Improving emergency treatment for patients with acute stroke: the PEARS research programme, including the PASTA cluster RCT

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Scientific summary

PEARS research programme and PASTA cluster RCT

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Scientific summary

Background

Intravenous thrombolysis and intra-arterial thrombectomy (IAT) are effective treatments for acute ischaemic stroke when they are delivered rapidly, but the emergency clinical pathway is complex. Individual patients are carefully selected for treatment after hospital admission by a specialist review of their clinical information and brain imaging to estimate the potential benefit versus harm. National audit data have reported suboptimal delivery, especially for thrombectomy, which is a relatively new technology available in only a limited number of centres.

During emergency admission, paramedics identify suspected stroke patients, but they do not specifically assist with thrombolysis assessment. Improvements in treatment speed and volume have been reported following targeted interventions to raise the ambulance priority for suspected stroke. In other specialties, simple tools can improve the communication of key information, but no structured paramedic assessment process has been developed to optimise hospital stroke thrombolysis delivery.

As thrombectomy requires interventional neuroradiology expertise and facilities that are available in regional neuroscience centres only, most patients require rapid secondary transfer following initial local assessment. At the start of this programme, it was unclear how many UK stroke patients were suitable for IAT, what the optimal configuration of centres was and whether or not stakeholders supported the inevitable trade-off between possible health gains centrally relative to patient displacement.

Aims and objectives

Work package 1

The aim was to determine the content, effectiveness and cost-effectiveness of an enhanced Paramedic Acute Stroke Treatment Assessment (PASTA) trial to facilitate emergency stroke treatment.

The objectives were to:

1. develop an enhanced paramedic role for assessment of patients with acute stroke symptoms by a review of relevant literature and qualitative assessment of factors influencing the role from public and professional perspectives
2. examine the paramedic intervention by a cluster randomised trial of cost-effectiveness and qualitative process evaluation of professional and public experiences
3. report a within-trial economic evaluation of the enhanced role compared with standard care.

Work package 2

The aim was to determine the clinical effectiveness, costs, cost-effectiveness and affordability of delivering IAT for acute ischaemic stroke patients.

The objectives were to:

1. develop a conceptual model of potential care pathways for IAT patients across NHS services, including pre-hospital, secondary and tertiary care settings
2. convert the conceptual model into a mathematical model, identify the evidence for parameterising key decision points, and estimate outcomes
3. understand patient, public and relevant professional groups' views on possible IAT service designs

4. estimate the effectiveness, incremental cost per quality-adjusted life-year (QALY) and other outcomes from an NHS and societal perspective of a national IAT service for stroke
5. develop an implementation plan for IAT in English stroke services that optimises access.

Methods

Work package 1

To describe relevant evidence of enhanced paramedic assessment, an electronic search of published literature (from January 1990 to September 2016) was focused on (1) structured hospital handovers and (2) paramedic-initiated care processes post handover. The materials identified were introduced into focus groups with health-care professionals and service users to develop the PASTA intervention.

A pragmatic multicentre cluster randomised controlled trial with a parallel process evaluation examined the clinical effectiveness and cost-effectiveness of the PASTA intervention versus standard care in three UK ambulance services serving 15 hospitals (from December 2015 to July 2018). Participants were enrolled post admission if a hospital specialist confirmed that they had experienced a stroke and if the paramedic assessment started < 4 hours after onset. The primary outcome was the proportion of patients receiving thrombolysis. The secondary outcomes included the time intervals and day 90 health, with poor status defined as modified Rankin Scale (mRS) score > 2 to represent dependency or death.

A within-trial economic evaluation until day 90 calculated the incremental cost per QALY from the perspective of the NHS and Personal Social Services. Costs comprised prospectively captured resource utilisation data from ambulance services, hospital, community rehabilitation and social services. The incremental cost per QALY was calculated using non-parametric bootstrapping.

