Title Page

Remote controlled CT scanning for decentralized diagnostics and treatment versus standard care in acute stroke

DIRECT-CT

Decentralized Imaging by REmote Computer Tomography for Cerebral infarct Thrombolysis

Protocol v1. 11.02.2025

Chief investigator: Agnethe Eltoft

Sponsor: University Hospital of North Norway

Study Protocol

Title {1}	**Remote controlled CT scanning for decentralized diagnostics and treatment versus standard care in acute stroke** DIRECT-CT Decentralized Imaging by REmote Computer Tomography for Cerebral infarct Thrombolysis
Trial registration {2a and 2b}	Trial identifier at clinical trials.gov
Protocol version	v1. 11.02.2025
Funding {4}	Helse Nord Health Trust
Author details {5a}	Agnethe Eltoft[1,2], Eivor Logstein[3], Monica Storkjørren[3], Susanne Ingebrigtsen[1], Maria Carlsson[4], Linn Hofsøy Steffensen[1,2], Mette Kjær[5], Maren Ranhoff Hov[6,7,8], Jørgen Ibsen[9], Anette Huse Farmen[10], Jon Våbenø[3], Ellisiv B. Mathiesen[1,2], Tor Ingebrigtsen[1,2] [1]Universitty hospital of North-Norway [2]The Arctic University of Norway [3]Helgeland Hospital Trust [4]Nordland Hospital Trust [5]Finnmark Hospital Trust [6]Oslo University Hospital [7]Oslo Metropolitan University [8]Stiftelsen Norsk Luftambulanse [9]Ringerrike Hospital [10]Innlandet Hospital Trust
Name and contact information for the trial sponsor {5b}	University Hospital of North-Norway Nevro, ortopedi- og rehabiliteringsklinikken Postboks 100 9038 Tromsø
Role of sponsor {5c}	The study sponsor is responsible for the conduct of the trial with regards to data collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication in collaboration with all study collaborators.

Protocol Summary - Synopsis

Study Title:	**Remote controlled computer tomography (CT) scanning for decentralized diagnostics and treatment versus standard care in acute stroke**
CTR Number:	2025-*to filled in*
Acronym	DIRECT-CT
Coordinating investigator	Agnethe Eltoft MD PHD
Study Rationale	The DIRECT-CT trial is designed to test the hypothesis that remote controlled CT scanning combined with real time audio-and video conference (AVC) guided assessment from an experienced hospital stroke team (telestroke) at decentralized medical centers (DMC) reduces time to intravenous thrombolytic (IVT) treatment compared to the standard pathway.
Benefit/Risk assessment	IVT is an effective treatment of disabling acute ischemic stroke (AIS) and leads to improved functional outcomes if administered within 4.5 hours after symptom onset. Since the treatment effect is highly time dependent, it is recommended to give IVT as soon as possible after symptom onset to patients with AIS without contraindications. A CT examination of the head must be performed prior to IVT to exclude intracranial hemorrhage. If an intracerebral hemorrhage (ICH) is detected rapid blood pressure lowering medication should be initiated. As of today, timely delivery of acute stroke treatment is challenging in several parts of Norway due to sparsely populated areas with long geographical distances between hospitals. Patients living in rural areas are at risk of not receiving timely acute stroke treatment. Due to the time sensitive nature of IVT, a decentralized approach to diagnostics and treatment is compelling. However, a CT scanner and medical expertise on acute stroke diagnostics and treatment is not readily available in pre-hospital settings in Norway. We therefore plan to 1) assess the feasibility of widespread implementation of a model with decentralized stroke diagnostics and treatment in rural areas with a stationary CT combined with audio-and video guided support from an experienced stroke team at the local hospital 2) compare treatment access, time metrics and outcomes for stroke patients in the DMC catchment area to patients from similar rural areas without access to decentralized diagnostics and treatment. The risk for patients is minimized through remote controlled CT scanning administered from the local hospital combined with telestroke guided assessment by an experienced stroke team and regular simulation trainings. All treatment, including thrombolytic therapy, and monitoring routines are performed according to the hospitals' standard operating procedures (SOP).

Objectives	<u>Primary objective:</u> • To compare time from Emergency Medical Communication (EMC) notification to IVT treatment between AIS patients in the intervention group comprising patients from geographical areas with an established service of prehospital stroke diagnostics and treatment at the DMC to the control group comprising patients from similar geographical areas undergoing diagnostics and treatment at their local hospital as per standard pathway. <u>Secondary objectives:</u> • To compare onset- to-treatment decision time between stroke simulation trainings performed at DMC to stroke simulation trainings at local hospital and between stroke simulation trainings performed at different DMCs • To compare between the intervention and control groups: - Door-to-needle time among IVT treated AIS patients - Door-to-time of blood pressure lowering medication in ICH patients - The percentage of AIS patients treated with IVT - The percentage of AIS patients treated with endovascular treatment (EVT) - The percentage of ICH patients treated with blood pressure lowering medication - The percentage of patients treated with neurosurgical procedures - Onset-to-treatment time (for IVT, EVT, blood pressure lowering medication and neurosurgical procedures) - Time from EMC notification to comprehensive stroke center admittance among patients with a large vessel occlusion (LVO) transferred for EVT. - The percentage of IVT treated patients achieving early neurological improvement (ENI) defined as obtaining National Institutes of Health Stroke Scale (NIHSS) score 0-1 or decrease in NIHSS score > 8 points at 24 h among IVT treated AIS patients - Change in NIHSS score from baseline to 24h among IVT treated AIS patients - Functional outcome defined by modified Rankin Scale (mRS) score at 90 days among IVT treated AIS patients - Functional outcome defined by modified Rankin Scale (mRS) score at 90 days among ICH patients - The rate of symptomatic intracranial hemorrhage (sICH) among IVT treated AIS patients - Length of hospital stay - Discharge destination - Mortality rates during hospitalization, at 30 days, 90 days and 1 year - The percentage of stroke patients transported by air ambulance - The percentage of LVO patients achieving reperfusion judged by TICI score after IVT and EVT - Quality of life at 90 days defined by EQ5D
Trial Configuration	A pragmatic multicenter, prospective, controlled, open label, registry-linked trial
Setting	Emergency departments, DMCs, acute stroke units in Norway
Sample size estimate	The sample size estimation consisting of 26 patients in each group provides a power of 0.80 to demonstrate a difference of 50 minutes between the group (μ1 - μ2 = 0.0 - 50.0 = -50.0) using a two-sided Mann-Whitney U, assuming that the actual data distribution is normal. This is based on a significance level (alpha) of 0.050 and a standard deviation of 60.0 in both groups. We estimate that 16-20% of all AIS patients are eligible for IVT, with a recruitment period of 3 years and an annual incidence of 65 AIS in the catchment areas of the DMCs, we should have potential to recruit 30-40

	patients in the intervention group during the study period.
Number of participants	52 (26 in each group)

