University of Nottingham
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ISRCTN97695350

TRANEXAMIC ACID FOR INTRACEREBRAL HAEMORRHAGE: TICH-3 TRIAL

INVESTIGATOR MEETING

Brittany Hare and Nikola Sprigg

On behalf TICH-3 Trial Team

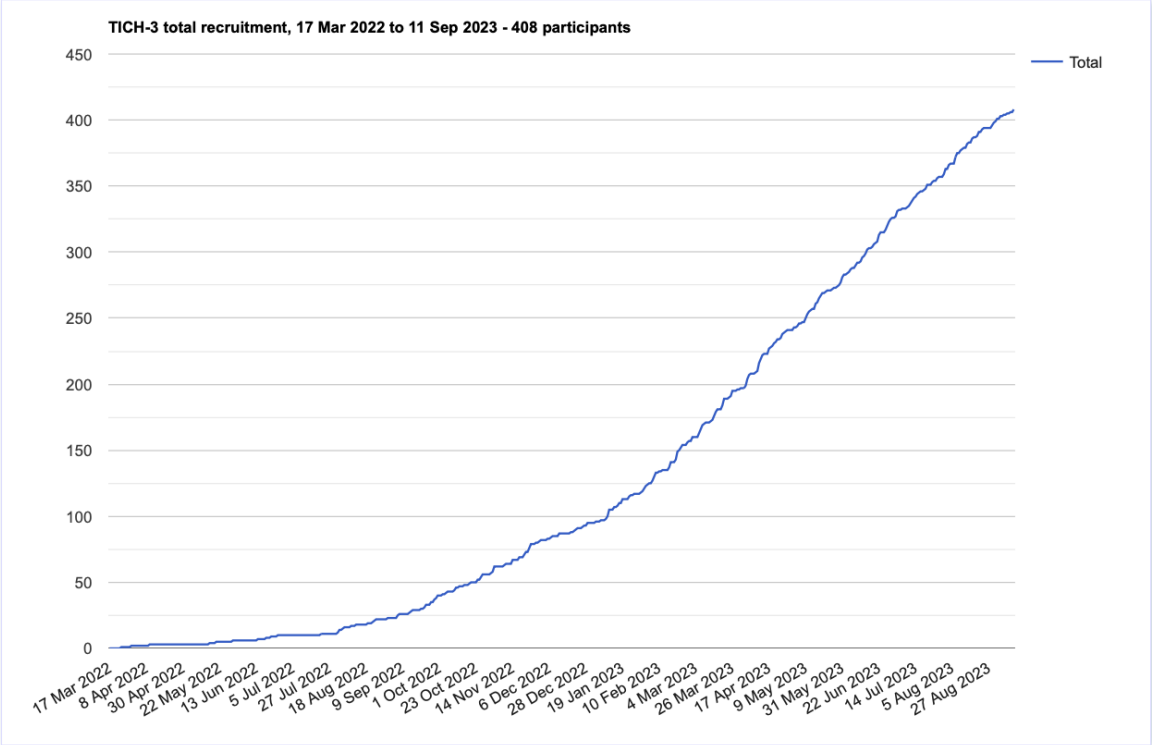
13th September 2023

Agenda

1. Recruitment update
2. Remote recruitment
3. Trial awareness
4. Pilot progression review
5. Co-enrolment with TICH-3
6. Upcoming events
7. Exclusions to the TICH-3 trial: CT scan image review
8. SWAT
9. Thank you
10. Questions?

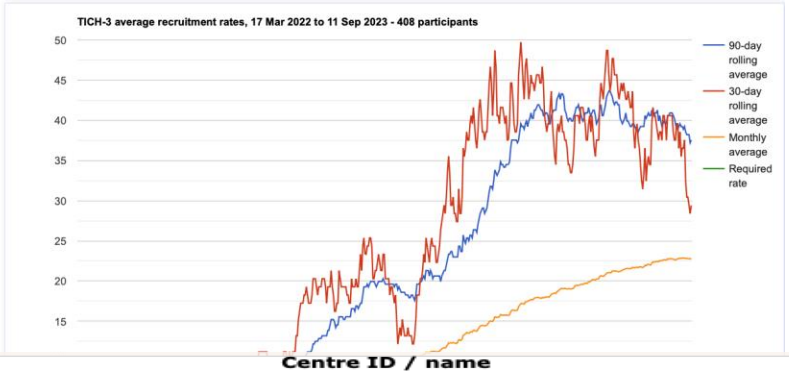
UK Recruitment Update

Site Status	No.
Sites open to recruitment	57
Recruited *(319 participants in total)*	*53*
Not recruited	*4*
In set up	13
Initial feasibility assessments	5
Declined for now (capacity issues)	8
Withdrawn	11



Thank you for all your recruitment into the TICH-3 trial, we couldn't do it without you!

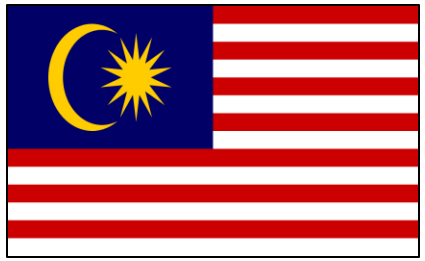
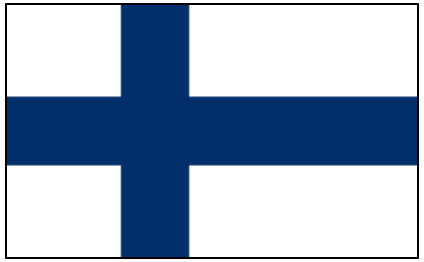
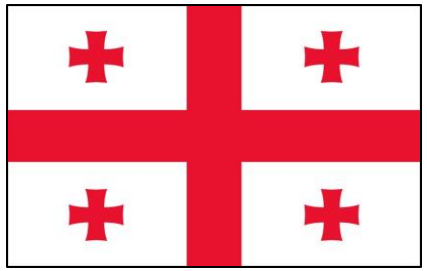
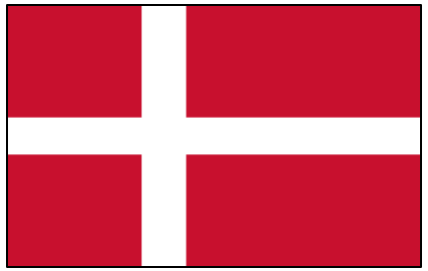
UK Recent dip in recruitment: ? Holidays/Strike?



