Prehospital screening of acute stroke with the National Institutes of Health Stroke Scale (ParaNASPP): a stepped-wedge, cluster-randomised controlled trial

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Lancet Neurol 2023; 22: 800–11

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Summary

Background Timely treatment of acute stroke depends on early identification and triage. Improved methods for recognition of stroke in the prehospital setting are needed. We aimed to assess whether use of the National Institutes of Health Stroke Scale (NIHSS) by paramedics in the ambulance could improve communication with the hospital, augment triage, and enhance diagnostic accuracy of acute stroke.

Methods The Paramedic Norwegian Acute Stroke Prehospital Project (ParaNASPP) was a stepped-wedge, single-blind, cluster-randomised controlled trial. Patients with suspected acute stroke, who were evaluated by paramedics from five ambulance stations in Oslo, Norway, were eligible for inclusion. The five ambulance stations (defined as clusters) all initially managed patients according to a standard stroke protocol (control group), with randomised sequential crossover of each station to the intervention group. The intervention consisted of supervised training on NIHSS scoring, a mobile application to aid scoring, and standardised communication with stroke physicians. Random allocation was done via a simple lottery draw by administrators at Oslo University Hospital, who were independent of the research team. Allocation concealment was not possible due to the nature of the intervention. The primary outcome was the positive predictive value (PPV) for prehospital identification of patients with a final discharge diagnosis of acute stroke, analysed by intention to treat. Prespecified secondary safety outcomes were median prehospital on-scene time and median door-to-needle time. This trial is registered with ClinicalTrials.gov, NCT04137874, and is completed.

Findings Between June 3, 2019, and July 1, 2021, 935 patients were evaluated by paramedics for suspected acute stroke. 134 patients met exclusion criteria or did not consent to participate. The primary analysis included 447 patients in the intervention group and 354 in the control group. There was no difference in PPV for prehospital identification of patients with a final discharge diagnosis of acute stroke between the intervention group (48·1%, 95% CI 43·4–52·8) and control group (45·8%, 40·5–51·1), with an estimated percentage points difference between groups of 2·3 (95% CI −4·6 to 9·3; p=0·51). Median prehospital on-scene time increased by 5 min in the intervention group (29 min [IQR 23–36] *vs* 24 min [19–31]; p<0·0001), whereas median door-to-needle time was similar between groups (26 min [21–36] *vs* 27 min [20–36]; p=0·90). No prehospital deaths were reported in either group.

Interpretation The intervention did not improve diagnostic accuracy in patients with suspected stroke. A general increase in prehospital time during the pandemic and the identification of smaller strokes that require more deliberation are possible explanations for the increased on-scene time. The ParaNASPP model is to be implemented in Norway from 2023, and will provide real-life data for further research.

Funding Norwegian Air Ambulance Foundation and Oslo University Hospital.

Introduction

Successful treatment of any stroke is time-dependent, and outcome depends on early identification and selection of patients for the right level of care.[1,2] Current guidelines recommend training of prehospital personnel in stroke symptom recognition and prenotification of the receiving hospital,[3] with the latter depending on the former.[4] Organisation of prehospital systems is heterogeneous, often semi-detached from the in-hospital services, and lacking in standardised stroke training. Although hospitals worldwide use the National Institutes of Health Stroke Scale (NIHSS) in the acute stroke setting,[5,6] there is no current consensus on which stroke scale to use in a prehospital setting.[7]

Several modified prehospital stroke scales derived from NIHSS have been developed, including the face, arm, speech, time (FAST) test,[7] which is the standard prehospital stroke screening tool in Norway. Many prehospital scales focus on identifying patients with severe strokes caused by large vessel occlusions (LVOs), to enable quick transfer to comprehensive stroke centres with endovascular capability.[8,9] Modified prehospital stroke scales, such as FAST, might be too restrictive as stroke screening tools, and might fail to

Research in context

Evidence before this study

We searched PubMed with the search terms "prehospital stroke scales", "prehospital NIHSS", "non-physician NIHSS", "prehospital stroke assessment", "NIHSS in LVO", and "mobile stroke units" for studies published in Norwegian and English between Jan 1, 2012 and Oct 31, 2022. We focused on studies reporting randomised controlled trials, stepped-wedge cluster trials, clinical trials, and cohort studies as well as systematic reviews and meta-analyses in prehospital stroke care. Only one study, the PASTA trial (2019), explored implementation of a structured protocol and checklists for paramedic stroke assessment to increase thrombolytic rates in a randomised control design. The PASTA checklist was based on structured handover and clinical assessment with a face, arm, speech, time (FAST) test, and concluded that paramedic training alone did not significantly influence treatment rate. Prehospital stroke scales are modified versions of the National Institutes of Health Stroke Scale (NIHSS) and are constructed to identify patients with large vessel occlusions (LVOs). The PRESTO trial compared the accuracy of eight prehospital stroke scales in detecting LVOs. Because LVOs occur in at most 30% of the general stroke population, most patients have non-LVO stroke with a heterogeneous symptom presentation; the NIHSS is the scale of choice for identification of both LVO and non-LVO strokes. We did not find any prehospital studies focusing on non-LVO symptoms in minor to moderate strokes. Several in-hospital conducted cohort and inter-rater agreement studies on the NIHSS have shown high levels of agreement when used by non-physicians. No studies considered whether prehospital NIHSS could be implemented in a large-scale prehospital system; however, promising results were presented in cohort studies from the helicopter emergency medical service and mobile stroke units. The prehospital NIHSS studies we found had poor methodological robustness because of their size and non-randomised design.

Added value of this study

To our knowledge, the ParaNASPP trial is the first large randomised clinical trial to explore prehospital NIHSS as a common language in the acute stroke chain, to improve care to all patients with stroke. The ParaNASPP model is to be implemented in Norway from 2023, and will provide real-life data for further research.