Eligibility criteria	**Inclusion criteria** Patients in the catchments areas of the intervention and control group presenting with • a clinical suspected diagnosis of stroke within symptom onset within the last 24 hours **Exclusion criteria** • patients presenting with a clinical suspected diagnosis of stroke more than 24 hours after symptom onset
Description of interventions	Patients presenting with acute stroke symptoms within the last 24 hours in the catchment area of the DMCs (Sørreisa, Senja, Brønnøy and Sømna) will be allocated to the intervention group. The intervention includes admittance to the DMC for initial diagnostic work up and acute treatment (if indicated). Paramedics examine the patient and assess stroke severity by NIHSS and G-FAST scoring overseen by a stroke physician at the local hospital through real time video conference. A remote controlled CT scan of the head is conducted, and the stroke team at the local hospital evaluates results and makes a treatment decision in real-time AVC. If treatment is indicated, this is administered by local personnel at the DMC before initiating transport to the local hospital or the comprehensive stroke center in case of LVO. Patients who are unable to reach the DMC prior to estimated admission time at their local hospital, will be treated at their local hospital as per standard pathway. Patients presenting with stroke symptoms in the catchment area of municipalities with comparable distance to the local hospital as the intervention group (Nordreisa, Kåfjord, Skjervøy, Kvænangen, Saltdal, Hamarøy, Steigen and Sørfold) comprise the control group. The control group will be treated as per standard pathway at their local hospital, adhering to local standard operating procedures (SOP) and current practice guidelines.
Duration of study	Planned prospective inclusion period 2025-2028, retrospective inclusion 2016-2025, study termination December 2033. Duration of study per participant: 90 days (+/- 2 weeks) follow-up.
Randomisation and blinding	This is an open label, open endpoint study. Eligible patients will be allocated according to geographical location at the time of stroke symptom onset. No randomization is planned.

Outcome measures	Primary outcome: • time from EMC notification to initiation IVT treatment Secondary outcome measures include • time from admittance to initiation of IVT treatment (door-to-needle time) • time from admittance to start of blood pressure lowering medication in ICH patients • IVT treatment (y/n) • EVT treatment (y/n) • Treatment with blood pressure lowering medication (y/n) • Neurosurgical procedures (y/n) • time from symptom onset to treatment (IVT, EVT, blood pressure lowering medication and neurosurgical procedures) • time from EMC notification to admittance at comprehensive stroke center • stroke severity score measured by NIHSS score (0-42) at admittance (DMC or local hospital), 2 h, 24 (± 6h) or discharge (within 7 days) • early neurological improvement, defined as a reduction of ≥8 points on the NHISS, or NIHSS score of 0-1 at 24 hours (22-36 h) (y/n) • functional outcome measured by the modified Rankin Scale score (mRS) at discharge and day 90 (± 2 weeks) • mRS category at day 90 (+/- 2 weeks) ○ excellent functional outcome (mRS 0-1) at day 90 (+/- 2 weeks) ○ good functional outcome (mRS 0-2) at day 90 (+/- 2weeks) ○ poor functional outcome (mRS 5-6) at day 90 (+/- 2 weeks) • occurrence of symptomatic intracranial hemorrhage (sICH) complications defined as intracranial hemorrhage on CT/MRI within 36 hours post IVT causally related to an increase of 4 points or more on the NIHSS (y/n) • transportation mode (ground or air ambulance) • any intracranial hemorrhage (ICH) on CT/MRI within 36 hours post IVT according to the Bleeding Classification Heidelberg (HBC) • TICI score in LVO patients (0-3) • quality of CT and CTA examination judged by radiologist as satisfactory (y/n) • final diagnosis • mortality during hospitalization, 30 days, 90 days and 1 year • Barthel score at discharge and day 90 (± 2 weeks) • EQ5D at day 90 (± 2 weeks) • length of hospitalization • discharge destination • groin puncture time
Statistical methods	The main analysis is planned when all patients have completed the study, all data have been entered, verified and validated and the database has been locked. The primary null hypothesis to be tested is that EMC notification- to treatment time is not different between patients in the intervention group and patients in the control group. The primary outcome will be analyzed by a non-parametric Mann–Whitney *U* test. Results are evaluated at 5% two-sided level of significance. Safety will be monitored continuously, and early stopping of the study will be considered if the number of sICH, patients with delayed treatment are excessively high in the intervention group or other safety concerns are detected.
Impact	If decentralized acute stroke treatment can be delivered safely and effectively in a prehospital setting at strategically located DMCs, this can increase the number of rural patients eligible for IVT and treatments access in the early phase after stroke onset when the treatment is most effective. Results from the present study represent an important contribution to ongoing international discussions regarding implementation of highly effective treatments for acute stroke.

Introduction

Background and rationale {6a}

Stroke is the leading cause of loss of disability-adjusted life years among the elderly (1). The number of hospital admissions in Norway is approximately 9-10 000 per year (2). Although the incidence is decreasing, the number of cases is still increasing because of an aging population (3). Ischemic strokes are the most common (80-85%), followed by intracerebral hemorrhage ICH (10-15%) and subarachnoid hemorrhage (SAH) (2-5%). Earlier access to diagnostics and treatment can provide health benefits to the population, reduce disability and thus decrease costs related to rehabilitation and care following stroke. In acute ischemic stroke (AIS), early intravenous thrombolysis treatment (IVT) is an important predictor of a good functional outcome(4, 5). For selected patients with AIS caused by a large vessel occlusion (LVO), timely endovascular treatment (EVT) with thrombectomy improves functional outcome (6-8). In patients with spontaneous non-traumatic ICH, an emerging body of evidence suggest that combining multiple interventions- anticoagulation reversal, blood pressure reduction, neurosurgical evaluation and management of pyrexia and hyperglycemia within time sensitive care bundles- is associated with reduced 30 day mortality (9) and improved outcomes (10).

Prior to IVT treatment, brain hemorrhage must be ruled out by a non-contrast computer tomography (CT) scan (4) and patients eligible for thrombectomy are identified by the detection of LVO on CT angiography (CTA). Prehospital administration of IVT in mobile stroke units- ambulances equipped with CT scanners- reduces time to thrombolysis (11) and provides absolute benefit compared to administration in emergency departments (12, 13). However, mobile stroke units are unlikely to be a feasible solution in in rural parts of Norway due to long distances and sparse population. Previous analyses suggest that each mobile stroke unit needs to be treat approximately 260 AIS patients annually to be cost-effective (14) with optimal cost-benefit achieved within an operating radius between 43 and 65 kilometers (15). Simulation studies have shown that CT in helicopters could provide even shorter time to thrombolysis (16). However, this technology is still under development and unavailable for implementation. A Norwegian clinical study (17) in a rural region in Southern Norway (Ål municipality) has shown that a prehospital CT model may initiate IVT therapy in AIS patients significantly earlier compared to conventional assessment at local hospitals. However, this model needs to be evaluated in other regions and on a larger scale.

