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KEY PERSONNEL

Chief Investigator	Dr Angus I. G. Ramsay UCL Department of Applied Health Research 1-19 Torrington Place, London WC1E 7HB e-mail: angus.ramsay@ucl.ac.uk
Study Coordinator	Ms Pei Li Ng UCL Department of Applied Health Research e-mail: pei.ng@ucl.ac.uk
Other team members	Dr Prasanna Aghoram – Dartford and Gravesham NHS Trust George Bray – UCL Mr Jeremy Dearling – Patient representative Prof Naomi Fulop – UCL Ms Claire Hall – South East Coast Ambulance Service NHS FT Dr David Hargroves – East Kent Hospitals University NHS FT Mr Patrick Hunter – London Ambulance Service NHS Trust Prof Rachael Hunter – UCL Prof Helen Snooks – Swansea University Dr Holly Walton - UCL Dr Robert Simister – UCLH NHS FT Ms Robyn Stephens – Stroke Association Ms Marney Williams – Patient representative Ms Victoria Williams – Maidstone and Tunbridge Wells NHS Trust
Sponsor	Mr Pushpsen Joshi UCLH/UCL Joint Research Office, 4th Floor, West 250 Euston Road London NW1 2PG
Funder	Health and Social Care Delivery Research Programme National Institute for Health and Social Care Research University of Southampton Alpha House, Enterprise Road Southampton SO16 7NS e-mail: hsdrinfo@nihr.ac.uk

KEY WORDS

- Stroke care
- Prehospital telemedicine
- Ambulance conveyance
- Quality and safety
- Patient and carer experience
- Cost-effectiveness

LIST OF ABBREVIATIONS

24/7	Twenty-four hours per day, seven days per week
COVID19	Coronavirus disease 2019
DiD	Difference-in-differences
ED	Hospital emergency departments
FT	NHS Foundation Trust
GP	General Practitioner
HES/ONS	Hospital Episodes Statistics
ICER	incremental cost-effectiveness ratio
INVOLVE	National Institute for Health Research body set up to support active public involvement in NHS, public health and social care research
LAS	London Ambulance Service NHS Trust
MSU	Mobile Stroke Unit
NC London	North Central London
NIHSS	National Institutes of Health Stroke Scale
PIS	Participant Information Sheet
PROSPERO	International Prospective Register of Systematic Reviews
QALY	Quality-adjusted life years
REC	Research Ethics Committee
RQ	Research Question
SECAmb	South East Coast Ambulance Service NHS Foundation Trust
SOPs	Standard Operating Procedures
SSC	Study Steering Committee
SSNAP	Sentinel Stroke National Audit Programme
TIA clinics	Transient Ischaemic Attack
UCL	University College London
UCLH	University College Hospitals NHS Foundation Trust

CONTENTS

1 STUDY OVERVIEW

Stroke is a major cause of death and disability in the UK and worldwide. Rapid access to hyperacute care for stroke patients saves lives and reduces disability but the absence of a pre-hospital test to diagnose stroke results in the transfer to stroke specialist units of acutely unwell patients who do not have stroke. This “stroke mimic” population, comprising up to 50% of all presentations to specialist stroke teams, receive delayed care away from their local care network and drain stroke service resource and attention away from the effective management of the stroke population.

During the COVID19 pandemic, some parts of England introduced “prehospital triage” services that let hospital-based stroke specialists use digital videoconferencing to communicate remotely with ambulance clinicians at the scene of 999 calls to assess suspected stroke patients. These aim to ensure patients are taken to the most appropriate service (or stay home, if appropriate). Video-assessment has been used to improve hospital team preparedness for inbound transfers to stroke services. However, very little is known about how pre-hospital triaging assessments can be implemented, how well they work, their impact on care, patient outcomes, and patient experience, and whether they provide value for money.

This research builds on the team’s recently completed rapid service evaluation of prehospital triage for stroke in North Central London (NC London) and East Kent – which focused on safety, effectiveness, and usability and a review of existing research evidence on systems that enable communication between ambulance crews and stroke physicians. PHOTONIC will provide important lessons on how prehospital triage for suspected stroke affects quality of care, patient outcomes, and whether it delivers value for money; it will also support future cooperation between hospital and ambulance systems.

The study will focus on four areas, NC London, East Kent, Maidstone (West Kent), and Darent Valley (West Kent), which have recently implemented prehospital triage. While these services are similar (using a digital platform to permit stroke and ambulance clinicians to assess patients on scene), some differ in terms of who is eligible for specialist assessment and which specialist conducts the assessment.

- First, the study will analyse how prehospital triage was set up, run, and experienced by patients, carers, and staff. Interviewees will include patients and carers; stroke, ambulance, and emergency teams; and service and system managers. Non-participant observations will be conducted on oversight and delivery of prehospital triage, and documents related to how the services are working will be analysed. The analysis will focus on how the services were put into action, and what helped or hindered this. We will also ask patients and carers how they experienced prehospital triage.
- Second, the study will analyse the impact of prehospital triage on healthcare services and patient outcomes. NHS data will be studied to analyse whether introducing prehospital triage results in: more patients being taken to the right hospital service; more patients remaining at home and avoiding hospital admission; patients (stroke and non-stroke) getting the right care more quickly, and if there are any adverse effects of prehospital triage; and improving how well patients do after their stroke. Analyses will compare performance before and after prehospital triage was introduced. Analyses will also compare the areas that are using prehospital triage with other parts of the UK that are not currently using it.

- Third, the study will analyse whether prehospital video triage services are delivering good value for money to the NHS. Again, analyses will compare performance before and after prehospital triage was introduced. Analyses will also compare the areas that are using prehospital triage with other parts of the UK that are not currently using it.

Throughout, the team will engage with people leading prehospital triage in monthly meetings, so they can make use of the findings as they develop. The team will develop a list of clinicians, politicians, charities, members of the public, and others who make decisions about healthcare and are interested in the research; the team will share quarterly newsletters and podcasts to describe how the research is going. The team will share the findings at research conferences and in academic journals, and make accessible summaries and videos for stakeholders. Finally, the team will run a workshop for people providing stroke and other services, patients and carers, charities, and international experts, to share and develop lessons for services across the UK that might want to introduce prehospital triage.

The team includes stroke survivors, stroke clinicians and service managers, charities, and academic researchers. Thanks to this, the team have expertise in the conditions and services to be studied, and in the research methods that will be used to study them.

The study will run from September 2021 to August 2023 inclusive.

2 BACKGROUND AND RATIONALE

Stroke is a major cause of death and disability.[1] Stroke patients have better care and outcomes if treated in a specialist unit.[2-5] Not every hospital has a specialist stroke unit: patients are commonly triaged by prehospital clinicians, bypassing the nearest emergency department if a patient is thought to be suffering a stroke. Many patients present with stroke-like symptoms but have another condition which 'mimics' a stroke. This may be difficult to determine in the prehospital setting with the assessment deemed 'false positive',[6] and the patient making an unnecessary journey to a specialist stroke team when in fact an alternative health care setting may be more appropriate (comprising up to 50% of all presentations to specialist stroke teams). This places avoidable pressure on ambulance and stroke services, with serious implications for quality of care for stroke and non-stroke patients.[7] Remote prehospital triage may increase appropriate patient transfer, improving effectiveness and efficiency of ambulance, stroke, and other services, and the quality of care and outcomes for stroke and non-stroke patients.

During the first wave of the COVID19 pandemic, ambulance, and stroke teams in North Central (NC) London and East Kent developed and implemented prehospital video triage services, which used digital tools technology to permit remote communication between ambulance clinicians and stroke specialists. Through these services, stroke specialists can assess the patient while the patient is still on scene of the 999 call. The aim was to optimise individual patients' care: to ensure that stroke patients were taken to a stroke unit, and to minimise the number of non-stroke patients making unnecessary journeys to a stroke unit or hospital emergency departments (ED) if they could be managed by their GP or as an outpatient; these issues are important at any time, but became particularly urgent during the pandemic.

Reviewing existing evidence

Through a current service evaluation (discussed below),[8] the team are conducting a two-phase literature review to assess the existing evidence base. The initial phase was a 'review of reviews' to identify existing systematic, scoping and narrative reviews on prehospital triage for

stroke. This exploratory work identified evidence about highly-equipped mobile stroke units (MSUs),[9, 10] while more relevant literature focused on the remote assessment of patients using two-way communication tools (commonly described as 'telestroke' or 'telemedicine'). Remote systems often rely on less complex medical diagnostic equipment (as found in MSUs) and enable sharing of audio and visual information between ambulance crews and stroke specialists to support clinical diagnosis and treatment.[11, 12] The literature on the use of remote prehospital triage was deemed to be valuable for both the rapid evaluation and future studies on this topic.