Implications of all the available evidence

The ParaNASPP trial showed that introducing prehospital NIHSS in a specially designed competence platform, including an electronic learning platform, digital simulation training, and a pictogram-based NIHSS application with direct communication to the stroke physician, improved care by reducing in-hospital time to CT and by increasing prehospital identification of patients with low NIHSS and subtle symptoms. However, it did not increase diagnostic accuracy. Further studies should explore algorithms in prehospital NIHSS to triage to the right level of care and aspect of symptom presentation in subgroups of patients (eg, different stroke subtypes) for further improvement of prehospital stroke assessment.

identify patients with acute stroke with smaller deficits who could still benefit from acute treatment.[10] Mistriage of patients puts strain on resources and delays correct treatment for patients both with and without stroke.[11] Use of stroke scales developed solely for the prehospital setting might contribute to miscommunication between prehospital and in-hospital services. The absence of a common language to describe acute stroke symptoms could ultimately lead to prolonged on-scene time.[12]

The NIHSS is the most validated tool for stroke assessment and treatment, addresses a more heterogeneous stroke population than the modified prehospital stroke scales,[5] and might facilitate recognition of subtler symptoms in patients with acute stroke. The NIHSS was found to be better than prehospital stroke scales in LVO detection,[8] but is regarded as too complex and time-consuming for prehospital settings.[6] However, a 2022 study showed that paramedics can be trained to use the NIHSS as an accurate stroke severity quantification tool in the field without any time delay.[13] Use of a common stroke scale might improve prehospital and in-hospital interaction, avoid miscommunication, and aid triage to the right level of care without unnecessary time delay.[13] Furthermore, enhanced paramedic assessment might influence quality of treatment decisions.[12,14]

The aim of the Paramedic Norwegian Acute Stroke Prehospital Project (ParaNASPP) was to explore whether specially trained paramedics using a mobile application to score the NIHSS could improve triage and diagnostic accuracy of patients with acute stroke, by standardising and facilitating communication between paramedics and stroke physicians.

Methods

Study design

The ParaNASPP trial was designed as a pragmatic, single-centre, stepped-wedge, cluster-randomised controlled intervention trial and was conducted in Oslo, Norway. This study design is regarded as pragmatic and robust[15] and is applicable in prehospital research where complexity and uncertainty are an inherent part of the setting.[16] Oslo University Hospital (OUH) is a comprehensive stroke centre that receives patients with suspected acute stroke. OUH has a 454 km² catchment area that covers the city of Oslo, with approximately 700 000 inhabitants, and is served by five ambulance stations.

A full description and details of the trial design have been published previously.[17] Randomisation at patient level or a crossover design would induce bias due to the nature of the intervention since a paramedic trained in

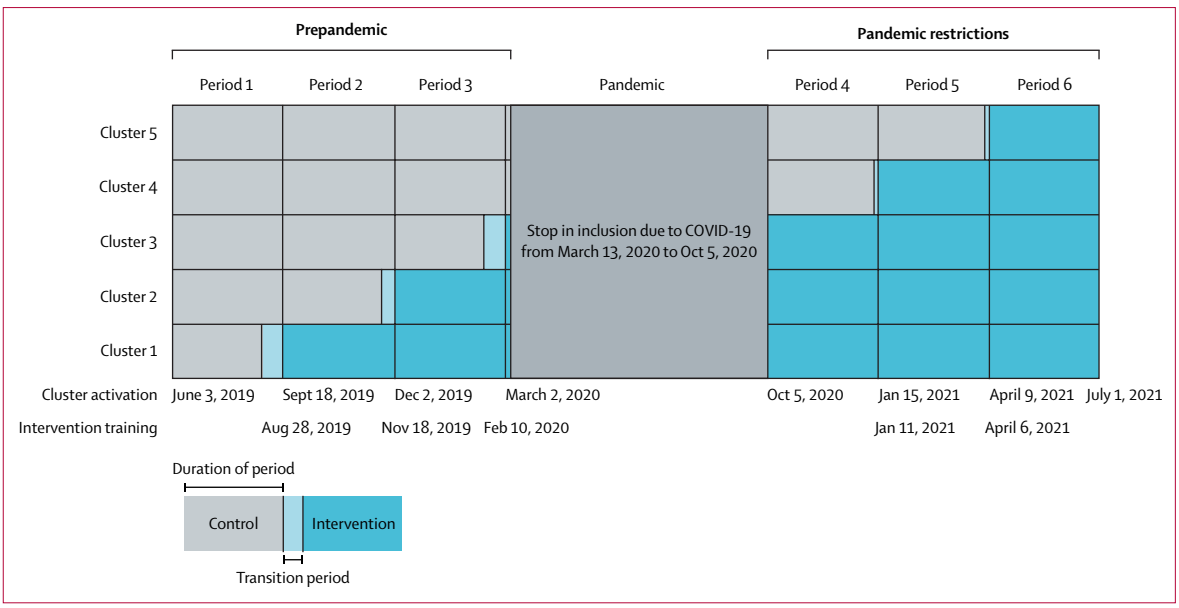

Figure 1: **Study design**
Study periods with duration of steps and transition periods. Dates represent start of the trial, intervention training, cluster activation, and termination of the trial.

the ParaNASPP model would be influenced by their new competencies and contaminate the former standard of care. Randomisation at the individual participant or patient level was therefore deemed not to be feasible, which supported randomisation at the cluster level—ie, each ambulance station acting as an individual cluster for patient recruitment. Therefore, the five ambulance stations serving OUH equal the five clusters in the trial (appendix p 2). Ambulance stations are natural clusters and a realistic approach for later implementation of the ParaNASPP model. The study design involved an initial period with all clusters in the control group before randomised, sequential crossover of all clusters from control to intervention (figure 1).

See **Online** for appendix

The Regional Committee for Medical Research Ethics South East Norway approved this trial (2018/2310).

Participants

In the Norwegian prehospital system, ambulance crews assess and triage patients in the field, but hospital admission in general requires consultation with a relevant on-call hospital physician (appendix p 3). Ambulance crews in Norway are a heterogeneous group with different levels of education. Emergency medical technicians are educated to a community college level, and emergency medical technicians and nurses can train to be paramedics via additional courses. A university bachelor's degree programme for paramedics has also been implemented. In Oslo, all ambulance teams contain at least one person with additional training. In this Article we use the term "paramedic" for simplicity. All 330 paramedics at the five stations participated in the trial.

Whenever a paramedic assessed a conscious patient aged 18 years and older with suspected acute stroke, with onset of symptoms or last seen well within 24 h, the patient was eligible for inclusion. If the patient's vital signs were stable, the paramedics conducted a focused medical history and physical examination, including stroke screening. For suspected acute stroke, paramedics consulted a stroke physician at OUH and included the patient in the trial if accepted for acute in-hospital assessment. Patients who were imprisoned, pregnant, or assessed by a prehospital physician before paramedic assessment were excluded.