A decentralized medical center (DMC) is a healthcare facility that provides a wide range of medical services in rural or remote areas. Such centers often represent a collaboration between specialized healthcare services including ambulance services and primary healthcare services. They may offer services such as emergency care, outpatient clinics, day surgery and rehabilitation. The primary goal of a DMC is to improve access to healthcare for people living in rural areas, reducing the need for them to travel long distances to larger hospitals. Telestroke refers to a telemedicine system where health care providers who have advanced training in treating strokes can use technology (audio-and video conference (AVC) and other communication tools) to evaluate and treat stroke patients in real-

time from a distance through collaboration with local emergency health care providers. We have developed a pilot-model at DMC-Midt Troms combining remote controlled prehospital CT examination with telestroke guided diagnostics and treatment of patients presenting with acute stroke symptoms in rural areas. No studies hereto have investigated whether this can be implemented on a larger scale and be extended to include CTA-diagnostics in a prehospital setting. We therefore plan to implement remote controlled CT scanning combined with telestroke guided assessment for prehospital decentralized diagnostics and treatment at DMCs and compare treatment times, rates and outcomes to a reference population from comparable districts in rural Norway.

Objectives {7}

The potential impact of implementing remote controlled prehospital CT scanning combined with telestroke guided assessment for decentralized diagnostics and thrombolysis on expediting and enhancing stroke treatment remains uncertain. Therefore, we aim to investigate the following: 1. Can the pilot-model at DMC Midt-Troms be effectively implemented and scaled to additional DMC facilities?

2. Are the emergency medical communication (EMC) notification-to-treatment times shorter, thrombolysis rates higher and outcomes improved for patients with AIS who have access to decentralized CT examination and IVT at a DMC, compared to a control group receiving standard care i.e. CT examination and treatment at the nearest hospital?

3. Are EMC notification-to-treatment times shorter and outcomes improved for patients with ICH who have access to decentralized CT examination and acute treatment at a DMC, compared to a control group receiving standard care i.e. CT examination and treatment at the nearest hospital? 4. Does the utilization of non-contrast CT and CTA at the DMC reduce the reliance on helicopter transport to local hospitals and decrease EMC notification-to-admittance times at the comprehensive stroke center for patients with LVO transferred for EVT, compared to a control group receiving CT examination at the nearest hospital?

Trial design {8}

This is a prospective open label, parallel group controlled observational clinical study investigating the effect of a health service innovation. The study assesses the superiority of a model with prehospital remote controlled CT scanning combined with telestroke guided assessment for decentralized diagnostics and acute stroke treatment at the DMCs compared to the standard pathway for stroke patients in rural Norway. The trial is designed in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) initiative guidelines.

Methods: Participants, interventions and outcomes

Participants are patients presenting with acute stroke symptoms in rural districts in Norway. In a pilot study at DMC Midt-Troms, we have implemented a cockpit solution by Syngo Virtual Cockpit® software for remote control of the stationary CT machine from the comprehensive stroke center University

Hospital of North-Norway (UNN), Tromsø. The EMC center routes the ambulance to DMC Midt-Troms when it is the nearest. A nurse at DMC and the ambulance personnel performs the clinical examination and positions the patient in the CT machine. Through AVC the examination is overseen by the stroke physician, images are interpreted by a radiologist at UNN, and the decision regarding acute treatment is made by the stroke physician at UNN, Tromsø. If indicated, IVT and blood pressure lowering medication is administered by the nurse at the DMC. The model from DMC Midt Troms may be implemented at other DMC locations. The first location is DMC Sør-Helgeland, where a similar model with remote control of the stationary CT and telestroke support from Helgeland Hospital, Sandnessjøen was implemented in clinical use from September 2024.

Patients presenting with acute stroke symptoms in the catchment area of DMC Midt-Troms (Sørreisa and Senja municipalities) and DMC Sør-Helgeland (Brønnøy and Sømna municipalities) comprise the intervention group.

The control group consists of

1) Patients presenting with acute stroke symptoms residing in municipalities in Nord-Troms (Nordreisa, Kåfjord, Skjervøy and Kvænangen) and Nordland (Saltdal, Hamarøy, Steigen and Sørfold) from the time of DMC model implementation until end of study. These patients are from areas that are geographically similar to Midt-Troms and Sør-Helgeland with regards to distance to the nearest hospital, but without access to prehospital CT diagnostics and acute stroke treatment.
2) Historical controls: Acute stroke patients from the same municipalities (both intervention and control group) presenting with stroke symptoms within a 5 year period prior to the implementation of prehospital diagnostics and treatment at the DMC.

If similar models for stroke diagnostics and treatment are established at other DMCs during the study period, we will attempt to also include these in the present study.

Outcome data will be retrieved from the patients' electronic health records (EHR) including prehospital (AMIS, eSTROKE) and intrahospital systems (DIPS, Sectra) and local registrations in the Norwegian Stroke Registry.

Eligibility criteria {10}

Inclusion criteria

All patients from the defined municipalities Senja, Sørreisa, Brønnøy, Sømna, Nordreisa, Kåfjord, Skjervøy, Kvænangen, Saltdal, Hamarøy, Steigen and Sørfold referred with

- a clinical suspected diagnosis of stroke within the last 24 hours

Exclusion criteria

- patient presenting with a clinical suspected diagnosis of stroke more than 24 hours after symptom

onset

Who will take informed consent? {26a}

Not applicable, for more details confer to {24} p.20.

Additional consent provisions for collection and use of participant data and biological specimens {26b}

Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies is not applicable.

Interventions

Explanation for the choice of comparators {6b}

The control group will comprise patients with a clinical suspected diagnosis of stroke who undergo a cerebral CT scan and neurological examination at their local hospital within 24 hours of symptom onset, defined as standard pathway. Patient presenting within 24 hours of symptom onset should according to national and international guidelines be considered for acute reperfusion treatment. The control group includes patients from municipalities that have similar distances to the local hospital and population size compared to municipalities in the intervention group.

Intervention description {11a}

All emergency calls to the EMC center (AMK 113), will be screened for stroke symptoms by the EMC dispatcher, as per normal procedures. If stroke symptoms are present, the stroke physician on-call at the local hospital will be noticed immediately and depending on fulfilment of inclusion criteria (listed above), patient location and expected arrival times, the patient will be allocated to the intervention (initial diagnostics and treatment at the DMC) or standard care (initial diagnostics and treatment at their local hospital). The EMC dispatcher will notify the DMC associated ambulance staff and GP on call and provide clinical history, if available. Trained paramedics will take the medical history and conduct a screening using the ABCDEs of trauma care. If the patient is stable, further investigations can proceed, including the NIHSS and G-FAST scoring. The patient will get two venous lines and be transported by ambulance to the DMC as soon as possible. An acute intra-hospital stroke alarm will be triggered at the local hospital noticing an in-hospital stroke team (a radiographer, a radiologist and the stroke physician on call) 10 minutes prior to expected patient arrival time at the DMC. The GP and nurse at the DMC receive a pre-notification prior to DMC arrival. At the DMC, paramedics will position the patient in the CT scanner and the CT scanning is remote controlled by the radiographer at the local hospital.