Centre ID / name	week	days	months	omised fol
United Kingdom (UK)				
C001 Nottingham, Queen's Medical Centre	-	1	15	**19**
C002 Watford, Watford General Hospital	-	-	3	**3**
C003 Exeter, Royal Devon and Exeter Hospital	-	-	8	**9**
C004 London, King's College Hospital	-	1	8	**10**
C005 Orpington, Princess Royal University Hospital	-	-	1	**2**
C006 Durham, University Hospital of North Durham	-	1	7	**12**
C007 London, Charing Cross Hospital	-	-	14	**16**
C008 Aberdeen, Aberdeen Royal Infirmary	-	-	14	**16**
C009 Somerset, Yeovil District Hospital	-	-	1	**3**
C010 Northumberland, Northumbria Specialist Emergency Care Hospital	-	-	3	**3**
C011 Portadown, Craigavon Area Hospital	-	-	3	**4**
C013 Bath, Royal United Hospital Bath	-	-	4	**4**
C014 Edinburgh, Royal Infirmary of Edinburgh	-	1	7	**9**
C015 Southampton, Southampton General Hospital	-	-	8	**9**
C016 Harrow, Northwick Park Hospital	-	-	4	**5**
C017 London, Royal London Hospital	-	-	10	**10**
C019 Middlesbrough, James Cook University Hospital	-	2	11	**11**
C020 Tyne and Wear, Sunderland Royal Hospital	-	1	2	**2**
C021 Belfast, Royal Victoria Hospital	-	-	7	**7**
C022 Airdrie, University Hospitals Monkland	-	-	4	**4**
C023 Salford, Salford Royal Hospital	-	-	5	**7**
C024 Kirkcaldy, Victoria Hospital	-	-	2	**2**
C025 Dorset, Dorset County Hospital	-	-	2	**2**
C026 Bury, Fairfield General Hospital	-	1	2	**2**
C027 Cambridge, Addenbrooke's Hospital	-	1	11	**11**
C028 Peterborough, Peterborough City Hospital	-	-	1	**1**
C029 Wirral, Arrowe Park Hospital	-	-	3	**3**
C030 Bradford, Bradford Royal Infirmary	-	-	2	**2**
C031 Leicester, Leicester Royal Infirmary	-	1	12	**12**
C032 County Fermanagh, South West Acute Hospital	-	-	1	**1**
C034 Derby, Royal Derby Hospital	-	-	17	**17**
C035 Milton Keynes, Milton Keynes University Hospital	-	-	3	**3**
C036 Leeds, Leeds General Infirmary	-	-	3	**3**
C037 Luton, Luton and Dunstable University Hospital	-	-	1	**1**
C038 York, York Hospital	-	1	10	**10**
C039 London, St. George's Hospital	-	-	14	**14**
C040 Wolverhampton, New Cross Hospital	-	-	3	**3**
C041 Canterbury, Kent, Kent & Canterbury Hospital	-	-	4	**4**
C042 Chester, Countess of Chester Hospital	-	1	4	**4**
C043 Swansea, Morriston Hospital	-	-	6	**6**
C044 Newcastle Upon Tyne, The Royal Victoria Infirmary	-	1	12	**12**
C045 Crewe, Leighton Hospital	-	-	1	**1**
C046 Stoke-on-Trent, Royal Stoke University Hospital	-	-	6	**6**
C047 Antrim, Antrim Area Hospital	-	-	1	**1**
C049 Dundee, Ninewells Hospital	-	-	2	**2**
C050 London, The National Hospital for Neurology & Neurosurgery (UCLH)	-	-	10	**10**
C051 Doncaster, Doncaster Royal Infirmary	-	-	3	**3**
C052 Cheltenham, Cheltenham General Hospital	-	-	1	**1**
C053 Sheffield, Royal Hallamshire Hospital	-	1	5	**5**
C054 Lincoln, Lincoln County Hospital	-	1	3	**3**
C056 Hull, Hull Royal Infirmary	-	1	6	**6**
C061 Essex, Basildon University Hospital	-	-	1	**1**
Summary for country UK Totals:	-	**16**	**291**	**317**
Summary for 52 centres Totals:	-	**16**	**291**	**317**

International Recruitment Update

	Sites open	Recruited
Malaysia	13/14	84
Finland	1/1	2
Georgia	3/4	6
Denmark	1/4	0
Italy	1/25	0
Totals	19/48	92


Remote recruitment

Eligibility

Confirming eligibility is defined as a medical decision, so must be undertake by a medically qualified doctor under the clinical trials regulations.

- The clinician does not need to be on the TICH-3 delegation log to confirm eligibility however they must be on the delegation log to take enrolment consent (code J).

Consent

Verbal consent is taken in the first instance, to receive the trial treatment, there would not be a consent form to sign if the patient has capacity to give consent or there is a relative giving consent on behalf of the patient.

- Oral consent can be taken remotely if the enrolling investigator is not on site either on the phone or via telemedicine.

- Oral consent can be given remotely by a relative, if the patient does not have capacity.

Eligibility assessment and method of obtaining consent must be documented in the patients' medical notes.