Deferred, written informed consent was obtained from the patients, or their next of kin, during hospitalisation by members of staff at the stroke unit for their de-identified participation in the trial. If consent was not obtained during hospitalisation, it was obtained retrospectively by the research team.

Randomisation and masking

The cluster randomisation was based on sequential conversion of the ambulance stations from control to intervention; hence, paramedics received intervention training based on station affiliation. The cluster sequence was randomised using a simple lottery draw. Five numbered notes were drawn to select the cluster activation order. This draw was done independently by the administration of the Prehospital Division at OUH and was masked from the research team. A few weeks in advance of activation, the research team was informed which cluster should receive training. It was not possible to conceal the allocation of clusters due to the nature of the intervention.

Procedures

The intervention consisted of training for paramedics to score the NIHSS, with use of a mobile application to aid the scoring and to standardise communication in the acute stroke chain (appendix p 4). All paramedics partaking in the intervention completed an e-learning programme consisting of general stroke education, symptoms and presentations of acute stroke, theoretical introduction to the NIHSS, cerebral vascular and functional anatomy, pathophysiology of acute stroke, and in-hospital procedures and treatment. After completing the e-learning programme, the paramedics underwent a standardised 1-day course with intensive NIHSS simulation training, led by the research team and experienced stroke physicians. Paramedics scored various simulation cases, supervised by the instructors who provided immediate feedback to enhance proficiency in the NIHSS.

The mobile application was developed in cooperation with stroke physicians, paramedics, graphic designers, and application developers for non-commercial use, and has been validated in a separate study.[18] The application is not considered a medical device (appendix pp 5–15).

The intervention version of the application allowed the paramedics to provide an NIHSS score for patients eligible for inclusion. The results from the prehospital NIHSS examination, along with vital parameters, use of anticoagulants, symptom onset, age, and sex, were transferred directly and in real time to the stroke physician, thereby standardising and facilitating the communication in prehospital prenotifications.

The control group followed standard prehospital procedures for suspected acute stroke, including FAST as a stroke screening tool for symptoms, and regular telephone communication with the stroke physicians before hospitalisation. Paramedics in the control group registered patients eligible for inclusion in a restricted version of the application, without any access to the NIHSS or in-application communication with the stroke physicians.

For both groups, a patient was included in the trial if a stroke physician accepted the patient to OUH (appendix p 3), and standard in-hospital protocol for assessment and treatment was applied. Follow-up visits for patients discharged with a stroke diagnosis were in accordance with national guidelines[19] at either 30 days or 90 days depending on discharge diagnosis, without extra study-specific consultations.

Outcomes

The primary outcome measure was positive predictive value (PPV) for prehospital identification of patients with a final discharge diagnosis of acute stroke. The PPV was calculated by dividing the numerator of true positive cases (patients with a final stroke diagnosis) by the denominator of true-positive and false-positive cases (patients with a non-stroke diagnosis). Acute stroke was defined as ICD-10 (International Classification of Diseases, version 10) diagnosis code at discharge: I60 non-traumatic subarachnoid haemorrhage, I61 non-traumatic intracerebral haemorrhage, I63 cerebral infarction, I67.6 non-pyogenic thrombosis of intracranial venous system, G45.3 amaurosis fugax, G45.8 other transient cerebral ischaemic attacks and related syndromes, and G45.9 transient cerebral ischaemic attack, unspecified. All other discharge diagnoses were defined as stroke mimics (non-stroke). Key secondary endpoints will also be assessed in subgroup populations, such as patients with a final diagnosis of stroke or patients treated with thrombolysis.

Secondary safety outcomes were neurological deficit, measured as prehospital NIHSS and NIHSS at admission; number of patients receiving thrombolysis; number of patients receiving thrombectomy; number of patients identified with LVO; number of patients identified with posterior stroke as per the Oxfordshire Community Stroke Project (OCSP); number of patients with suspected acute stroke admitted to the stroke unit; prehospital on-scene time; time from ambulance arrival hospital to first CT; time from onset to arrival at hospital; time from onset to thrombolysis; door-to-needle time; and functional outcome measured by modified Rankin Scale (mRS), reported both as an ordinal scale and dichotomised into good outcome (mRS 0–2) and poor outcome (mRS 3–6).

Secondary endpoints from the published protocol article[15] that will be presented in later publications include: absolute change in NIHSS from admission to 2 h, 24 h, and at discharge; number of patients with post-thrombolytic symptomatic intracerebral haemorrhage; modified Thrombolysis in Cerebral Infarction score; door-to-needle time for blood pressure lowering in patients with intracerebral haemorrhage; door-to-groin puncture time; NIHSS at discharge; NIHSS at 90 days; and Alberta stroke program early CT score. The inter-rater agreement between paramedics and stroke physicians has been published.[20]

Statistical analysis

During the planning of this trial, the stepped-wedge design was just emerging, and design-specific CONSORT guidelines and methods for sample size calculation did not yet exist.[21] Unpublished data from OUH suggested that in 2017, approximately 700 (39%) of 1800 patients admitted to the emergency department at OUH with a suspected acute stroke had a stroke diagnosis at discharge. Our aim was to increase this proportion to 49%. A two-sided test for independent data with α 5% and power (1–β) 80% was used in the calculations, giving a requirement of 808 patients.

The historical data did not specify the prehospital pathway of the patients admitted to the stroke unit, but a 72-week study period was estimated to be sufficient to reach the recruitment goal. Practical considerations affected the scheduled intervals, resulting in an inclusion