The available evidence on using digital tools and telestroke notes the potential to support effective assessment of suspected stroke patients.[13, 14]. However, technical challenges (e.g. signal quality) are identified as a potential obstacle to the process.[13, 14] For example, a recent review describes how prehospital triage might contribute to quality and safety of stroke care, but identifies important knowledge gaps including limited rigorous evidence on how prehospital triage is implemented,[14, 15] its effectiveness in influencing clinical decisions,[13-15] and its impact on patient outcomes, patient experience, and cost-effectiveness.[15] A rapid 'review of reviews' therefore identified some important potential gaps, in particular, around the patient perspective, patient safety, implementation, costs, and how technology may change communication dynamics between health professionals and between health professionals and patients. It was also observed that some reviews were restricted by searching for clinical outcomes and none had been conducted across databases during the COVID19 pandemic as new stroke service models were rolled out and digital transformation expedited within health systems. In addition, the team recently completed a review of the literature on implementation and outcomes (both clinical and non-clinical) arising from the introduction of prehospital triage systems for stroke (registered on PROSPERO). This review was completed in September 2021.

This study will address the important gaps in knowledge identified to date, building on the team's recent and thorough reviews of the published research evidence. The team will provide robust data on the impact of prehospital triage, analysing impact on patient destination, care delivery, and cost-effectiveness, using a multi-site study design with national and regional controls. The team will study implementation and patient experience with in-depth qualitative analyses that go beyond assessments of technological usability or clinical measures. The team will also use qualitative methods to explore the influence of initiatives introduced to strengthen clinical leadership for stroke (e.g., Integrated Stroke Delivery Networks) and system leadership more generally (e.g. Integrated Care Systems).

The study team have led research on reconfiguration of acute stroke services,[2-4, 16-18] 24/7 working in London stroke services,[7, 19] and use of evidence about stroke service change ; as well as other prehospital interventions to improve the emergency care of patients with stroke.[20-22] The study builds on a current rapid service evaluation, led by several of the team,[8] which is delivering reviews of the evidence, clinician views on usability, safety, and timelines of implementation of prehospital triage in NC London and East Kent.[8] The interim data indicate that the new services are working effectively, with stroke and ambulance teams highly supportive of the principles and approach of the new services; important questions are emerging in relation to how best to ensure stroke teams have the capacity to deliver these remote assessments alongside delivering other aspects of specialist stroke care.

The team have established that the anticipated findings are of interest and importance to national and regional leadership for stroke and ambulance services, for example in enhancing delivery of the NHS Long Term Plan in relation to prehospital and acute care for stroke patients.

Why this research is needed now

Improving prehospital and acute stroke care has been identified as a priority in UK national policy[23, 24] and by the Stroke Association.[25] Appropriate patient transfer is vital to stroke systems, particularly in rural areas, and to permit timely access to specialist stroke care, including key interventions such as clot-busting drugs (thrombolysis) and clot-removal (mechanical thrombectomy); it is also a focus of the National Stroke Service Model, currently being developed by NHS England. The study builds on research in a recent NIHR themed review on stroke.[26] It may also be relevant to other health service contexts that rely on appropriate patient transfer. Lessons on implementation will contribute to the national priority of rapid deployment and scale-up of digital technologies. Ensuring this deployment and scale-up is undertaken efficiently will be key as health services are likely to face funding challenges due the long-term effects of the pandemic on the healthcare system and economy more broadly.

In preparing this application the team have engaged with stroke survivors, clinicians, and representatives of the Stroke Association and NHS England. All have confirmed the importance of this research and its potential impact on future organisation and delivery of stroke care, and indicated their interest in learning of the findings as soon as possible. Several key figures have agreed to join the Study Steering Committee, including the National Clinical Director for Stroke (who provided a letter of support for this work), the Welsh Ambulance Services Trust, the Chair of the recently-formed National Ambulance Stroke Leads group, and a number of patient representatives – one of whom stated that this study offers *"A huge benefit to patient outcomes and rewarding for all the people involved in this difficult branch of medicine"*.

3 AIM(S) AND OBJECTIVES

The study will build on the team's recent rapid service evaluation of prehospital video triage in NC London and East Kent to address implementation and impact of prehospital triage. The research questions are:

1. Which factors influence implementation, use, and expansion of prehospital triage for suspected stroke patients, in terms of planning, governance, and workforce?
2. How is prehospital triage experienced by patients and carers (of different backgrounds), stroke and ambulance services, emergency departments, primary care, TIA clinics, hospital managers, system leaders, and charities?
3. Does prehospital triage impact on appropriate patient transfer, care delivery, and patient outcomes across the prehospital and acute stroke pathways?
4. Is prehospital triage for stroke cost-effective?
5. What are the lessons for planning, implementing, and evaluating prehospital triage (for stroke and other conditions)?

3.1 Primary Objective

To develop lessons on implementation and experiences of prehospital video triage, and its impact on care delivery, patient outcomes, and cost-effectiveness.

3.2 Secondary Objectives

1. To use qualitative methods to study which factors influence implementation, use, and expansion of prehospital triage for suspected stroke patients, in terms of planning, governance, and workforce.

2. To use qualitative methods to study how prehospital video triage for suspected stroke is experienced by patients and carers (of different backgrounds), stroke and ambulance services, emergency departments, primary care, TIA clinics, hospital managers, system leaders, and charities.
3. To use quantitative methods to assess in what ways prehospital video triage for suspected stroke impacts on appropriate patient transfer, care delivery, and patient outcomes across prehospital and acute stroke pathways.
4. To use health economic methods to assess cost-effectiveness of prehospital video triage for suspected stroke.
5. To integrate qualitative and quantitative findings and conduct a stakeholder workshop in order to identify lessons for planning, implementing, and evaluating prehospital triage (for stroke and other conditions).

4 STUDY DESIGN & METHODS OF DATA COLLECTION

Design and conceptual framework

This is a mixed method, multisite study of the implementation and impact of prehospital triage for suspected stroke in four areas of the English NHS. The study draws on the literature review and qualitative work already undertaken in the team's rapid evaluation, but makes important additional contributions in terms of focus, sample, and methods. The study will combine ***qualitative analysis*** (of stakeholder interviews, non-participant observations, and relevant documentation), ***quantitative analysis*** of national and local datasets, and ***cost-effectiveness analyses*** (including analysis of implementation costs) (Figure 1).

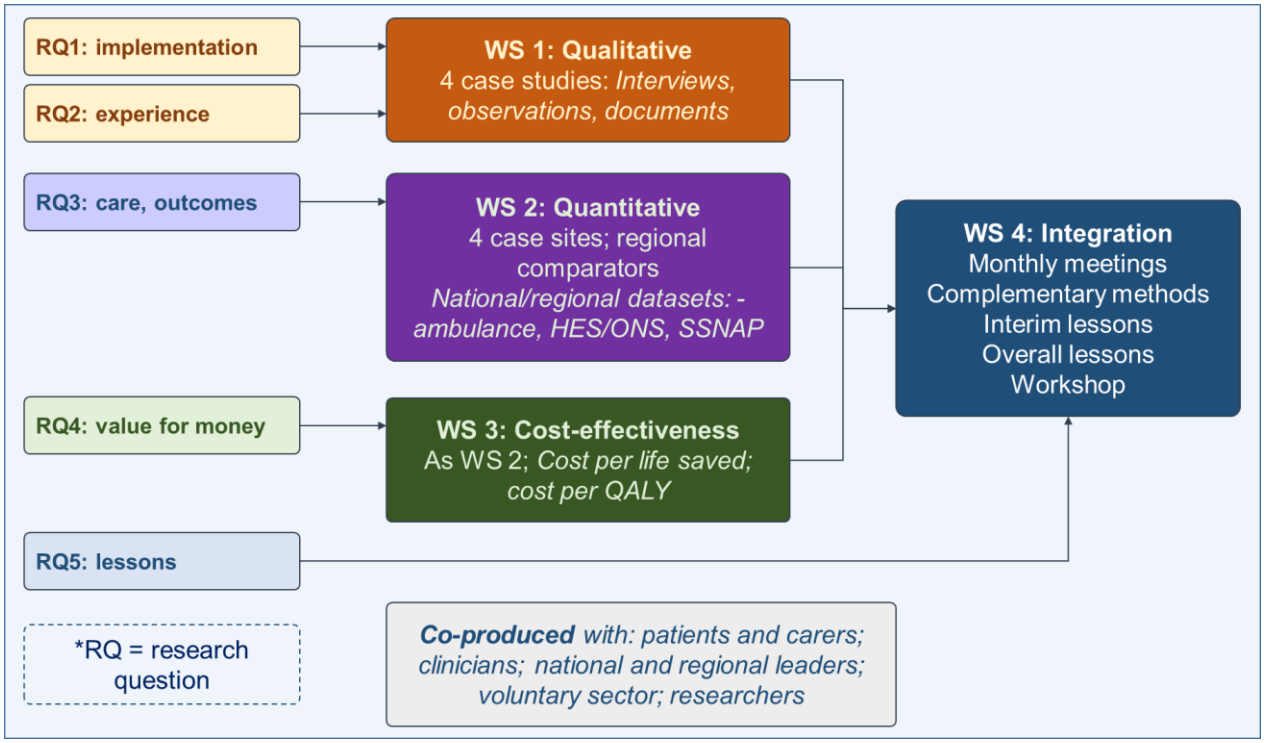

Figure 1. Overview of PHOTONIC study design

This study will be informed by thinking on long term process analysis, using inductive and deductive approaches to describe unique examples in their context as they evolve over time, while also seeking to generate wider lessons through cross-case comparison.[27]