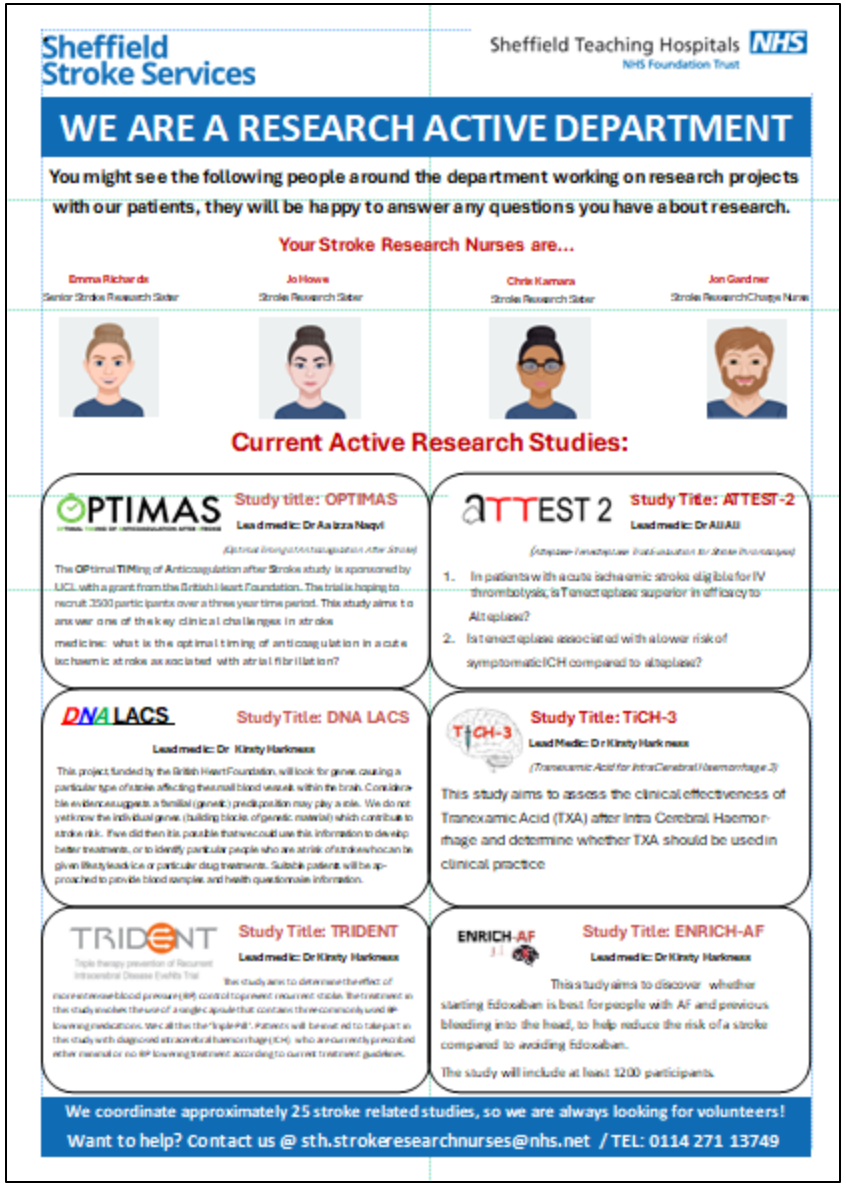
Trial Awareness

Please keep the TICH-3 Trial on the agenda at your local site to maximise chances of recruitment.

Example of one of our TICH-3 sites increasing awareness of TICH-3 at their site.

General aim is to help the frequently changing clinical staff know who the team are, what they do and a brief prompt for trial awareness on HASU.

There is a poster for ED available on the TICH-3 documents page https://stroke.nottingham.ac.uk/docs/TICH-3/Trial_documents/TICH-3%20poster%20for%20ED%20v2.1%2015.08.2023.pdf



Sheffield Stroke Services

Sheffield Teaching Hospitals NHS
NHS Foundation Trust

WE ARE A RESEARCH ACTIVE DEPARTMENT

You might see the following people around the department working on research projects with our patients, they will be happy to answer any questions you have about research.

Your Stroke Research Nurses are...

Emma Richards — Senior Stroke Research Sister
Jo Howe — Stroke Research Sister
Chris Kamara — Stroke Research Sister
Jon Gardner — Stroke Research Charge Nurse

Current Active Research Studies:

OPTIMAS — Study title: OPTIMAS
Lead medic: Dr Aaliza Naqvi

The OPtimal TIMing of Anticoagulation after Stroke study is sponsored by UCL with a grant from the British Heart Foundation. The trial is hoping to recruit 2500 participants over a three year time period. This study aims to answer one of the key clinical challenges in stroke medicine: what is the optimal timing of anticoagulation in acute ischaemic stroke associated with atrial fibrillation?

ATTEST 2 — Study Title: ATTEST-2
Lead medic: Dr Ali Ali

1. In patients with acute ischaemic stroke eligible for IV thrombolysis, is Tenecteplase superior in efficacy to Alteplase?
2. Is tenecteplase associated with a lower risk of symptomatic ICH compared to alteplase?

DNA LACS — Study Title: DNA LACS
Lead medic: Dr Kirsty Harkness

This project funded by the British Heart Foundation, will look for genes causing a particular type of stroke affecting the small blood vessels within the brain. Considerable evidence suggests a familial (genetic) predisposition may play a role. We do not yet know the individual genes (building blocks of genetic material) which contribute to stroke risk. If we did then it is possible that we could use this information to develop better treatments, or to identify particular people who are at risk of stroke who can be given lifestyle advice or particular drug treatments. Suitable patients will be approached to provide blood samples and health questionnaire information.

TICH-3 — Study Title: TICH-3
Lead Medic: Dr Kirsty Harkness
(Tranexamic Acid for IntraCerebral Haemorrhage 3)

This study aims to assess the clinical effectiveness of Tranexamic Acid (TXA) after Intra Cerebral Haemorrhage and determine whether TXA should be used in clinical practice

