eschenfeldt PC, Schwamm LH, Hur C. Optimization of prehospital triage of patients with suspected ischemic stroke. *Stroke*. 2018;49:2532–2535. doi: 10.1161/STROKEAHA.118.022041
18. Holodinsky JK, Williamson TS, Demchuk AM, Zhao H, Zhu L, Francis MJ, Goyal M, Hill MD, Kamal N. Modeling stroke patient transport for all patients with suspected large-vessel occlusion. *JAMA Neurol*. 2018;75:1477–1486. doi: 10.1001/jamaneurol.2018.2424
19. Venema E, Groot AE, Lingsma HF, Hinsenveld W, Treurniet KM, Chalos V, Zinkstok SM, Mulder M, de Ridder IR, Marquering HA, et al. Effect of interhospital transfer on endovascular treatment for acute ischemic stroke. *Stroke*. 2019;50:923–930. doi: 10.1161/STROKEAHA.118.024091
20. Phan TG, Beare R, Srikanth V, Ma H. Googling service boundaries for endovascular clot retrieval (ECR) hub hospitals in metropolitan Sydney. *Front Neurol*. 2019;10:708. doi: 10.3389/fneur.2019.00708
21. Mullen MT, Branas CC, Kasner SE, Wolff C, Williams JC, Albright KC, Carr BG. Optimization modeling to maximize population access to comprehensive stroke centers. *Neurology*. 2015;84:1196–1205. doi: 10.1212/WNL.0000000000001390
22. Bogle BM, Asimos AW, Rosamond WD. Regional evaluation of the severity-based stroke triage algorithm for emergency medical services using discrete event simulation. *Stroke*. 2017;48:2827–2835. doi: 10.1161/STROKEAHA.117.017905
23. Schlemm L, Endres M, Scheitz JF, Ernst M, Nolte CH, Schlemm E. Comparative evaluation of 10 prehospital triage strategy paradigms for patients with suspected acute ischemic stroke. *J Am Heart Assoc*. 2019;8:e012665. doi: 10.1161/JAHA.119.012665
24. Bosson N, Gausche-Hill M, Saver JL, Sanossian N, Tadeo R, Clare C, Perez L, Williams M, Rasnake S, Nguyen PL, et al. Increased access to and use of endovascular therapy following implementation of a 2-tiered regional stroke system. *Stroke*. 2020;51:908–913. doi: 10.1161/STROKEAHA.119.027756
25. Sarraj A, Savitz S, Pujara D, Kamal H, Carroll K, Shaker F, Reddy S, Parsha K, Fournier LE, Jones EM, et al. Endovascular thrombectomy for acute ischemic strokes: current US access paradigms and optimization methodology. *Stroke*. 2020;51:1207–1217. doi: 10.1161/STROKEAHA.120.028850

26. Venema E, Burke JF, Roozenbeek B, Nelson J, Lingsma HF, Dippel DWJ, Kent DM. Prehospital triage strategies for the transportation of suspected stroke patients in the United States. *Stroke*. 2020;51:3310–3319. doi: 10.1161/STROKEAHA.120.031144
27. Abilleira S, Perez de la Ossa N, Jimenez X, Cardona P, Cocho D, Purroy F, Serena J, Roman LS, Urra X, Vilaro M, et al. Transfer to the Local Stroke Center versus Direct Transfer to Endovascular Center of Acute Stroke Patients with Suspected Large Vessel Occlusion in the Catalan territory (RACECAT): study protocol of a cluster randomized within a cohort trial. *Int J Stroke*. 2019;14:734–744. doi: 10.1177/1747493019852176
28. Perez de la Ossa N, Abilleira S, Jovin TG, Garcia-Tornel A, Jimenez X, Urra X, Cardona P, Cocho D, Purroy F, Serena J, et al. Effect of direct transportation to thrombectomy-capable center vs local stroke center on neurological outcomes in patients with suspected large-vessel occlusion stroke in nonurban areas: the RACECAT randomized clinical trial. *Jama*. 2022;327:1782–1794. doi: 10.1001/jama.2022.4404
29. Feil K, Remi J, Kupper C, Herzberg M, Dorn F, Kunz WG, Reidler P, Levin J, Huttemann K, Tiedt S, et al. Inter-hospital transfer for mechanical thrombectomy within the supraregional stroke network NEVAS. *J Neurol*. 2021;268:623–631. doi: 10.1007/s00415-020-10165-2
30. Clark PJ, Evans FC. Distance to nearest neighbor as a measure of spatial relationships in populations. *Ecology*. 1954;35:445–453. doi: 10.2307/1931034
31. Behrndtz A, Johnsen SP, Valentin JB, Gude MF, Blauenfeldt RA, Andersen G, Majoie CB, Fisher M, Simonsen CZ. TRIAGE-STROKE: Treatment strategy in Acute larGE vessel occlusion: Prioritize IV or endovascular treatment-a randomized trial. *Int J Stroke*. 2020;15:103–108. doi: 10.1177/1747493019869830
32. Almekhlafi MA, Goyal M, Dippel DWJ, Majoie C, Campbell BCV, Muir KW, Demchuk AM, Bracard S, Guillemin F, Jovin TG, et al. Healthy life-year costs of treatment speed from arrival to endovascular thrombectomy in patients with ischemic stroke: a meta-analysis of individual patient data from 7 randomized clinical trials. *JAMA Neurol*. 2021;78:709–717. doi: 10.1001/jamaneurol.2021.1055
33. Saver JL, Goyal M, van der Lugt A, Menon BK, Majoie CB, Dippel DW, Campbell BC, Nogueira RG, Demchuk AM, Tomasello A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316:1279–1288. doi: 10.1001/jama.2016.13647
34. Froehler MT, Saver JL, Zaidat OO, Jahan R, Aziz-Sultan MA, Klucznik RP, Haussen DC, Hellinger FR Jr, Yavagal DR, Yao TL, et al. Interhospital transfer before thrombectomy is associated with delayed treatment and worse outcome in the STRATIS registry (Systematic Evaluation of Patients Treated With Neurothrombectomy Devices for Acute Ischemic Stroke). *Circulation*. 2017;136:2311–2321. doi: 10.1161/CIRCULATIONAHA.117.028920
35. Kate MP, Jeerakathil T, Buck BH, Khan K, Nomani AZ, Butt A, Thirunavukkarasu S, Nowacki T, Kalashyan H, Lloret-Villas MI, et al. Pre-hospital triage of suspected acute stroke patients in a mobile stroke unit in the rural Alberta. *Sci Rep*. 2021;11:4988. doi: 10.1038/s41598-021-84441-0