Data S1. Supplemental Methods and Results

Mathematical description of the model

An outline of the probabilistic model used in our study is presented in Figure 1 and the Methods section in the main text. Here, we describe the model in detail using mathematical terms. Table S3 contains a list definitions used in the following formulae.

First, we defined a function to estimate the change of disability-adjusted life days (DALDs) associated with transport to the nearest comprehensive stroke center (CSC) as compared to the nearest primary stroke center (PSC) as a function of demographic, clinical, and geographic input parameters:

$$\Delta = f \left( \ldots, t, t, t \right).$$

The total change of DALDs is calculated as the weighted mean of the change of DALDs associated with transport to the nearest CSC for patients in each of the four final diagnostic categories:

$$\Delta DALD = \sum_{d \in D}(\Delta DALD_d \times p_d^{RISK}).$$

For patients with hemorrhagic stroke (HS) and stroke mimic (SM), we assumed no change of DALDs associated with transport to the nearest CSC as compared to transport to the nearest PSC:

$$\Delta DALD_{HS,SM} = 0.$$

For patients with acute ischemic stroke (AIS) without large vessel occlusion (LVO), the loss of DALDs associated with transport to the nearest CSC is calculated as:

$$\Delta DALD_{AIS\text{ without LVO}} = \left( \min \left( t^{SCS}_{IVT}, t^{max}_{IVT} \right) - \min \left( t^{PSC}_{IVT}, t^{max}_{IVT} \right) \right) \times e^{WHSS,age,sex}_{AIS\text{ without LVO}}.$$

For patients with AIS with LVO, recanalization can occur after i.v. thrombolysis (IVT), after mechanical thrombectomy (MT), or not at all. Thus, we calculate the expected time of recanalization, depending on the transport destination, as:

$$t^{PSC}_R = \begin{cases} \mathcal{P}^{IVT}_R \times \left( 1 - \mathcal{P}^{MT}_R \right) \times \left( o_{TEMS} + t^{PSC}_{IVT} + t^{IVT}_R / 2 \right) + \ldots, \\ \left( 1 - \mathcal{P}^{IVT}_R \right) \times \mathcal{P}^{MT}_R \times \left( o_{TEMS} + t^{PSC}_{IVT} + DO + t_{transfer} + DTG + GTR \right) + \ldots, \\ (1 - \mathcal{P}^{IVT}_R) \times (1 - \mathcal{P}^{MT}_R) \times \left( t^{max}_{GP} + GTR \right) \end{cases}$$

$$t^{CSC}_R = \begin{cases} \mathcal{P}^{IVT}_R \times \left( 1 - \mathcal{P}^{MT}_R \right) \times \left( o_{TEMS} + t^{CSC}_{IVT} + t^{IVT}_R / 2 \right) + \ldots, \\ \left( 1 - \mathcal{P}^{IVT}_R \right) \times \mathcal{P}^{MT}_R \times \left( o_{TEMS} + t^{CSC}_{IVT} + NTG + GTR \right) + \ldots, \\ (1 - \mathcal{P}^{IVT}_R) \times (1 - \mathcal{P}^{MT}_R) \times \left( t^{max}_{GP} + GTR \right) \end{cases}$$
In addition, the time window for IVT to take effect ($t_{R}^{IVT}$) and the probability of early recanalization after IVT ($P_{R}^{IVT}$) is adjusted if recanalization from MT would be expected to be achieved shortly after administration of IVT. If the expected time-to-IVT or time-to-groin puncture are greater than $t_{R}^{max}$ and $t_{MT}^{max}$, respectively, then the corresponding probabilities to achieve recanalization with IVT or MT are set to zero.

Accordingly, the gain of DALDs for patients with AIS and LVO is estimated as:

$$\Delta DALD_{AIS with LVO} = \left(\min(t_{R}^{PSC}, t_{GP}^{max} + GTR) - \min(t_{R}^{CSC}, t_{GP}^{max} + GTR)\right) \times E_{AIS with LVO}^{NHSagesex}.$$  

**Second**, we calculated two-dimensional prehospital triage strategy paradigm-specific transport destination decision rule maps for each geography according to Figure 2 in the main text. These maps determine if a given patient at one of the sampled locations should be transported to the nearest PSC or CSC, taking into account demographic (age, sex), clinical (stroke symptom severity), geographic parameters (transport times, transfer time) and treatment time performance metrics. For triage strategy paradigms V and VI, estimated outcome as outlined above was used to determine transport destination. For the following, let $t_{S}^{age,sex}$ denote the transport decision for a given patient at the sampled point $s$ under triage strategy paradigm $Z$.

**Third**, we estimated the population-wide impact of different prehospital triage strategies. Let $\mathcal{S}$ be the set of sampled points in a given geography, $\mathcal{U}$ the set of the statistical geographical units for which data on the sex-specific age distribution was available (one single unit in abstract scenarios), and $n_{sex,age}^{U}$ the total number of individuals of a given age and sex living in a given statistical geographical unit. In addition, let $m_{u \in \mathcal{U}}$ be the total number of sampled points belonging to a given statistical geographical unit.

The following function was used to estimate the annual incidence of acute stroke as a function of age and sex ($m$: male, $f$: female) in a given statistical geographical unit:  

$$I_{stroke}^{age,sex,u} = \left((sex = m) \times 0.0671 \times \text{age}^{5.946} \times n_{m,age}^{U} + (sex = f) \times 6.95 \times \text{age}^{4.844} \times n_{f,age}^{U}\right) \times 10^{-12}.$$  

The annual incidence of acute stroke in each statistical geographical unit and in the whole region was then calculated as:

$$I_{stroke}^{u} = \sum_{age=35}^{100} (I_{stroke}^{age,m,u} + I_{stroke}^{age,f,u}),$$

$$I_{stroke} = \sum_{u \in \mathcal{U}} I_{stroke}^{u}.$$  

The annual incidence of EMS-calls for suspected acute stroke was derived from the annual incidence of acute stroke in each statistical geographical unit and in the whole region was then estimated using the following formula:

$$\Delta DALYs =$$

$$I_{stroke}/PF \times P_{IVT} \times \sum_{sex \in \mathcal{S}} \sum_{age=35}^{100} \sum_{RACE=0}^{9} (t_{S}^{age,sex} = CSC) \times \Delta DALD \times \frac{I_{stroke}^{age,sex,u}}{I_{stroke}^{u}} \times \frac{m_{u(s)}}{m_{u}} \times P_{R=\text{RACE}}.$$
Sampling of data points and calculation of transport times

Using the R package osrm-r for each real-world geographic scenario the boundary of the region of interest was defined as a spatial polygon. 10,000 points were then sampled from a regular spatial grid restricted to this polygon. For each point the Euclidean distance to the nearest location accessible by car was computed and points were discarded if that distance exceeded the spatial granularity of the sampling grid. The remaining points thus avoided uninhabited and unreachable areas such as parks and lakes as well as islands without road connection and were used as simulated stroke incident locations. OSRM with a custom transport profile representing the driving speeds and accessibility restrictions of an emergency vehicle (Table S5) was used to compute travel times between stroke locations and stroke centers as well as transport times between PSCs and CSCs.

