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Time intervals and distances travelled for prehospital ambulance stroke care: data from the randomised-controlled ambulance-based Rapid Intervention with Glyceryl trinitrate in Hypertensive stroke Trial-2 (RIGHT-2)

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ABSTRACT

Objectives Ambulances offer the first opportunity to evaluate hyperacute stroke treatments. In this study, we investigated the conduct of a hyperacute stroke study in the ambulance-based setting with a particular focus on timings and logistics of trial delivery.

Design Multicentre prospective, single-blind, parallel group randomised controlled trial.

Setting Eight National Health Service ambulance services in England and Wales; 54 acute stroke centres.

Participants Paramedics enrolled 1149 patients assessed as likely to have a stroke, with Face, Arm, Speech and Time score (2 or 3), within 4 hours of symptom onset and systolic blood pressure >120 mm Hg.

Interventions Paramedics administered randomly assigned active transdermal glyceryl trinitrate or sham.

Primary and secondary outcomes Modified Rankin scale at day 90. This paper focuses on response time intervals, distances travelled and baseline characteristics of patients, compared between ambulance services.

Results Paramedics enrolled 1149 patients between September 2015 and May 2018. Final diagnosis: intracerebral haemorrhage 13%, ischaemic stroke 52%, transient ischaemic attack 9% and mimic 26%. Timings (min) were (median (25–75 centile)): onset to emergency call 19 (5–64); onset to randomisation 71 (45–116); total time at scene 33 (26–46); depart scene to hospital 15 (10–23); randomisation to hospital 24 (16–34) and onset to hospital 97 (71–141). Ambulances travelled (km) 10 (4–19) from scene to hospital. Timings and distances differed between ambulance service, for example, onset to randomisation (fastest 53 min, slowest 77 min; p<0.001), distance from scene to hospital (least 4 km, most 20 km; p<0.001).

Conclusion We completed a large prehospital stroke trial involving a simple-to-administer intervention across multiple ambulance services. The time from onset to randomisation and modest distances travelled support the applicability of future large-scale paramedic-delivered ambulance-based stroke trials in urban and rural locations.

Trial registration number ISRCTN26986053.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The first multicentre paramedic-delivered ambulance-based randomised controlled trial in stroke in the UK.
- ⇒ Ambulance response time intervals and distances are collated and reported for 1149 patients assessed as likely to have a stroke.
- ⇒ The time interval between arrival at hospital and the ambulance becoming available for the next emergency call (hospital turnaround) is not captured, but worth considering for future trials.
- ⇒ Timing and logistic data may not be fully representative of all urban and rural locations due to non-participation of some hospitals and ambulance stations within ambulance service regional areas.

INTRODUCTION

Routine prehospital management of suspected acute stroke involves rapid identification of suspected stroke using a validated stroke screening tool, prompt transport, pre-arrival notification and primary stabilisation to the nearest appropriate receiving stroke centre.[1] The mainstays for hyperacute management of stroke in hospital include urgent neuroimaging, stroke unit care, reperfusion therapy for ischaemic stroke and blood pressure (BP) lowering for intracerebral haemorrhage.[2] For reperfusion therapies, shortening the time from symptom onset to treatment improves functional outcome and this has become the aim of prehospital and in-hospital acute stroke services.[3–6] Thus, ambulance services play a crucial role in assessing, identifying and conveying patients with suspected stroke to primary and comprehensive stroke centres, which may include bypassing local emergency departments.

Timely prehospital care for stroke is dependent on several factors that include rapid recognition of potential stroke and calling for help,[7] ambulance response times encompassing symptom onset to arrival at hospital,[8] distance from scene to hospital[9] and the accuracy of identifying patients with true stroke or transient ischaemic attack from those with a stroke mimic.[10] There are a small, but growing number of studies that explore randomised paramedic-initiated interventions commencing in the ambulance for acute stroke. However, few studies have systematically analysed these parameters and the factors that influence them in acute prehospital stroke practice.[4 9 11 12]

Here, we report the logistics underlying patient recruitment to the Rapid Intervention with Glyceryl trinitrate in Hypertensive stroke Trial-2 (RIGHT-2), a large ambulance-based stroke trial in the UK that investigated the efficacy of transdermal glyceryl trinitrate as a paramedic-delivered intervention in suspected acute stroke. Specifically, ambulance response times and distance travelled across multiple organisations in this setting are assessed.