TRIDENT — Study Title: TRIDENT
Lead medic: Dr Kirsty Harkness

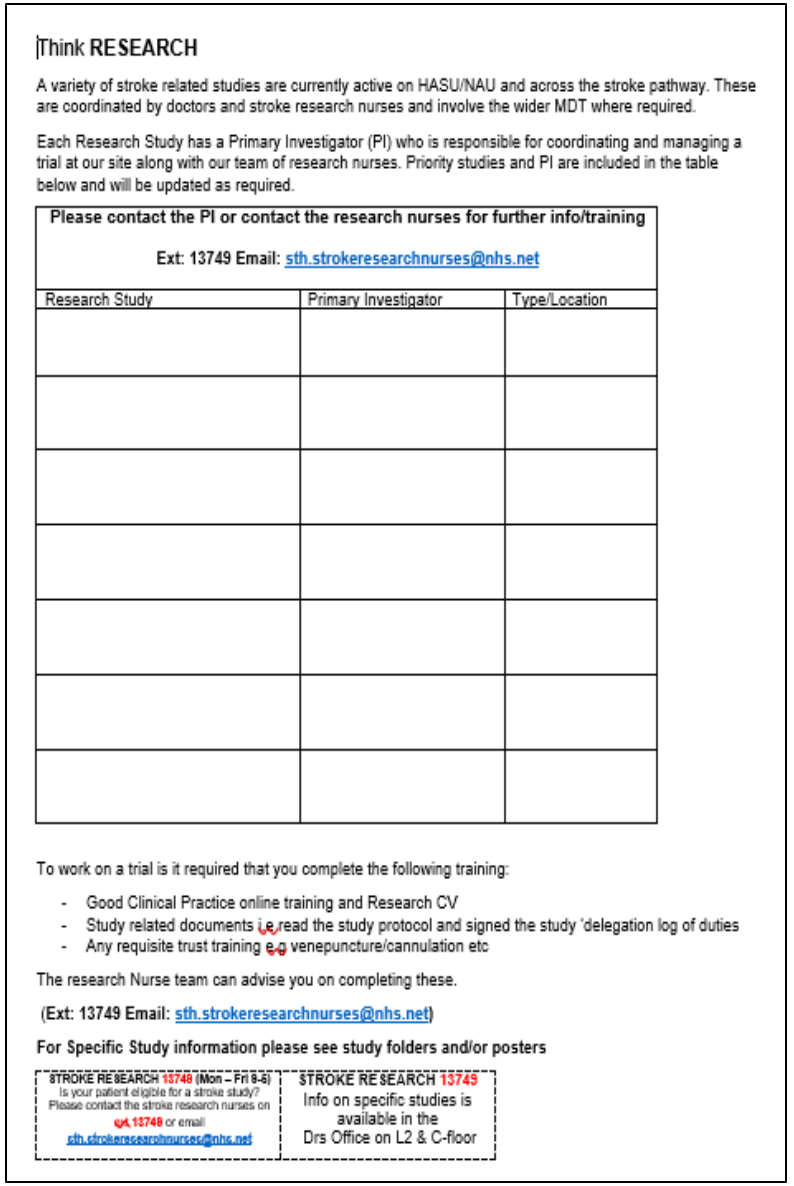
The study aims to determine the effect of more intensive blood pressure (BP) control compared to current routine care, the treatment in the study involves the use of a single capsule that contains three commonly used BP lowering medications. We call this the "triple pill". Patients will be randomised to take part in the study with diagnosed intracerebral haemorrhage (ICH), who are currently prescribed either monotherapy or no BP lowering treatment according to current treatment guidelines.

ENRICH-AF — Study Title: ENRICH-AF
Lead medic: Dr Kirsty Harkness

This study aims to discover whether starting Edoxaban is best for people with AF and previous bleeding into the head, to help reduce the risk of a stroke compared to avoiding Edoxaban.

The study will include at least 1200 participants.

We coordinate approximately 25 stroke related studies, so we are always looking for volunteers!
Want to help? Contact us @ sth.strokeresearchnurses@nhs.net / TEL: 0114 271 13749



Think RESEARCH

A variety of stroke related studies are currently active on HASU/NAU and across the stroke pathway. These are coordinated by doctors and stroke research nurses and involve the wider MDT where required.

Each Research Study has a Primary Investigator (PI) who is responsible for coordinating and managing a trial at our site along with our team of research nurses. Priority studies and PI are included in the table below and will be updated as required.

Please contact the PI or contact the research nurses for further info/training

Ext: 13749 Email: sth.strokeresearchnurses@nhs.net

Research Study	Primary Investigator	Type/Location

To work on a trial is it required that you complete the following training:

- Good Clinical Practice online training and Research CV
- Study related documents i.e read the study protocol and signed the study 'delegation log of duties
- Any requisite trust training e.g venepuncture/cannulation etc

The research Nurse team can advise you on completing these.

(Ext: 13749 Email: sth.strokeresearchnurses@nhs.net)

For Specific Study information please see study folders and/or posters

STROKE RESEARCH 13748 (Mon – Fri 8-5)
Is your patient eligible for a stroke study?
Please contact the stroke research nurses on ext 13748 or email sth.strokeresearchnurses@nhs.net

STROKE RESEARCH 13749
Info on specific studies is available in the Drs Office on L2 & C-floor