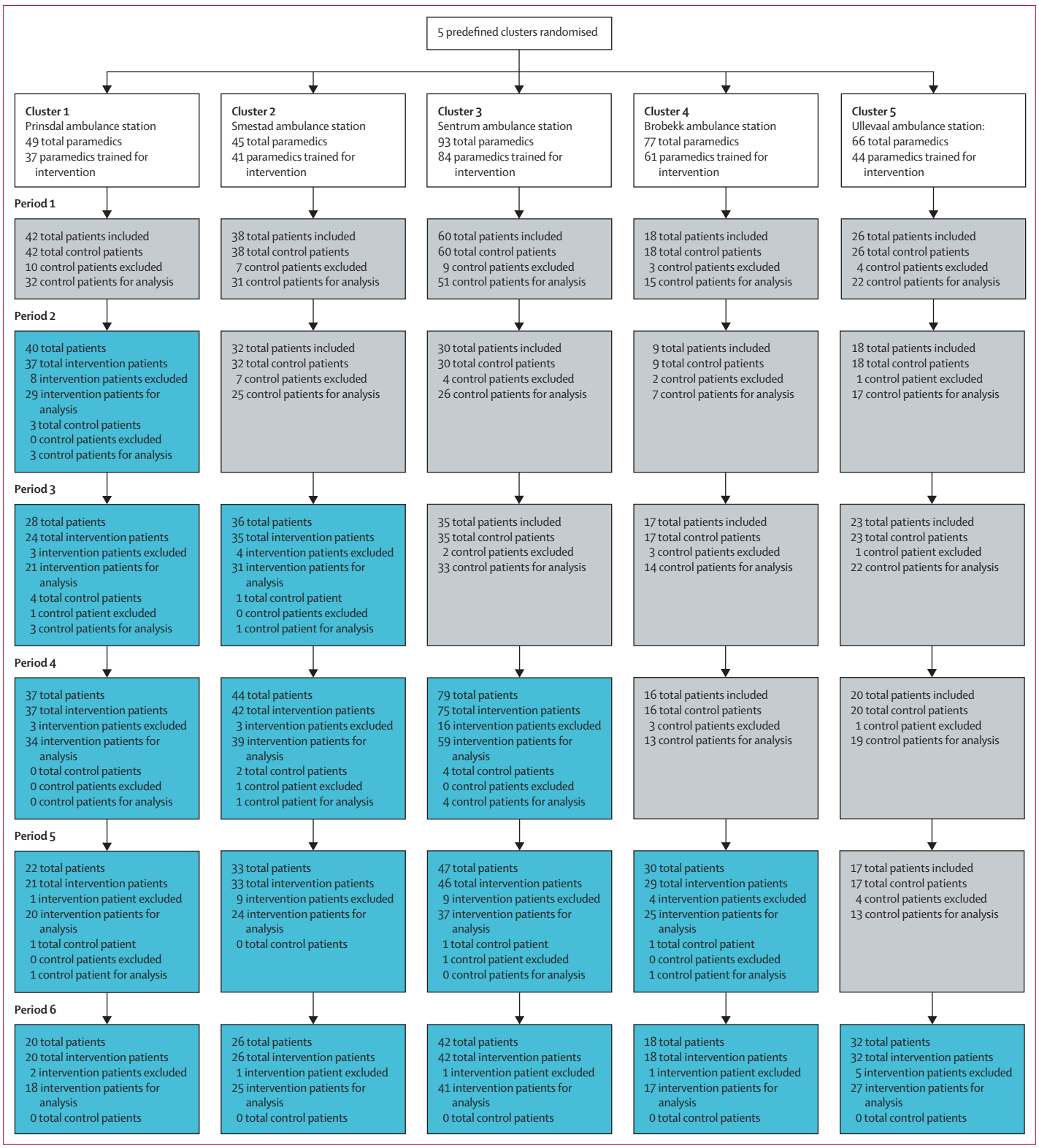

Figure 2: **Flowchart of participating clusters and patients**
Intervention group: 517 total patients included. 70 total patients meeting exclusion criteria (47 no consent obtained, 8 not identifiable, 2 symptom onset >24 h, 9 prior physician assessment, 1 <18 years). 447 total patients included for final analysis. Control group: 418 total patients included. 64 total patients meeting exclusion criteria (25 no consent obtained, 3 not identifiable, 6 symptom onset >24 h, 24 prior physician assessment, 6 unconscious). 354 total patients included for final analysis.

period of 78 weeks (figure 1). All clusters started in the control group, and by the end of the last crossover all paramedics had received intervention training; inclusion in the control group ended at this point. Patient inclusion was stopped 12 weeks after the last cluster activation step, regardless of the number of patients included. The trial finished after the final patient with a stroke diagnosis had completed outpatient follow-up.

Concern from the hospital administration due to the ongoing COVID-19 pandemic made us temporarily pause data inclusion from March 13 to Oct 5, 2020 (figure 1). The third cluster crossed over to the intervention group 1 week before the 7-month-long break. To preserve newly acquired skills and knowledge for the intervention clusters, a training version of the application was made available; however, the option to include patients was closed. Due to social distancing regulations, the intervention training was converted to a validated digital format before training the fourth cluster.[20]

The statistical analysis plan was finalised before the last patient inclusion, and all analyses were done according to this plan. A stepped-wedge design allows for paired analyses of data, but in this trial all intervention and control inclusions are pooled in their respective groups, and hence are treated as independent variables. The primary outcome was reported as PPV (95% CI). The p value was calculated using the χ^2 test. As our primary endpoint was PPV, and with there being no standard regression model with PPV as the outcome variable, we performed a post-hoc sensitivity analysis to explore potential temporal effects during the study, using a logistic regression model adjusted for time with odds ratios (ORs) as the corresponding effect size measure.

For secondary safety outcomes, the χ^2 test for comparing groups of categorical data and the Mann-Whitney *U* test for comparing groups of continuous non-normally distributed data were used. An mRS shift analysis was performed using an ordered logistic regression to assess functional outcome, which was reported as adjusted common OR with 95% CI for patients with a final stroke diagnosis, and which was adjusted for age and stroke severity (measured as NIHSS at admission). mRS was reported as adjusted OR, both as an ordinal scale (0–6) and as a dichotomised variable where mRS 3–6 defines an unfavourable outcome.[22] To provide the difference between medians of the two groups, a bootstrap analysis was conducted, and the results are reported as difference between medians (95% CI).

Continuous data are presented as mean (SD) for symmetrical data, and median (IQR) for skewed data. Categorical data are presented as absolute numbers and percentages. p values less than 0·05 are considered statistically significant. All p values are two-sided. The intention-to-treat principle was followed for all outcomes. No adjustments were made for multiple outcome assessments.