METHODS

RIGHT-2 trial

RIGHT-2 commenced recruitment in September 2015 with the first participant recruited on 22 October 2015.

RIGHT-2 was a multicentre prospective, single-blind, parallel group randomised controlled trial; the protocol, statistical analysis plan, baseline data, main results and subgroup results in participants with a final diagnosis of intracerebral haemorrhage are published.[13–17] Briefly, adult patients with suspected stroke presenting to the emergency service via an emergency call were recruited if they: were FAST-positive (facial weakness, arm weakness, speech abnormality; with test score 2 or 3), had systolic BP of >120 mm Hg, were within 4 hours of symptom onset, presented to trial-trained paramedics from eight UK ambulance services and were to be taken to a trial-participating hospital. Patients were randomised to receive transdermal glyceryl trinitrate (GTN) or sham patch in the ambulance and this was continued for three further days during hospital admission.[13] The study was undertaken across eight UK ambulance services (AS): East of England AS (EEAS), East Midlands AS (EMAS), London AS (LAS), South-Central AS (SCAS), South-West AS (SWAS), Welsh AS (WAS), West-Midlands AS (WMAS) and Yorkshire AS (YAS). All participating ambulance services used FAST identification and protocols consistent with national guidelines.

For each eligible patient, the enrolling paramedic assessed capacity and obtained patient or proxy consent (from a relative on the scene, or from the paramedic witnessed by a colleague), completed a written case report form to capture in-ambulance baseline and on-treatment data and applied the transdermal patch of GTN or sham dressing.[13] Ambulance-related data not recorded at source were confirmed by research paramedics from participating ambulance services after review of control room timing logs or patient care records, and then entered into the trial database.

Timings and distances

Timings were obtained from each ambulance service (time of emergency call, resource dispatch, scene arrival and departure, hospital arrival) and from paramedic records (consent for trial enrolment, randomisation, application of study treatment). Paramedic-documented history provided the time of symptom onset or, where unclear, the last known well time.

Distance measurements were calculated from the address or postcode of the emergency location, where available, to the expected stopping point for the ambulance at the destination hospital (accident and emergency or stroke unit entrance) to the nearest 10 metres using Google Maps; one ambulance service was unable to provide postcode information due to time constraints. One ambulance service was able to provide the linear distance from the location of the ambulance at the point of dispatch to the scene of the emergency.

A comparison of urban versus rural ambulance services arbitrarily divided ASs by <25% rural versus >25% rural (as defined in table 1; online supplemental table I).

Comparison of trial and non-trial patients

One ambulance service provided response time interval and distance data for a cohort (n=49) of patients with confirmed stroke who were not enrolled into RIGHT-2 (attended by non-trial trained paramedics) but were transported to the same specialist stroke centres participating in the trial.

Statistical analysis

Time intervals (in min), distances (in km) and baseline characteristics were compared between ambulance services using χ^2 and Kruskal-Wallis (one-way analysis of variance on ranks) tests. Multiple comparison procedures (Dunn's with Bonferroni correction) were used to assess which ambulance service differed from the others. Spearman and point-biserial correlations were performed to identify the relationship between baseline variables, times and distances. Data are number (%), median (IQR) or mean (SD). Statistical significance was defined overall at p<0.05, and at p<0.001 for correlation matrices and multiple comparisons. Statistical analyses were conducted with SPSS V.24 (IBM, New York, USA).

Patient and public involvement

This study was supported by public members of the trial steering committee who were involved throughout, including in trial design, development, conduct, periodic review and dissemination of results.