In addition to osrm-r, the following R packages were used in the analysis: leaflet, rgdal, OpenStreetMap, raster, gdata, sf, geosphere, cleangeo, mapview, ggsci, RColorBrewer, webshot, and scales.

1.3 Calculation of transport times in abstract geographic scenarios

For the estimation of transport times in abstract geographic scenarios, we randomly sampled points in the specific urban and specific rural geographic scenario and calculated both Euclidean distances in km and transport times in minutes to all available stroke centers. Data were fitted using a one-term power series model. Results of the fit were used to convert Euclidean distances to transport times in the abstract geographic scenarios (Figure S5).

1.4 Model parameters

See Tables S1 and S2 and Figures S1 – S4.

1.5 Geographic scenarios

See Table S4.

1.6 Prehospital stroke triage strategy paradigm-associated transport destination decision rules in abstract geographic scenarios

See Figure S6.

1.7 Univariate sensitivity analyses: door-out time

See Figures S7 – S9.

1.8 Numerical results

See Tables S6 – S8.
### Table S1. Model parameters – 1

| Parameter                                                                 | Base case value, 95% CI | Distr. in PSA | Distribution parameters | Comment          |
|---------------------------------------------------------------------------|--------------------------|---------------|-------------------------|------------------|
| Probability of patients seen by EMS for suspected acute stroke having final diagnosis of ‘AIS with LVO’, per RACE score category |                          |               | A: 2; B: 63             | See Figure S1.    |
| RACE 0: 0.03                                                             |                          |               | A: 2; B: 158            |                  |
| RACE 1: 0.01                                                             |                          |               | A: 10; B: 223           |                  |
| RACE 2: 0.04                                                             |                          |               | A: 13; B: 146           |                  |
| RACE 3: 0.08                                                             |                          |               | A: 21; B: 146           |                  |
| RACE 4: 0.13                                                             |                          |               | A: 36; B: 114           |                  |
| RACE 5: 0.24                                                             |                          |               | A: 63; B: 162           |                  |
| RACE 6: 0.28                                                             |                          |               | A: 62; B: 93            |                  |
| RACE 7: 0.40                                                             |                          | Beta          | A: 58; B: 77            |                  |
| RACE 8: 0.43                                                             |                          |               | A: 42; B: 42            |                  |
| RACE 9: 0.50                                                             |                          |               |                         |                  |
| Probability of patients seen by EMS for suspected acute stroke having final diagnosis of ‘AIS without LVO’, per RACE score category |                          | Beta          | A: 37; B: 28            | See Figure S1.    |
| RACE 0: 0.57                                                             |                          |               | A: 98; B: 62            |                  |
| RACE 1: 0.61                                                             |                          |               | A: 123; B: 110          |                  |
| RACE 2: 0.53                                                             |                          |               | A: 73; B: 86            |                  |
| RACE 3: 0.46                                                             |                          | Beta          | A: 77; B: 90            |                  |
| RACE 4: 0.46                                                             |                          |               | A: 56; B: 94            |                  |
| RACE 5: 0.37                                                             |                          |               | A: 59; B: 166           |                  |
| RACE 6: 0.26                                                             |                          |               | A: 42; B: 113           |                  |
| RACE 7: 0.27                                                             |                          |               | A: 36; B: 99            |                  |
| RACE 8: 0.27                                                             |                          |               | A: 13; B: 71            |                  |
| RACE 9: 0.15                                                             |                          |               |                         |                  |
| Probability of patients seen by EMS for suspected acute stroke having final diagnosis of ‘hemorrhagic stroke’, per RACE score category |                          | Beta          | A: 3; B: 62             | See Figure S1.    |
| RACE 0: 0.05                                                             |                          |               | A: 15; B: 145           |                  |
| RACE 1: 0.09                                                             |                          |               | A: 19; B: 214           |                  |
| RACE 2: 0.08                                                             |                          |               | A: 29; B: 130           |                  |
| RACE 3: 0.18                                                             |                          |               | A: 34; B: 133           |                  |
| RACE 4: 0.20                                                             |                          |               | A: 38; B: 112           |                  |
| RACE 5: 0.25                                                             |                          |               | A: 81; B: 144           |                  |
| RACE 6: 0.36                                                             |                          | Beta          | A: 40; B: 115           |                  |
| RACE 7: 0.26                                                             |                          |               | A: 37; B: 98            |                  |
| RACE 8: 0.27                                                             |                          |               | A: 23; B: 61            |                  |
| RACE 9: 0.27                                                             |                          |               |                         |                  |
| Parameter                                                                 | Base case value, 95% CI | Distr. in PSA | Distribution parameters | Comment |
|--------------------------------------------------------------------------|--------------------------|---------------|-------------------------|---------|
| Probability of patients seen by EMS for suspected acute stroke having final diagnosis of ‘stroke mimic’, per RACE score category | RACE 0: 0.35 RACE 1: 0.28 RACE 2: 0.35 RACE 3: 0.28 RACE 4: 0.21 RACE 5: 0.13 RACE 6: 0.10 RACE 7: 0.07 RACE 8: 0.03 RACE 9: 0.07 | Beta | A: 23; B: 42 A: 45; B: 115 A: 81; B: 152 A: 44; B: 115 A: 35; B: 132 A: 20; B: 130 A: 33; B: 203 A: 11; B: 144 A: 4; B: 131 A: 6; B: 78 | See Figure S1. |
| Probability of RACE score 0 – 9 per EMS call for suspected stroke        | RACE 0: 0.06 RACE 1: 0.13 RACE 2: 0.18 RACE 3: 0.11 RACE 4: 0.11 RACE 5: 0.09 RACE 6: 0.13 RACE 7: 0.08 RACE 8: 0.07 RACE 9: 0.04 | Beta | A: 85; B: 1448 A: 198; B: 1335 A: 273; B: 1260 A: 175; B: 1358 A: 172; B: 1361 A: 144; B: 1389 A: 200; B: 1333 A: 127; B: 1406 A: 101; B: 1432 A: 57; B: 1476 | See Figure S2 for details on adjustment for selective recruitment of more severely affected patients. |
| National Institutes of Health Stroke Scale score per RACE score category  | RACE 0: 3.40 RACE 1: 3.65 RACE 2: 5.11 RACE 3: 7.83 RACE 4: 10.05 RACE 5: 12.35 RACE 6: 17.37 RACE 7: 18.15 RACE 8: 19.26 RACE 9: 19.71 | Gamma | k: 1.14; θ: 2.97 k: 2.36; θ: 1.55 k: 1.44; θ: 3.55 k: 1.91; θ: 4.09 k: 2.30; θ: 4.39 k: 2.19; θ: 5.64 k: 4.52; θ: 3.84 k: 11.21; θ: 1.62 k: 18.26; θ: 1.06 k: 19.96; θ: 1.16 | See Figure S3. |