The research will be guided by a recent framework describing key factors that influence how digital service innovations are implemented, sustained, and spread. Factors include innovation characteristics, implementation approaches, organisational characteristics, wider system context, and diffusion approaches.[28]

Setting/context for this study

This research will take place in four areas of London and South East England where prehospital triage for stroke has been established. The focus of the research is on prehospital ambulance care and acute care settings, including stroke and emergency departments, but will also explore the organisations within which these services sit, and the wider context, including local/regional governance and commissioning, the voluntary sector, and other patient representative groups. In preparing the research application the team engaged with ambulance service leads in England and Wales, and clinical leads in Scotland (through the National Ambulance Stroke Leads group), who confirmed no other areas have implemented services of this kind at equivalent scale. Through this engagement with wider networks, the team were made aware of activity on prehospital triage for stroke in the East of England (piloted using video platform 'Visionable', with potential for scale-up), North East England (plans to introduce a service, beginning with a pilot), and London (aims to roll out NC London model across the city). The team have engaged with people leading this activity in each area to ensure they are aware of this research, and they will to be added to the prospective stakeholder list (discussed further under Dissemination).

The study will analyse four case sites where prehospital triage has been implemented, summarised in Table 1. While similar in terms of platform and function, these case sites vary on a number of key features of the conceptual framework, including intervention characteristics (e.g., 24/7 coverage or patient eligibility), organisational characteristics (e.g. NHS Foundation trust status and academic links), and wider context (e.g., stroke system, rurality).

Table 1. Characteristics of case sites

Characteristics	**Case site**			
	East Kent	*NC London*	*Maidstone*	*Darent Valley*
Intervention characteristics				
Implemented from	Apr-2020	May-2020	Oct-2020	Nov-2020
Platform	Facetime	Facetime	Facetime	Facetime
Eligibility for assessment	All suspected strokes[1]	All suspected strokes	All suspected strokes	Diagnostic uncertainty
Assessor	Consultant/ registrar	Consultant/ registrar	Stroke nurse, then consultant if needed	Stroke nurse, then consultant if needed
Hours active	24/7	24/7	Stroke nurse: 24/7 Consultant: 8am-8pm Mon-Fri	8am-6pm Mon-Fri

Organisation characteristics				
Acute FT-status	Yes	Yes	No	No
Acute Teaching	Yes	Yes	No	No
ED & Stroke unit co-located	No	No	Yes	Yes
Ambulance service	SECAmb	LAS	SECAmb	SECAmb
Wider context				
Acute stroke system	Centralising	Centralised 2010	Centralising	Centralising
Rurality	Rural	Urban	Rural	Rural

Note. [1]East Kent eligibility was initially for patients where there was diagnostic uncertainty, and changed to all suspected strokes in September 2020.

Workstream 1: implementation and experiences [RQs 1&2; months 1-24]

The study will use a range of qualitative methods to analyse implementation and sustainability of prehospital triage services for stroke, and stakeholder experiences of these services, including patient, carer, and healthcare professional perspectives. The approach will draw on the chosen conceptual framework for implementation and sustainability of digital innovation,[28] and it will be informed by the developing findings from the team's recent service evaluation of the NC London and East Kent services.

Stakeholder interviews

In each of the four case sites, up to 30 interviews will be conducted with a wide range of stakeholders to ensure suitable coverage of the services studied and the context in which they operate. Interviewees will include stroke and non-stroke (initially suspected to be stroke) patients and their carers, including patients with different decisions resulting from assessment (i.e., transferred to stroke unit, transferred to emergency department, referred to TIA clinic, advised to stay home). The team will work closely with clinical colleagues (including local research nurses) and purposively sample interviewees to ensure that a diverse range of patients and carers is recruited, in order to reflect local socio-demographic factors, including ethnicity, socio-economic status, language capabilities (e.g. non-English speakers) and living situation (e.g. patients who live alone). Interviews will also be conducted with clinical and managerial staff in ambulance services, acute stroke teams, and emergency departments, senior organisational management, and representatives of the wider context (Table 2).

Interviews will be guided by semi-structured topic guides. These will be developed in collaboration with the clinician, stroke patient, and voluntary sector co-investigators, and informed by conceptual framework, the wider literature on implementation of prehospital triage for stroke, and the team's extensive experience of evaluating implementation and sustainability of innovations in stroke care settings. The topic guides will be tailored to different stakeholder perspectives and experiences: for example the patient and carer interviews might focus more on the individual's personal experience of the service (for example, what it was like to be assessed in advance of reaching hospital), while clinician interviews might focus more on

development, governance, and day-to-day delivery of the service, and stakeholders representing the wider context may be asked about oversight and system-level implications of the services.

Table 2. Summary of stakeholder interviews and non-participant observations

Method	Source	Per case	Total
Stakeholder Interviews	Stroke patients and carers	5	20
	Non-stroke patients and carers	5	20
	Ambulance staff	5	20
	Stroke staff	5	20
	Emergency department staff	4	16
	Senior management[1]	3	12
	Wider context(e.g. system leaders, commissioners, patient groups)	3	12
	TOTAL	**30**	**120**
Non-participant observations	Prehospital triage assessments	10	40
	Triage service oversight	4	16
	Stroke service governance	4	16
	Ambulance governance[1]	4	16
	Wider governance	4	16
	Training events	4	16
	TOTAL	**30**	**120**

Note. [1]Because three sites are served by the same ambulance service, the number of higher-level interviews and observations may be lower, as fewer senior management representatives and trust-level meetings will cover all three case sites.

Non-participant observations

Non-participant observations of a range of activities related to delivery and oversight of the prehospital triage services will be conducted (Table 2). In order to understand how the prehospital triage service is delivered researchers will attend participating stroke units to observe stroke physicians conducting remote assessments. To understand how staff are introduced to the service researchers will observe training sessions conducted in stroke and ambulance settings. To understand how these services are led and managed, researchers will observe governance meetings at different levels, including team (e.g. triage service and clinical

governance meetings), organisation (governance and safety meetings), and system (e.g. NHS England and Integrated Stroke Delivery Network meetings) levels. Observations will be conducted in-person or virtually, depending on the type of event, safety issues, and advice from the team's clinical partners.

Data will be collected in the form of field notes, handwritten and electronically transcribed for storage and analysis by the researcher. Field notes will be collected using a semi-structured template reflecting key themes identified in the conceptual framework and the wider literature on implementation of prehospital triage for stroke, developed in collaboration with clinician, stroke patient, and voluntary sector co-investigators. Themes will include:

- Nature of the event observed (assessment, meeting, training).
- Participants in the activity (clinicians, managers, others).
- Nature of interactions (focus, quality of communication, who leads discussion).
- Outcomes of the activity (decisions reached, learning achieved).
- Factors influencing communication and decision-making (including technical and interpersonal issues).

Key documents

Researchers will also request relevant documents from participating organisations and stakeholders for analysis. To understand how services are organised and delivered, researchers will request service plans, business cases, and transfer protocols. To understand management and oversight of the services over time, researchers will request meeting documentation (minutes, agendas, supporting papers) from initiation of the services onwards. To understand how staff are introduced to and skilled to deliver these services, researchers will request communications and training materials (including introductory videos, information pamphlets and 'frequently asked questions', and posters).

Workstream 2: impact on care delivery and outcomes [RQ3; months 1-22]

The study will analyse delivery and outcomes of care related to prehospital triage, using patient-level data. This will be a quasi-experimental design, comparing the case site areas against national controls, before and after the introduction of prehospital triage.

Case sites and controls

The analyses will focus on performance in the four case sites. For the comparative analyses of prehospital care the control cohort will include combined data from four ambulance NHS Trusts where prehospital triage services for stroke are not being used: London Ambulance Service NHS Trust (excluding NC London), South East Coast Ambulance NHS Foundation Trust (excluding East Kent, Maidstone, and Darent Valley), West Midlands Ambulance Service NHS Foundation Trust (WMAS), and North East Ambulance Service NHS Foundation Trust (NEAS). For the comparative analyses of delivery of stroke clinical interventions within hospital services the analyses will use a national control drawn from the Sentinel Stroke National Audit Programme (SSNAP). All patients submitted to these datasets will be included in prehospital and in/post hospital analyses.

