Flash-Mob TTP Audit

Audit protocol, version 2.0

30th September 2019

KEY DATES	
Local audit registration period	1st August to 13th October 2019
"Flash-Mob" data collection period	14th October to 6th December 2019
Preliminary results presented	April 2020
Final report and manuscript	Quarter 3 2020

Contents

Short title Flash-Mob TTP Audit

Long title Nationwide audit of treatment delays in patients presenting with acute TTP to UK hospitals

1. Contact details

1.1 Management committee

Name	Position
Dr. Rory McCulloch	Vice chair HaemSTAR, Haematology trainee, University Hospitals Plymouth NHS Trust
Dr. Pip Nicolson	Chair HaemSTAR, Haematology trainee, University Hospitals Birmingham NHS Foundation Trust
Dr. Rebecca Shaw	HaemSTAR representative for Mersey, Haematology trainee, Royal Liverpool and Broadgreen University Hospitals NHS Trust
Dr. Alex Langridge	HaemSTAR lead for communications, Haematology trainee, City Hospitals Sunderland NHS Foundation Trust
Dr. Tom Bull	HaemSTAR website officer, Haematology trainee, Cambridge University Hospitals NHS Foundation Trust
Dr. Zara Sayar	HaemSTAR representative for Central London, Haematology trainee, University College London Hospitals NHS Foundation Trust
Dr. David Tucker	HaemSTAR alumnus, Consultant Haematologist, Royal Cornwall Hospitals NHS Trust
Dr. Steven Lane	Statistician, Department of Biostatistics, University of Liverpool
Dr. Laura Magill	Trials Manager, Birmingham Surgical Trials Consortium, University of Birmingham
Prof. Marie Scully	Consultant Haematologist, University College London Hospitals NHS Foundation Trust

1.2 Data management

Name	Position
Dr. Rita Perry	Project Manager, Birmingham Surgical Trials Consortium, University of Birmingham Email: BhamRed@contacts.bham.ac.uk
Dr. Michala Pettitt	Data Manager, Birmingham Surgical Trials Consortium, University of Birmingham

1.4 Key contact

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2. Abbreviations

ADAMTS13	A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13
ASM	Annual Scientific Meeting
BCTU	Birmingham Clinical Trials Unit
BiSTC	Birmingham Surgical Trials Consortium
BSH	British Society of Haematology
CNS	Central nervous system
CRN	Clinical Research Network
FBC	Full blood count
FFP	Fresh frozen plasma
MAHA	Microangiopathic haemolytic anaemia
NHS	National Health Service
PEX	Plasma exchange
REDCap	Research electronic data capture
TTP	Thrombotic thrombocytopenic purpura
UK	United Kingdom

3. Audit synopsis

Title	Flash-Mob TTP audit: Nationwide audit of treatment delays in patients presenting with acute TTP to UK hospitals
Audit management	Co-ordinated through the nationwide HaemSTAR network and open to all UK sites with experience managing acute TTP.
Audit aim	To assess the early management of acute TTP in UK hospitals.
Audit design	Multicentre, retrospective UK-based audit of early management of patients presenting with acute TTP.
Audit standard	Scully *et al* (2012) Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. *Br J Haematol.* 158, 323-335.
Audit population	
Inclusion criteria	Adult patients aged 18 years and older. First presentation of TTP, including both acquired and congenital TTP. ADAMTS13 activity level <10% during acute episode. Hospital admission occurring on, or after, 1st June 2014 and before 1st June 2019.
Exclusion criteria	Previous history of TTP.
Estimated sample size	200 patients
Number of sites	40
Endpoints	
Primary	Rate of patients initiating therapeutic plasma exchange within 8 hours of presentation as per BSH guidelines.
Secondary	Evaluate initial management of acute TTP against BSH guideline recommendations including use of steroids, early initiation of rituximab in presence of CNS and/or cardiac involvement, use of FFP transfusions prior to PEX, and the avoidance of platelet transfusions. Evaluate the contributory factors for excessive delay in starting PEX. Evaluate variations in practice according to secondary and tertiary care setting and geographic location. Evaluate impact of treatment delays on 30-day mortality rate and duration of inpatient stay.
Audit schedule	
Audit timelines	Registration of audit at eligible centres: August to October 2019. Identification of eligible patients: August to October 2019 Flash-Mob data collection: October to December 2019 Abstract based on preliminary analysis submitted to BSH 2019 Local results disseminated: Quarter 2 2019 Final report and manuscript: Quarter 3 2019