The paramedics will provide the stroke team with the clinical history, point-of-care laboratory blood tests, the time of symptom onset, and any known clinical contraindication of thrombolysis. The intra-hospital stroke physician will overlook the NIHSS and G-FAST scoring performed by paramedics in real time AVC. The radiologist will interpret the CT scan by teleradiology, and a treatment decision

will be made by the stroke physician. If acute therapy is indicated according to inclusion/exclusion criteria in current guidelines and local SOPs, the paramedic or local nurse will prepare and give IVT in AIS patients and follow relevant treatment protocols for ICH patients. Both thrombolytic medications (alteplase (ALP) and tenecteplase (TNK)) are approved for the indication AIS, with similar efficacy and safety profile. Alteplase 0.9 mg/kg, with a maximum total dose of 90 mg, is administered with 10% of the total dose given as an initial intravenous bolus over 1 minute and the remaining 90% of the total dose as a continuous intravenous infusion over 60 minutes. Tenecteplase 0.25 mg/kg (maximum 25 mg) is given as a single intravenous bolus. Blood pressure should be maintained below 180/105 mmHg during the first 24 hours after IVT.

Relevant treatment protocols in ICH include early intensive blood pressure lowering, glycemic control, and early treatment of pyrexia, early reversal of anticoagulation, early avoidance of do-not-resuscitate orders, and referral pathways for intensive care and neurosurgery. Intensive BP lowering aims to reach a systolic target of 130–140 mmHg within 30 minutes of commencing treatment, and to maintain this BP level for the first 7 days (for patients presenting with blood pressure <200 mmHg). If blood pressure ≥200 and <220, target BP of 160 mmHg should be targeted at 30 minutes, and 130–140 mmHg should be achieved in 60 minutes. If BP ≥220, target BP of 160 mmHg and should be achieved in 60 minutes. Early reversal treatment of ongoing oral anticoagulation (OAC) is relevant in situations of either an elevated INR with the use of warfarin or where there has been recent use (<48 hours) of a direct oral anticoagulant (DOAC). The appropriate reversal agent should then be administered within 30 minutes according to local SOPs.

After acute treatment, the patient will remain on strict bedrest and vital signs, neurological signs and blood pressure will be monitored every 15 min. until hospital admittance. The patient will be transferred to their local hospital unless a LVO is detected. In cases with LVO and eligibility for thrombectomy or ICH with need of surgical care, transportation is initiated as soon as possible to the nearest comprehensive stroke center.

Paramedics in the catchment areas of the DMC will be trained in NIHSS, and G-FAST scoring which will be performed at the first medical contact and repeated on arrival at the DMC. The findings will be promptly discussed with the stroke physician on-call at the local hospital. NIHSS score≥8 or G-FAST score≥3 are predefined indicators of suspected LVO in Helse-Nord region. If present, the neurologist at the comprehensive stroke center will be promptly contacted, and the patient may be evaluated for direct transportation to the comprehensive stroke center.

Patients with acute stroke symptoms who are unable to arrive at the DMC before the estimated admission time at their local hospital, will be transported to their local for diagnostics and treatment per standard pathway, following national stroke guidelines.

Criteria for discontinuing or modifying allocated interventions {11b} If the CT scanner at the DMC is indisposed due to technical issues or for some other reason, the patients will be routed to their local hospital or directly to the comprehensive stroke center according to standard care and local procedures. Technical issues refer to any issues or malfunctions related to hardware, software, connectivity, or operational processes that hinder the successful completion of imaging, image transmission, or communication between the DMC and the stroke center. These may include, but are not limited to, scanner calibration errors, network disruptions, image quality degradation, or challenges in coordinating remote radiographer support.

To minimize the risk of such issues, extensive technical testing has been conducted prior to the operational phase at each DMC to ensure system reliability under various conditions. In the event of a technical problem, the stroke physician is to be contacted immediately to reassess the patient's condition and determine whether an alternative hospital should be designated for treatment. This is included in the local SOP and ensures that patient care remains uninterrupted despite potential technical challenges. In addition, all technical issues will be reported to the technical department for evaluation and risk mitigation.

Strategies to improve adherence to interventions {11c}

Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence, include simulation training in multidisciplinary teams and will be performed regularly (at least once a month) to keep all personnel trained and updated on procedures. During simulation training as well as in operational clinical practice, time metrics will be monitored including door-to needle time, door-to-CT scan time, door-to-treatment decision time as well as reporting of technical issues.

Relevant concomitant care permitted or prohibited during the trial {11d} No relevant concomitant care and interventions that are permitted or prohibited during the trial have been identified.

Provisions for post-trial care {30}

Supplementary treatments and care will be performed within the public health care sector according to local SOPs and national guidelines for acute stroke treatment. Participants are covered by the Norwegian Patient Injury Compensation which provides compensation of injuries that occur within the healthcare system, including those arising from clinical trials.

Outcomes {12}

Primary outcome:

- time from EMC notification to initiation IVT treatment

Secondary outcome measures include

• time from admittance to initiation of IVT treatment (door-to-needle time)

• time from admittance to start of blood pressure lowering medication in ICH patients • IVT treatment (y/n)

• EVT treatment (y/n)

• Treatment with blood pressure lowering medication (y/n)

• Neurosurgical procedures (y/n)

• time from symptom onset to treatment (IVT, EVT, blood pressure lowering medication and neurosurgical procedures)

• time from EMC notification to admission comprehensive stroke center for LVO patients • stroke severity score measured by NIHSS score (0-42) at admittance (DMC or local hospital), 2 h, 24 (± 6h) or discharge (within 7 days)

• early neurological improvement, defined as a reduction of ≥8 points on the NHISS, or NIHSS score of 0-1 at 24 hours (22-36 h) (y/n)

• functional outcome measured by the modified Rankin Scale score (mRS) at discharge and day 90 (± 2 weeks)

• mRS category at day 90 (+/- 2 weeks)
    - excellent functional outcome (mRS 0-1) at day 90 (+/- 2 weeks)
    - good functional outcome (mRS 0-2) at day 90 (+/- 2weeks)
    - poor functional outcome (mRS 5-6) at day 90 (+/- 2 weeks)

• occurrence of symptomatic intracranial hemorrhage (sICH) complications defined as intracranial hemorrhage on CT/MRI within 36 hours post IVT causally related to an increase of 4 points or more on the NIHSS (y/n)

• transportation mode (ground or air ambulance)

• any intracranial hemorrhage (ICH) on CT/MRI within 36 hours post IVT categorized according to the Bleeding Classification Heidelberg (HBC)

• thrombolysis in cerebral infarction TICI score in LVO patients (0-3)

• quality of CT and CTA examination judged by radiologist as satisfactory (y/n) • final diagnosis

• mortality during hospitalization, 30 days, 90 days and 1 year

• Barthel score at discharge and day 90 (± 2 weeks)

• EQ5D at day 90 (± 2 weeks)

• length of hospitalization

• discharge destination

• groin puncture time

Other relevant study variables:

Age, gender, history of known comorbidity and medications including history of anticoagulation or antiplatelet use, prehospital NIHSS, G-FAST score, vital signs, NIHSS in-hospital (day 0, 2 hours after IVT, 24h, and at discharge), hyperacute CT diagnosis, CT-angiography (CTA) findings, MRI lesion

volume within 48 hours after hospital admission, time from symptom onset to EMC notification, time spent on site by paramedics, time spent in transportation. Blood samples (glucose level, INR and thrombocyte count) are required to assess IVT eligibility and will be performed and analyzed according to the local SOPs.