Table 1 Characteristics of participating ambulance service as of 31 May 2018. Data are numbers (%)

	E&W	EEAS	EMAS	LAS	SCAS	SWAS	WAS	WMAS	YAS
Time in trial (months)	32	27	32	14	4	27	22	14	29
Patients	1149	178	218	202	7	265	89	37	153
Participating hospitals	54	5	10	3	1	13	4	5	13
Area (km^2)	122 065	19 424	16 710	1605	9204	25 899	20 735	12 949	15 539
Population									
Overall (×1000)	53 000	5800	4800	8600	7000	5300	2900	5600	5338
Living in rural areas* (%)	17.6	28.9	26.7	0.2	20.4	31.6	32.8	15.1	17.5
Strokes (/year)†	90 781	9145	9246	13 118	7763	10 442	7400	8701	7931
Adjusted ratio /1000	1.71	1.58	1.92	1.52	1.11	1.97	2.55	1.55	1.49
Call volume (/day)	24 661	2800	2500	5193	1479	3077	1331	3000	2336
Participating ambulance stations	270	24	50	23	3	73	34	17	63
Paramedics employed	22 000	2000	1111	2864	1780	1788	1310	1300	1592
Trained in RIGHT-2	1492	145	193	325	63	313	165	124	142
Paramedics who recruited	516	58	75	120	6	112	47	23	75
Patients/paramedic	2.22	3.06	2.90	1.68	1.16	2.37	1.89	1.60	2.04

*2011 Census.[18]
†Number of patients with suspected stroke assessed face-to-face 2015/2016.
EEAS, East of England Ambulance Service NHS Trust; EMAS, East Midlands Ambulance Service NHS Trust; E&W, England and Wales; LAS, London Ambulance Service; RIGHT-2, Rapid Intervention with Glyceryl trinitrate in Hypertensive stroke Trial-2; SCAS, South-Central Ambulance Service NHS Foundation Trust; SWAS, South-West Ambulance Service NHS Foundation Trust; WAS, Welsh Ambulance Service NHS Trust; WMAS, West-Midlands Ambulance Services; YAS, Yorkshire Ambulance Service NHS Trust.

RESULTS

RIGHT-2 recruited 1149 patients between September 2015 and May 2018. Table 1 outlines patient recruitment across the various participating ambulance services, which collectively covered an area of 122 065 km^2 in England and Wales (ie, 42% of the land area of these countries). Ambulance services varied considerably in size (1605 km^2 vs 25 899 km^2), population served per service (2.9 million vs 8.6 million)[18] and annual stroke events (7400 vs 13 118) (table 1). Altogether 1492 paramedics volunteered to be trained in the trial, of whom 516 (36%) recruited at least one patient. Where two or more trial paramedics were present at the scene, the paramedic initiating randomisation was credited. On average, 2.2 patients were recruited by each paramedic who enrolled at least one patient although this varied between ambulance services (1.1 vs 3.1).

Patient characteristics

Of the 1149 patients recruited, average age was 73 (15) years, women 48%, BP 162 (25)/92 (18) mm Hg, Glasgow Coma Scale (GCS) 13.9 (1.7) and FAST score of three 60% (online supplemental table II). The final diagnosis varied between ambulance services, with the rate of conditions mimicking acute neurovascular disease ranging from 14.3% to 36.1%. This is consistent with other prehospital trials without physician presence or mobile stroke unit care, and the rate of stroke mimic reported here is explored elsewhere.[19] Baseline temperature also varied. Otherwise, baseline characteristics did not differ between ambulance service. As age increased, BP and glucose were higher, and heart rate, FAST and GCS lower (online supplemental table III). Informed consent was provided by 603 (53%) patients, 431 (38%) relatives and 115 (10%) paramedics witnessed by a colleague on scene.