Data from Carrera et al.\(^5\). CI stands for confidence interval; PSA, probabilistic sensitivity analysis; EMS, emergency medical services; AIS, acute ischemic stroke; LVO, large vessel occlusion; RACE, rapid arterial occlusion evaluation scale (score).
| Parameter                                                                 | Base case value, 95% CI | Distribution type | Distribution parameters       | Reference                     | Comment                                                                 |
|--------------------------------------------------------------------------|-------------------------|-------------------|-------------------------------|------------------------------|--------------------------------------------------------------------------|
| Probability of eligibility for i.v. thrombolysis                         | 25%                     |                   |                               | Carrera et al.⁵               | Eligibility assumed to be ascertainable prehospitalistically.             |
| Probability of early recanalization of LVO within 70 minutes after i.v. thrombolysis | 20% (15 – 26%)           | Beta              | A: 60.63; B: 237.70           | Seners et al.⁶, Holodinsky et al.⁷ | Linear adjustment for shorter time periods, i.e. expected recanalization through MT achieved less than 70 minutes after start of i.v. thrombolysis |
| Probability of successful recanalization of LVO following MT             | 80% (70 – 90%)           | Beta              | A: 53.34; B: 13.56            | Holodinsky et al.⁷            | Width of confidence interval estimate based on professional experience due to lack of data. |
| Door-to-needle time at primary stroke centers                            | 30 min (20 – 60 min)    | Gamma             | k: 26.85; θ: 1.13             |                              | Additional constraint in PSA that door-to-needle time at primary stroke centers is at least as long as door-to-needle time at comprehensive stroke centers. |
| Door-to-needle time at comprehensive stroke centers                     | 30 min (20 – 60 min)    | Gamma             | k: 26.85; θ: 1.13             |                              |                                                                          |
| Needle-to-groin puncture time at comprehensive stroke centers           | 30 min (20 – 60 min)    | Gamma             | k: 26.85; θ: 1.13             |                              |                                                                          |
| Door-to-groin puncture time at comprehensive stroke centers after secondary transfer from a primary stroke centers | 30 min (20 – 60 min)    | Gamma             | k: 26.85; θ: 1.13             |                              |                                                                          |
| Groin puncture-to-recanalization time (if MT is technically successful)  | 30 min (20 – 60 min)    |                   | k: 26.85; θ: 1.13             | Holodinsky et al.⁷           |                                                                          |
| Parameter                                                                 | Base case value, 95% CI | Distribution type | Distribution parameters | Reference       | Comment                                                                 |
|--------------------------------------------------------------------------|--------------------------|-------------------|-------------------------|-----------------|-------------------------------------------------------------------------|
| Door-out time at primary stroke centers before secondary transfer (time   | I: 45 min (30 – 60 min)  | Gamma              | $k$: 37.55; $\theta$: 1.21 | Carrera et al. 5 | The impact of shorter door-out times (II) was explored in univariate   |
| recognition of LVO through imaging / administration of i.v. thrombolysis  | II: 15 min (5 – 20 min)  |                   | $k$: 15.00; $\theta$: 1.00 |                 | sensitivity analyses.                                                    |
| and departure of the patient to the comprehensive stroke center)         |                           |                   |                         |                 |                                                                         |
| Maximum time from symptom onset-to-i.v. thrombolysis                     | 270 min                  |                   |                         | Powers et al. 8  |                                                                         |
| Maximum time from symptom onset-to-groin puncture                        | 360 min                  |                   |                         | Powers et al. 8  |                                                                         |

CI stands for confidence interval; PSA, probabilistic sensitivity analysis; EMS, emergency medical services; AIS, acute ischemic stroke; LVO, large vessel occlusion; RACE, rapid arterial occlusion evaluation scale (score); MT, mechanical thrombectomy
Table S3. Definitions

| Def. | Parameter                          | Def. | Parameter                                                                 |
|------|------------------------------------|------|---------------------------------------------------------------------------|
| DTN  | door-to-needle time                | D    | Set of possible final diagnoses: AIS with LVO, AIS without LVO, hemorrhagic stroke, stroke mimic |
| DO   | door-out time                      | \(d \in \Delta\) | Relative frequency of one of the four final diagnoses in each RACE score category 0 – 9. |
| DTG  | door-to-groin puncture time        | \(P_{R=X}\) | Relative frequency of patients with a RACE score of X among patients seen by EMS personnel for suspected acute stroke. |
| NTG  | needle-to-groin puncture time      | \(\text{Gain of DALDs per minute faster recanalization of LVO.}\) | |
| GTR  | groin puncture-to-reperfusion time | \(\text{Gain of DALDs per minute faster access to IVT.}\) | |
| OTEMS| onset-to-EMS time                  | \(P_{IVT}\) | Probability of achieving recanalization of LVO with IVT |
| \(t_{\max}^\text{IVT}\) | Maximum time from symptom onset-to-IVT | \(t_{IVT}\) | Time window within which recanalization of LVO after IVT can occur. |
| \(t_{\max}^\text{GP}\) | Maximum time from symptom onset-to-groin puncture | \(P_{MT}\) | Probability of achieving recanalization of LVO with MT |
| RACE | Rapid arterial occlusion evaluation scale (score) | \(P_{IVT}\) | Relative frequency of eligibility for IVT |
| \(t_{\text{PSC}}^\text{IVT}\) | Time-to-thrombolysis at the nearest PSC (transport time + DTN) | | |
| \(t_{\text{CSC}}^\text{IVT}\) | Time-to-thrombolysis at the nearest CSC (transport time + DTN) | | |
| \(t_{\text{transfer}}\) | Transport time from nearest PSC to CSC | | |

See Tables 1, S1, and S2 and Figures S1 – S4 for values. IVT stands for i.v. thrombolysis; AIS, acute ischemic stroke; LVO, large vessel occlusion; EMS, emergency medical services; DALDs, disability-adjusted life days; NIHSS, National Institutes of Health Stroke Scale (score).
| Parameter                                         | Specific real-world urban scenario: Berlin I (‘as is’)* | Specific real-world urban scenario: Berlin II (theoretical, centralized MT-services)* | Abstract urban scenario | Specific real-world rural scenario: Schleswig-Holstein† | Abstract rural Scenario† |
|--------------------------------------------------|-------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------|--------------------------------------------------------|--------------------------|
| Surface area – km²                                | 852 km²                                               | 852 km²                                                                             | (15 km)² x π = 706 km² | 15,763 km²                                             | (70 km)² x π = 15,394 km² |
| Total population – n                              | 3.6 Mio                                               | 3.6 Mio                                                                             | 3.6 Mio                 | 2.9 Mio                                                | 2.9 Mio                  |
| Mean population density – km⁻²                   | 4,052                                                 | 4,052                                                                               | 5,099                   | 182                                                    | 188                      |
| Estimated annual incidence of acute stroke‡      | 9,328                                                 | 9,328                                                                               | 9,328                   | 7,586                                                  | 7,586                    |
| Estimated annual incidence of Code Stroke activation by EMS§ | 2,292                                                 | 2,292                                                                               | 2,292                   | 1,864                                                  | 1,864                    |
| Spatial granularity of population data            | 447 statistical units (Lebensweltlich orientierte Räume) | 447 statistical units (Lebensweltlich orientierte Räume)                            | 1, spatially homogenous population | 1,112 communities (Gemeinden)                        | 1, spatially homogenous population |
| Total number of PSC / CSCs                       | 4 / 10                                                 | 11 / 3                                                                              | 1 – 5 / 1 - 5           | 7 / 6                                                   | 1 – 5 / 1 - 5            |