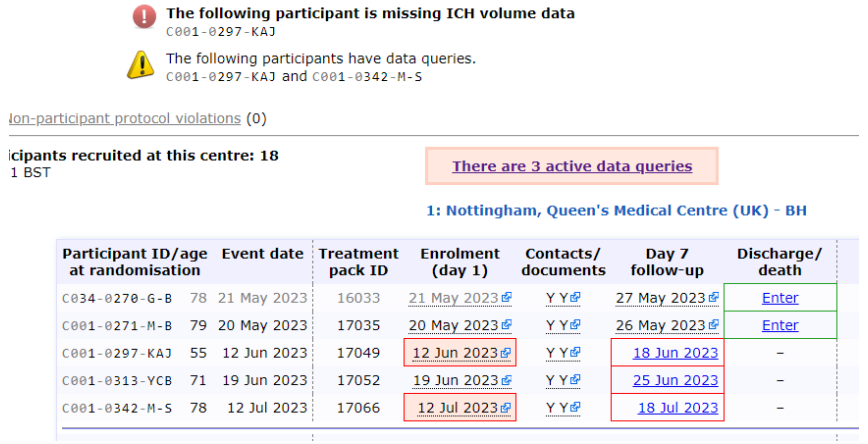
Pilot Progression Review

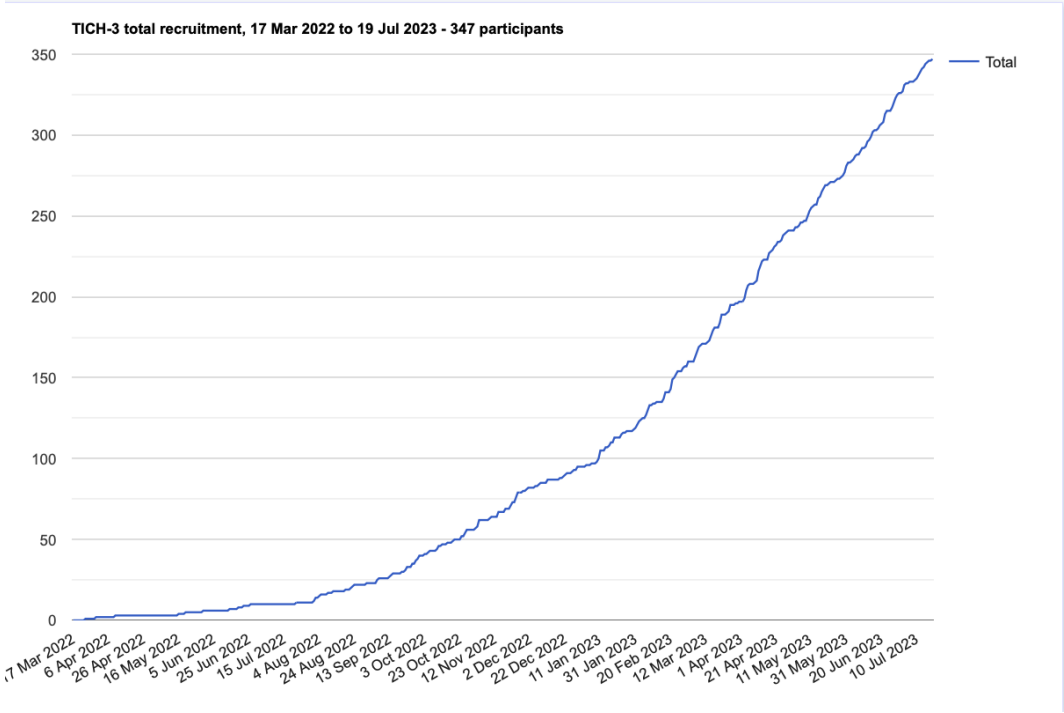
Upcoming committee meetings
DMC 14/09/2023
TSC 19/09/2023

Outstanding data
Please can you ensure any data queries have been completed prior to the upcoming DMC meeting.
> You can review if your site has any data queries by going to the 'participant list' on the TICH-3 website

There is guidance available on the TICH-3 documents page for completing data correction requests
https://stroke.nottingham.ac.uk/docs/TICH-3/UK_site_training/TICH-3%20Data%20corrections%20guidance%20Final%20v1.0%2007.03.2023.pdf

Please also remember to complete day 7 eCRF and the death/discharge eCRF when appropriate.

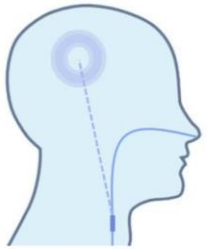




Co-enrolment with TICH-3

Co-enrolment is permitted, and sponsor approved for the following University of Nottingham sponsored trials (contract with site not required)

- MAPS-2 (IC now up-to 24 hours to enrol)
- PhEAST



Co-enrolment has been agreed with the following non-University of Nottingham sponsored CTIMPs (contract with site REQUIRED before co-enrolment is permitted)

- TRIDENT
- ENRICH-AF (MASTER CONTRACT NOW AGREED)

If you are taking part in either trial, please let us know so your site (PI and R&I) can document they agree to co-enrolment at your site.

Please let us know if there are any other trials you may wish to co-enrol with so that we can begin the contracts process.

There is a co-enrolment log on the TICH-3 documents page
https://stroke.nottingham.ac.uk/sif/docs/?sid=TICH-3

Upcoming events

- ESO Winter School, Edinburgh, 25th – 27th Sept 2023
- WICH 2023 Toronto, 8 – 9th October 2023
- World Stroke Congress Toronto,10-12 October 2023
- UKSF ICC Birmingham, 4 to 6 December 2023

Exclusions to the TICH-3 trial: CT scan image review

Other differentials to consider while assessing a patient for eligibility

Objectives

- Due to the emergency nature of the trial, most patients are being recruited prior to the formal radiology report.
- This training is to help avoid any errors while recruiting for TICH-3
- If in doubt, please contact the Radiology consultant or Stroke consultant to review the images and provide a verbal report

Inclusion criteria

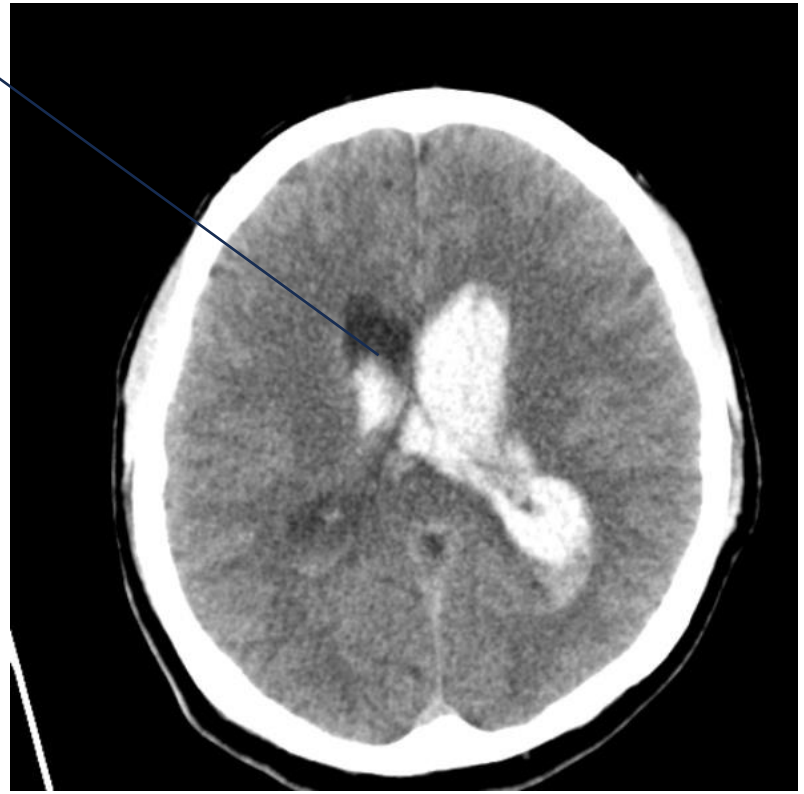
- Spontaneous ICH (confirmed on brain imaging) < 4.5 h of onset