	Intervention (n=447)	Control (n=354)
Age, years	74 (62–83)	74 (63–83)
Sex		
Women	201 (45%)	179 (51%)
Men	246 (55%)	175 (49%)
Past medical history		
Atrial fibrillation	83 (19%)	67 (19%)
Hypertension	226 (51%)	167 (47%)
Hypercholesterolaemia	169 (38%)	137 (39%)
Diabetes	64 (14%)	41 (12%)
Transient ischaemic attack	38 (9%)	34 (10%)
Ischaemic stroke	82 (18%)	78 (22%)
Coronary disease	46 (10%)	55 (15%)
Intracerebral haemorrhage	13 (3%)	7 (2%)
Anticoagulant use	88 (20%)	72 (20%)
Antiplatelet use	135 (30%)	110 (31%)
Antihypertensive use	199 (44%)	142 (40%)
Statin use	159 (36%)	130 (37%)
Currently smoking	57 (13%)	56 (16%)
Living alone	163 (37%)	131 (37%)
Premorbid mRS		
0–2	360 (83%)	280 (81%)
3–5	73 (17%)	65 (18%)
Time from onset to EMCC call, min	37 (13–107)	32 (8–94)

Data are mean (SD), n (%), or median (IQR). Baseline data for patients, collected at time of inclusion. mRS=modified Rankin Scale. EMCC=emergency medical communication centre.

Table 1: **Baseline characteristics of the intention-to-treat population**

Documentation quality varied for both prehospital and in-hospital data. To minimise occurrence of missing data, we used free-text fields for interpretation when possible. This would be the case for the variables mRS, NIHSS, OCSP classification, Trial of Org 10172 in Acute Stroke Treatment (TOAST), and presence of LVO. If ambiguity was present, we strived for consensus in the research group. If consensus was unattainable, the datapoint was defined as missing. Missing data were imputed if more than 5% were missing. Any imputed data are indicated in the results.

To assess whether more posterior circulation strokes were identified in the intervention group, we carried out post-hoc analyses according to the OCSP and TOAST, to assess whether the aetiology of strokes differed between the groups. Due to the unselected nature of the prehospital patient population, we decided to include post-hoc analyses of the number of patients assessed for acute treatment.

An independent data safety and monitoring committee carried out an interim analysis after activation of the third cluster. The prehospital intervention was deemed not to influence the occurrence of any in-hospital adverse events, but might affect time from ambulance arrival on scene to treatment. The committee reviewed the

	Intervention (n=447)	Control (n=354)	Difference (95% CI)	p value
Prehospital NIHSS	2 (1–6)	NA	..	NA
NIHSS at admission	2 (0–5)	2 (0·5–6·5)	0 (–2 to 0)*	0·015†
NIHSS at admission if final diagnosis of stroke	3 (1–6)	5 (2–10)	–2 (–5 to –2)*	0·0002†
Patients receiving thrombolysis	85 (19%)	60 (17%)	2 (–3 to 7)	0·45‡
Patients initially assessed for thrombectomy only	16 (4%)	19 (5%)	–2 (–5 to 1)	0·43‡
Patients with suspected acute stroke admitted to the stroke unit	294 (66%)	214 (61%)	5 (–1 to 12)	0·12‡
Patients with non-stroke diagnosis admitted to the stroke unit	113 (49%)	99 (52%)	–3 (–12 to 7)	0·56‡
Patients with non-stroke diagnosis receiving thrombolysis	9 (2%)	9 (3%)	–1 (–5 to 3)	0·62‡
Ischaemic stroke (cerebral infarction diagnosis)	148 (33%)	112 (32%)	..	..
Patients with cerebral infarction diagnosis identified with LVO, anterior and posterior	33/148 (22%)	52/112 (46%)	..	0·0002‡
TOAST classification among patients with cerebral infarction diagnosis	..	..	..	0·30‡
Large artery atherosclerosis	39/148 (26%)	31/112 (28%)	..	..
Cardioembolic	18/148 (12%)	16/112 (14%)	..	..
Small vessel occlusion	44/148 (30%)	22/112 (20%)	..	..
Stroke of other determined aetiology	8/148 (5%)	4/112 (4%)	..	..
Stroke of undetermined aetiology	19/148 (13%)	15/112 (13%)	..	..
Missing documentation	20/148 (14%)	24/112 (21%)	..	..
OCSP classification among patients with cerebral infarction diagnosis	..	..	..	0·0003‡
Total anterior circulation infarction	7/148 (5%)	24/112 (21%)	..	<0·0001‡
Partial anterior circulation infarction	71/148 (48%)	36/112 (32%)	..	0·015‡
Lacunar infarction	20/148 (14%)	13/112 (12%)	..	0·78
Posterior circulation infarction	31/148 (21%)	19/112 (17%)	..	0·51‡
Missing documentation	19/148 (13%)	20/112 (18%)	..	..

Data are median (IQR), n (%), or n/N (%), unless otherwise stated. NIHSS=National Institutes of Health Stroke Scale. NA=not applicable. LVO=large vessel occlusion (identified from the radiology reports and including intracranial internal carotid, M1, M2, A1, intracranial vertebral artery, basilar artery, and P1 occlusions). TOAST=Trial of Org 10172 in Acute Stroke Treatment. OCSP=Oxfordshire Community Stroke Project. *A bootstrap analysis was done to calculate the difference between groups (95% CI). †p values were calculated with the Mann-Whitney *U* test. ‡p values were calculated with the χ^2 test.

Table 2: **: Patients' stroke characteristics and treatments**

prehospital on-scene time and door-to-needle time, the two intervals considered most likely to be affected by the intervention. More time spent would be a safety concern, and an increase in the first interval would only be acceptable if the latter were equally or more reduced.

All statistical analyses were performed with Stata (version 16.1) and R (version 3.4.4).

The trial is registered with ClinicalTrials.gov, NCT04137874.

Role of the funding source

The Norwegian Air Ambulance Foundation, a non-governmental organisation for research and development, funded software programming of the eSTROKE application and its implementation in the study. The core research team (MG, HFB, ECS, and MRH) were employed by the Foundation during the trial. The funders of the study had no other role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Between June 3, 2019, and July 1, 2021, 935 patients were evaluated by paramedics, and the follow-up period lasted until the last patient's 90-day follow-up on Oct 13, 2021. During the trial, 267 of the 330 paramedics were trained for intervention, allocated to five different clusters (figure 2; appendix p 16).

Figure 2 shows the patient flow for both groups and the number of patients included at each step of the trial. 134 (14%) of the 935 evaluated patients met exclusion criteria or did not consent to participation. As a result, 801 patients were included in the primary analysis (447 [56%] in the intervention group and 354 [44%] in the control group). 355 (79%) patients in the intervention group were included during the pandemic, compared with only 50 (14%) patients in the control group in the same period (p<0·0001).