Data

Table 3 presents annual activity levels in terms of prehospital care (patients who have been coded as *suspected stroke/neurological* by ambulance crews) and acute stroke care (number of

strokes reported in the national audit, the vast majority of whom are conveyed by ambulance). To enable the controlled before and after design, data covering a 40-month period (April 2019 to August 2022 inclusive) will be requested, permitting a minimum of 12 months 'before' data and minimum of 26 months 'after' data.

Table 3. Annual activity for quantitative analysis

Metric	*Control*[A]	Case sites			
		East Kent	***NC London***	***Maidstone***	***Darent Valley***
Stroke patients treated in hospital[B]	85,549[C]	970[D]	1457	789[E]	515
Ambulance calls for suspected stroke/neurological event[F]	46724	1729	2529	2620	984

Note. [A]Control for stroke patients is national, whereas the control for Ambulance data combines four NHS Ambulance trusts –meaning the stroke patient control is proportionally larger than the ambulance data control. [B]Stroke case numbers drawn from the Stroke Sentinel National Audit Programme (SSNAP) data for April 2019 to March 2020. [C]National data cover England, Wales, and Northern Ireland, excluding strokes reported for the case sites. [D]East Kent data combine strokes reported for two sites: Queen Elizabeth the Queen Mother Hospital and William Harvey Hospital. [E]Maidstone data combine strokes reported for two sites: Maidstone General Hospital and Tunbridge Wells Hospital, the latter of which closed in late 2019, with stroke activity transferred to Maidstone. [F]Ambulance call sample based on estimates of 12 months of calls where ambulance crews have categorised patients as 'suspected stroke/neurological event', as provided by LAS, SECAmb, WMAS, and NEAS.

To study prehospital care, analyses will focus on job cycle time (from 999 call to 'ambulance free' time, where the ambulance is ready for its next dispatch); and initial patient destination. As these patient-level data are not held nationally the team will request these data from local ambulance services identified above. The team have confirmed with these organisations that the data are collected reliably and are available for request; and the costs agreed for these data requests have been included in the budget. Over the course of data requests researchers will work closely with Ambulance service representatives to ensure consistency of definitions and data collection. To study delivery of acute stroke care and stroke patient functional independence, researchers will analyse patient-level stroke national clinical audit data requested from SSNAP, and data collected by stroke teams using prehospital video triage. To study patient outcomes (patient mortality and length of hospital stay), researchers will analyse Hospital Episode Statistics data linked with Office for National Statistics mortality data, requested at patient-level from NHS Digital.

Table 4. Quantitative data sources

Source	Data	Measures	Time
Local ambulance	Patient-level	• Call categorisation, Emergency Operations Centre	Apr 2019-

	Patients categorised by ambulance crews as *suspected stroke/neurological*	• Job cycle length, disaggregated by Time to dispatch; to scene; on scene; to hospital; Total job cycle • Patient destination	Aug 2022
Local stroke units	Patient-level	Stroke services using prehospital triage are collecting data on destination and diagnosis of all patients categorised as non-stroke	Apr 2019-Aug 2022
SSNAP	Patient-level Data for patients categorised as *stroke*	• Type of stroke (infarction/haemorrhage) • Stroke severity (NIHSS[1]) on arrival • Patient characteristics (e.g. sex, age) • Arrival mode (e.g. by ambulance, in-hospital) • Eligibility for thrombolysis • Eligibility for mechanical thrombectomy Time from a) symptom onset, b) 999 call, and c) arrival at hospital to... • brain scan • admission to stroke unit • thrombolysis (if eligible) • mechanical thrombectomy (if eligible) • assessment by consultant physician assessment • assessment by stroke specialist nurse • swallow screen Outcomes: • Functional independence: patients with Modified Rankin Scale score (established measure of stroke patient disability) of 0-2 (or return to baseline if baseline score is more than 2)	Apr 2019-Aug 2022
HES/ONS	Patient-level ED attendances (with dates); Stroke attendances	Emergency hospital admissions with dates and length of hospital stay All-cause patient mortality at 30 and 90 days	Apr 2019-Aug 2022

Note. [1]NIHSS=National Institutes of Health Stroke Scale.

Workstream 3: cost-effectiveness [RQ4; months 1-24]

In addition to understanding the effectiveness of pre-hospital triage it is also important to evaluate the cost-effectiveness of the intervention. Where possible the analyses will seek to understand if different triage systems deliver variable outcomes and costs, thereby informing any wider national scale-up.

The health economic analysis will focus on the case study sites and national and regional controls (Table 3). The analyses will draw on the same data sources as requested for Workstream 2 (Table 4), along with national reference costs and Trust estimates of service costs.

The analyses will estimate the costs of prehospital triage (from NHS and personal social services perspectives). Estimated outcomes (life years or quality-adjusted life years (QALY)) will be derived from the outcomes in the data and evidence in the literature. The analyses will estimate cost-effectiveness as the difference in cost between comparators divided by the difference in outcomes to give an incremental cost-effectiveness ratio (ICER) per life year saved and per quality-adjusted life year gained. A difference-in-differences (DiD) analysis will be used to determine the effect size, while the cost of care will be estimated using national reference costs further informed by exploring the resource use and cost of prehospital triage systems, captured in interviews with Trusts.

5 STUDY SCHEDULE

- Recruitment of interviewees will commence once ethical approval and local research governance permissions have been obtained.
- Interviewees will include patients and their carers, and staff (Section 7)
- Approaching potential interviewees:
    - Research nurses embedded within the clinical services will work with the clinical team to identify patient interviewees who meet the inclusion criteria. Once the clinical team confirm that a patient is willing to be approached, the research nurses will then discuss the research with the patient (Section 6). If patients are happy to be contacted by a researcher, the research nurse will either pass on the researcher's contact details to the patient or ask the patient if they are happy for their details to be passed onto the researcher.
    - Researchers will approach potential staff interviewees, guided by inclusion and exclusion criteria (Section 6).
- Recruitment: Researchers will contact potential interviewees and share study information. Potential interviewees will have at least 48 hours in which to consider whether they would like to take part.
- Consent: interviews will take place only with written, informed consent.
- Participation: interviews will last approximately 45 minutes and will be guided by a semi-structured topic guide.
- Follow-up:
    - Patient and carer interviews will be single events; there will be no follow-up interviews.
    - Staff interviews may sometimes involve follow-up events, e.g. in the event that there is a significant change in services.
- Withdrawal: Interviewees will be free to withdraw at any time, up to two weeks after the interview has taken place. If they withdraw, all interview data provided will be removed from the dataset and destroyed securely.
- End of study will be reached when all data have been collected and analysed, and draft final report submitted to funder (deadline 14th September 2023).

6 ELIGIBILITY CRITERIA

6.1 Inclusion Criteria

For the qualitative work, interviews will be conducted with patients (and their carers, if appropriate) and members of staff with experience of prehospital video triage for suspected stroke.

The study will recruit patients who:

- are over 18 years of age
- any sex or gender
- have capacity to give informed consent
- underwent prehospital video triage for suspected stroke in participating services (NC London, East Kent, Darent Valley, Maidstone)
- were transferred to stroke unit or emergency department, referred to TIA clinic, or advised to stay home
- represent a range of backgrounds (including ethnicity, first language, socioeconomic status, home living arrangement)

The study will seek to recruit carers of recruited patient interviewees (e.g. family member or partner) to take part in a joint interview with the patient.

The study will seek to recruit staff with a range of roles related to prehospital video triage:

- Working in the participating areas (NC London, East Kent, Darent Valley, Maidstone)
- Ambulance staff (clinicians and managers)
- Stroke staff (clinicians and managers)
- Emergency department staff (clinicians and managers)
- Senior management (e.g. of hospital and ambulance organisations)
- Wider context (e.g. system leaders, commissioners, patient groups)

6.2 Exclusion Criteria

Participants will be excluded if they are under 18 years of age.

Patient participants will be excluded from the study if they have not undergone prehospital video triage for suspected stroke in the participating areas.

Staff participants will be excluded if they have not been involved in prehospital video triage for suspected stroke in the participating areas.

7 RECRUITMENT

Stakeholder interviews

A range of stakeholders will be interviewed (see Table 2), guided by the research questions. Adult patients and carers who have experienced the prehospital triage services will be interviewed, with the aim of understanding how people experienced different outcomes of assessment (transfer to stroke unit or emergency department, referral to TIA clinic, advised to stay home). It is important that the research examines how these new services are experienced by patients and carers whose first language is not English and will thus seek to recruit at least

one such person in each case, conducting these interviews using UCL-approved interpreter services.