Time intervals

The time intervals for various stages in the journey from stroke scene to hospital are shown in online supplemental table IV. Overall, the median time from symptom onset to emergency call was 19 (IQR 5–64) min and this did not differ between ambulance services (online supplemental tables IV and V). The median time from emergency call to ambulance dispatch was 3 (1–7) min and varied between ambulance service (1 min vs 5 min). An ambulance resource arrived at the scene within 8 (5–13) min from being dispatched (and 10 (6–16) minutes if only including RIGHT-2 trained paramedics) with this varying between ambulance service (8 min vs 12 min).

The median time from onset of symptoms to randomisation was 71 (45–116) minutes (table 2, figure 1) and this varied between ambulance service (53 min vs 77 min). Significantly, randomisation occurred within 30 and 60 min of symptom onset in 104 (9.1%) and 491 (42.9%) participants, respectively (table 2). Ambulance resources spent a median of 33 (26–46) minutes on scene, though this varied between ambulance services (29 min vs 43 min) (online supplemental table IV). Importantly, time on scene did not differ significantly when comparing RIGHT-2 patients vs non-RIGHT-2 patients 34 (26–44) and

Table 2 Timings: symptom onset to randomisation (OTR) (min). Data are N (%), median (25–75 centile); comparison by Kruskal-Wallis test

Min	E&W	EEAS	EMAS	LAS	SCAS	SWAS	WAS	WMAS	YAS	p
OTR										
N (%)	1149	178 (15.5)	218 (19.0)	202 (17.6)	7 (0.6)	265 (23.1)	89 (7.7)	37 (3.2)	153 (13.3)	
Median (25–75 centile)	71 (45–116)	73 (47–120)	59 (35–100)	77 (51–124)	53 (45–65)	75 (49–107)	75 (48–123)	60 (32–115)	70 (45–118)	0.001
N (%)										<0.001
≤30	104 (9.1)	15 (8.4)	38 (17.4)	11 (5.4)	1 (14.3)	16 (6.0)	7 (7.9)	6 (16.2)	10 (6.5)	
31–60	387 (33.8)	63 (35.4)	82 (37.6)	61 (30.2)	3 (42.9)	82 (30.9)	28 (31.5)	13 (35.1)	56 (36.6)	
61–90	258 (22.5)	32 (18.0)	34 (15.6)	51 (25.2)	0 (0.0)	77 (29.1)	19 (21.3)	5 (13.5)	38 (24.8)	
91–120	136 (15.1)	25 (14.0)	19 (8.7)	25 (12.4)	0 (0.0)	36 (13.6)	13 (14.6)	5 (13.5)	13 (8.5)	
121–180	173 (15.1)	30 (16.9)	33 (15.1)	28 (13.9)	0 (0.0)	40 (15.1)	16 (18.0)	6 (16.2)	20 (13.1)	
181–240	76 (6.6)	12 (6.7)	9 (4.1)	20 (9.9)	0 (0.0)	13 (4.9)	5 (5.6)	2 (5.4)	15 (9.8)	
>240	15 (1.2)	1 (0.5)	3 (1.4)	6 (3.0)	1 (14.3)	1 (0.4)	1 (1.1)	0 (0.0)	2 (0.7)	

EEAS, East of England Ambulance Service NHS Trust; EMAS, East Midlands Ambulance Service NHS Trust; E&W, England and Wales; LAS, London Ambulance Service; SCAS, South-Central Ambulance Service NHS Foundation Trust; SWAS, South-West Ambulance Service NHS Foundation Trust; WAS, Welsh Ambulance Service NHS Trust; WMAS, West-Midlands Ambulance Services; YAS, Yorkshire Ambulance Service NHS Trust.

32 (23–41) min, respectively (online supplemental table VI). Transfer time from scene to hospital was a median of 15 (10–23) min, but varied between ambulance service (9 min vs 24 min) (online supplemental table IV). The overall time from symptom onset to arrival at hospital was 97 (71–141) minutes and also varied between ambulance services (86 min vs 109 min) (online supplemental table VII). Time at scene was strongly positively correlated with time from scene to hospital (table 3).