Schedule of Activities (SoA)

Procedure	Intervention Period					Follow-up[π] 90 days +/- 2 weeks
	Pre hospital	0 hours Baseline**	+ 2 h	+ 24 h (22-36 h)	+ 7 days or earlier discharge	
Demography*	X	X				
Current and prior medical conditions and medication*	X	X				
Vital signs*	X	X	X	X		
NIHSS score*	X	X	X	X	X	
Imaging* Head CT/CTA(CTP) or MRI (MRA/MRP)		X		X		
Inclusion and exclusion criteria		X				
Laboratory analysis*		X				
Intervention DMC diagnostics and reperfusion treatment and times		X				
12-lead ECG*			X			
SAE/AE*	X	X	X	X	X	
mRS		X			X	X
Barthel					X	X
EQ5D-5L						X
*SOP for thrombolysis, ** Baseline is at admittance to DMC and local hospital,[π]by dedicated study nurse						

Sample size {14}

The primary outcome will be EMC notification to treatment time in the intervention group compared to the control group. The sample size estimation consisting of 26 patients in each group provides a power of 0.80 to demonstrate a difference of 50 minutes between the group (μ1 - μ2 = 0.0 - 50.0 = -50.0) using a two-sided Mann-Whitney U, assuming that the actual data distribution is normal. This is based on a significance level (alpha) of 0.050 and a standard deviation of 60.0 in both groups.

We estimate that 16-20% of all AIS patients are eligible for IVT, with a recruitment period of 3 years and an annual incidence of 65 AIS in the catchment areas of the DMCs, we should have potential to recruit 30-40 patients in the intervention group during the study period. We estimate that 16-20% of all AIS patients are eligible for IVT, with a recruitment period of 3 years and an annual incidence of 65 AIS in the catchment areas of the DMCs, we would have the potential to recruit 30-40 patients in the intervention group.

Recruitment {15}

All emergency calls to the EMC center (AMK 113), from the catchment areas, will be screened for stroke symptoms by the EMC dispatcher, as per normal procedures. If stroke symptoms are present, the stroke physician on-call at the local hospital will be noticed immediately and depending on fulfilment of the inclusion criteria, patient location and expected arrival times, the patient will be allocated to intervention (initial diagnostics and treatment at the DMC) or standard care ((initial diagnostics and treatment at their local hospital).

Assignment of interventions: allocation

Sequence generation {16a}

Patients presenting with stroke symptoms in the catchment area of the DMC will be allocated to the intervention when the CT machine at the DMC is the nearest. In each specific situation this depends on the location of the patient and prehospital resources, weather and traffic conditions. Patients with acute stroke symptoms who are unable to arrive at the DMC before the estimated admission time at their local hospital will be transported to their local for diagnostics and treatment, following standard pathway and national stroke guidelines. All other patients presenting with stroke symptoms will be handled according to SOP at their local hospital.

Concealment mechanism {16b}

Patients are allocated to the control group or the intervention group according to their geographical location at the time of EMC notification. No randomization or concealment is planned due to the fixed location of the model at DMC and the expected low number of cases.

Implementation {16c}

Allocation will be based on geographical location. The assignment to intervention will be performed by EMC dispatcher in agreement with the stroke physician on call at the time of EMC notification.

Assignment of interventions: Blinding

Who will be blinded {17a/b}

No blinding of trial participants, care providers, outcome assessors or data analysts is planned.

Data collection and management

Plans for assessment and collection of outcomes {18a}

All relevant data are prospectively recorded as part of routine clinical practice in both prehospital and in-hospital EHR and are mandatorily reported to the Norwegian Stroke Registry. Quantitative data collected from EHR in this study will be entered into patient specific electronic case report forms (eCRFs) in the REDCAP system. The relevant prehospital and in-hospital EHR systems are AMIS, eSTROKE, DIPS and SECTRA. A procedure for harmonized prospective data collection will be implemented by introducing a template for journal notes for pre-hospital and in hospital personnel at all sites to ensure complete data collection for both the intervention and control groups. The paramedics and EMC dispatcher will collect the prehospital data on time-metrics, history of known comorbidity and medications including history of anticoagulation or antiplatelet use, vital signs, stroke severity according to NIHSS stroke scale and G-FAST (both at first medical contact and upon arrival at the DMC), CT scan time, acute treatment time and occurrence of any treatment complications or other adverse events. In hospital doctors will register time of hospital admission, admission and follow-up NIHSS score, vital signs, history of known comorbidity and medications, CT scan time, acute treatment time and occurrence of any treatment complications or other adverse events. mRS and Barthel score will be assessed in the hospital upon arrival and at day 7 or the day of discharge (whichever comes first). A new CT scan or preferably a MRI scan, will be obtained within 36 hours of hospital admission in all IVT treated patients. Follow-up assessments at 90 days (±2 weeks) after stroke, will be performed by telephone interview by a nurse as part of the routine reporting to the Norwegian Stroke Registry. We will collect data on vital status up to one year from trial entry from EHR. Hospital admission lists will be searched by local stroke unit personal every week for relevant patients and in case of missing data the treating physician may be approached to fill in this information.

Plans to promote participant retention and complete follow-up {18b}

Follow-up tests 90 days (±2 weeks) after acute stroke, will be conducted by telephone interview by a nurse as part of the routine reporting to the Norwegian Stroke Registry. Unless rejected, the study nurse will contact participants by several attempts to retrieve complete data for 90-day follow-up as this is to be mandatorily reported to the Norwegian Stroke Registry. If the patient fails to respond to the follow-up telephone interview, data will be imputed from recordings at discharge (last observation carried forward).

Data management {19}

All prospectively collected quantitative data will be registered in the patient's EHR. Dedicated study personnel (PhD candidate and study nurse) will collect and enter data from the EHR in an electronic case report form (eCRF) using the REDCap system. In order to ensure the quality of data transferal (from source data to the database), the data entry will be double checked.

Confidentiality {27}

All data are stored de-identified with an individual code for each participant in the Helse-Nord's secure research server, accessible only to specified study personnel. The code list is kept on a separate server. The database is password protected and unavailable to non-study personnel.

Plans for collection, laboratory evaluation and storage of biological specimens for genetic or molecular analysis in this trial/future use {33}

Collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis is not planned in the current trial. However, some blood samples are required to assess IVT eligibility and will be performed and analyzed according to the local SOPs.

Statistical methods

Statistical methods for primary and secondary outcomes {20a}

Objective 1: Can the the pilot-model at DMC Midt-Troms be effectively implemented and scaled to additional DMC facilities?

Null hypotheses: Door-to-needle times do not differ between the new DMC model and the standard local hospital model. Furthermore, we will test the null hypothesis that door-to needle times at DMC Midt-Troms is not different from door-to-needle times at DMC Sør-Helgeland or any other DMC which implements the DMC model.

Statistical method: Door-to needle times will be compared by Mann–Whitney *U* test. 2-sample, 2-sided equality. Comparisons will be made separately for the simulation training setting and the clinical setting.

Objective 2a: Are EMC notification-to-treatment times shorter for AIS patients who have access to decentralized CT examination and thrombolysis treatment at a DMC, compared to a control group receiving standard care i.e. CT examination at the nearest hospital?