4. About HaemSTAR

HaemSTAR is a UK-wide network of clinical haematology registrars that is supported by the National Institute of Health Research (NIHR) non-malignant clinical research network (CRN). It has a national steering group who decide strategy and prioritise network activity. It has lead members in each regional NIHR Local (L)CRN who co-ordinate local research activity and the involvement of haematology registrar colleagues.

The overarching aim of HaemSTAR is to promote clinical research in non-malignant haematology. It does this in four ways: by increasing recruitment to non-malignant haematology trials nationally; by providing a platform for worthy audits to be run on a national scale; by developing and rolling out its own national studies which align with NIHR research priorities; and by exposing clinical haematology registrars to NHS Trust Research and Development (R&D) departments and the NIHR in order to develop Principle Investigator (PI) skills which are not currently part of the haematology registrar training curriculum.

This project follows HaemSTAR's successful Flash-Mob audit of intravenous immunoglobulin use in immune thrombocytopenia. The HaemSTAR network collected data from 978 patients across 39 sites in the UK within a 12-week period. Preliminary data was presented at the British Society of Haematology ASM 2019 (HaemSTAR Investigators, 2019).

Authorship

HaemSTAR authorship policy provides PubMed-citable collaborator status to all collaborators involved in a study as detailed at http://haemstar.org/authorship-policy. An example of this can be seen here: https://www.ncbi.nlm.nih.gov/pubmed/24826894

Further information

- Visit our website at HaemSTAR.org Follow us on Twitter @HaemSTAR_UK

5. Background and rationale

Thrombotic thrombocytopenic purpura (TTP) is a very rare, life threatening condition. It is a recognised medical emergency and prompt diagnosis and initiation of therapy is imperative. Plasma exchange (PEX) remains the only treatment shown to impact significantly on acute mortality (Rock *et al*, 1991) and early treatment initiation is critical with up to 50% of TTP deaths occurring within 24 hours of presentation (Scully *et al*, 2008).

Prompt initiation of PEX faces many logistical challenges. The average UK NHS Trust may diagnose only one case of TTP per year, presenting symptoms are often non-specific and first point of contact is normally with non-Haematologists in the primary or secondary care setting making timely diagnosis challenging.

Once TTP is recognised arrangements for PEX, including central line insertion, must be made. Most centres do not have provision for a 24-hour PEX service meaning either local ad hoc arrangements are made, or transfer to a regional tertiary centre must be co-ordinated, which can be a complex and time-consuming task.

The recognised problems in acute TTP management have provoked recent proposals for a national service with appointed TTP specialist centres and provision for rapid hospital transfer (Dutt & Scully, 2015). A national TTP service, funded directly through NHS England, currently remains under negotiation.

Although the challenges of acute care are recognised there is currently no comprehensive record of treatment delays experienced by patients presenting with acute TTP in UK hospitals. Local audit has limited value in such a rare disease, but a collaborative national audit has potential to highlight important recurring issues. This audit will, for the first time, evaluate the extent of recurrent barriers to early treatment initiation and will provide valuable information to inform and shape the design of future national care provision.

6. Audit standard

The British Society of Haematology guideline published in 2012 provides comprehensive, evidence-based guidance on acute management of TTP and forms the standard against which this audit will be measured (Scully *et al*, 2012).