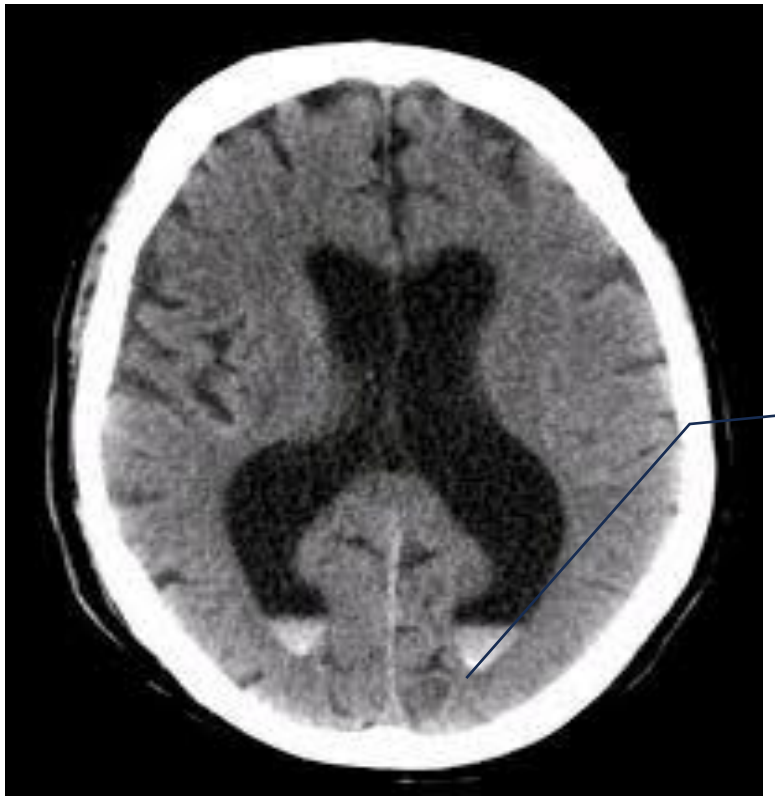
CT (or MRI) is conducted pre-recruitment in line with standard care, the haematoma volume measurement will help assess whether the participant is eligible.

Note - ICH secondary to ruptured aneurysm or vascular malformation or brain tumor or ischaemic stroke (haemorrhagic transformation of infarct, HTI) or thrombolysis or venous infarct is NOT spontaneous ICH

Isolated IVH is an exclusion

Intraventricular hemorrhage



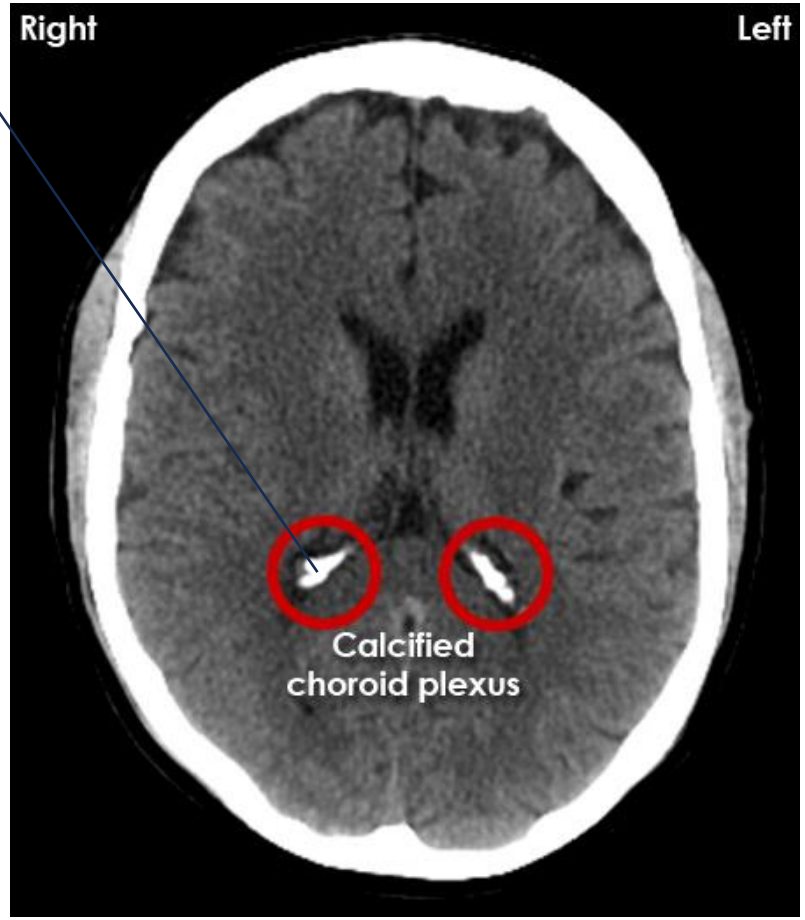


Pooling of the blood bilaterally

Be aware of calcified choroid plexus

Hyperdensities in the posterior horns of the lateral ventricles could be mistaken for hemorrhage.