A post hoc analysis considered whether or not routine hospital specialist availability for thrombolysis decision-making had any bearing on treatment delivery and cost-effectiveness. Workforce information reported in the Sentinel Stroke National Audit Programme (SSNAP) Acute Organisational Audit 2016 was used to categorise hospitals as compliant or non-compliant with the current standard regarding provision of a specialist thrombolysis service (King's College London. *Sentinel Stroke National Audit Programme*. London: School of Population Health and Environmental Studies, King's College London; 2016. URL: www.strokeaudit.org).

To describe paramedic, hospital professional and patient experiences related to the PASTA intervention, audio-recordings of semistructured interviews were analysed thematically by two researchers independently.

Work package 2

Surveys were used to establish views regarding service models for IAT provision. In November 2014, clinical leads in all 24 regional neuroscience centres in England were surveyed to enable us to understand the current characteristics of their services. To achieve expert consensus about optimal configuration, a Delphi panel from the British Association of Stroke Physicians reviewed 12 possible service options between November 2015 and March 2016. Clinicians then ranked the most preferred options using a Likert scale.

To understand the public views regarding the trade-off between travel time/displacement and access to IAT treatment, an online survey for stroke patients was advertised by the Stroke Association and National Institute for Health and Care Research (NIHR) Clinical Research Network (which ran from January to May 2017). Using the outputs from surveys and service modelling, a best–worst scaling (BWS) survey was distributed to all Healthwatch services in England in June 2019 to seek the preferred options for service organisation attributes.

To explore the role of an air ambulance during secondary transfer of patients farthest from regional neuroscience centres, an online survey was sent to nine Helicopter Emergency Medical Services (HEMS) serving 'unavoidably small and remote' hospitals (NHS England definition: < 200,000 population and > 1 hour' travel from the nearest major hospital) [Advisory Committee on Resource Allocation, NHS.

Advisory Committee on Resource Allocation (ACRA) (2015) 36 – Costs of Unavoidable Smallness due to Remoteness. 2016. URL: www.england.nhs.uk/publication/advisory-committee-on-resource-allocation-acra-2015-36-costs-of-unavoidable-smallness-due-to-remoteness/ (accessed 28 September 2021)].

To build a model that reflected the latest evidence for thrombectomy effectiveness, a search strategy was applied to five electronic bibliographies and three international trial registries to identify randomised clinical trials published from January 2009 to February 2015 for data meta-analysis.

To estimate the number of UK patients eligible for IAT, regardless of geographical or service constraints, a decision tree was constructed from published trials and national registry data (SSNAP for England, Wales and Northern Ireland; and the Scottish Stroke Care Audit). Microcosting methods were applied to clinical records of individual IAT patients at five UK regional centres (2015–18). Resources used within the 72 hours following stroke were collected for direct admission and secondary transfer service models. A discrete-event simulation (DES) was constructed from the decision tree and IAT costing information to predict per-patient outcomes and financial consequences for different service configurations. Two key scenarios were modelled: (1) increasing IAT provision from 24 to 30 centres to achieve better population-level coverage and (2) secondary helicopter transfer of eligible patients from remote hospitals.

The DES was converted into a web-based application, allowing commissioners and providers to examine the potential health and economic impact of changing service configuration within their locality [the Interface for Thrombectomy Economic Modelling and outcomeS (ITEMS)].

Results

Work package 1

A narrative review of 36 shortlisted studies highlighted that paramedic information collection and communication skills can be enhanced. Fifteen focus groups and interviews to develop the PASTA pathway were undertaken in north-east England, north-west England and Wales (20 patients; 103 professionals). The resulting intervention comprised additional pre-hospital information collection, structured hospital handover, practical assistance up to 15 minutes post handover, a pre-departure care checklist and clinician feedback.