Key standards relevant to the audit are listed below:

- In view of the high risk of preventable, early deaths in TTP, treatment with PEX should be initiated as soon as possible, preferably within 4–8 hours, regardless of the time of day at presentation, if a patient presents with a MAHA and thrombocytopenia in the absence of any other identifiable clinical cause.
- Intravenous daily methylprednisolone or high dose oral prednisolone should be considered.
- In acute idiopathic TTP with neurological/cardiac pathology, which are associated with a high mortality, rituximab should be considered on admission, in conjunction with PEX and steroids.
- Platelet transfusions are contraindicated in TTP unless there is life-threatening haemorrhage.
- If any delay in starting PEX then give FFP infusion.

7. Aims and objectives

7.1 Aims

The main aim of this audit is to assess early management of acute TTP in UK hospitals.

7.2 Objectives

Primary: Rate of patients presenting with acute TTP initiating therapeutic plasma exchange within 8 hours of presentation, as per BSH guidelines (*see section 8 for definition of time delay*).

Secondary:

These relate to specific points in the BSH guidelines:

- Rate of steroid administration within 24 hours of presentation
- Rate of rituximab administration within 48 hours of presentation in the presence of CNS and/or cardiac involvement
- Rate of FFP infusions given where PEX is delayed due to hospital transfer
- Rate of platelet infusions given in the absence of bleeding prior to initiating PEX

The audit will evaluate contributory factors for excessive time delay in PEX initiation to help determine areas for future improved practice. It will also evaluate variations in practice according to secondary and tertiary care setting that may inform a future care model. Potential implications of delayed PEX will be assessed through 30-day mortality rates and total hospital inpatient days. It is anticipated that the audit will identify areas for future prospective research.

8. Definition of audit end-points

There are unavoidable limitations to any definition of time delay between presentation and initiation of PEX, and the BSH guideline does not provide a strict definition. Importantly this audit uses objective, electronically recorded times to provide definitions. These are easily auditable and provide data that is reliable, consistent and reproducible.

Electronic recordings used to define primary outcome:

- Date and time that first full blood count (FBC) with blood film reporting fragments or schistocytes ***received*** by laboratory. This time-point will be used to "start the clock" in the primary objective measure and will define time of initial presentation.
- Date and time plasma released from blood bank for first plasma exchange. This time-point will be used to "stop the clock" in the primary objective measure and will define time patient initiates plasma exchange.

The audit will record additional electronically recorded timings that will provide context to delays in PEX initiation. These include:

- Date and time of acute hospital admission, as recorded on hospital IT system.

If transferred to tertiary centre,

- Date and time discharged from presenting hospital, as recorded on hospital IT system.
- Date and time of admission to tertiary centre, as recorded on hospital IT system.

Accepting compromised reliability two additional time points will be audited that rely on documentation in hospital notes. These are:

- Date and time possible diagnosis of TTP first documented in hospital notes.
- Date and time central line inserted for PEX.

9. Audit design

This is a multicentre, retrospective UK-based audit of early management of acute TTP in routine clinical practice over a 5-year time period. Data will be collected from centres across the UK experienced in the management of acute TTP. Data will be collected on at least 200 patients and will aim to recruit from at least 40 UK centres, including both secondary and tertiary care centres. Participants treated for acute TTP and meeting eligibility criteria will be identified by local clinical teams.

Data will be collected that covers a patient's inpatient stay, and if the patient underwent hospital transfer will include information from both the presenting hospital and tertiary referral centre. Designated regional audit leads will be responsible for ensuring data is collected from both sites and data will be linked retrospectively by matching dates and hospitals at the end of the data collection period. In cases where this method is not deemed reliable the submitting centres will be asked to link selected cases with OpenPseudonymiser (www.openpseudonymiser.org).

The data collection phase will follow the "Flash-Mob" model previously adopted by HaemSTAR (HaemSTAR Investigators, 2019). All data will be collected within the 8-week period 14/10/2019 to 06/12/2019 and will be co-ordinated through the national HaemSTAR network.