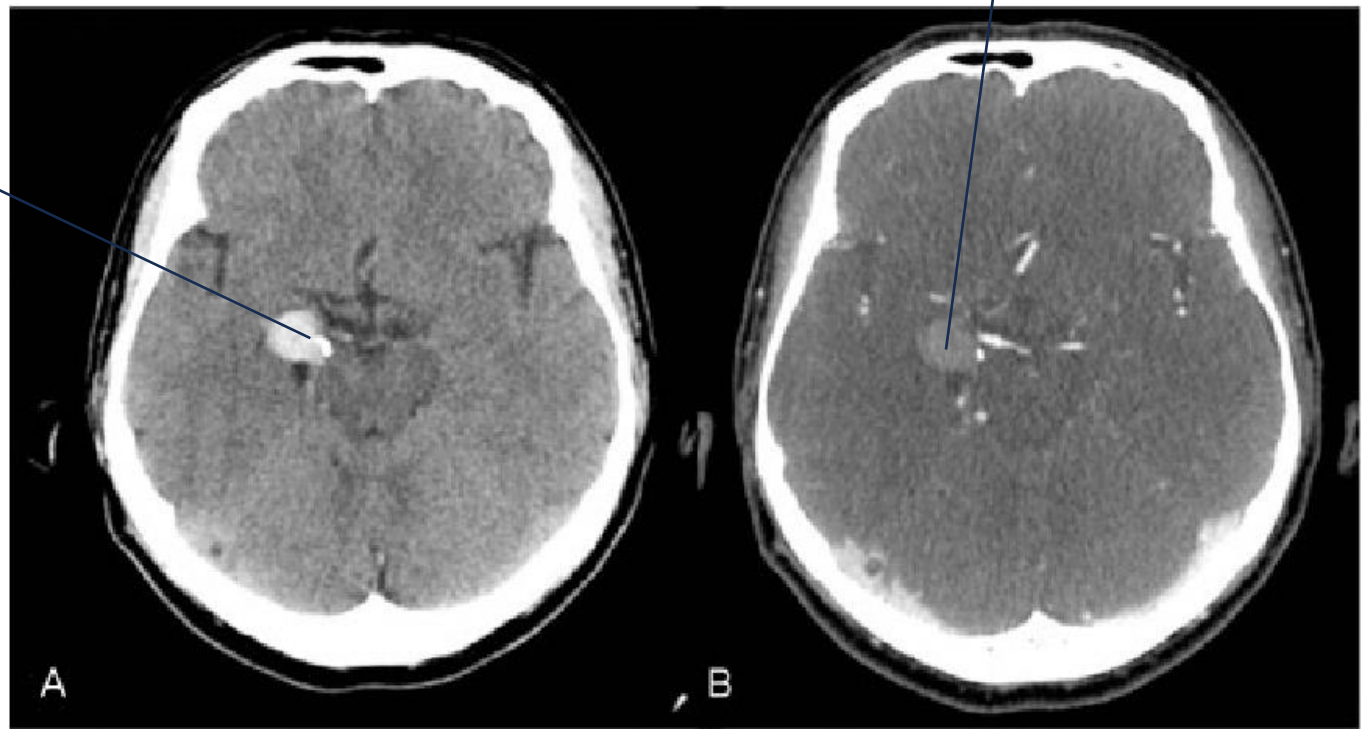
A. Isolated IVH is an exclusion
B. Bilateral small hyperdensities – think about alternatives



Thrombosed/ruptured aneurysm is an exclusion

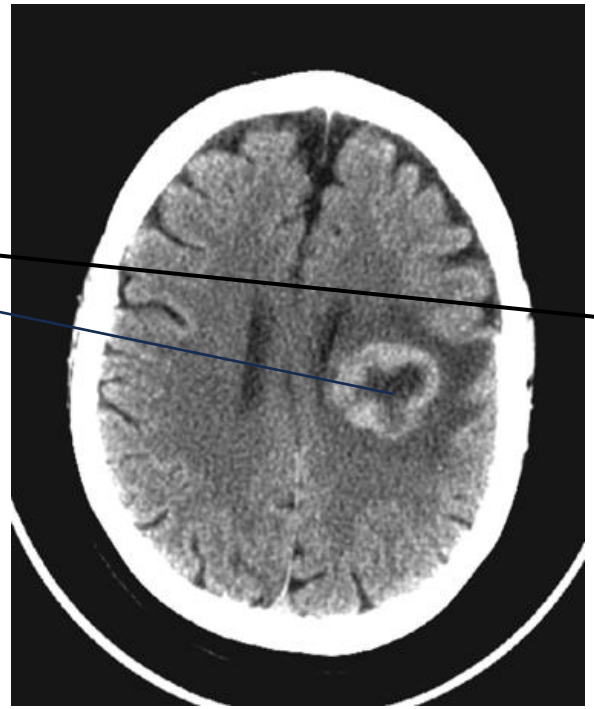
If there is a lesion around the location of the circle of willis, or there is concomitant SAH. THINK of thrombosed aneurysm or ruptured aneurysm.