*Geographic and demographic data for Berlin from (9) and (10). The distribution of MT-capable stroke centers in the scenario ‘Berlin I’ corresponds to the current situation, in ‘Berlin II’ to a theoretical setting with centralized MT-services. †Geographic and demographic data for Schleswig-Holstein from (11) and (12). ‡Annual incidence of acute stroke per 1,000,000 estimated as 0.00000006708 × age⁵.₉⁴⁶ for men and 0.000000695 × age⁴.₃₄₄ for women. §Estimated under the assumption that the annual incidence of Code Stroke activation by EMS is proportional to the annual incidence of acute stroke, and that an estimated annual incidence of acute stroke of 15,473 corresponds to 3,900 Code Stroke activations by EMS (data from the region of Catalonia, Spain⁵, 1₃). EMS stands for emergency medical services; PSC, primary stroke center; CSC, comprehensive stroke center.
| Road type       | Driving speed (km h\(^{-2}\)) |
|-----------------|--------------------------------|
| Motorway        | 140                            |
| Motorway link   | 80                             |
| Trunk           | 120                            |
| Trunk link      | 60                             |
| Primary         | 100                            |
| Primary link    | 50                             |
| Secondary       | 80                             |
| Secondary link  | 40                             |
| Tertiary        | 60                             |
| Tertiary link   | 30                             |
| Unclassified    | 40                             |
| Residential     | 40                             |
| Living street   | 30                             |
| Service         | 25                             |
Table S6. Patient-related outcome measures outcome measures in specific real-world geographic scenarios, including univariate and probabilistic sensitivity analyses.

| Scenario I       | Drip-‘n’-ship (reference) | - | - | 12.69 (3.33-31.84) | 6.16 (2.93-12.35) | 2.62 (-1.81-13.01) | 2.34 (-3.24-12.15) |
|------------------|---------------------------|---|---|-------------------|-------------------|-------------------|-------------------|
| Scenario II      | Mothershipe                | 17.90 (8.74-33.06) | 14.38 (6.33-30.49) | 14.15 (3.58-27.38) | 10.07 (1.35-21.21) | 6.16 (2.93-12.35) | 3.17 (-0.74-11.30) | 4.35 (0.49-9.67) |
| Scenario III     | Additional transport time threshold | 17.90 (8.74-33.06) | 14.15 (3.58-27.38) | 13.07 (1.35-21.21) | 12.69 (3.33-31.84) | 6.16 (2.93-12.35) | 3.17 (-0.74-11.30) | 4.35 (0.49-9.67) |
| Scenario IV      | Fixed cutoff score         | 16.06 (8.22-28.56) | 14.64 (7.03-27.75) | 15.80 (7.17-31.06) | 16.06 (8.22-28.56) | 14.64 (7.03-27.75) | 15.80 (7.17-31.06) | 6.19 (3.87-10.90) | 4.76 (1.95-11.87) | 5.44 (1.99-12.53) |
| Scenario V       | Fixed cutoff score with probabilistic outcome determination | 16.06 (8.22-28.56) | 14.64 (7.03-27.75) | 15.80 (7.17-31.06) | 16.06 (8.22-28.56) | 14.64 (7.03-27.75) | 15.80 (7.17-31.06) | 6.19 (3.87-10.90) | 4.76 (1.95-11.87) | 5.44 (1.99-12.53) |
| Scenario VI      | Optimal variable cutoff scores | 18.24 (9.35-33.24) | 15.91 (7.85-30.94) | 17.15 (8.24-34.06) | 6.01 (4.22-12.57) | 5.10 (2.66-13.64) | 6.14 (3.42-14.20) |
| Scenario VII     | Optimal LVO detection device | 19.80 (10.77-34.84) | 19.14 (10.52-33.87) | 22.27 (11.82-38.81) | 8.06 (5.34-14.23) | 7.39 (4.76-15.65) | 8.83 (5.75-17.14) |
| Scenario IX      | Mobile IVT unit            | 25.64 (15.58-41.17) | 25.47 (15.52-45.10) | 39.73 (23.82-57.83) | 13.91 (10.57-26.02) | 13.72 (10.38-29.16) | 22.31 (17.88-36.68) |
| Scenario X       | Mobile MT unit             | 30.29 (18.49-50.69) | 32.09 (19.22-57.53) | 55.76 (34.22-83.37) | 18.56 (14.13-37.22) | 20.33 (15.41-42.39) | 34.16 (26.78-56.64) |

| Population-wide total gain of DALYs |
|-----------------------------------|
| Scenario I I                      | Drip-‘n’-ship (reference) | - | - | 18.22 (2.48-30.24) | 18.22 (2.48-30.24) | 9.85 (2.51-20.83) | 9.85 (2.51-20.83) | 2.92 (0.22-4.68) | 2.92 (0.22-4.68) | 3.33 (-2.30-9.06) | 3.33 (-2.30-9.06) | 1.55 (-2.15-5.20) | 1.55 (-2.15-5.20) |
| Scenario II                      | Mothershipe                | 8.48 (0.14-13.15) | 18.22 (2.48-30.24) | 9.85 (2.51-20.83) | 2.92 (0.22-4.68) | 3.33 (-2.30-9.06) | 3.33 (-2.30-9.06) | 1.55 (-2.15-5.20) | 1.55 (-2.15-5.20) |
| Scenario III                     | Additional transport time threshold | 8.48 (0.14-13.15) | 17.93 (0.38-28.81) | 10.15 (0.40-16.31) | 2.92 (0.22-4.68) | 4.01 (-0.94-9.17) | 2.89 (0.32-5.58) |
| Scenario IV                      | Fixed cutoff score         | 7.60 (0.12-11.92) | 18.55 (2.34-29.27) | 12.26 (4.75-20.55) | 2.93 (0.21-4.30) | 6.03 (2.46-9.75) | 3.61 (1.32-6.00) |
| Scenario V                      | Fixed cutoff score with probabilistic outcome determination | 7.60 (0.12-11.92) | 18.55 (2.34-29.27) | 12.26 (4.75-20.55) | 2.93 (0.21-4.30) | 6.08 (3.00-9.75) | 3.80 (2.05-6.07) |
| Scenario VI                     | Optimal variable cutoff scores | 8.64 (0.14-13.30) | 20.16 (2.55-31.54) | 13.31 (5.18-22.70) | 3.23 (0.24-4.81) | 6.46 (3.38-10.54) | 4.07 (2.27-6.60) |
| Scenario VII                     | Optimal LVO detection device | 9.37 (0.15-14.26) | 24.26 (2.76-36.85) | 17.29 (6.44-25.91) | 3.82 (0.27-5.30) | 9.36 (5.11-13.26) | 5.86 (3.82-8.27) |
| Scenario IX                     | Optimal LVO detection device with probabilistic outcome determination | 9.37 (0.15-14.26) | 24.26 (2.76-36.85) | 17.29 (6.44-25.91) | 3.82 (0.27-5.30) | 9.36 (5.11-13.26) | 5.86 (3.82-8.27) |
| Scenario X                     | Mobile IVT unit            | 12.14 (0.26-17.74) | 32.28 (3.99-47.02) | 30.85 (12.83-43.19) | 6.59 (0.54-7.46) | 17.38 (10.45-21.79) | 14.80 (9.11-18.15) |
| Scenario X                     | Mobile MT unit             | 14.35 (0.32-20.77) | 40.66 (5.21-58.53) | 43.28 (17.78-62.08) | 8.79 (0.72-10.27) | 25.77 (14.33-33.23) | 22.67 (13.14-29.20) |
Table S6. Patient-related outcome measures outcome measures in specific real-world geographic scenarios (continued)