The PASTA trial involved 121 ambulance stations and 1540 paramedics. Out of 11,478 stroke patients screened, 1214 were enrolled (mean age 75 years; 48% of patients were female). Baseline characteristics were well matched. The PASTA paramedics took an average of 13.4 minutes longer [95% confidence interval (CI) 9.4 to 17.4 minutes; $p < 0.001$] than the standard care paramedics to complete patient care episodes (i.e. 'clear' a patient), mainly because of an additional 8.8 minutes spent in hospital (95% CI 6.5 to 11.0 minutes; $p < 0.001$). There was no significant additional time spent on scene [PASTA intervention 26.0 minutes, standard care 24.2 minutes, difference 1.61 minutes (95% CI −0.2 to 3.4 minutes; $p = 0.08$)]. Door-to-needle times were not significantly different for thrombolysis patients [PASTA intervention 59 minutes, standard care 54 minutes, difference 5 minutes (95% CI −1 to 11 minutes; $p = 0.12$)].

There was no significant difference in the proportion of patients receiving thrombolysis between the PASTA [197/500 (39.4%)] and standard care groups [319/714 (44.7%)], but there was an unexpected trend in the opposite direction [adjusted odds ratio (aOR) 0.81, 95% CI 0.61 to 1.08; $p = 0.15$; intracluster correlation coefficient 0.00]. Although lacking statistical significance, at day 90 there was a non-significant trend towards fewer poor outcomes (i.e. a mRS score ≥ 3) among intervention patients [PASTA intervention, 313/489 (64.0%); standard care, 461/690 (66.8%); aOR 0.86, 95% CI 0.60 to 1.2; $p = 0.39$]. There was no evidence of a QALY difference between groups in either complete-case (0.007, 95% CI −0.003 to 0.018) or imputed data (0.005, 95% CI −0.004 to 0.015). The total costs were significantly lower in the PASTA intervention group for both complete-case (−£1473, 95% CI −£2736 to −£219) and imputed data sets (−£1086, 95% CI −£2236 to −£13). Over a range of values for willingness to pay per QALY, there was a > 97.5% chance that the PASTA intervention would be considered cost-effective.

In a secondary analysis, eight hospitals ($n = 506$) that were not fully compliant with the national standard for specialist availability achieved a statistically significant absolute reduction in the PASTA thrombolysis rate of 9.8%, compared with standard care [99/276 (35.9%) vs. 105/230 (45.7%); unadjusted odds ratio (OR) 0.67, 95% CI 0.47 to 0.95; $p = 0.03$], with a significant cost reduction (–£2952, 95% CI –£4988 to –£917) and a non-significant QALY gain (0.009, 95% CI –0.008 to 0.025).

During the process evaluation, 26 interviews with intervention paramedics across the three ambulance services (north-east England, 11; north-west England, 10; Wales, 5) identified four key themes: (1) the PASTA intervention complemented their skill set and confidence; (2) hospital pre-notification contained more appropriate information than standard care; (3) the 'scripted' format for handover was viewed as the primary benefit; and (4) assisting care after handover in hospital was harder to achieve. These themes were reinforced during interviews with 25 hospital staff. Patient recruitment was discontinued after six interviews, as no participants were able to recall ambulance care details.

Work package 2

The survey responses from 18 neuroscience centres showed considerable service variation: one had 24 hours per day, 7 days per week IAT provision, two centres had 7-day provision during normal hours, 12 delivered IAT on weekdays and three had no regular provision. Patient selection criteria also varied. A median of 10 (interquartile range 16) stroke patients had IAT performed per centre during the previous year.

Expert consensus from 11 stroke physicians and a survey of specialist society membership ($n = 64$) supported a current model involving secondary transfer of patients ('drip and ship') with large artery occlusion stroke for IAT based on initial local imaging. A public survey proposing this model received 147 responses (i.e. 27 stroke survivors, 51 relatives/carers and 69 other), with the majority supporting centralised IAT provision and secondary transfer up to 30 miles. A subsequent BWS survey was completed by 105 respondents [mean age 37 years (range 18–86 years); 70% female; 18% urban, 56% suburban, 26% rural; 18% stroke survivors, 32% relatives/carers and 50% others]. The most preferred service attribute was access to greater medical expertise, and secondary transfers with travel times of up to 45 minutes to receive IAT were considered acceptable. The results of the HEMS survey showed that all nine air ambulance services were willing to provide secondary transfers for IAT, although three indicated that additional funding and/or organisational changes would be required.