The team recognises that the issues covered in interviews of this kind may be stressful for patient, carer, and staff participants. Therefore, researchers will work closely with patient, voluntary sector, and clinical partners to ensure the interview process and topics minimise participant burden and risk of stress. The team will also ensure these activities are conducted only with full ethical and research governance approvals. The majority of participants (and all patient and carer participants) will take part in a single interview, lasting approximately 45 minutes, at a time and location of their choosing, with participation entirely voluntary and only with fully informed consent.

Patient and carer interviews: Research nurses embedded within the clinical services will work with the clinical team to identify and approach potential patient interviewees who reflect the research sample, covering a range of experiences of the prehospital video triage service (transfer to stroke unit or emergency department, referral to TIA clinic, advised to stay home) and a range of patient backgrounds (ethnicity, first language not English, socioeconomic status, home living arrangement). Once the clinical team confirm that a patient is willing to be approached, the research nurses will then discuss the research with the patient. They will share the Participant Information Sheet and discuss what the research will involve. The research nurses will also ask the patient if they have a carer (e.g. partner or family member) who might also wish to take part in the interview; if a carer is identified, the research nurse will also share study information with them. If patients (and carers, if appropriate) are happy to be contacted by a researcher, the research nurse will either pass on the researcher's contact details to the patient or ask the patient if they are happy for their details to be passed onto the researcher.

Therefore, the research team will only receive personal contact details of patients and carers who have agreed for this information to be passed on to them.

In line with good practice and UCL requirements, recruitment documentation (i.e., patient information sheets, carer information sheets and consent forms) will make clear the anticipated burden and risks of participating and emphasise the voluntary nature of participation. To ensure non-English speakers may take part in the patient and carer interviews, the interview Participant Information Sheets (Patient and Carer) will be translated into 12 commonly spoken languages by a professional translation company, and the team have budgeted for professional interpreters to facilitate a proportion of the interviews. There will be no payments to cover patient or carer participation: interviews will be conducted remotely (by telephone or online) or in the patient's or carer's home, meaning no reimbursement for travel will be required. Research nurses will maintain anonymised log will be kept of recruitment approaches and the research team will log interviews completed.

Staff interviews: Researchers will approach potential staff participants initially by sharing study information by e-mail or post. In line with good practice and UCL requirements, recruitment documentation (i.e., information and consent forms) will make clear the anticipated burden and risks of participating and emphasise the voluntary nature of participation.

Non-participant observations

The approach to recruitment, consent, and conduct of observations will be informed by the team's previous work in stroke and other clinical settings, and advice from our clinician and patient co-investigators.[7, 29] Researchers will seek to ensure that staff are fully aware of the

research both before and during observations (e.g. through presentations to staff meetings), that staff have the opportunity to provide informed consent, and that they are assured that the researcher will withdraw from any situation where it is felt that observation is not appropriate or might interfere with provision of care.

Permission to observe ***staff training sessions or meetings*** will be obtained from activity leads (e.g. lead consultant, trainer, or meeting chair) in advance of the observed activities taking place. Participant information sheets will be circulated with meeting papers to all attendees. On first attendance (e.g. at meetings), the researcher will brief attendees on the study's aims, what participation entails, and that they may decline to participate at any time. At subsequent meetings, the researcher will announce him/herself as a non-participant observer, and confirm that he/she is happy to answer any questions in relation to the research.

Observations of ambulance and stroke clinicians conducting triage consultations will be conducted by researchers who will be based in the stroke unit. We will conduct observations only with written consent from stroke clinicians and verbal consent from both ambulance clinicians and patients; the researcher will only enter the space where the consultation is taking place once consent has been provided by all and commence taking written fieldnotes; no patient-identifiable information will be recorded/noted in these fieldnotes (***further details provided under 'consent', overleaf***).

With all observations, if at any point the clinicians feel it has become inappropriate for the observation to continue, they will inform the researcher of this, and the researcher will withdraw.
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8 CONSENT

Stakeholder interviews

Researchers will approach potential participants initially by sharing study information (Participant Information Sheet) by e-mail or post. The Participant Information Sheets explain the purpose and nature of the research, what participation involves, its benefits (or lack of benefits), risks, and burdens. The Participant Information Sheets also make clear that there is no obligation to participate, and that participants are free to refuse to participate or withdraw up to 14 days after the interview with no implication for their care or status. To enable a wide range of participation, the recruitment documents will be professionally translated into 12 commonly spoken non-English languages.

Potential participants will be given at least 48 hours to decide whether they would like to take part in the interview. If participants would like to take part remotely they will be asked to complete a consent form (written or electronic) and return it to the research team in advance of the interview. If individuals would like to take part in an interview, a mutually convenient time and platform (phone, teams or zoom) will be decided.

A member of the research team will consent participants. Individuals will be asked to complete consent forms (written or electronically) prior to taking part in the interview. Participants who complete the consent form by hand will be asked to sign two copies (one for the researcher and one for the participant). Participants who consent electronically will be sent a copy of the completed consent form for their records. Participants will be asked to return the consent form

in one of two ways: a) posting the consent form back to the researcher, or b) emailing the consent form back to the researcher (either by scanning a handwritten copy or by completing the consent form electronically). Participants will be asked to send the consent form in advance of the interview. Interviews will not take place unless the researcher has received the signed consent form. Participants will have the opportunity to ask questions at any time. Interpreter services will be provided to support participants who do not have English as a first language.

Non-participant observations of professional activity

Prehospital video triage assessments: We have developed our approach to obtaining consent for observations in collaboration with our clinician and patient collaborators. Observations of ambulance and stroke clinicians conducting triage consultations will be conducted by researchers who will be based in the stroke unit.

Researchers will obtain written consent from all stroke physicians providing prehospital video triage in advance of observations commencing. It will not be possible to seek individual consent from all ambulance clinicians involved in prehospital video triage, therefore before commencing any observations, researchers will attend ambulance staff meetings to discuss the research and obtain verbal consent from ambulance teams. Similarly, it will not be possible to obtain written consent from suspected stroke patients; therefore, the clinicians conducting the assessment will obtain patient verbal consent for these observations of professional activity to be conducted before the researcher enters the space where the triage assessment is to be conducted.

When the stroke clinician is alerted to an incoming triage call, the researcher will withdraw so that the researcher can neither see nor hear the initial discussion between clinicians and patient. If the stroke clinician and ambulance clinician conducting the triage assessment are satisfied that the patient has capacity to give consent, they will ask the patient for verbal consent for the observation to take place. If the clinicians are not satisfied that the patient has capacity to give consent, no request will be made, and no observation will take place. If the patient provides verbal consent, and the clinicians are still satisfied that the patient has capacity to provide this consent, the clinicians will invite the researcher to enter the space where the triage consultation is being conducted, so that the researcher may commence taking fieldnotes. No patient-identifiable information will be recorded/noted in these fieldnotes

With all observations, if at any point the clinicians feel it has become inappropriate for the observation to continue, they will inform the researcher of this and the researcher will withdraw immediately.

Meetings and training activities: Permission to observe the meetings will be obtained from the Chair/session lead in advance of the meeting taking place. Agreement for the observation to take place will also be requested from those taking part in the meeting and agreement will be documented in the minutes.

All participant data will be treated anonymously, and will not be identified by name in any reports. As with the interviews, these activities will be conducted only with full ethical and research governance approvals.

9 DATA ANALYSIS

This section covers four main analyses:

1. Qualitative analysis of implementation and experiences of prehospital video triage

2. Quantitative analysis of patient conveyance, care delivery, and patient outcomes
3. Health economic analysis of cost-effectiveness
4. Synthesis of analyses

Workstream 1. Implementation and experiences of prehospital video triage

The qualitative research will take a case study approach,[27, 30] focusing on implementation and sustainability of each studied service. Each case will be formed of the prehospital triage service being studied and the organisational and wider context within which it is located. For each case, timelines of how prehospital triage was implemented will be developed. Researchers will analyse local adaptations and progress, considering influential factors identified in the conceptual framework (innovation characteristics, characteristics of those delivering the new service and the organisations in which they are based, diffusion and implementation approaches, and the wider system context). The research will consider potential influence on factors analysed in the quantitative and cost-effectiveness analyses; researchers will also explore implications for equalities and diversity (e.g. access to/experience in digital systems, language barriers, disabilities), and experiences of stroke and non-stroke patients and carers.