Null hypotheses: EMC notification-to-treatment times do not differ between the intervention group and control group.

Statistical method: EMC notification-to-treatment times will be compared by Mann–Whitney *U* test. 2-sample, 2-sided equality.

Objective 2b: Are thrombolysis rates higher among AIS patients in regions with access to initial CT examination and IVT treatment at a DMC, compared to the control group receiving diagnostics and IVT treatment at the nearest hospital?

Null hypotheses: The percentage of AIS patients undergoing IVT treatment does not differ between the intervention group and control group.

Statistical method: Percentage of patients treated with thrombolysis will be compared between the intervention group and the control groups by means of binary logistic regression adjusted for relevant covariates (age, sex, NIHSS score and time from symptom onset to EMC notification time).

Objective 2c: Are outcomes improved for AIS patients with access to prehospital CT diagnostics and IVT treatment at a DMC, compared to the control group receiving CT examination at the nearest hospital?

Null hypotheses: Functional outcomes defined as mRS score at 90 days do not differ between patients in the intervention group and patients in the control group.
Outcomes will be defined on an ordinal scale as mRS (0-6) and as binary outcomes (excellent functional outcome (mRS 0-1), good functional outcome (mRS 0-2), and poor functional outcome (mRS 5-6)
Statistical method: Functional outcome will be compared between the intervention group and the control groups by means of ordinal and binary logistic regression (as appropriate) and will be adjusted for relevant covariates (age, sex, NIHSS score and time from symptom onset to EMC notification time).

Objective 3a: Are EMC notification-to-treatment times shorter for ICH patients who have access to decentralized CT examination and acute treatment at a DMC, compared to a control group receiving standard care i.e. CT examination and treatment at the nearest hospital?
Null hypotheses: EMC notification-to-treatment times do not differ between the intervention group and control group.
Statistical method: EMC notification-to-treatment times will be compared by Mann–Whitney *U* test. 2-sample, 2-sided equality.

Objective 3b: Are outcomes improved for ICH patients who have access to decentralized CT examination and acute treatment at a DMC, compared to a control group receiving standard care i.e. CT examination and treatment at the nearest hospital?
Null hypotheses: Functional outcomes defined as mRS score at 90 days do not differ between ICH patients in the intervention group and patients in the control group.
Outcomes will be defined on an ordinal scale as mRS (0-6) and as binary outcomes (excellent functional outcome (mRS 0-1), good functional outcome (mRS 0-2), and poor functional outcome (mRS 5-6)
Statistical method: Functional outcome will be compared between the intervention group and the control groups by means of ordinal and binary logistic regression (as appropriate) and will be adjusted for relevant covariates (age, sex and NIHSS score).

Objective 4a: Does the CT examination and thrombolysis treatment at a DMC reduce the reliance on air ambulance transport to hospitals?
Null hypotheses: The percentage of air ambulance transfers of stroke patients do not differ between the intervention and control groups.
Statistical method: Percentage of patients transferred by air ambulance will be compared between the intervention and the control groups by means of binary logistic regression adjusted for relevant covariates (age, sex, NIHSS score).

Objective 4b. Does the utilization of CTA at a DMC reduce EMC notification-to-admittance times at the comprehensive stroke center for patients with LVO transferred for EVT, compared to a control group

receiving CT examination at the nearest hospital?
Null hypotheses: EMC notification-to-admission times do not differ between the intervention group and control group.
Statistical method: EMC notification-to-admission times will be compared by Mann–Whitney *U* test. 2-sample, 2-sided equality.

For other clinical events we will estimate odds ratios and 95% confidence intervals using binary logistic regression. All analyses will use 5 % two-sided level of significance. Health economic variables and cost effectiveness related to implementing a decentralized IVT service will be evaluated by estimating costs per quality adjusted life years utilizing the generic outcome variable EQ5D.

Interim analyses {21b}

No interim analyses will be performed.

Methods for additional analyses (e.g. subgroup analyses) {20b}

Due to the explorative nature of subsequent analyses related to functional outcome, life quality and health economics statistical analysis cannot be outlined in detail. Due to the low number of study participants planned for inclusion, no subgroup analyses are pre-planned. Mixed model analyses accounting for between-center differences will be performed. Propensity score matching may be considered.

Methods in analysis to handle protocol non-adherence and any statistical methods to handle missing data {20c}

We will analyze the data according to the intention-to-treat principle. This means that patients presenting with stroke symptoms in the municipalities defined as the intervention group will be analyzed in the intervention group independent of whether they received initial assessment at the DMC or not. In addition, per-protocol analyses will be performed, excluding all patients from the intervention group who were assessed by the standard of care pathway at their local hospital. We will utilize multiple imputation to account for missing data.

Plans to give access to the full protocol, participant level-data and statistical code {31c}

Data privacy legislation limits public access to the dataset.

Oversight and monitoring

Composition of the coordinating centre and trial steering committee {5d}

The trial Steering committee comprises Tor Ingebrigtsen, Ellisiv Mathiesen, Agnethe Eltoft, Maria Carlsson, Monica Storkjørren, Linn Hofsøy Steffensen and the user representative Melissa Birkeland. They will meet biannually to discuss the conduct and progression of the trial.
The executive working group will consist of the project leader and main supervisor Agnethe Eltoft, PhD candidate Eivor Logstein, a research nurse (50% position), and co-supervisors Jon Våbenø and Tor Ingebrigtsen. They are in charge of running the trial day-to-day and providing organizational support, and will meet every second week throughout the study period.
In addition, a local project team is established at each DMC comprising the local project group:

DMC Sør-Helgeland:

a. Project leader: Monica Storkjørren, HSYK
b. Paramedic: Steffen Hollup, HSYK
c. Primary physician and DMC nurse: Birgit Aune (nurse) and Tonje Johansen (Head of Brønnøy legevakt) and Olga Benum (primary physician)
d. Radiographer UNN: Kurt Bøckman Gschib, Radiographer Sandnessjøen: Hege Paulsen and Anna Elisabeth Øyen , Radiographer Brønnøysund: Maren Schanche Ottesen

DMC- Midt Troms:

e. Project leader: Linn Hofsøy Steffensen
f. Paramedics/ Ambulance/EMC:Tina Aas
g. DMC nurse and Primary physician: Marit Storli, Aslak Lian
h. Radiographer at UNN: Gschib, Kurt Bøckman
i. Radiographer DMC-Midt Troms: Anne Marte Nikolaisen
j. Neurologist and radiologists at UNN: Agnethe Eltoft, Susanne Ingebrigtsen, Ellisiv B. Mathiesen, Jon Andre Totland
k. HN-IKT: Øyvind Ursin, Steinar Nyhus

The local project group will meet at least semiannually for half day seminars in addition to simulation trainings every 2 weeks. Ad hoc meetings will be arranged when necessary.

Composition of the data monitoring committee, its role and reporting structure {21a}

We follow NorCRIN's Guideline for clinical interventional and observational studies with UNN as the research responsible institution. Risk assessment according to NorCRIN's Risk Assessment for clinical studies shows a low implementation risk. An independent safety committee consisting of two experienced stroke neurologists will review all safety data after 5, 10,15, and 20 patients have been evaluated for thrombolysis at each DMC.