The median age was 74 years (IQR 63–83), and 380 (47%) of the 801 patients were women. Stroke risk factors at baseline (ie, at the time of inclusion) were balanced between the two groups, although the proportion of patients with a history of coronary disease was higher in the control group than in the intervention group (p=0·026; table 1).

The primary endpoint did not differ between groups, with a PPV for prehospital identification of patients with a final discharge diagnosis of acute stroke of

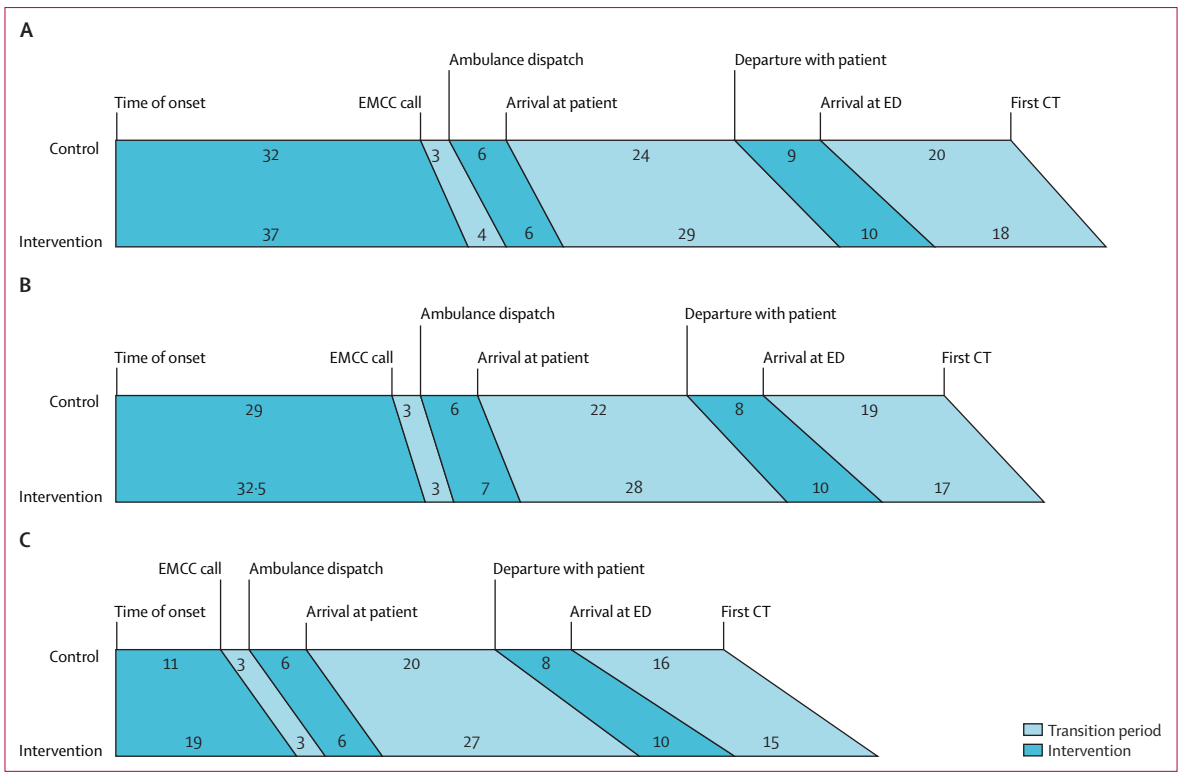

Figure 3: **Timeline showing intervals in minutes between all registered timestamps from onset to first CT for the control group and the intervention group**
(A) All patients. (B) Patients with a final diagnosis of stroke. (C) Patients treated with thrombolysis. Numbers are time in minutes. EMCC=emergency medical communication centre. ED=emergency department at Oslo University Hospital.

48·1% (95% CI 43·4 to 52·8) in the intervention group and 45·8% (40·5 to 51·1) in the control group, and an estimated percentage points difference between groups of 2·3 (95% CI –4·6 to 9·3; p=0·51). In the post-hoc sensitivity analysis exploring temporal effects, the addition of time to the logistic regression model did not alter the results of no difference for a final diagnosis of stroke between the two groups.

Of the patients with a final stroke diagnosis, there was no difference between the groups regarding subtypes of stroke (table 2 and appendix p 17). The groups were also similar regarding patients without a stroke diagnosis (ie, stroke mimics; table 2 and appendix p 18). These analyses were done post-hoc to further describe our patient population.

Patients in the intervention group had a significantly lower median NIHSS score on admission (2·0 [IQR 0·0–5·0]) than did those in the control group (2·0 [0·5–6·5]; p=0·015). For patients with a final diagnosis of stroke, the median NIHSS at admission was 3 (1–6) in the intervention group and 5 (2–10) in the control group (p=0·0002; table 2). There were more LVO strokes in the control group (52 [46%]) than in the intervention group (33 [22%]; p=0·0002), and a significantly higher proportion of both the total population (23 [7%] *vs* 13 [3%]; p=0·015) and of the patients with ischaemic stroke diagnosis (23 [21%] *vs* 13 [9%]; p=0·0066) were treated with thrombectomy. We found no differences between the groups regarding admission to the stroke unit and thrombolysis rates. OCSP classification was significantly different between the groups (p=0·0003), with more partial anterior strokes in the intervention group (71 [48%] *vs* 36 [32%]) and fewer total anterior strokes (seven [5%] *vs* 24 [21%]; table 2).

Prehospital time intervals were longer in the intervention group for most of the intervals measured (figure 3); on-scene time was longer in the intervention group at 29 min (23–36) versus 24 min (19–31) in the control group. Total prehospital time was significantly longer in the intervention group, whereas time from ambulance arrival at hospital to first CT was significantly shorter in the intervention group (table 3). For patients discharged with a final diagnosis of stroke, median time from arrival to hospital to first CT was 17 (IQR 14–29) min for the intervention group and 19 (15–25) min for the control group (p=0·056). For door-to-needle time, we found no significant differences between the groups, with 26 min (21–36) in the intervention group versus 27 min (20–36) in the control group (p=0·90; table 3). There were no prehospital deaths reported in either group.