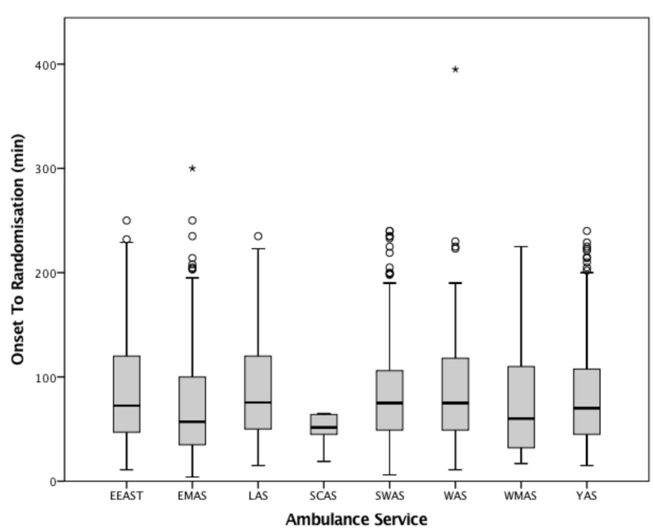

Figure 1 Box plot of onset to randomisation. EEAS, East of England Ambulance Service NHS Trust; EMAS, East Midlands Ambulance Service NHS Trust; LAS, London Ambulance Service; SCAS, South-Central Ambulance Service NHS Foundation Trust; SWAS, South-West Ambulance Service NHS Foundation Trust; WAS, Welsh Ambulance Service NHS Trust; WMAS, West-Midlands Ambulance Services; YAS, Yorkshire Ambulance Service NHS Trust.

Distances

The median distance travelled from the postcode of the suspected stroke scene to the receiving hospital was 10.0 (4.4–18.4) km, with considerable variation between ambulance services (4.1 km vs 19.9 km) (online supplemental table VIII). Time from scene to hospital was moderately positively correlated with distance from scene to hospital (online supplemental figure I:A-G present geographical distribution of randomisation by ambulance service).

Urban versus rural services

When comparing urban and rural ambulance services (online supplemental table I), there was no difference in receipt of the emergency call to dispatching a resource to scene, nor a difference in onset of symptoms to randomisation. The time spent at scene was marginally longer in rural locations and, as anticipated, both conveyance time and distance to the stroke centre was statistically different.

Comparison of trial and non-trial patients

In the ambulance service with times available for patients not enrolled in the trial, on scene to hospital arrival differed among patients enrolled and not enrolled in RIGHT-2, 10 (0.4–64.7) vs 16 (7.6–24.0) min (online supplemental table VIII). The median distance from dispatch location to scene in the ambulance service with this available (EMAS) was 7.3 km (3.5–12.0).

DISCUSSION

In this large national prehospital trial, 516 paramedics from eight ambulance services across England and Wales successfully recruited 1149 participants and transported them to 54 hospitals. Paramedics assessed and diagnosed suspected stroke, consented patients and initiated

Table 3 Univariate Correlation between severity of symptoms, timings and distance from scene to hospital. Data are Spearman's coefficient (p-value)

	OTR	FAST	GCS	Scene	OTH	STH	Km
OTC	0.836 (<0.001)	−0.130 (<0.001)	0.086 (0.003)	0.05 (0.088)	0.802 (<0.001)	0.007 (0.80)	−0.070 (0.033)
OTR		−0.135 (<0.001)	0.102 (0.001)	0.263 (<0.001)	0.941 (<0.001)	0.244 (<0.001)	−0.61 (0.61)
FAST			−0.157 (<0.001)	−0.066 (0.026)	−0.133 (<0.001)	−0.046 (0.12)	0.803 (0.93)
GCS				−0.008 (0.80)	0.115 (<0.001)	0.084 (0.004)	0.076 (0.017)
Scene					0.326 (<0.001)	0.791 (<0.001)	0.104 (0.002)
OTH						0.403 (<0.001)	0.216 (<0.001)
STH							0.554 (<0.001)