Adverse event reporting and harms {22}

All patients will be monitored carefully during treatment and follow-up, and procedures for management of reactions and reporting of adverse (AE) and serious adverse events (SAE) are given in the protocol and in local local SOP.

Definition of AE:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the study intervention, whether or not considered related to the study intervention. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the study intervention.

A SAE is any untoward medical occurrence that:

- results in death
- is life threatening
- requires hospitalisation or prolongation of an existing hospitalization
- results in disability/incapacity

Medical and scientific judgement should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious.

Some SAEs are expected such as intracranial hemorrhage following IVT. All patients with neurological deterioration will therefore undergo emergency head CT. Based on the image findings, treatment will either be initiated on site, in accordance with in-hospital procedures, or the patient will be transported directly to the comprehensive stroke center for neurosurgery. Local personnel have SOPs and training for handling acute complications including angioedema and contrast reactions and are qualified to take care of acute respiratory and cardiac failure. In cases of complications, air ambulance will be alarmed instantly. Examples of other expected SAE are delayed or missed treatment, intracranial hemorrhage, recurrent ischemic stroke, myocardial infarction, or death.

The study is not blinded and all adverse events serious or not will be reported and evaluated within the local project groups, independent safety committee, executive working group and steering committee. If any signs of harm, the study design and procedures will be adjusted and if any evidence of harm the study will be stopped.

In case of unexpected serious adverse events, the trial coordinating investigator Agnethe Eltoft should be notified immediately and within 24 hours at the latest. Serious adverse events that are expected will be reported as endpoints in the eCRF and should additionally be reported by email or phone to the trial

coordinating investigator within 2 workdays.

Frequency and plans for auditing trial conduct {23}

An independent safety committee consisting of two experienced stroke neurologists will review all safety data after 5, 10,15, and 20 patients have been evaluated for thrombolysis at the DMC. The committee will stop the study if they find evidence for an unacceptable increase in symptom onset to treatment time, logistical problems or increase of symptomatic cerebral bleedings (sICH) (more than 4%) or deaths.

Plans for communicating important protocol amendments to relevant parties (e.g. trial participants, ethical committees) {25}

Important protocol modifications (e.g., changes to eligibility criteria, outcomes, analyses) will be swiftly communicated by the steering committee to the relevant parties including the executive working group, local project groups and Regional Committees for Medical and Health Research Ethics (REC). The local project groups are responsible for communicating protocol modifications to pre- and intrahospital personnel and updating local SOPs accordingly.

Dissemination plans {31a}

Target audiences and stakeholders/users of the project outcomes are the general population, health care providers, regional and national health authorities and policy makers. The protocol, primary results and results of any sub-studies will be submitted to English language peer-reviewed journals. All publications will be in accordance with the Vancouver Requirements. Patients and the public will also be informed through newsletters and in member journals owned by the user organization National Association for Heart and Lung Diseases and Aphasia. We aim to post information on social medias such as Facebook. We aim for rapid communication of the results at relevant national and international conferences.

Planned National Collaborations:

Currently, two other projects in the northern part of Norway (Alta) and the southern part of Norway (Hallingdal) have been implemented to deliver rural CT examination and acute stroke treatment. We have initiated collaborations with these two projects and plan to coordinate and harmonize data collection with these sites and future sites where a similar model is implemented. If new sites are included in the present study, a protocol amendment will be made, and a notification of the change will be sent REC. Due to an expected low number of patients at each site, we plan to merge data from all operating sites to assess effects of the decentralized stroke service on functional outcomes and health economics.

Expected benefit

If prehospital stroke treatment can be delivered safely and effectively at strategically located DMCs, this will increase the number of rural patients eligible for IVT and treatment access in the early phase after stroke onset when the treatment is most effective. Results from the present study represent an important contribution to ongoing international discussions regarding implementation of highly effective reperfusion treatment. This study can provide new knowledge regarding organization and resource allocation for acute stroke diagnostics and treatment in Norway and other rural areas. It may provide evidence that geographical inequalities in stroke care may be diminished by utilizing already available resources more efficiently. There are currently no additional DMCs in northern Norway where this model ca be implemented with the currently available resources. However, the strategy could be relevant for several other DMCs, such as Nord-Troms, Steigen, Longyearbyen, and Karasjok, if a limited investment in CT technology is made. Beyond the purchase of equipment for radiology and telemedicine, the daily expenses related to operating this service are expected to be low. Furthermore, the experience gained from this project will provide a substantial knowledge base, particularly if CT in helicopters becomes a possibility in the long term.

There are several innovative aspects of the project. Firstly, stroke diagnostics and treatment is performed outside of the hospital utilizing advanced software equipment for remote controlling a CT scanner and AVC to facilitate diagnostic precision and treatment decision making. Secondly, knowledge in diagnostics and treatment of stroke patients is transferred to prehospital and community health personnel.

Midt-Troms, Sør-Helgeland, Alta and Hallingdal Sjukustugu are so far the only DMCs in Norway where CT scanning of the brain is available as a 24/7 service in a prehospital setting. If our study succeeds in showing better access and decreased time to treatment in rural areas at low cost, this model of stroke organization based on decentralized stationary CT scanners, could be implemented at other sites in Norway and potentially in other rural areas worldwide. Prehospital CT diagnostics may further be extended to aid the triage of other emergency medical conditions in rural areas such as traumatic head injury. The project may have both medical and health economic benefits as mutilating sequelae after stroke can be diminished by adequate and timely delivered acute stroke treatment, and patients will survive with improved functional and cognitive status. Thus, expenses related to rehabilitation, nursing home care and other public health services may be reduced. The projects outputs and knowledge have the potential to address the UN Sustainable Development Goal of good health and well-being.

Ethics approval and consent to participate {24}

The trial will be conducted in accordance with the MRC Guidelines for Good Clinical Practice in Clinical Trials, the Council of Europe's Convention on Human rights and Biomedicine (CETS No.: 164), the ICH guideline for Good Clinical Practice (ICH E6 R3)) and the Declaration of Helsinki (Helsinki, October 2024). The trial will obtain ethical approval by Regional Committees for Medical and Health Research Ethics (REC).

Obtaining informed consent from all participants at all sites with different will be challenging and informed consent is not planned for several reasons:
-the study aims to assess the benefits of implementing a healthcare service for the delivery of guideline-recommended treatment
-data collection is part of standard clinical registration in the electronic health record as well as mandatory reporting to the Norwegian Stroke Registry.
- Due to the disabling nature of stroke, patients may have deficits on admission which makes them unable to give an informed consent. Excluding patients with severe deficits or incapacitated due to preexisting cognitive impairment will jeopardize the generalizability of this trial.

To ensure participants' privacy, all data will be handled in accordance with applicable data protection laws and regulations. The data will be de-identified before analysis. Access to the data will be restricted to authorized research personnel, and all electronic data will be stored on secure servers with appropriate security measures. Furthermore, all reporting of results will be conducted in a manner that does not reveal the identity of the participants.