There was a shift in distribution in the ordinal logistic regression analysis of the mRS (figure 4) favouring the intervention group, with an adjusted common OR of

	Intervention	Control	Difference (95% CI)	p value
Prespecified safety measurement time intervals				
Prehospital on-scene time, min	29 (23–36)	24 (19–31)	5 (2 to 6)†	<0·0001
Door-to-needle time, min	26 (21–36)	27 (20–36)	–2 (–6 to 4)	0·90
Other time intervals				
Time from ambulance arrival hospital to first CT, min	18 (14–39)	20 (16–34)	–2 (–5 to –2)	0·0001
Time from ambulance arrival hospital to first CT if final stroke diagnosis, min	17 (14–29)	19 (15–25)	–2 (–5 to –2)	0·056
Time from ambulance arrival hospital to first CT if "code stroke", min*	16 (13–19)	18 (15–22)	–2 (–4 to –1)	<0·0001
Time from onset to arrival at hospital, min	91 (64–159)	82 (51–144)	10 (–3 to 21)	0·0083
Time from onset to thrombolysis, min	106 (81–132)	85 (65–115)	21 (–1 to 37)	0·006

Data are median (IQR), unless otherwise stated. A bootstrap analysis was done to calculate the difference between groups (95% CI). p values were calculated with the Mann-Whitney *U* test. *"Code stroke" refers to being met by the full stroke team and put on a fast-track pathway for patients considered eligible for acute reperfusion therapy

Table 3: **Prespecified safety measurements, and other time intervals in the acute stroke chain**

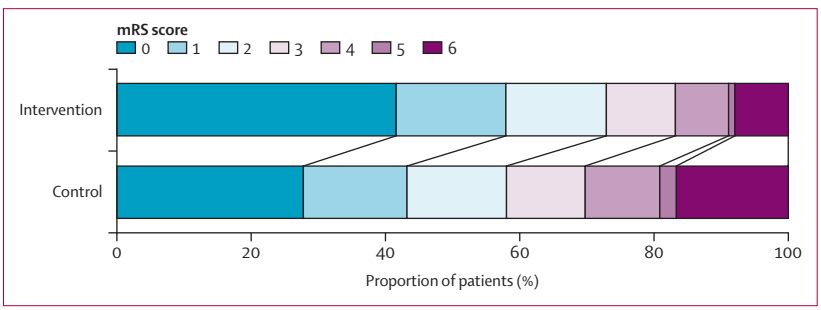

Figure 4: **Distribution of functional outcome according to mRS scores for patients with a final diagnosis of stroke**
mRS=modified Rankin Scale.

1·55 (95% CI 1·06–2·29) for a beneficial shift in mRS (p=0·025). For the adjusted logistic regression analysis of dichotomised mRS there was no difference in outcome (0–2 *vs* 3–6), with an adjusted OR of 1·60 (0·95–2·67; p=0·076).

Discussion

In this prehospital, pragmatic interventional trial there was no difference in PPV for a final diagnosis of stroke between groups. NIHSS scores at admission were lower in the intervention group both for the total patient population and for the patients with a final diagnosis of stroke, suggesting that patients with a lower symptom presentation were identified, and the ParaNASPP intervention established a common language for prehospital notification and acceptance for in-hospital assessment.

Only 1–2% of all emergency calls are estimated to end up with a final diagnosis of stroke,[23] illustrating that paramedics face a challenging reality with assessment and recognition of stroke symptoms in a vast and unselected population. Diagnosis of stroke remains an in-hospital decision, often after complete workup of the patient. In our data, 50% of the patients with a final non-stroke diagnosis were admitted to the stroke unit, meaning that the stroke physicians maintained the paramedics' suspicion of stroke after an initial assessment of these patients, and only after further workup were able to rule out a diagnosis of stroke. This emphasises the complexity and diagnostic uncertainty of acute stroke, and the need for standardised competence and communication between the paramedics and the in-hospital stroke team.

In our trial, paramedics in the control group used FAST, a screening tool known to inherently favour identification of severe strokes.[8] The median NIHSS at admission in the control group was higher, reflected by the proportions of LVO strokes, total anterior strokes, and thrombectomies, all of which were much higher than in both the intervention group and the general stroke population.[24,25] These strokes of moderate to major severity have a more classic symptom presentation and are more straightforward for the paramedics to recognise, and for the stroke physician to accept for hospitalisation. Recent studies exploring prehospital identification of stroke symptoms have primarily focused on the detection of LVO strokes. The PRESTO study[8] comparing eight prehospital scales showed that none of the scales was superior to the NIHSS. The nature of acute stroke symptoms and diagnosis are more complex and heterogeneous than a simple yes or no to LVOs.

In the ParaNASPP trial we explored prehospital NIHSS as part of a standardised clinical assessment, including vital signs, symptom onset, history of anticoagulant drug use, age, and sex for a more detailed work up, with the ultimate aim of identifying more patients with a stroke diagnosis. Median NIHSS at admission was lower in the ParaNASPP intervention group for patients with a final stroke diagnosis, compared with the control group. This suggests that supervised training and prehospital NIHSS assessment might increase identification of patients with subtle stroke symptoms. In addition to identification of more subtle stroke symptoms, the NIHSS has shown

superiority to prehospital stroke scales in identifying LVOs,[8] providing paramedics with a clinical tool for assessment of a heterogeneous stroke population.

Subtle stroke presentations might be less alarming for the patients, more difficult for the emergency medical communication centre operator to identify as a stroke, and require a more thorough examination by the paramedics before the decision can be made to contact a stroke physician. The decision to accept these patients for hospital assessment might also require more deliberation than when stroke suspicion is unambiguous. These qualities are found in other studies to increase prehospital delay for patients with subtle stroke symptoms[26,27] and might explain the tendency for prehospital delay seen in the ParaNASPP intervention group. These patients are less likely to be identified with FAST and are typically triaged to a lower level of care, such as a primary care doctor or a local emergency room, with delayed or missed opportunities for acute treatment and secondary prophylaxis. Even with longer prehospital times, which are presumably a safety concern, we found better functional outcomes in the intervention group, although the beneficial functional outcome might have been influenced by unidentified confounding factors. Rapid prehospital assessment of patients with suspected acute stroke is important, and digital structured real-time communication with the stroke physician might reduce time delays. Time from door to CT was significantly reduced in the intervention group, in contrast to other studies that showed an increase in door-to-CT times for patients with a low NIHSS,[28] and the prehospital competence and communication might be key to improving effectiveness in the acute stroke chain for the entire stroke population.