| Additional population-wide total gain of DALYs in addition to less complex triage strategies | Univariate sensitivity analysis: I | Univariate sensitivity analysis: II |
|---------------------------------------|----------------------------------|----------------------------------|
|                                       | Berlin I | Berlin II | Schleswig-Holstein | Berlin I | Berlin II | Schleswig-Holstein |
| Scenario I Drip-'n'-ship (reference)  | -       | -        | -                  | -       | -        | -                  |
| Scenario II Mothership                | 8.48 (0.14-13.15) | 18.22 (2.48-30.24) | 9.85 (2.51-20.83) | 2.92 (0.22-4.68) | 3.33 (-2.30-9.06) | 1.55 (-2.15-5.20) |
| Scenario III Additional transport time threshold | 0.00 (0.00-0.00) | -0.29 (-2.11-0.47) | 0.30 (-6.54-3.57) | 0.00 (0.00-0.00) | 0.69 (-0.94-0.80) | 1.34 (-0.66-1.34) |
| Scenario IV Fixed cutoff score        | -0.87 (-1.91-0.00) | 0.33 (-2.88-2.32) | 2.12 (-0.53-3.21) | 0.02 (-0.37-0.44) | 2.02 (-0.44-2.46) | 0.72 (0.10-1.00) |
| Scenario V Fixed cutoff score with probabilistic outcome determination | -0.87 (-1.91-0.00) | 0.00 (-2.88-0.00) | 0.00 (-0.53-0.37) | 0.00 (-0.37-0.03) | 0.04 (-0.44-0.54) | 0.19 (0.00-0.72) |
| Scenario VI Optimal variable cutoff scores | 0.16 (0.00-0.37) | 1.61 (0.04-2.41) | 1.05 (0.24-2.00) | 0.29 (0.00-0.29) | 0.39 (0.18-0.78) | 0.28 (0.14-0.52) |
| Scenario VII Optimal LVO detection device | 0.74 (0.00-0.98) | 4.10 (0.19-5.36) | 3.98 (1.17-5.29) | 0.59 (0.03-0.74) | 2.90 (0.71-3.39) | 1.78 (0.77-2.06) |
| Scenario IX Optimal LVO detection device with probabilistic outcome determination | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) |
| Scenario IX Mobile IVT unit           | 2.77 (0.07-3.81) | 8.02 (1.59-11.16) | 13.56 (4.98-18.85) | 2.77 (0.26-3.59) | 8.02 (5.25-9.85) | 8.94 (5.00-11.35) |
| Scenario X Mobile MT unit             | 2.20 (0.06-3.13) | 8.38 (1.08-11.94) | 12.44 (4.70-17.84) | 2.20 (0.19-2.81) | 8.38 (3.88-11.45) | 7.87 (4.03-11.05) |

Time to IVT per AIS patient in the equipoise region

|                                       | Scenario I Drip-'n'-ship | Scenario II Mothership | Scenario III Additional transport time threshold | Scenario IV Fixed cutoff score with probabilistic outcome determination | Scenario V Fixed cutoff score with probabilistic outcome determination | Scenario VI Optimal variable cutoff scores | Scenario VII Optimal LVO detection device with probabilistic outcome determination |
|---------------------------------------|--------------------------|-------------------------|-----------------------------------------------|-------------------------------------------------------------------|-------------------------------------------------------------------|---------------------------------------------|-----------------------------------------------------------------------------------|
|                                       | 68 (61-82) | 68 (61-82) | 83 (76-96) | 70 (63-83) | 70 (63-83) | 70 (63-83) | 69 (62-83) |
|                                       | 72 (65-85) | 77 (70-90) | 100 (92-113) | 72 (68-85) | 72 (68-85) | 72 (68-85) | 69 (62-83) |
|                                       | 72 (65-85) | 75 (68-88) | 87 (79-100) | 72 (68-85) | 72 (68-85) | 72 (68-85) | 69 (62-83) |
|                                       | 70 (63-83) | 72 (65-86) | 90 (83-103) | 70 (65-83) | 72 (66-85) | 83 (76-96) | 71 (65-84) |
|                                       | 70 (63-83) | 72 (65-86) | 90 (83-101) | 70 (65-83) | 71 (66-85) | 81 (76-94) | 81 (74-94) |
|                                       | 71 (64-84) | 73 (67-87) | 90 (85-102) | 70 (66-84) | 72 (67-84) | 82 (76-94) | 81 (74-94) |
|                                       | 69 (62-83) | 71 (64-85) | 88 (81-101) | 69 (65-83) | 71 (65-84) | 81 (74-94) | 81 (74-94) |
|                                       | 69 (62-83) | 71 (64-85) | 88 (81-101) | 69 (65-83) | 71 (65-84) | 81 (74-94) | 81 (74-94) |
|                                       | 60 (49-73) | 60 (49-73) | 60 (49-73) | 60 (49-73) | 60 (49-73) | 60 (49-73) | 60 (49-73) |
|                                       | 60 (49-73) | 60 (49-73) | 60 (49-73) | 60 (49-73) | 60 (49-73) | 60 (49-73) | 60 (49-73) |
|                                       |            |            |            |            |            |            |            |
Table S6. Patient-related outcome measures in specific real-world geographic scenarios (continued)