FAST, Face, Arm, Speech, Time score; GCS, Glasgow Coma Scale; Km, distance (km) from scene to hospital.; OTC, onset to emergency call; OTH, onset to hospital; OTR, onset to randomisation; Scene, total time spent at scene; STH, time from scene to reach hospital.

randomised treatment. Key timings were: onset to emergency call 19 min, onset to scene 40 min, onset to randomisation 71 min, time at scene 33 min, randomisation to hospital 24 min and depart scene to hospital arrival 15 min; all but the first two differed between ambulance services. The average distance travelled by one ambulance service from dispatch location to scene was 7.3 km and 10.0 km from scene to hospital for all participating ambulance services.

Prehospital time intervals in acute stroke have been described previously,[9 20–24] but rarely in randomised trials.[4 11 12] The symptom onset to randomisation time of 71 min in RIGHT-2 is consistent with two previous UK ambulance-based stroke trials (RIGHT was 55 min and Paramedic Initiated Lisinopril For Acute Stroke Treatment (PIL-FAST) was 70 min)[25 26] although these were small single centre pilot studies undertaken largely in urban settings. The large US Field Administration of Stroke Therapy - Magnesium trial[27] (FAST-MAG) reported a median of 45 min from symptom onset to receipt of study drug. Nevertheless, these times are all longer than UK multicentre ambulance-based trials outside of stroke, notably the AIRWAYS-2 and PARAMEDIC-2 trials in cardiac arrest.[28 29] In PARAMEDIC-2, the onset of symptoms to initiation of treatment in the intervention group was just 21.5 min. The most important driver of this difference is most likely shorter onset to call times for patients who had cardiac arrest than for stroke, and suspected stroke may require more complex assessment both by call handlers and by paramedics on scene. Additional contributors are that cardiac arrest is allocated the highest dispatch priority, an immediate response and patients receive immediate trial treatment with emergency waiver of consent.

The explanation for differences in timings is probably multifactorial but the degree of urban versus rural population is one likely explanation. This was apparent for time spent at the scene and both time and distance to hospital. As expected, there were no differences for receipt of call to dispatch, arrival of RIGHT-2 trained paramedic at scene nor onset of symptoms to randomisation.

There are several strengths of this study. First, RIGHT-2 involved 8 of 11 ambulance services in England and Wales. Of those not participating, two were unable to join because they were involved in another ambulance-based stroke trial[30] and the other involved hospitals that were concerned about adversely impacting on recruitment to commercial trials. Among 1492 trained paramedics in RIGHT-2 procedures 516 consented and randomised a large number of participants, adhered to the protocol and completed specific data recording. It is noted that there are marked differences in recruit numbers between ambulance services. This, in part, is accounted for due to low recruitment during the initial recruitment phase requiring broadening of ambulance services from 5 to 8 and stroke centres from 30 to 54. Furthermore, recruitment hours initially limited to typical working hours for research staff availability were extended to encompass 24/7 recruitment reflective of real-world ambulance care to not limit participation and maximise inclusion. Conflictingly, a small number of stroke centres closed recruitment to ambulances once target numbers of participants had been received and before the end of the recruitment phase highlighting the challenging reliance on dual centres when dealing with research in prehospital stroke.

Second, the consent model applied in RIGHT-2 is unlike any other large-scale ambulance-based studies worldwide to date and builds on previous UK based prehospital stroke pilots.[25 31] Other prehospital trials in stroke have relied on models of either informed consent,[32] deferred consent[33] or consent by doctor (present or remote).[27 34] Stroke is complex due to the varying nature of severity of presentations where patients' ability to consent in an informed manner to participate in a clinical study should not be overlooked preserving patient autonomy in accordance with the Declaration of Helsinki.[35 36] Notwithstanding the complexities of emergency presentations that could impact on decision-making, mental capacity or short intervention windows and the impact these situations bring to truly informed patient consent, the combined consent approach in RIGHT-2 acknowledges patient autonomy without precluding participation from those who are unable to voice their opinion or who lack presence of a proxy to consent on their behalf.[36] Mechanisms to safeguard consent were built into the protocol through reconfirmation of consent once in hospital for both the prehospital and in-hospital elements, respectively, and patient and public representatives were fully embedded within protocol development and steering group oversight of the trial.[13]

