Delays experienced in in setting up new clinical trials post COVID.

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INTRODUCTION

ICH causes more than **1.7 million** strokes worldwide per year

mortality of over **40%**

Haematoma expansion Is the most common cause of death after ICH

Intracerebral haemorrhage (ICH) can be absolutely devastating resulting in severe disability or death. There is no effective drug treatment and only a small proportion of patients benefit from surgery. Haematoma expansion is common and occurs early after ICH.

Drugs that stop bleeding, such as tranexamic acid, are effective in other bleeding conditions and could potentially reduce haematoma expansion

TICH-3 aims to assess whether giving tranexamic acid after hyperacute (within 4.5 hours of onset) spontaneous ICH prevents haematoma expansion and reduces death and disability.

TICH-3 is a Phase III pragmatic Randomised Controlled Trial embedded into the clinical pathway using initial verbal consent and simple randomisation. There are no additional clinical assessments and minimal data collection up to day-7 post randomisation. TICH-3 does not routinely collect all SAEs, only pre-specified safety events, reducing the burden on sites.

Site set up post-COVID has demonstrated new challenges and we aimed to explore the barriers to site set up in the post-pandemic era.

METHOD

The TICH-3 trial has a large recruitment target of 5,500 participants of which 3,900 are to be recruited from UK sites. The trial aims to have a minimum of 85 eligible UK sites recruiting participants for this target to be feasible.

In late 2019 an online form was circulated to UK hyperacute stroke units, including the 109 UK sites that were involved in the previous TICH-2 trial, to collate expressions of interest (EOI) for TICH-3.

Contact with sites that expressed interest began July 2021 whilst ethical approval was ongoing. Full ethical approval was granted 18/11/2021. The sites that were responsive and completed eligibility screening were sent the local document package (LDP) and non-commercial agreement in December 2021 to begin local feasibility assessments.

We present the proportions of sites in various stages of site set up and the commonest causes of delays.

Any questions or interest please contact
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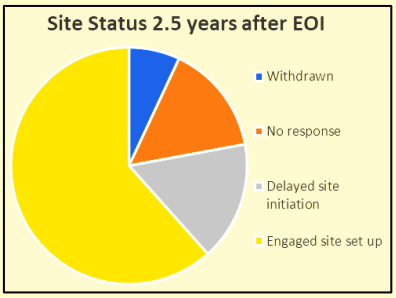
RESULTS

Data was analysed 21st September 2022. EOIs were received from 86 UK sites, of which 71 (86%) were received pre-COVID-19 pandemic.



Of the 86 sites:

- 6 (7%) withdrawn largely due to staffing capacity issues including impact of COVID
- **13 (15%)** sites have not responded since submitting the EOI
- **14 (16%)** delayed initiation of site set up due to COVID-19 associated capacity issues, overall lack of support for hyperacute activity, clinical workload effecting staffing and Principal Investigator (PI) availability
- **53 (62%)** were sent the local document package following eligibility screening and fulfilling site selection

Of the 53 sites receiving the LDP:

- **27 (51%)** sites were active within 9 months; 0 (0%) within 3 months and 11 (21%) within 5 months
- **26 (49%)** of the sites are still in the site set up stage, nearly 10 months since feasibility assessments began

Of the 26 still in site set up, the barriers are categorised below:

- **1 (4%)** new EOI
- **2 (8%)** costing issues
- **3 (12%)** lack of PI capacity to complete research tasks for set up such as training and authorising delegation log
- **4 (15%)** lack of capacity due to clinical workload and PI availability
- **7 (27%)** delays with research and development office (R&D) to begin feasibility assessments and execute local approvals
- **9 (35%)** no specified reason but slow responses and actions from research team and R&D

Even though the barriers have been categorised above with the sites main reason for delay, there was a lot of intertwining of the same issues across the sites. There appears to be a circular affect that COVID has increased pressure on clinical workload, causing staff sickness/isolation requirements again impacting clinical pressures therefore impacting availability of staff for hyperacute stroke activity including absence of available PI's for research. Costings is therefore more stringent for research activity due to the economical deficient caused by COVID and R&D capacity only assessing one trial at a time.

POTENTIAL RELEVANCE AND IMPACT

The data presented highlights the ongoing problems and delays experienced in trial initiation in hyperacute stroke units due to COVID-19, despite a streamlined trial methodology embedded in the clinical pathway.

The impact of COVID-19 is still prevalent with staff illness, the increased burden on the NHS, delays in R&D approvals for site initiation and lack of PI availability. Research reset is causing concern for a lot of clinical trials as there is a lot of delays to site initiation and therefore difficulty in hitting recruitment targets.

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https://stroke.nottingham.ac.uk/

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