10. Audit participants

10.1 Inclusion Criteria

Potential participants must satisfy the following criteria to be included in the audit:

- Adult patient aged 18 years and older
- Acute episode represents ***first*** presentation of TTP (may include acquired or congenital TTP)
- ADAMTS13 activity level <10% measured during acute episode
- Hospital admission occurring on, or after, 1st June 2014 and before 1st June 2019

10.2 Exclusion criteria

Potential participants meeting any of the following criteria will not be included in the audit:

- Past history of TTP

10.3 Identification of participants

Patients treated for acute TTP will be identified by the local clinical teams. To optimise audit coverage the HaemSTAR network will assist local centres in identifying eligible patients. Methods of patient identification will include:

Local teams:

- Identify patients treated at centre by identifying ADAMTS13 activity levels <10% on local laboratory records and check patient eligibility against other criteria.
- Identify local patients registered on the UK TTP registry and check patient eligibility against other criteria.

Regional leads:

- Liaise with local leads and inform contacts at registered centres of any patients who were transferred to/from their centre for further management. Secure NHS email accounts will be used to liaise and minimal patient data will be shared (i.e. NHS number). This data will not be shared with the management committee.

10.4 Eligible centres

Any hospital with ≥1 case of TTP that meets eligibility criteria and has a haematology trainee presence may participate. In exceptional circumstances a centre without trainee presence may participate at the discretion of the management committee.

11. Data management

11.1 Participant numbering

Participants will be identified by the local clinical team. Anonymous data about these patients will be entered into a web-based system which will be maintained by the Birmingham Surgical Trials Consortium. On registration with the system all patients will receive a unique study number and no patient identifiable information will be stored within the system. Basic demographics will be recorded to ensure patient eligibility and provide context to treatment delays.

11.2 Data collection

Information regarding participant demographics and details of management of acute TTP (appendix 1) will be entered by local clinical teams and stored online through a secure server running the Research Electronic Data Capture (REDCap) web application hosted at the University of Birmingham (https://bistc.redcap.bham.ac.uk/). REDCap is a web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources (Harris 2009; Harris 2019).

Login information and passwords for REDCap will be generated for each collaborator after confirmation of audit registration. This will allow collaborators to enter and review data from their own centre. They will not have access to data from other centres.

11.3 Data confidentiality and security

Clinical teams at participating sites will ensure that participants' anonymity is maintained when entering data into the REDCap system. REDCap has been used extensively to electronically capture and store sensitive health data in a secure and encrypted format for similar projects within the NHS.

Patient demographics have been minimised to protect patient anonymity. Age ranges will be recorded, instead of specific age, and gender will not be recorded, unless the patient was pregnant as this is deemed a clinically significant characteristic. The name of the treating hospital and referral centre will be recorded as will the dates of admission to allow linking of patient data. Only local leads who work at the centres where the patients were treated will be able to identify patients. The data manager and management committee, who will analyse the data, will not be able to identify patients.

Data will be collected and stored in accordance with the Data Protection Act, 2018. Direct access to the audit data will be restricted to members of the management committee and

audit team at Birmingham Surgical Trials Consortium. Access to the database will be overseen by the data manager.

11.4 Archiving

Data will be stored securely and on encrypted and certified servers at the University of Birmingham. Data will not be shared with any third parties.

The only local data to be stored will be password protected spreadsheets linking unique hospital identifiers and system assigned identifiers. These will be held in local centres on encrypted servers. This information will not be shared with the central management committee.

11.5 Follow up

As this is a retrospective audit, no follow up of participants is required.