Third, the protocol required flexibility and adaptation to align with individual operational processes specific to each ambulance service to ensure successful delivery of the trial. Fourth, detailed logistic information on timing and distances travelled were collected. Last, the results highlight the successful delivery of a simple, ambulance-based intervention with 43% of the patients receiving the intervention within 2 hours of symptom onset without compromising time on scene required to complete additional research activity.

There are also several study limitations. First, it is recognised that not every receiving stroke unit within each ambulance service region could participate in RIGHT-2 due to capacity and competing research,[30 37] (this included concurrent commercial and post-arrival trials). Therefore, it must be considered that the timing and logistic data of participating hospitals may not be fully representative of all urban and rural locations. However, the intention was not to assess the differences between urban and rural settings, but to shed light on the conduct and deliverability of a prehospital intervention in stroke where time and distance may impede access to specialist stroke services. Furthermore, stroke unit hours of operation varied across the 54 centres with a small number of sites not accepting patients outside working hours which impacted paramedics' decisions to randomise. This reduces the reflection of real-world emergency stroke care. The duration of recruitment varied between regions due to complexities in setting up multicentre research

Additionally, it is acknowledged that the recruitment criteria were broad which resulted in a higher than anticipated proportion of stroke mimics. To mitigate this, mobile stroke unit care is an emerging field where imaging and definitive care delivery at the scene reduces time delays in stroke[38] and could offer improved confidence and precision of diagnosis for prehospital trial enrolment.

Recognising that 516 of 1492 RIGHT-2 trained paramedics (36%) identified and randomised eligible patients, this is consistent with other trials in prehospital stroke.[25] This, in part, is due to the voluntary participation of paramedics in research where records suggest that only one-third of the paramedic workforce participate.[39] Further, in a UK system where response time is one benchmark of the quality of ambulance service provision, ambulance dispatchers are not able to assign specific research-trained personnel to specific emergency calls, instead allocating the nearest available resource to attend. Low recruitment must be considered during the development of ambulance-based trials and this factor alone has previously resulted in extended recruitment phases, retraining of researchers and extensive study drug availability to achieve preplanned sample sizes.[27 33 40]

Finally, this paper does not capture the time interval between arrival at hospital and handover to the hospital team, nor the time of the ambulance becoming available for the next emergency call (hospital turnaround). During the hospital turnaround period, ambulance staff handover the patient to hospital staff, complete relevant documentation and prepare the vehicle for the next assignment. A rapid hospital turnaround is important for making the vehicle available for waiting emergency calls. While the addition of research activity at scene may not delay enrolled patient treatment, it is possible that delay required to complete additional research activity steps after patient handover may prolong the turnaround phase.

In summary, we completed a large prehospital stroke trial involving a simple-to-administer intervention across multiple ambulance services. The time from onset to randomisation and modest distances travelled support the applicability of future large-scale paramedic-delivered ambulance-based stroke trials in urban and rural locations.

Nevertheless, prehospital time intervals and distances from scene-to-hospital varied by ambulance service and this was, at least in part, explained by the type of urban versus rural population. Although our results may not be generalisable to all ambulance service settings, they do inform future developments in ambulance-based stroke care and provide support to the deliverability of future large-scale multicentre pre-hospital paramedic-delivered ambulance-based acute stroke trials.

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Contributors PMB, also chief investigator and guarantor, and MD conceived the study. All authors contributed to the planning, design and conduct. LJH was responsible for data curation. PS and LJW supported with statistical analysis. All authors contributed to the reporting, analysis and interpretation of the results. MD and PMB led the writing of the manuscript with critical revision from JPA, PS, LJW, LJH, DH, JW and ANS.

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Patient consent for publication Not applicable.

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