Ethical issues are related to delivering IVT treatment outside of a hospital with less specialized personnel and remote controlling the CT scan. However, the model for prehospital diagnostics and IVT treatment is implemented as part of regular clinical practice and the treatment and medicines applied are according to best clinical practice guidelines. All patients will be monitored carefully during treatment and follow-up, and procedures for management of adverse drug reactions, and reporting of adverse and serious adverse events are given in the protocol and local SOPs. Possible risks that might endanger achieving the project objectives are related to feasibility, safety issues and low rate of patient recruitment. If such issues arise, we will strive to sort them out and if we do not succeed the study will be halted.

Competing interests {28}

The authors declare that they have no competing interests.

References

1. Tollånes MC, Knudsen AK, Vollset SE, Kinge JM, Skirbekk V, Øverland S. Disease burden in Norway in 2016. Tidsskr Nor Laegeforen. 2018;138(15).
2. Norsk Sf, hjerneslagregister. Norsk hjerneslagregister årsrapport for 2022. 2023.
3. Norrving B, Barrick J, Davalos A, Dichgans M, Cordonnier C, Guekht A, et al. Action Plan for Stroke in Europe 2018-2030. Eur Stroke J. 2018;3(4):309-36.
4. Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, et al. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta analysis of individual patient data from randomised trials. Lancet. 2014;384(9958):1929-35.
5. Lees KR, Emberson J, Blackwell L, Bluhmki E, Davis SM, Donnan GA, et al. Effects of Alteplase for Acute Stroke on the Distribution of Functional Outcomes. Stroke. 2016;47(9):2373-9.
6. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet. 2016;387(10029):1723-31.
7. Jovin TG, Nogueira RG, Lansberg MG, Demchuk AM, Martins SO, Mocco J, et al. Thrombectomy for

anterior circulation stroke beyond 6 h from time last known well (AURORA): a systematic review and individual patient data meta-analysis. Lancet. 2022;399(10321):249-58.
8. Malik A, Drumm B, D'Anna L, Brooks I, Low B, Raha O, et al. Mechanical thrombectomy in acute basilar artery stroke: a systematic review and Meta-analysis of randomized controlled trials. BMC Neurology. 2022;22(1):415.
9. Parry-Jones AR, Sammut-Powell C, Paroutoglou K, Birleson E, Rowland J, Lee S, et al. An Intracerebral Hemorrhage Care Bundle Is Associated with Lower Case Fatality. Ann Neurol. 2019;86(4):495-503. 10. Ma L, Hu X, Song L, Chen X, Ouyang M, Billot L, et al. The third Intensive Care Bundle with Blood Pressure Reduction in Acute Cerebral Haemorrhage Trial (INTERACT3): an international, stepped wedge cluster randomised controlled trial. Lancet. 2023;402(10395):27-40.
11. Turc G, Hadziahmetovic M, Walter S, Churilov L, Larsen K, Grotta JC, et al. Comparison of Mobile Stroke Unit With Usual Care for Acute Ischemic Stroke Management: A Systematic Review and Meta-analysis. JAMA Neurol. 2022;79(3):281-90.
12. Grotta JC, Yamal JM, Parker SA, Rajan SS, Gonzales NR, Jones WJ, et al. Prospective, Multicenter, Controlled Trial of Mobile Stroke Units. NEJM. 2021;385(11):971-81.
13. Ebinger M, Siegerink B, Kunz A, Wendt M, Weber JE, Schwabauer E, et al. Association Between Dispatch of Mobile Stroke Units and Functional Outcomes Among Patients With Acute Ischemic Stroke in Berlin. JAMA. 2021;325(5):454-66.
14. Lund UH, Stoinska-Schneider A, Larsen K, Bache KG, Robberstad B. Cost-Effectiveness of Mobile Stroke Unit Care in Norway. Stroke. 2022;53(10):3173-81.
15. Dietrich M, Walter S, Ragoschke-Schumm A, Helwig S, Levine S, Balucani C, et al. Is prehospital treatment of acute stroke too expensive? An economic evaluation based on the first trial. Cerebrovasc Dis. 2014;38(6):457- 63.
16. Christensen E, Fagerheim Bugge H, Hagemo J, Larsen K, Harring AK, Gleditsch J, et al. Prehospital stroke diagnostics using three different simulation methods: A pragmatic pilot study. Eur Stroke J. 2024;9(4):1016-24.
17. Ibsen J, Hov MR, Tokerud GE, Fuglum J, Linnerud Krogstad M, Stugaard M, et al. Prehospital computed tomography in a rural district for rapid diagnosis and treatment of stroke. Eur Stroke J. 2024:23969873241267084.

Appendix 1:

G-FAST:

≥3 of 4 symptoms present this indicates large vessel occlusion of the anterior circulation (AUC for G-FAST (0·80, 0·76–0·84).

Comparison of eight prehospital stroke scales to detect intracranial large-vessel occlusion in suspected stroke (PRESTO): a prospective observational study
Duvekot, Martijne H CDippel, Diederik W.J. et al.
The Lancet Neurology, Volume 20, Issue 3, 213 - 22

National Institutes of Health Stroke Scale

Score = 0 No stroke
Score = 1-4 Minor stroke
Score = 5-15 Moderate stroke
Score = 15-20 Moderate to severe stroke
Score = 21-42 Severe stroke

National Institutes of Health Stroke Scale score	
1a. Level of consciousness	0 = Alert; keenly responsive 1 = Not alert, but arousable by minor stimulation 2 = Not alert; requires repeated stimulation 3 = Unresponsive or responds only with reflex
1b. Level of consciousness questions: What is the month? What is your age?	0 = Answers two questions correctly 1 = Answers one question correctly 2 = Answers neither question correctly
1c. Level of consciousness commands: Open and close your eyes. Grip and release your hand.	0 = Performs both tasks correctly 1 = Performs one task correctly 2 = Performs neither task correctly
2. Best gaze	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation
3. Visual	0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia
4. Facial palsy	0 = Normal symmetric movements 1 = Minor paralysis 2 = Partial paralysis 3 = Complete paralysis of one or both sides
5. Motor arm 5a. Left arm 5b. Right arm	0 = No drift 1 = Drift 2 = Some effort against gravity 3 = No effort against gravity; limb falls 4 = No movement
6. Motor leg 6a. Left leg 6b. Right leg	0 = No drift 1 = Drift 2 = Some effort against gravity 3 = No effort against gravity 4 = No movement
7. Limb ataxia	0 = Absent 1 = Present in one limb 2 = Present in two limbs
8. Sensory	0 = Normal; no sensory loss 1 = Mild-to-moderate sensory loss 2 = Severe to total sensory loss
9. Best language	0 = No aphasia; normal 1 = Mild to moderate aphasia 2 = Severe aphasia 3 = Mute, global aphasia
10. Dysarthria	0 = Normal 1 = Mild to moderate dysarthria 2 = Severe dysarthria
11. Extinction and inattention	0 = No abnormality 1 = Visual, tactile, auditory, spatial, or personal inattention 2 = Profound hemi-inattention or extinction
Total score = 0-42.	