Recent guidelines recommend training of prehospital personnel and development of a standardised prehospital tool for symptom assessment.[29] The effect of training paramedics was highlighted in the PASTA trial,[14] where paramedics in the intervention group were instructed to assess suspected stroke symptoms with FAST. Additional information on symptom severity, medical history, and onset time was reported to the stroke physician before hospitalisation. The study failed to reach the primary endpoint of increasing the thrombolytic rate, and the results of the PASTA trial showed that fewer patients in the intervention group received reperfusion treatment when compared with standard care. The authors concluded that the training of paramedics did not influence treatment rates, but might affect the quality of treatment decisions.[14] Exploring whether prehospital competence enhancement influences hospital quality measures, such as thrombolytic rates, is challenging, because these measures are affected by several factors. The focus of most stroke teams in the past decade has been to streamline emergency department care for patients with acute stroke so as to treat as many as possible. Hence, thrombolytic treatment rates might have already achieved optimal performance in several centres. Correct triage to care, to protect the limited resources in the acute stroke chain, is a remaining challenge in stroke treatment. The consequence of aiming for high sensitivity and a high thrombolytic rate might be a high rate of patients with false positives who are brought to the hospital. By choosing FAST for prehospital assessment of stroke symptoms, minor strokes might be missed, and the specificity will be lower than published for NIHSS.[30]

The ParaNASPP results suggest that prehospital NIHSS as a screening tool is superior to FAST at identifying minor strokes without missing the major strokes. For clearer stroke symptoms, a full NIHSS might not be reasonable or necessary for prehospital screening. In future studies, we will investigate a built-in algorithm in the application that supports the decision to communicate with the stroke physician based on results on specific items in the NIHSS instead of completing a full NIHSS as default. Because acute treatment in stroke is highly time-dependent,[1,2] the effort for efficiency is indisputable. Nonetheless, high quality needs to take precedence given the consequences of mistriage. As the NIHSS is the prevailing in-hospital stroke scale,[5,29] and the shortcomings of existing prehospital stroke scales are well known,[4,29] training paramedics and implementing prehospital NIHSS might be a logical progression of prehospital stroke care. This progression would provide better prehospital stroke assessment, which would be beneficial in terms of improved triage for all patients with stroke, a common language, and improved prenotification in the acute stroke chain.

There might have been an underinclusion of participants in general in the control group, because registration was not required to communicate with the stroke physician before arrival at the hospital. Inclusion in the control group hinged on adherence to the study protocol, and registration might have been arbitrarily omitted. We do not suspect this to be the case in the intervention group, because training and a new tool were provided. However, in patients with severe stroke symptoms, inclusion might have been deliberately omitted and replaced by a simple load-and-go approach. These factors might have affected the stroke population in the control and the intervention group.

A weakness of a stepped-wedge design is the insufficient protection against secular changes taking place during the inclusion period, as more clusters are exposed to the intervention towards the end. This trial enrolled patients from 2019 to 2021, and the COVID-19 pandemic began while the last half of clusters were yet to cross over, which might have influenced the results. At the hospital, COVID-19 screening before entering became mandatory. However, data are not available to precisely quantify this time delay. Unpublished data from the Division of Prehospital Services, OUH, show

a 5 min increase (18·6 *vs* 23·8) in median prehospital on-scene time for all acute and urgent ambulance dispatches during the pandemic, and similar findings have been presented in other prehospital studies.[31,32] The nature of the stepped-wedge design, with more intervention patients enrolled with pandemic restrictions, might have confounded the increased on-scene interval and limited the possibility to show the effect of the intervention on time variables both prehospital and in-hospital. Pre-pandemic, at the time of the scheduled interim safety analysis, the data monitoring safety committee had no concerns.

The results from this trial rely on the educational level of paramedics and the organisation of the emergency medical services in Norway, and might not be fully adaptable to prehospital services in other countries with different organisation and education models. The results from this trial need to be replicated in different emergency medical service systems.

In conclusion, the ParaNASPP trial did not increase the PPV and diagnostic accuracy of final stroke diagnosis. However, the lower NIHSS score at admission indicates that subtler strokes were identified, thereby improving triage for a part of the stroke population that is easily unrecognised in the prehospital setting. Through customised training of paramedics and a mobile application, NIHSS might be introduced in the prehospital setting, creating a common language between paramedics and stroke physicians that standardises communication and saves in-hospital time. The ParaNASPP trial highlights the pivotal role of paramedics in the acute stroke chain and is the first step towards a standardised approach to assessment of patients with prehospital suspected acute stroke.

Contributors

All authors had full access to the final dataset and approved the final submitted version of this report. MRH, ECS, and JR contributed to study conceptualisation. MG and HFB contributed to data curation. MRH, ECS, KGB, MR, HFB, and JR contributed to methodology and formal analysis. MRH and ECS contributed to project administration and resources. MRH contributed to funding acquisition. MRH, ECS, MT, and JKJ supervised the study. MG and HFB validated the data. MG, HFB, ECS, and MRH wrote the original draft. MG, HFB, JR, JKJ, MT, HIH, KGB, KL, ACB, ECS, and MRH contributed to manuscript review and editing. MG, HFB, JR, ECS, and MRH accessed and verified the data and were responsible for the decision to submit the manuscript.

Declaration of interests

We declare no competing interests.

Data sharing

The data is available for the researchers in this study and can be made available for new projects upon reasonable request and provided if ethical approval is granted.

Acknowledgments

We thank the Norwegian Air Ambulance Foundation; the Ambulance Service of Oslo University Hospital; Ola Borstad, Head of Ambulance Department, OUH; Roger Bakke, Head of Competence at Ambulance Department, OUH; Kjell Otto Fremstad, Head of Department of Development at Norwegian Air Ambulance Foundation; Bjørn Fossen, System Manager at Norwegian Air Ambulance Foundation; Fredrik Kaupang, Application Developer at Norwegian Air Ambulance Technology; Maren Hauge, Research Nurse at Stroke Unit, OUH; Erik Eriksen, Stroke Physician at Stroke Unit, OUH; and Svein Håkon Ingebretsen, Stroke Physician at Stroke Unit, OUH.

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