11.6 Data analysis

The statistical methodology for this national audit has been discussed with expert statisticians. The data will be analysed using descriptive methods and presented using summary statistics, including means, median, counts and measures of variability. Multilevel-logistic regression models will also be used to allow for within centre clustering. The sample size is projected to include over 40 centres within the UK. We estimate that each hospital will treat 1 acute TTP patient per year. Over the 5-year time frame for retrospective data collection this equates to 5 cases per centre. This extrapolates to 200 patients being included. We will however, be happy to exceed this number in terms of both number of centres and number of patients.

For public disclosures of audit results, such as oral presentations and publication, patient data will be presented collectively and will not allow individual patients to be identified within it. The performance of individual hospitals will not be disclosed and all subgroup analysis will include large patient cohorts to protect patient anonymity.

12. Quality assurance

12.1 Protocol

This protocol was designed by the members of the management committee, with guidance from an expert advisory group comprising members of the West Midlands NIHR LCRN and the Birmingham Clinical Trials Unit (BCTU). Audit standards and audit methodology were developed in order to adhere to guidelines produced by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Initiative (von Elm et al 2007). The protocol was refined further following discussion at HaemSTAR meetings.

12.2 Protecting patient anonymity

As TTP is very rare this audit has been designed with particular attention to protecting patient confidentiality. The audit and data management plans have been discussed with the following professionals: Director of the Birmingham Clinical Trials Unit, Head of Operations at Cancer Research UK Clinical Trials Unit (CRCTU), Manager of Information Governance at University Hospitals Birmingham NHS Foundation Trust and the Caldicott Guardian at University Hospitals Plymouth NHS Trust. All are satisfied that the protocol is an audit and does not compromise patient anonymity.

To ensure the perspective of patients was included we consulted Jo McIntyre, founder of the TTP Network, the largest UK charity for patients with TTP. She reviewed the protocol and shared it with charity members via a patient forum. Feedback from patients was supportive of the audit's aims and no concerns regarding patient anonymity were raised.

12.3 Pilot

A pilot audit was undertaken in March 2019 to assess feasibility. Results were reviewed at the HaemSTAR meeting in April 2019 prompting recommendation that the audit should be expanded to a national level. A second pilot was undertaken in August 2019. Following review at the HaemSTAR meeting in September 2019 the protocol was finalised.

12.4 Data completeness

Following data collection, only data sets with >40% data completeness will be accepted for pooled national analysis. Centres with >60% missing data points will be excluded and collaborators from those centres withdrawn from the published list of citable collaborators.

13. Co-ordination of the "Flash-Mob" audit

The organisation of this national audit, undertaken in a limited time frame, will be carefully co-ordinated through the national HaemSTAR framework. The roles of various collaborator groups are described below.

13.1 Audit collaborator groups

- *Management committee:* a core group of haematology trainees and consultants plus data management and statistician are responsible for protocol design, data handling, analysis and drafting of the paper. The management committee are responsible for use of data resulting from the project.
- *Regional leads:* a network of Haematology trainees across the UK responsible for co-ordinating teams at local hospitals. The regional leads act as a link between local teams and the management committee. They are the first point of contact for local collaborators. Each regional lead will aim to recruit 4-5 local-teams within their designated region. If patients were transferred during their acute admission regional leads will help ensure relevant data is collected from both hospitals. To qualify for authorship, regional leads must recruit at least three local-teams unless agreed in advance with the management committee.
- *Local teams:* each local centre requires a team of collaborators consisting of one supervising consultant and a team of haematology and medical trainees. Local team sizes will vary according to size of hospital but should comprise a minimum of 2 (1 trainee and 1 supervising consultant) and a maximum of 5. Local teams will contribute to identification of eligible patients and are responsible for data collection. One collaborator should be selected to act as the 'local lead'. A maximum of 5 collaborators per centre-team will be listed as 'PubMed' citable collaborators. A collaborator must have evidence of data collection via their REDCap login to be eligible for collaborator status.

In exceptional circumstances, where local teams anticipate a very high volume of patients being eligible for inclusion, they may contact the management committee for permission to add an additional collaborator to their team.