The analysis will follow the principles of long term process analysis,[27] where change is temporally-embedded and influenced by events, activities, and choices operating at different levels (e.g. the *micro* or team-level, the *meso* or organisational/regional level, and the *macro* or national system level).[31] The analysis will take an iterative approach, using inductive (theory-building) and deductive (theory-testing) approaches to describe the unique case sites in their context as they evolve over time, while also seeking to generate wider lessons through cross-case integration at two stages of the study.[27]

The analysis will be developed with a subgroup of co-investigators who have qualitative expertise (AIGR, NJF, and JL). Interpretation of findings will be contributed to by the whole research team, including clinicians, patients, and voluntary sector representatives. Validity will be assessed in relation to Patton's four criteria of validity (verification, rival explanations, negative examples, and triangulation).

Workstream 2. Patient conveyance, care delivery, and patient outcomes

The hypothesis is that prehospital video triage will a) reduce the number of inappropriate patient transfers to specialist stroke units, which will b) result in hyperacute treatments being delivered to stroke patients more quickly and reliably than elsewhere, and therefore c) that stroke patients treated by such services will have better outcomes than those treated by services that do not use prehospital video triage. To test these hypotheses, the analysis will use a controlled before-and-after design to estimate the impact of prehospital triage on ambulance journeys for suspected stroke patients:

Patient destination: the hypothesis is that there will be a significant reduction in the proportion of patients classified as 'suspected stroke/neurological' who are transferred to hospitals with specialist stroke units following implementation of prehospital triage services, relative to control sites.

The study will also analyse 'Job cycle' length (i.e., time from initial 999 call received through to 'ambulance free'), disaggregated by key processes (Table 4)

Furthermore, the analysis will estimate the impact on stroke patients receiving key clinical interventions, including:

- Time from onset of symptoms to receiving clinical interventions (to assess potential impact of increased time on scene to conduct prehospital triage)
- Time from arrival at hospital to receiving clinical interventions (to assess potential benefits of prehospital triage and advance knowledge of patients on effective running of stroke teams)
- Impact of these services on the following key outcomes
    - Patient mortality at 90 days (the primary outcome)
    - Patient functional outcome (as measured with the Modified Rankin Scale)

These patient-level analyses will compare areas using prehospital triage (NC London, East Kent, Maidstone and Darent Valley) with other areas of England where prehospital triage is not used (hereafter referred to as the 'comparator') (Table 3), using propensity score matching (taking care to use only patient variables that should not be altered by the triage intervention, e.g. sex and age).[32] A difference in differences (DiD) approach will be employed to understand the impact of the 'treatment effect' prehospital triage on outcomes (primary outcome: patient mortality at 90 days). DiD aims to generate causal effect estimates by comparing the change in the outcome from before to after the introduction of an intervention in the group exposed to the intervention, to the change in outcome from before to after the intervention in a group not exposed to the intervention. Provided a valid control group has been identified, the difference between the two differences can be said to represent the impact of the intervention.

As outlined above, the analysis will include a minimum of 12 months 'before' data and up to 26 months 'after' data. Given the sample sizes (Table 4), the team do not anticipate concerns about statistical power, but during the early stages of the study researchers will engage with clinical partners and data owners to understand the data in depth, and will conduct robustness tests alongside the main analyses.

Workstream timeline:

- Months 1-5: researchers work with clinical collaborators and data owners to gain a deeper understanding of the data available, specify data requests.
- Months 5-15: data requests submitted and data received to be prepared for analysis.
- Months 13-22: main analyses conducted, leaving time for integration of findings (see WS4).

Workstream 3: cost-effectiveness [RQ4; months 1-24]

In addition to understanding the effectiveness of pre-hospital triage it is also important to evaluate the cost-effectiveness of the intervention. Where possible the analyses will seek to understand if different triage systems deliver variable outcomes and costs, thereby informing any wider national scale-up.

The health economic analysis will focus on the case study sites and national and regional controls (Table 3). The analyses will draw on the same data sources as requested for Workstream 2 (Table 4), along with national reference costs and Trust estimates of service costs.

The analyses will estimate the costs of prehospital triage (from NHS and personal social services perspectives). Estimated outcomes (life years or quality-adjusted life years) will be derived from the outcomes in the data and evidence in the literature. The analyses will estimate cost-effectiveness as the difference in cost between comparators divided by the difference in outcomes to give an incremental cost-effectiveness ratio (ICER) per life year saved and per quality-adjusted life year gained. A DiD analysis will be used to determine the effect size, while the cost of care will be estimated using national reference costs further informed by exploring the resource use and cost of prehospital triage systems, captured in interviews with Trusts.

The economic evaluation will compare the costs and outcomes of pre-hospital triage to no triage using decision analytic modelling.[33] Patient pathways will follow those of published papers including Hunter et al 2018,[16, 18] amended for the triage setting. The researchers will work with clinicians to determine the appropriateness of published models and any need to amend the pathway and stroke management given pre-hospital triage. Analysis of patient subgroups will be guided in part by the data and also confirmed with clinicians as to whether the subgroups are clinically relevant and feasible in terms of informing broader adoption decisions.

The time horizon will be ten years, this aligns with other similar literature.[16, 18, 33, 34] Mortality estimates will be derived from the linked HES/ONS data. Quality-adjusted life year (QALY) estimates will be derived from the literature that has evaluated stroke interventions including those addressing delays in presentation. The analyses will also apply QALY estimates to other events that can be documented in the linked data, such as length of stay and readmissions where these are available in the literature.[16, 18, 33, 34] The base case analysis will consider the incremental cost per QALY gained, additionally the analysis will also estimate the additional cost per life year gained, as a sensitivity analysis, on the expectation that there will be minimal primary QoL data specific to pre-hospital triage. Other sensitivity and scenario analysis will be undertaken in order to evidence the uncertainty in the economic evaluation results, including the estimation of cost effectiveness acceptably curves and net monetary benefit estimates.[16, 18, 33] The analysis will undertake budget impact modelling to understand future implementation costs and cost savings and to which part of the health care system they accrue.

Workstream timeline:

- Months 1-4: data specification.
- Months 7-15: data requests and preparation, interviews with Trust to understand resource implications of prehospital triage, including any additional training and implementation costs
- Months 16-24: data analysis and integrating findings (see WS4).

Missing data

While the ambulance, SSNAP, and HES/ONS datasets have high levels of participation/completeness, we acknowledge that there may be some missing data. Further, this issue may have become more pronounced during the COVID19 pandemic. The team also recognise that it is possible that missing data may occur systemically rather than randomly in these datasets.[35] In response, sensitivity analyses will be conducted, employing a reference-based multiple imputation approach, as recommended in current best practice guidelines with respect to addressing missing data and why it is missing.[35, 36]

Workstream 4: integrating analyses, generating lessons, stakeholder workshop (RQ5; months 2-24]

The analyses will be integrated throughout the study in monthly team meetings. There will also be three key stages of integration, where researchers on Workstreams 1, 2, and 3 will work with clinical and patient collaborators.

- Months 1-4: ensuring study designs are complementary (e.g. qualitative research explores issues that may emerge from the quantitative) for presentation to and feedback from Study Steering Committee (SSC).
- Months 10-12: generating interim lessons to share with stakeholders and SSC; researchers will incorporate feedback into research design (e.g. additional quantitative/economic measures or interview topics).
- Months 20-24: identifying key lessons to be shared with SSC and incorporating feedback from final SSC meeting. A stakeholder workshop will identify how lessons may apply to different settings. The workshop will be conducted both digitally and in-person (to maximise accessibility) and themes fed into the final report.

10 PATIENT AND PUBLIC INVOLVEMENT (PPI)

Patients and the public were central to the study from the outset. The team includes two stroke survivors (Jeremy Dearling and Marney Williams) and a Stroke Association representative (Josh Edwards).

The patient representatives provided detailed feedback on wording and content of the research application. This included clarifying the language used in the plain English summary and research questions; patient representatives also influenced how the case for the research was presented (e.g. identifying ways in which the research might benefit the NHS at system-level, and encouraging us to foreground the need for prompt, appropriate care for both stroke and non-stroke patients), the study design (e.g. helping us clarify the approach to conducting and analysing interviews), and knowledge mobilisation strategy (e.g. identifying several relevant dissemination opportunities). The team incorporated this valuable feedback throughout. In addition, over the course of preparing this study the team consulted with other patient representatives, Janet Holah and Brian Russell of the SECAmb patient representative group, who confirmed that they are fully supportive of the purpose and approach of this work and have agreed to join the Study Steering Committee.

The stroke survivor representatives are full members of the Study team. They will thus participate in the monthly team meetings and contribute to all aspects of the research that they wish to, e.g. research strategy, recruitment documents, interpretation of findings, co-authoring articles and summaries, and presenting at events.

The Chief Investigator has an extensive record of working productively in developing and delivering research with patient representatives (e.g. recently coproducing a PPI strategy for the NIHR HS&DR Rapid Service Evaluation Team programme).

The Study Steering Committee will include patients, carers and the voluntary sector; so far the team have recruited Janet Holah and Brian Russell (mentioned above) and Colin Oliver of the Stroke Association in Scotland.