The literature search identified eight randomised clinical trials eligible for the meta-analyses ($n = 1841$ contributing cases). Patients treated with IAT were significantly more likely to be functionally independent (i.e. a mRS score < 3) at 90 days' follow-up (OR 2.39, 95% CI 1.88 to 3.04). These results suggest that, compared with best medical care, IAT had no effect on the rate of mortality or symptomatic intracerebral haemorrhage.

An evidence-driven decision tree estimated that, in the UK, 10,140–11,530 (12%) stroke admissions would be eligible for IAT each year, with only a small proportion requiring advanced imaging. Retrospective microcosting showed that the main expenditure during IAT provision was the actual procedure, accounting for 73% (£7930) of the total 24-hour cost. The total mean cost within 72 hours was £12,440. There was no statistically significant difference in 24-hour costs between direct admissions and those admitted following secondary transfer (mean difference –£368, 95% CI –£1016 to £279; $p = 0.26$).

A DES based on the decision tree estimated that the addition of six neuroscience centres to improve English population coverage would generate 190 QALYs (95% CI –6 to 399 QALYs) and a saving to the health-care system of £1,864,000 per year (95% CI –£1,204,000 to £5,017,000 saving per year). Over 5 years, there would be a return on capital investment of £8M. However, the modelling did not consider the capital costs of new services. By improving IAT access for patients who initially presented to remote hospitals, helicopter transfer was associated with a greater mean probability of living independently at 90 days (0.57), compared with using ground-based ambulances (0.53), and an incremental cost-effectiveness ratio over a lifetime horizon of £28,027 per QALY gained.

The DES was converted into the web-based ITEMS application, enabling a selection of local key variables, such as service configuration, rurality and procedure costs, to generate a cost-effectiveness output display (90 day mRS score and lifetime QALYs).

Limitations

It is important to recognise that the association with specialist availability found in work package (WP) 1 was a hypothesis-generating post hoc analysis, and mechanisms remain unclear for any influence on treatment decisions, health and economic outcomes. The modelling work in WP2 did not include capital expenditure and other costs associated with establishing new health-care infrastructure and cannot account for unforeseen developments in future services or technologies, and all surveys reflect views from respondents only.

Conclusions

The key for successful NHS implementation of emergency stroke treatments is to take a whole-pathway approach. A novel ambulance assessment did not improve the volume and speed of thrombolysis delivery at local hospitals, but an unexpected combination of thrombolysis, health and economic outcomes led us to consider whether a structured handover and/or multidisciplinary checklist could improve the selection of patients for thrombolysis, particularly at sites with lower levels of specialist availability. As qualitative evidence indicates clinical acceptability, implementation could be considered in stroke services with unavoidably low levels of specialist availability for thrombolysis decision-making.

A more complex pathway to provide IAT at regional centres could increase the probability of a good outcome for up to 12% of UK stroke admissions. Increasing access to IAT has strong professional and public support, even if the pathway requires secondary transfer over a significant distance following initial local assessment. Modelling work based on national registries identified changes in acute stroke service configuration that are highly likely to produce cost-saving health benefits by improving access to IAT in localities furthest from regional neuroscience centres assuming that capital costs are available (six additional sites and/or use of helicopter transfers).

Future research should consider:

1. prospective evaluation of whether or not structured information collection and communication by paramedics can influence emergency clinical guideline adherence in hospital and subsequent care costs for acute stroke patients
2. further validation and development of the DES output, with inclusion of parameters reflecting ambulance service resources and the PASTA trial evidence
3. adding new parameters to a combined IAT and thrombolysis DES that might have a significant impact, such as ambulance telemedicine.

Trial registration

This trial is registered as ISRCTN12418919 and the systematic review protocols are registered as PROSPERO CRD42014010785 and PROSPERO CRD42015016649.

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