- *Local leads:* each centre will require 1 collaborator to act as the "local lead". The lead is responsible for: 1) ensuring the audit is registered locally; 2) contacting the supervising consultant; 3) sending the management committee the contact details of the collaborators from their centre; 4) making sure all deadlines are met (see front sheet); 5) ensuring all data is submitted from their centre; and 6) helping with data collection. These individuals will be listed in the final authorship as local leads, in recognition of their contribution.
- *Supervising consultant:* one consultant per centre is eligible for collaborative PubMed citable collaborator status if they meet the following criteria: 1) Supports local audit registration; 2) Circulates information about the audit and the audit

protocol to consultant colleagues; 3) Facilitates presentation of local audit results at a departmental audit meeting; 4) Completes workplace-based assessments for trainees (ePortfolio), if asked. Consultants should ensure collaborators act in accordance within governance guidelines and should facilitate implementation of post-audit interventions, if required.

13.2 Local registration of audit

It is the responsibility of the local centre-team at each site to identify a local supervising consultant haematologist and to ensure that the audit is registered appropriately. Confirmation that this is not research is available in Appendix 2. A letter addressed to trust audit officers is available in Appendix 4 to aid the process. Examples of audit registration forms can be found on the HaemSTAR website. When registering this as a clinical audit you should emphasise that:

- The audit will measure current practice against established standards.
- It is a national audit.

REDCap accounts will not be issued until evidence is sent to the management committee showing the successful registration with the audit department, including the email address of the local audit officer.

Two permanent contacts at each hospital are required (supervising consultant and audit officer) to return hospital specific results.

13.3 Dissemination and publication of results

The results of the audit will be disseminated through:

- Local presentations – teams at all centres will need to provide the contact details of the local consultant supervisor and the local audit officer.
- Presentation at national and international meetings.
- Publication in a peer-reviewed haematology journal.

Patient outcomes will only be published/presented collectively and no individual patient will be identifiable within the results analysis. The performance of specific hospitals will not be disclosed within any public presentation of results.

14. Financial arrangements

This study is supported by the Scientific and Academic Coagulation Consortium Katie Bolam Research Award and the Birmingham Clinical Trials Unit. Support in the form of finance and/or expertise from these organisations have been used to design and host the secure online data collection forms. The REDCap system used is provided by the BiSTC and hosted by the University of Birmingham.

No registration fee is payable by units to join the project or to enter data online. Similarly, no financial reimbursement will be made to units or investigators for their involvement in the project.

15. References

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16. Appendices

16.1 Appendix 1: Audit pro forma

PART A: Eligibility and demographics	
Eligibility and demographics	
Did hospital admission occur on, or after, 1st June 2014 and before 1st June 2019?	Y/N
Age at time of acute episode	≥18 years to <40 years; ≥40 years to <50 years; ≥50 years to <60 years; ≥60 years to <70 years; ≥70 years to <80 years; ≥80 years.
Pregnant at time of acute TTP episode	Y/N
Was this the first presentation of TTP?	Y/N
Was ADAMTS13 activity <10% during acute TTP episode?	Y/N
Treating hospital	
Name of treating hospital	*Free text*
Is this site a recognised tertiary referral centre for TTP?	Y/N
Did the patient present to this site, or were they transferred from another site?	"Site of presentation" go to part B only, or "Transferred from another site for management of TTP" go to part C only, or "Transferred from another site before diagnosis of TTP considered" go to part D.
PART B: Site of presentation	
Baseline characteristics	
Date and time of hospital admission (electronic record)	DD/MM/YYYY 00:00
Date and time that admission full blood count received in laboratory (electronic record)	DD/MM/YYYY 00:00 (electronic record)
Presenting platelet count (x 10^9/L)	Number
Presenting haemoglobin (g/L)	Number *(automatic question if <20)*
Are fragments or schistocytes reported in blood film?	Y/N/Blood film not reported
Did patient have a full blood count sent at general practice/outpatients prior to hospital admission with a blood film reporting fragments or schistocytes?	Y/N
If "Yes" to answer subsequent questions:	
Location where full blood count sent from	General practice/ Outpatient Clinic/Antenatal Department/Other
Date and time full blood count was received in laboratory (electronic record)	DD/MM/YYYY 00:00
Platelet count (x 10^9/L)	Number
Haemoglobin (g/L)	Number
If no fragments on admission blood film, and no earlier test, ask subsequent question:	