To facilitate effective involvement in all these activities, the team will share meeting papers sufficiently far in advance with patient and carer representatives. The team have budgeted for all patient contributions in line with good practice identified by INVOLVE.

11 FUNDING AND SUPPLY OF EQUIPMENT

The study funding has been reviewed by the UCLH/UCL Joint Research Office, and deemed sufficient to cover the requirements of the study.

The research costs for the study have been supported by the National Institute for Health Research Health Services and Delivery Research programme (ref NIHR133779; £592,411.19, 1st September 2021-31st August 2023).

No equipment is being supplied through this research and the Chief Investigator has no personal relationship with the organisations funding or sponsoring the research.

12 DATA HANDLING AND MANAGEMENT

The study is compliant with the requirements of General Data Protection Regulation (2016/679) and the UK Data Protection Act (2018). All investigators and study site staff will comply with the requirements of the General Data Protection Regulation (2016/679) with regards to the collection, storage, processing, and disclosure of personal information, and will uphold the Act's core principles. UCL is the data controller; the UCL Data Protection Officer is Alex Potts (a.potts@ucl.ac.uk). The data processors are Angus Ramsay, Naomi Fulop, Holly Walton, Rachael Hunter, and George Bray (all UCL).

DATA MANAGEMENT

Data will be managed in line with legal and regulatory requirements, including the General Data Protection Regulation (GDPR) and the Data Protection Act (2018), and necessary research approvals.

Dr Angus Ramsay will act as the data controller for this study. He will process, store and dispose of all data in accordance with all applicable legal and regulatory requirements, including the General Data Protection Regulation (GDPR) and the Data Protection Act (2018) and any amendments thereto. Data will not be transferred to any party not identified in this protocol and are not to be processed and/or transferred other than in accordance with the patients' consent.

Qualitative data (interviews and observations)

Research nurses embedded within the clinical services in participating NHS organisations will work with the clinical team to identify and approach potential patient interviewees. If patients are agreeable, research nurses will share contact details of potential interviewees with the research team. These contact details will be stored securely on the UCL Data Safe Haven (a secure electronic environment, certified to ISO27001 information security standard and conforms to the NHS Information Governance Toolkit).

Interviews (qualitative data) will be recorded on an encrypted, password-protected digital recorder (only the researcher will know the password). Data will be collected by a team of qualitative researchers from University College London.

Patient consent forms and audio-recordings of interviews will be securely transferred using the Data Transfer portal onto the UCL Data Safe Haven. Audio-recordings will be transferred directly from the encrypted Dictaphone to the UCL Data Safe Haven File Transfer Portal. Once transferred onto the Data Safe haven, the data will be cleared from the encrypted digital recorder. Patient consent forms received via post will be posted to the UCL team members at

the UCL Department of Applied Health Research, 1-19 Torrington Place, London WC1E 7HB and stored securely within UCL offices. Patient consent forms received via post will be stored securely in locked filing cabinets within the secure UCL Department of Applied Health Research office.

Interviews with people who do not have English as a first language may be facilitated by professional interpreters provided through a UCL-approved contractor (Agroni Research limited). This activity will be subject of a service level agreement between UCL and Agroni specifying the confidential nature of these interviews.

Digital audio-recordings of interviews will be sent to a UCL-approved contractor for transcription (TP transcription limited). Transcripts will be fully anonymised (names and places) and organised by participant codes. Anonymised transcripts and other relevant data will be stored in a secure folder to which only the named researchers (UCL qualitative team) have access. Only the research team will have access to participants' personal data (i.e. name and contact details). A password protected spreadsheet of interviewees and their contact details will also be held on the Data Safe Haven. Participant identifier codes will be stored in the DSH and kept separate from study data.

Quantitative data (care delivery and outcomes)

Quantitative data will come from management information systems owned by Ambulance services (London Ambulance Service NHS Trust, South East Coast Ambulance Service NHS Foundation Trust, West Midlands Ambulance Service NHS Foundation Trust, and North East Ambulance Service NHS Foundation Trust), the Sentinel Stroke National Audit Programme (SSNAP, which sits within the Health Quality Improvement Partnership (HQIP)), and NHS Digital. The access and use of these data for this study will be governed by formal data sharing agreements with these organisations. All quantitative data will be transferred to University College London via secure FTP and analysed on a secure server (UCL Data Safe Haven) based at University College London, which acts as the data processor and data controller. The data will be accessed only by named UCL researchers with expertise in and responsibility for analyses that make use of these data.

13 PEER AND REGULATORY REVIEW

The study has been peer reviewed in accordance with the requirements outlined by UCL. The Sponsor considers the procedure for obtaining funding from the NIHR Health Services and Delivery Research programme to be of sufficient rigour and independence to be considered an adequate peer review.

The study was deemed to require regulatory approval via NHS REC Favourable Opinion and HRA Approval. Before any site can enrol patients into the study, the Chief Investigator/Principal Investigator or designee will ensure that the appropriate regulatory approvals have been issued, and NHS Confirmations of Capacity and Capability and Sponsor green lights are in place.

For any amendments to the study, the Chief Investigator or designee, in agreement with the Sponsor, will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments as well as the study delivery team) to confirm ongoing Capacity and Capability for the study.

All correspondence with the Sponsor, REC and HRA will be retained. The Chief Investigator will notify the Sponsor and REC of the end of the study.

It is the Chief Investigator's responsibility to produce the annual progress reports when required; an annual progress report (APR) will be submitted to the Sponsor and REC within 30 days of the anniversary date on which the favourable opinion was issued, and annually until the study is declared ended.

If the study is ended prematurely, the Chief Investigator will notify the Sponsor and REC, including the reasons for the premature termination.

Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the Sponsor and to the REC and HRA.

14 ASSESSMENT AND MANAGEMENT OF RISK

This research is anticipated to be of low risk to participants. The main risks and how the team will manage them are outlined below.

Patient and staff interviews: Conducting interviews with patients and carers about their experience of receiving prehospital triage services for a suspected stroke may potentially cause distress as these will involve patients discussing their experiences of receiving care whilst being unwell. Additionally, some staff may find discussing aspects of services sensitive or stressful. To address these concerns and ensure that questions within the topic guides are sensitively presented, the team will seek feedback on the interview topic guides from the research team and PPI members. The team will pilot the interview topic guides to ensure that the wording of questions are appropriate for patients and carers. The information sheets state that participation is voluntary and that participants are free to withdraw. The Patient and Carer participant information sheets also signpost patients to further support (where necessary and relevant), e.g. the Patient Advice Liaison Service (PALS). Secondly, interviews will ask patients and staff to reflect on their experiences of receiving prehospital triage services for suspected stroke, and thus patients and staff may be hesitant to raise criticism. To address this, the participant information sheet will highlight that researchers are independent of those delivering care and that there are no right or wrong answers. The PIS highlights that information will be fully anonymised (including names and places) and will emphasise that the researchers want to learn about things that do not work well so that they can be improved in future.

Professional observations: It is possible that participants taking part in the observations could feel uncomfortable having an observer watch aspects of their work. However, the PIS emphasises that the researchers are independent of stroke services and will abide by professional codes. In addition, the PIS makes clear that participants are free to withdraw (or ask the researcher to withdraw, if appropriate) at any time.

Loss of anonymity in data: Another risk – inherent to any study involving collection of qualitative data – relates to the loss of anonymity e.g. in terms of a data breach or the linking of an individuals' statements to the individual who made these statements. As discussed under Section 12, the secure handling and management of data is a key priority on this study, and processes mitigating the associated risks are in place. In addition, recruitment documentation notes that the team cannot completely guarantee that an individual could not work out participant identity, and the option for participants not to be quoted in reports is provided.

Lone working: The patient, carer and staff interviews and professional observations may require researchers to conduct lone working. To mitigate risks associated with lone working, we have the following processes in place. Firstly, most of the interviews with patients, carers and staff will take place online or over the telephone, unless there are circumstances in which patients prefer a face-to-face interview or find telephone or online methods inaccessible. If data collection takes place in person (COVID guidelines permitting) e.g. in participants' homes, we will follow UCL lone working policy and will ensure that another researcher within the team knows where the researcher is at all times and that the researcher conducting any face-to-face interviews checks in with the other researcher when they arrive at the destination and when they leave the destination. If the researcher feels unsafe at any time they will leave the location immediately.

15 RECORDING AND REPORTING OF EVENTS AND INCIDENTS

As outlined above, this study is anticipated to be low risk. Should adverse incidents occur, they will be raised and escalated appropriately. In the event of any incidents or concerns raised by participants, the Chief Investigator will discuss the issue with his academic and clinical colleagues urgently, and if appropriate notify the Sponsor (via research-incidents@ucl.ac.uk) and host sites, and documented in the Trial Master File/Investigator Site File via study-specific incident logs (and related correspondence).