| Scenario I                  | Berlin I | Berlin II | Schleswig-Holstein | Univariate sensitivity analysis: I | Berlin I | Berlin II | Schleswig-Holstein |
|-----------------------------|----------|-----------|-------------------|-----------------------------------|----------|-----------|-------------------|
| Time to MT per AIS patient with LVO in the equipoise region          |          |           |                   |                                   |          |           |                   |
| Scenario I                 | Drip-'n'-ship | 153 (137-182) | 158 (143-192) | 190 (174-217) | 123 (114-142) | 128 (119-146) | 145 (135-163) |
| Scenario II                | Mothership | 102 (93-121) | 107 (98-126) | 130 (120-148) | 102 (95-117) | 107 (98-122) | 119 (110-135) |
| Scenario III               | Additional transport time threshold | 102 (93-121) | 110 (102-178) | 150 (139-209) | 102 (95-117) | 108 (101-124) | 124 (116-140) |
| Scenario IV                | Fixed cutoff score | 112 (102-130) | 117 (107-137) | 142 (132-160) | 106 (98-122) | 111 (103-127) | 124 (115-141) |
| Scenario V                 | Fixed cutoff score with probabilistic outcome determination | 112 (102-130) | 117 (107-137) | 142 (132-161) | 106 (98-122) | 111 (103-128) | 126 (116-143) |
| Scenario VI                | Optimal variable cutoff scores | 103 (93-122) | 110 (100-128) | 136 (125-155) | 103 (96-119) | 110 (99-127) | 124 (113-141) |
| Scenario VII               | Optimal LVO detection device | 102 (93-121) | 107 (98-126) | 130 (120-148) | 102 (95-117) | 107 (98-122) | 119 (110-135) |
| Scenario IX                | Optimal LVO detection device with probabilistic outcome determination | 102 (93-121) | 107 (98-126) | 130 (120-148) | 102 (95-117) | 107 (98-122) | 119 (110-135) |
| Scenario IX                | Mobile IVT unit | 102 (93-121) | 107 (98-126) | 130 (120-148) | 102 (95-117) | 107 (98-122) | 119 (110-135) |
| Scenario X                 | Mobile MT unit | 90 (74-109) | 90 (74-109) | 90 (74-109) | 90 (74-105) | 90 (74-105) | 90 (74-105) |

For a description of triage strategy paradigms, see Figure 2 in the main text. DALD stands for disability-adjusted life day; EMS, emergency medical services; IVT, i.v. thrombolysis; DALY, disability-adjusted life year; LVO, large vessel occlusion; AIS, acute ischemic stroke.
Table S7. Health system-related outcome measures in specific real-world geographic scenarios, including univariate and probabilistic sensitivity analyses.

| Scenario     | Proportion of patients triaged to a primary stroke center | Proportion of patients triaged to a comprehensive stroke center (without secondary transfers) |
|--------------|--------------------------------------------------------|------------------------------------------------------------------------------------------|
|              | Univariate sensitivity analysis: I | Univariate sensitivity analysis: II |
|              | Berlin I | Berlin II | Schleswig-Holstein | Berlin I | Berlin II | Schleswig-Holstein |
| Scenario I   | Drip-'n'-ship | 0.30 (0.01-0.30) | 0.81 (0.07-0.81) | 0.61 (0.23-0.61) | 0.30 (0.01-0.30) | 0.81 (0.24-0.81) | 0.52 (0.20-0.52) |
| Scenario II  | Mothership | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) |
| Scenario III | Additional transport time threshold | 0.00 (0.00-0.00) | 0.06 (0.06-0.06) | 0.22 (0.22-0.22) | 0.00 (0.00-0.00) | 0.06 (0.06-0.06) | 0.09 (0.09-0.09) |
| Scenario IV  | Fixed cutoff score | 0.18 (0.00-0.18) | 0.48 (0.04-0.49) | 0.36 (0.14-0.37) | 0.18 (0.01-0.18) | 0.48 (0.14-0.49) | 0.31 (0.12-0.31) |
| Scenario V   | Fixed cutoff score with probabilistic outcome determination | 0.18 (0.00-0.18) | 0.48 (0.04-0.49) | 0.36 (0.14-0.39) | 0.18 (0.01-0.18) | 0.48 (0.14-0.54) | 0.32 (0.12-0.36) |
| Scenario VI  | Optimal variable cutoff scores | 0.05 (0.00-0.08) | 0.27 (0.02-0.35) | 0.24 (0.08-0.31) | 0.09 (0.00-0.12) | 0.39 (0.05-0.50) | 0.27 (0.06-0.33) |
| Scenario VII | Optimal LVO detection device | 0.25 (0.00-0.25) | 0.67 (0.05-0.68) | 0.50 (0.19-0.51) | 0.25 (0.01-0.25) | 0.67 (0.20-0.67) | 0.43 (0.17-0.43) |
| Scenario IX  | Optimal LVO detection device with probabilistic outcome determination | 0.25 (0.00-0.25) | 0.67 (0.05-0.68) | 0.50 (0.19-0.51) | 0.25 (0.01-0.25) | 0.67 (0.20-0.67) | 0.43 (0.17-0.43) |
| Scenario IX  | Mobile IVT unit | 0.25 (0.00-0.25) | 0.67 (0.05-0.68) | 0.50 (0.19-0.51) | 0.25 (0.01-0.25) | 0.67 (0.20-0.67) | 0.43 (0.17-0.43) |
| Scenario X   | Mobile MT unit | 0.25 (0.00-0.25) | 0.67 (0.05-0.68) | 0.50 (0.19-0.51) | 0.25 (0.01-0.25) | 0.67 (0.20-0.67) | 0.43 (0.17-0.43) |

Proportion of patients triaged to a comprehensive stroke center (without secondary transfers):

| Scenario I   | Drip-'n'-ship | 0.70 (0.70-0.99) | 0.19 (0.19-0.93) | 0.39 (0.39-0.77) | 0.70 (0.70-0.99) | 0.19 (0.19-0.76) | 0.48 (0.48-0.80) |
| Scenario II  | Mothership | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) |
| Scenario III | Additional transport time threshold | 1.00 (1.00-1.00) | 0.94 (0.94-0.94) | 0.78 (0.78-0.78) | 1.00 (1.00-1.00) | 0.94 (0.94-0.94) | 0.91 (0.91-0.91) |
| Scenario IV  | Fixed cutoff score | 0.82 (0.82-1.00) | 0.52 (0.51-0.96) | 0.64 (0.63-0.86) | 0.82 (0.82-0.99) | 0.52 (0.51-0.86) | 0.69 (0.69-0.88) |
| Scenario V   | Fixed cutoff score with probabilistic outcome determination | 0.82 (0.82-1.00) | 0.52 (0.51-0.96) | 0.64 (0.61-0.86) | 0.82 (0.82-0.99) | 0.52 (0.46-0.86) | 0.68 (0.64-0.88) |
| Scenario VI  | Optimal variable cutoff scores | 0.95 (0.92-1.00) | 0.73 (0.65-0.98) | 0.76 (0.69-0.92) | 0.91 (0.88-1.00) | 0.61 (0.50-0.95) | 0.73 (0.67-0.94) |
| Scenario VII | Optimal LVO detection device | 0.75 (0.75-1.00) | 0.33 (0.32-0.95) | 0.50 (0.49-0.81) | 0.75 (0.75-0.99) | 0.33 (0.33-0.80) | 0.57 (0.57-0.83) |
| Scenario IX  | Optimal LVO detection device with probabilistic outcome determination | 0.75 (0.75-1.00) | 0.33 (0.32-0.95) | 0.50 (0.49-0.81) | 0.75 (0.75-0.99) | 0.33 (0.33-0.80) | 0.57 (0.57-0.83) |
| Scenario IX  | Mobile IVT unit | 0.75 (0.75-1.00) | 0.33 (0.32-0.95) | 0.50 (0.49-0.81) | 0.75 (0.75-0.99) | 0.33 (0.33-0.80) | 0.57 (0.57-0.83) |
| Scenario X   | Mobile MT unit | 0.75 (0.75-1.00) | 0.33 (0.32-0.95) | 0.50 (0.49-0.81) | 0.75 (0.75-0.99) | 0.33 (0.33-0.80) | 0.57 (0.57-0.83) |
Table S7. Health system-related outcome measures in specific real-world geographic scenarios, including univariate and probabilistic sensitivity analyses (continued).