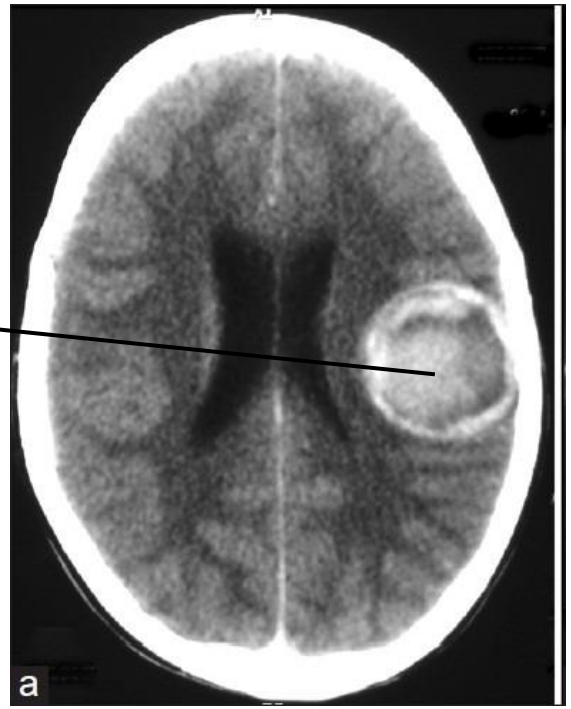
CTA showing thrombosed aneurysm



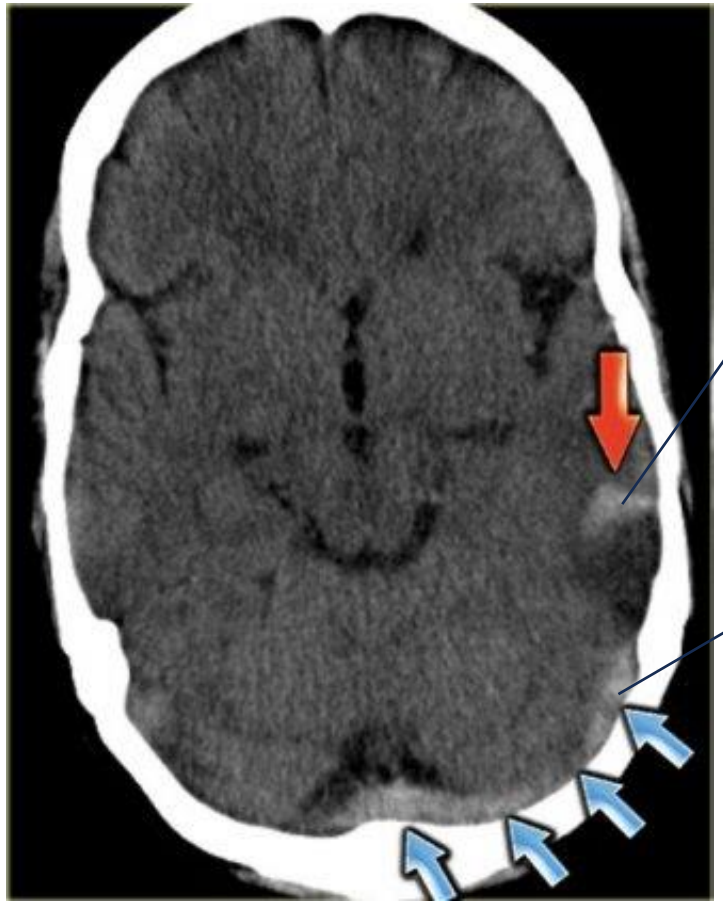
Secondary causes i.e tumors/ abscess are an exclusion

Multi-density, well-defined lesions with odema =Think about space occupying i.e tumor, abscess





Cerebral venous sinus thrombosis hemorrhage is an exclusion

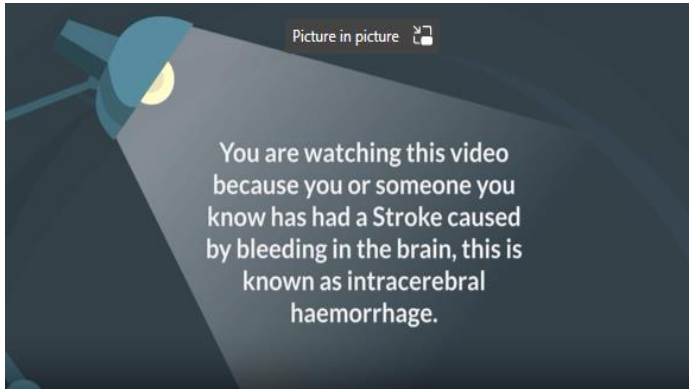


In patients' presenting with headaches, remember to consider CVST. Here the patient has had a CVST that has caused an infarct and hemorrhagic transformation.

Look for hyper density in the confluence and sagittal sinus

Study Within A Trial (SWAT)

Does the addition of access to an animated video, translated into 4 commonly spoken languages as well as English improve recruitment and retention into the TICH-3 trial?



- Population: Patients and their families considering joining the TICH-3 trial at initial or deferred consent
- Intervention: Access to an animated video + Patient Information Sheet (PIS)
- Comparator: PIS alone
- Outcomes: i) recruitment and retention of participants into TICH-3, ii) recruitment and retention of participants from ethnic minority groups/non-native English speakers into TICH-3

- Design: Cluster randomisation at site level with minimisation on ethnic minority proportion, size of hospital and prevalence of ICH.

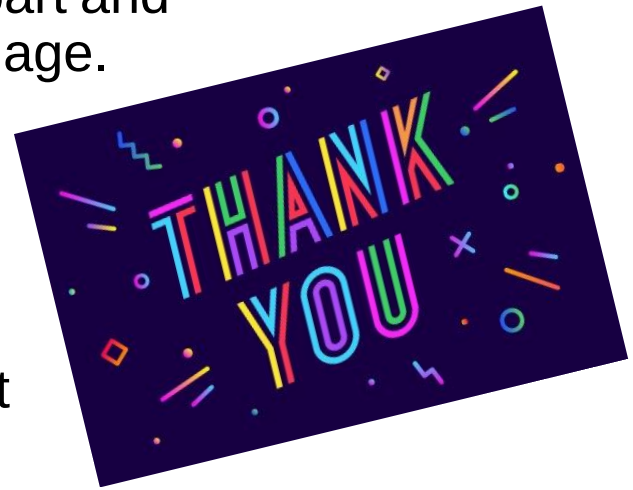
Study Within A Trial (SWAT) Results

Sites accessing SWAT Video	24
Viewings	291
Bengali	7
English	260
Polish	9
Punjabi	8
Urdu	7

Acknowledgements

TICH-3 would not be possible without:

All our participants and their families – we thank them for agreeing to take part and help us try to find better treatments for stroke due to intracerebral haemorrhage.



Thank you also to:

- TICH-3 Investigators
- TICH-3 staff Nottingham Stroke Trials Unit, Nottingham Clinical Trials Unit
- TICH-3 co-applicants
- Collaborators including Andrew Willis
- Nottingham Stroke Research Partnership Group - PPIE
- TICH-3 trial steering committee, data monitoring committee
- Funders – NIHR HTA

The Centre for Ethnic Health Research
national centre for tackling health inequalities

TICH-3 is funded by National Institute of Health and Care Research (Health Technology Assessment 19/59) NIHR129917

FUNDED BY NIHR | National Institute for Health and Care Research

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Any questions?

Q&A

Q: *"We found that TXA is prescribed and administered (with advice from Neuro) as part of reversal for patients on NOACS".* Royal Cornwall Hospital.

A: *"We occasionally see this at sites, there is little information that TXA will help with bleeding for patients on NOACS. If you site has TXA as part of standard care then you should not enrol to trial".*

Follow up comment from Cornwall Royal Infirmary; "We take advice from Derriford, TXA is not part of standard care but it has happened".

A: Prof Sprigg added; "This is why the study is double blind to maintain the integrity of the data".

Q&A

Q: “We are getting our bleep nurses put on the delegation log, we want to get them database access, is there training they can do to enable them to have access” (Addenbrookes, Cambridge)

A: The training slides are available on the TICH-3 documents page https://stroke.nottingham.ac.uk/sif/docs/?sid=TICH-3 and then once complete they can use the self referral link http://tich-3.ac.uk/?ZSelfRef

SWAT Feedback

"We found it helpful and used it to consent someone who only spoke Polish, as did their family. We wouldn't have been able to recruit them without it" Addenbrookes, Cambridge

"Our team find it really useful for all our patients – only really used the English version. But to supplement the consent conversation especially within the initial time frame is really useful" Lincoln County Hospital.