In line with UCL policy (https://www.ucl.ac.uk/legal-services/guidance/reporting-loss-personal-data), any data breach (e.g. loss of personal data) will be logged and reported by the Chief Investigator as soon as the breach is discovered. A report will be submitted to the UCL Information Security Group, detailing the nature of the breach, volume of information involved, and the sensitivity of the data. Based on subsequent analysis of the breach, processes will be updated to minimise risk of the breach recurring. The Sponsor will be responsible for investigating, reviewing, or escalating to a serious breach if required.

15.1 Personal Data Breaches

In some instances, despite risk management and mitigations, personal data breaches may occur throughout the duration of the study. GDPR broadly defines personal data breaches as a security incident that has affected the confidentiality, integrity or availability of personal data. In short, there will be a personal data breach whenever any personal data is lost, destroyed, corrupted or disclosed; if someone accesses the data or passes it on without proper authorisation; or if the data is made unavailable, for example, when it has been encrypted by ransomware, or accidentally lost or destroyed.

Personal data breaches will be immediately reported to the UCL Information Security Group (ISG) and the UCL Data Protection Officer is Alex Potts (a.potts@ucl.ac.uk), (as per form and guidance: https://www.ucl.ac.uk/legal-services/guidance/reporting-loss-personal-data), and to the Sponsor via the UCL REDCAP incident reporting form (https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo). The following information will be provided: full details as to the nature of the breach, an indication as to the volume of material involved, and the sensitivity of the breach (and any timeframes that apply). Sites will additionally follow their Trust incident reporting mechanisms and will document this within their TMF/ISFs.

15.2 Protocol deviations and notification of protocol violations

Protocol deviations are usually an unintended departure from the expected conduct of the study protocol/SOPs, which does not need to be reported to the Sponsor. The CI will monitor protocol deviations, and if found to frequently recur, will discuss in the first instance with the Sponsor to determine re-classification and reporting requirements.

A protocol violation is a breach which is likely to effect to a significant degree: –

(a) the safety or physical or mental integrity of the participants of the study; or

(b) the scientific value of the study

The CI and Sponsor will be notified immediately of any case where the above definition applies via research-incidents@ucl.ac.uk or the UCL REDCAP incident reporting form.

15.3 NHS Serious Incidents and near misses

A serious incident or near miss is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:

a. It is an accident or other incident which results in injury or ill health.

b. It is contrary to specified or expected standard of patient care or service.

c. It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.

d. It puts the Trust in an adverse position with potential loss of reputation.

e. It puts Trust property or assets in an adverse position or at risk.

Serious Incidents and near misses will be reported to the Sponsor and Trust Quality & Safety department as soon as the study team becomes aware of them.

15.4 Complaints from research participants

In the first instance, research participant complaints (patients or healthy volunteers) will be reported to the CI/PI to investigate, as documented in the patient information sheet(s), and to the Sponsor via research-incidents@ucl.ac.uk, following the *UCL Complaints from Research Subjects about UCL Sponsored Studies and Trials* policy. For participants who are NHS patients, complaints will be reported to the NHS Complaints Manager at the Trust where the recruitment and study procedures was undertaken. Complaints from NHS patients are handled under NHS complaints policies and procedures, with involvement from PALS and the Sponsor where necessary.

16 MONITORING AND AUDITING

The Chief Investigator will ensure there adequate quality and number of monitoring activities will be conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality.

The Chief Investigator will inform the Sponsor should he have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

17 TRAINING

The Chief Investigator will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files.

Research nurses making initial approaches to potential patient interviewees will receive training that covers the nature of the research study, how patients are to be approached, and how information (e.g. contact details, approach numbers, incidents) are to be reported.

All researchers working on this study are expert in the methods they are employing. In addition, researchers conducting qualitative research will undergo appropriate training and certification to conduct research with patients (e.g. Good Clinical Practice training) as part of obtaining their research passport, and this will be refreshed if necessary over the lifetime of the study.

18 INDEMNITY ARRANGEMENTS

University College London holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, as this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participant of the clinical study. University College London does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

Participants may also be able to claim compensation for injury caused by participation in this clinical study without the need to prove negligence on the part of University College London or another party. Participants who sustain injury and wish to make a claim for compensation should be advised to do so in writing in the first instance to the Chief Investigator, who will pass the claim to the Sponsor's Insurers, via the Sponsor's office.

Hospitals selected to participate in this clinical study shall provide clinical negligence insurance cover for harm caused by their employees and a copy of the relevant insurance policy or summary shall be provided to University College London upon request.

Additionally, UCL does not accept liability for sites such as GP surgeries in primary care; investigators/collaborators based in these types of sites must ensure that their activity on the study is covered under their own professional indemnity.

19 ARCHIVING

UCL and each participating site recognise that there is an obligation to archive study-related documents at the end of the study (as such end is defined within this protocol). The Chief Investigator confirms that he/she will archive the study master file at UCL for the period stipulated in the protocol and in line with all relevant legal and statutory requirements. The Principal Investigator at each participating site agrees to archive his/her respective site's study documents in line with all relevant legal and statutory requirements. Study documents will be archived for a minimum of 5 years from the study end, and no longer than 20 years from the study end.

The Trial Master File will be archived at UCL, in accordance with the UCL Retentions Schedule and Policy. It will be archived for a minimum of 5 years from the study end, and no longer than 20 years from study end.

20 PUBLICATION AND DISSEMINATION

The team has substantial expertise and experience in generating highly influential lessons. For example, efforts to mobilise the team's research findings on stroke service reconfiguration resulted in the work being cited in the NHS Five Year Forward View, the National Clinical Guideline for Stroke, and the NHS Long Term Plan. Drawing on their past experience, the team will work closely with collaborators (including the Stroke Association, patient representatives, and clinical leaders in stroke and ambulance settings) throughout this study to mobilise learning at local, national and international levels.

To maximise the impact of this research, the team will develop a range of products:

- Articles in academic and professional journals – based on main analyses and integration of findings
- Presentations of equivalent findings at relevant national research conferences.
- Accessible summaries in text and video formats presenting key findings to sit alongside published papers and the final report
- Presentations of findings tailored to participating sites, including clinical teams and patient groups
- Quarterly podcasts discussing the study as it develops, introducing team members, and highlighting relevant issues
- Quarterly newsletters presenting key updates on study progress (e.g., outputs and events)
- The team will share text and video summaries of the work – including the overall study design and specific methods.
- The team will host a webinar describing the study and enabling wider stakeholder feedback (e.g. through Q&A), to be shared on the study website.
- Study website – an accessible repository of information about the study, including the outputs described above.

The team believe the findings will be highly relevant to stroke systems across the UK that have not introduced prehospital triage. However, timely appropriate patient transfer is crucial to many emergency specialist conditions and ambulance clinicians are central to deciding where many patients are treated. Therefore findings may apply to other high priority care settings; the team will explore this with the Study Steering Committee (SSC) and Stakeholder Workshop. From the pre-launch phase onward, the team will develop and engage a stakeholder list dedicated to this study. This will include patients and the public, charities, health services, healthcare leaders, service commissioners, and researchers – to build interest in the work at national and regional levels. The team will seek to access a range of key organisations and groups, including NHS England and Improvement, and relevant prehospital and acute stroke working groups (including those overseeing delivery of the NHS Long Term Plan) and Health Education England; the team will engage with professional organisations, such as relevant professional/training bodies (e.g. Royal College of Physicians, Royal College of Nursing, College of Paramedics, Royal College of Emergency Medicine, and British Association of Stroke Physicians). At regional level the team will engage with local system leadership with responsibility for delivering high quality

prehospital, acute, and stroke care, including Integrated Care Systems, Integrated Stroke Delivery Networks, and local authorities. To increase awareness across the stroke community the team will engage with the National Stroke Assembly, World Stroke Day Forum, and voluntary organisations such as Different Strokes and the Stroke Association, and participate in relevant engagement activities, such as 'tweetathons'. To maximise engagement beyond the stroke setting, the team will seek to build awareness via the press and social media, and related user groups, such as groups supporting older people, ethnic minorities, and hard to reach communities.

The team will share formative feedback with participating sites, so they can use the research as it develops. The team will share quarterly newsletters and podcasts, to give insights on the research and team members. The team will share findings at professional and academic conferences and in high impact academic and professional journals. All outputs will come with accessible summaries (coproduced with patients and clinicians).

The team has a strong track record of achieving meaningful research impact through active mobilisation approaches. In the event that the research is successful, the findings are anticipated to contribute to national health policy, clinical guidance for stroke and prehospital systems, local care pathways across the UK (and potentially the commissioning of these pathways), and educational outputs, such as training packages for use within healthcare and academic settings.

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