| Scenario            | Berlin I | Berlin II | Schleswig-Holstein | Berlin I | Berlin II | Schleswig-Holstein |
|---------------------|----------|-----------|--------------------|----------|-----------|--------------------|
| **Total number of secondary transfers (patients with acute ischemic stroke and large vessel occlusion triaged to a primary stroke center)** |          |           |                    |          |           |                    |
| Scenario I          | Drip-'n'-ship | 492 (9.533) | 1316 (114-1427) | 801 (298-869) | 492 (22-537) | 1316 (385-1437) | 685 (262-748) |
| Scenario II         | Mothership | 0 (0-0)   | 0 (0-0)            | 0 (0-0)   | 0 (0-0)   | 0 (0-0)            | 0 (0-0) |
| Scenario III        | Additional transport time threshold | 0 (0-0) | 91 (83-99) | 288 (263-314) | 0 (0-0) | 91 (83-99) | 124 (113-135) |
| Scenario IV         | Fixed cutoff score | 97 (2-130) | 261 (21-347) | 159 (57-211) | 97 (5-132) | 261 (83-353) | 136 (57-184) |
| Scenario V          | Fixed cutoff score with probabilistic outcome determination | 97 (2-130) | 261 (21-347) | 159 (57-240) | 97 (5-132) | 284 (83-474) | 183 (57-288) |
| Scenario VI         | Optimal variable cutoff scores | 13 (0-22) | 94 (2-150) | 91 (21-169) | 32 (1-65) | 216 (19-433) | 143 (25-250) |
| Scenario VII        | Optimal LVO detection device | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) |
| Scenario VIII       | Optimal LVO detection device with probabilistic outcome determination | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) |
| Scenario IX         | Mobile IVT unit | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) |
| Scenario X          | Mobile MT unit | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0 (0-0) |

| Proportion of patients with LVO in the equipoise region triaged correctly | Berlin I | Berlin II | Schleswig-Holstein | Berlin I | Berlin II | Schleswig-Holstein |
|---------------------|----------|-----------|--------------------|----------|-----------|--------------------|
| Scenario I          | Drip-'n'-ship | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.02) |
| Scenario II         | Mothership | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (0.98-1.00) |
| Scenario III        | Additional transport time threshold | 1.00 (1.00-1.00) | 0.93 (0.16-0.93) | 0.64 (0.05-0.64) | 1.00 (1.00-1.00) | 0.93 (0.77-0.93) | 0.82 (0.54-0.84) |
| Scenario IV         | Fixed cutoff score | 0.80 (0.75-0.85) | 0.80 (0.75-0.85) | 0.80 (0.75-0.85) | 0.80 (0.75-0.81) | 0.80 (0.75-0.81) | 0.80 (0.75-0.81) |
| Scenario V          | Fixed cutoff score with probabilistic outcome determination | 0.80 (0.75-0.85) | 0.80 (0.75-0.85) | 0.80 (0.70-0.85) | 0.80 (0.75-0.81) | 0.78 (0.64-0.81) | 0.73 (0.58-0.80) |
| Scenario VI         | Optimal variable cutoff scores | 0.97 (0.95-1.00) | 0.93 (0.88-0.98) | 0.89 (0.80-0.95) | 0.94 (0.87-0.97) | 0.84 (0.67-0.95) | 0.79 (0.63-0.91) |
| Scenario VII        | Optimal LVO detection device | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (0.98-1.00) |
| Scenario VIII       | Optimal LVO detection device with probabilistic outcome determination | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) |
| Scenario IX         | Mobile IVT unit | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) |
| Scenario X          | Mobile MT unit | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) |
For a description of triage strategy paradigms, see Figure 2 in the main text.

Table S7. Health system-related outcome measures in specific real-world geographic scenarios, including univariate and probabilistic sensitivity analyses (continued).

| Proportion of patients without LVO in the equipoise region triaged correctly | Univariate sensitivity analysis: I | Univariate sensitivity analysis: II |
|---|---|---|
| Berlin I | Berlin II | Schleswig-Holstein | Berlin I | Berlin II | Schleswig-Holstein |
| Scenario I | Drip-‘n’-ship | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) |
| Scenario II | Mothership | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) |
| Scenario III | Additional transport time threshold | 0.00 (0.00-0.00) | 0.07 (0.07-0.84) | 0.36 (0.36-0.95) | 0.00 (0.00-0.00) | 0.07 (0.07-0.23) |
| Scenario IV | Fixed cutoff score | 0.73 (0.69-0.76) | 0.73 (0.69-0.76) | 0.73 (0.69-0.76) | 0.73 (0.71-0.76) | 0.73 (0.71-0.76) |
| Scenario V | Fixed cutoff score with probabilistic outcome determination | 0.73 (0.69-0.76) | 0.73 (0.69-0.76) | 0.73 (0.69-0.77) | 0.73 (0.71-0.76) | 0.73 (0.72-0.78) |
| Scenario VI | Optimal variable cutoff scores | 0.23 (0.04-0.39) | 0.43 (0.16-0.55) | 0.51 (0.32-0.62) | 0.40 (0.23-0.51) | 0.60 (0.25-0.72) |
| Scenario VII | Optimal LVO detection device | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) |
| Scenario IX | Additional transport time threshold | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) | 1.00 (1.00-1.00) |
| Scenario X | Mobile IVT unit | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) |
| Scenario XII | Mobile MT unit | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) | 0.00 (0.00-0.00) |

For a description of triage strategy paradigms, see Figure 2 in the main text.
Table S8. Theoretical outcome measures in specific real-world geographic scenarios, including univariate and probabilistic sensitivity analyses.

|                                                                                      | Univariate sensitivity analysis: I | Univariate sensitivity analysis: II |
|--------------------------------------------------------------------------------------|------------------------------------|-------------------------------------|
|                                                                                      | Berlin I                           | Berlin II                           | Schleswig-Holstein                  |
| Relative size of the equipoise region, calculated according to estimated number of Code Stroke activations by EMS | 0.3 (0.01-0.3)                     | 0.81 (0.2-0.81)                     | 0.61 (0.28-0.61)                   |
| Relative size of the equipoise region                                               | identical to analysis I            |
| Spatial frequency of optimal variable cutoff score (% of the equipoise region, triage strategy paradigm VI) | 0.92 (0.78-1.00)                  | 0.83 (0.54-1.00)                    | 0.70 (0.53-1.00)                   |
| Optimal variable cutoff score < 5                                                  | 0.00 (0.00-0.01)                   | 0.00 (0.00-0.11)                    | 0.07 (0.00-0.26)                   |
| Optimal variable cutoff score = 5                                                  | 0.08 (0.00-0.22)                   | 0.17 (0.00-0.43)                    | 0.23 (0.00-0.35)                   |
| Optimal variable cutoff score > 5                                                  | 1.00 (1.00-1.00)                   | 1.00 (1.00-1.00)                    | 1.00 (0.93-1.00)                   |
| Spatial frequency of fixed cutoff score = 5 (% of the equipoise region, triage strategy paradigm V) | 1.00 (0.91-1.00)                  | 0.95 (0.79-1.00)                    | 0.93 (0.78-1.00)                   |
| Fixed cutoff score = 5                                                             | 0.09 (0.00-0.15)                   | 0.21 (0.00-0.62)                    | 0.22 (0.10-0.50)                   |
|                                                                                      | 0.39 (0.06-0.47)                   | 0.29 (0.04-0.40)                    |

For a description of triage strategy paradigms, see Figure 2 in the main text. EMS stands for emergency medical services.
Figure S1. Probability density functions of probabilities for final diagnoses according to RACE score.

Gray boxes represent 95% probability mass intervals. AIS stands for acute ischemic stroke; LVO, large vessel occlusion; HS, hemorrhagic stroke; SM, stroke mimic; RACE, rapid arterial occlusion evaluation scale. Based on data from Carrera et al.\textsuperscript{5}
Based on data from Carrera et al.\textsuperscript{5} In this study, patients with more severe stroke symptoms (higher RACE/NIHSS scores) were more likely to receive a RACE score evaluation and be included in the study. To compensate for this effect, we applied a linear correction factor to the reported frequencies of patient in each RACE score category:

\[ f = -0.068 \times RACE + 0.728. \]

The correction factor was chosen such that the overall mean stroke symptom severity would match that of the entire population of patients with Stroke Code Activation by EMS, including patients that did not receive a RACE score evaluation in the study. Gray boxes represent 95% probability mass intervals. RACE stands for rapid arterial occlusion evaluation scale; NIHSS, National Institutes of Health Stroke Scale.

Figure S2. Probability density functions of the relative frequencies of each RACE score category encountered by emergency medical services (EMS) personnel in the prehospital setting.
Figure S3. Probability density functions of National Institutes of Health Stroke Scale (NIHSS) scores according to RACE score.

Gray boxes represent 95% probability mass intervals. RACE stands for rapid arterial occlusion evaluation scale. Based on data from Carrera et al.5
Figure S4. Reduction of DALDs per minute faster treatment for acute ischemic stroke patients.

**Upper left:** Reduction of disability-adjusted life days (DALDs) per minute faster access to successful recanalization for female acute ischemic stroke (AIS) patients with large vessel occlusion (LVO). **Upper right:** Reduction of DALDs per minute faster access to successful recanalization for male AIS patients with LVO. **Lower left:** Reduction of DALDs per minute faster access to i.v. thrombolysis for female AIS patients without LVO. **Lower right:** Reduction of DALDs per minute faster access to i.v. thrombolysis for male AIS patients without LVO. The upper and lower surface in each panel represent boundaries of the 95% probability mass intervals, the middle surface the mean.

Based on data from Meretoja et al.\textsuperscript{14,15} (Point estimates fitted using a locally weighted smoothing linear regression [span 0.2]). NIHSS stands for National Institutes of Health Stroke Scale.
Figure S5. Fit of transport times vs. Euclidean distances in specific real-world geographic scenarios.

The grey areas represent the 95% non-simultaneous prediction intervals for a given observation.
Figure S6. Prehospital stroke triage strategy paradigm-associated transport destination decision rule maps in abstract urban and rural geographic scenarios.

Shown are results for an exemplary 70-year-old male patient with suspected acute stroke in abstract urban (half radius 7.5 km) and rural (half radius 35 km) geographic scenarios. Patients with a RACE score greater than or equal to the color-coded RACE cutoff score would be transported to the nearest CSC instead of the nearest PSC. A dash ‘-’ signifies transport of all patients to the nearest CSC due to lack of equipoise because of a shorter transport time (light color) or PSC (‘RACE cutoff score ≥ 10’, dark color). For a detailed description of the three shown triage strategy paradigms (TSP III, V, and VI), see Figure 2 in main text.

RACE stands for rapid arterial occlusion evaluation scale; TSP, triage strategy paradigm; CSC, comprehensive stroke center; PSC, primary stroke center.
Figure S7. Impact of prehospital triage strategy paradigms on patient-centered outcome parameters in specific real-world geographic scenarios

Boxplots show data for prehospital triage strategy paradigms I – X from probabilistic sensitivity analyses; vertical extent of the boxes represent the interquartile range, the horizontal line the base case result, the whiskers extend to include 95% of all values. Currently available triage strategy paradigms (I – VI) are shown in shades of blue, the remaining paradigms (VII – X) in shades of red. Gain of DALYs is calculated with reference to triage strategy paradigm I (drip-'n'-ship approach). The last row depicts the additional gain in DALYs associated with each triage strategy paradigm over and above all less complex triage strategy paradigms. For a description of triage strategy paradigms, see Figure 2 in the main text.

Panel A represents the base case scenario with a door-out time of 45 minutes, Panel B a door-out time of 15 minutes.

DALY stands for disability-adjusted life year; IVT, i.v. thrombolysis; MT, mechanical thrombectomy.
Figure S8. Impact of prehospital triage strategy paradigms on health system-related outcome parameters in specific real-world geographic scenarios

Boxplots show data for prehospital triage strategy paradigms I – X from probabilistic sensitivity analyses; vertical extent of the boxes represent the interquartile range, the horizontal line the base case result, the whiskers extend to include 95% of all values. Currently available triage strategy paradigms (I – VI) are shown in shades of blue, the remaining paradigms (VII – X) in shades of red. Gain of DALYs is calculated with reference to triage strategy paradigm I (drip-’n’-ship approach). The last row depicts the additional gain in DALYs associated with each triage strategy paradigm over and above all less complex triage strategy paradigms. For a description of triage strategy paradigms, see Figure 2 in the main text.

Panel A represents the base case scenario with a door-out time of 45 minutes, Panel B a door-out time of 15 minutes.

DALY stands for disability-adjusted life year; IVT, i.v. thrombolysis; MT, mechanical thrombectomy.
Boxplots show results for prehospital triage strategy paradigms I – X from repeated random generation of abstract rural and urban geographic scenarios with between 1 – 5 primary stroke centers and 1 – 5 comprehensive stroke centers according to the relative size of the equipoise region (ER). Vertical extent of the boxes represent the interquartile range, the horizontal line the mean, the whiskers extend to include 95% of all values. Currently available triage strategy paradigms (I – VI) are shown in shades of blue, the remaining paradigms (VII – X) in shades of red. In the first row, gain of DALYs is calculated with reference to triage strategy paradigm I (drip-‘n’-ship approach). The second row depicts the additional gain in DALYs associated with each triage strategy paradigm over and above all less complex triage strategy paradigms. For a description of triage strategy paradigms, see Figure 2 in the main text.

Panel A represents the base case scenario with a door-out time of 45 minutes, Panel B a door-out time of 15 minutes.

PSC stands for primary stroke center; CSC, comprehensive stroke center.
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