Please document date and time (sample received in laboratory) of first blood film to report fragments or schistocytes during this hospital admission.	DD/MM/YYYY 00:00 Or "No blood film reporting fragments or schistocytes during admission"
When was a diagnosis of TTP first objectively considered in the notes?	DD/MM/YYYY 00:00 (if recorded) "TTP not objectively considered"
Date and time first ADAMTS13 activity assay received in laboratory	DD/MM/YYYY 00:00 (electronic record) "Not sent at this hospital"
Clinical symptoms to suggest CNS involvement within 48 hours of hospital admission?	Y/N/Unknown
Troponin checked within 24 hours of admission	Y/N
Was Troponin raised above laboratory upper limit of normal?	Y/N/"Not done at this hospital"
Treatment	
Once diagnosis considered was patient treated actively for TTP with intention to start plasma exchange?	Yes No – too unwell No – diagnosis of TTP not considered during hospital stay No – other (provide free text)
Date of first steroids (time if available)	DD/MM/YYYY 00:00 (provide option "steroids not given)
Was an FFP transfusion given prior to starting PEX/hospital transfer?	Y/N
Were platelets transfused?	Y/N – If Yes "Did patient have life threatening haemorrhage?" Y/N
▪ Date of first platelet transfusion	DD/MM/YYYY
Date of central line insertion (time if available)	DD/MM/YYYY 00:00 (provide option "not done at this hospital"
Was patient intubated at this hospital prior to plasma exchange or hospital transfer?	Yes/No/Unknown
Did patient commence plasma exchange at this hospital?	Y/N
▪ Ward where first plasma exchange administered	Renal unit/Haematology unit/ICU/Other/Unknown
▪ Date and time octaplas (or plasma) released from blood bank for first plasma exchange	DD/MM/YYYY 00:00 (electronic record)
Did patient receive rituximab at this hospital?	Y/N
▪ Date of first rituximab infusion	DD/MM/YYYY
Was patient transferred to a tertiary centre?	Y/N
▪ Was this transfer arranged specifically for TTP management?	Y/N
▪ Name of tertiary centre transferred to	Free text
▪ Date and time of discharge for transfer	DD/MM/YYYY 00:00 (electronic record)

Aftercare	
Was patient alive day +30 after initial admission?	Y/N – if "No" Number of days from admission to death/Unknown
Date of hospital discharge	DD/MM/YYYY or "Died"
Destination at discharge	Hospital transfer/Home/Rehab centre/Died/Other
From review of clinical notes what do you feel were the most important contributory factors for delay in starting PEX or hospital transfer? (Rank up to 3 options considered significant, with 1. being the most important factor. If there were none then leave blank)	• Delayed diagnosis • Unable to get central line inserted promptly • Difficulty co-ordinating hospital transfer (If select this "Please describe issues" free text) • Difficulty co-ordinating local plasma exchange • Other (free text)
Was plasma exchange/hospital transfer delayed while an ADAMTS13 level was awaited?	Yes/No/Unknown
If diagnosis of TTP was delayed ≥24 hours from hospital admission please state the initial working diagnosis.	• Acute coronary syndrome • Acute stroke • Acute sepsis • Obstetric related pathology • Autoimmune cytopenia (i.e. immune thrombocytopenia or autoimmune haemolytic anaemia) • Other

Part C: TTP tertiary referral centre

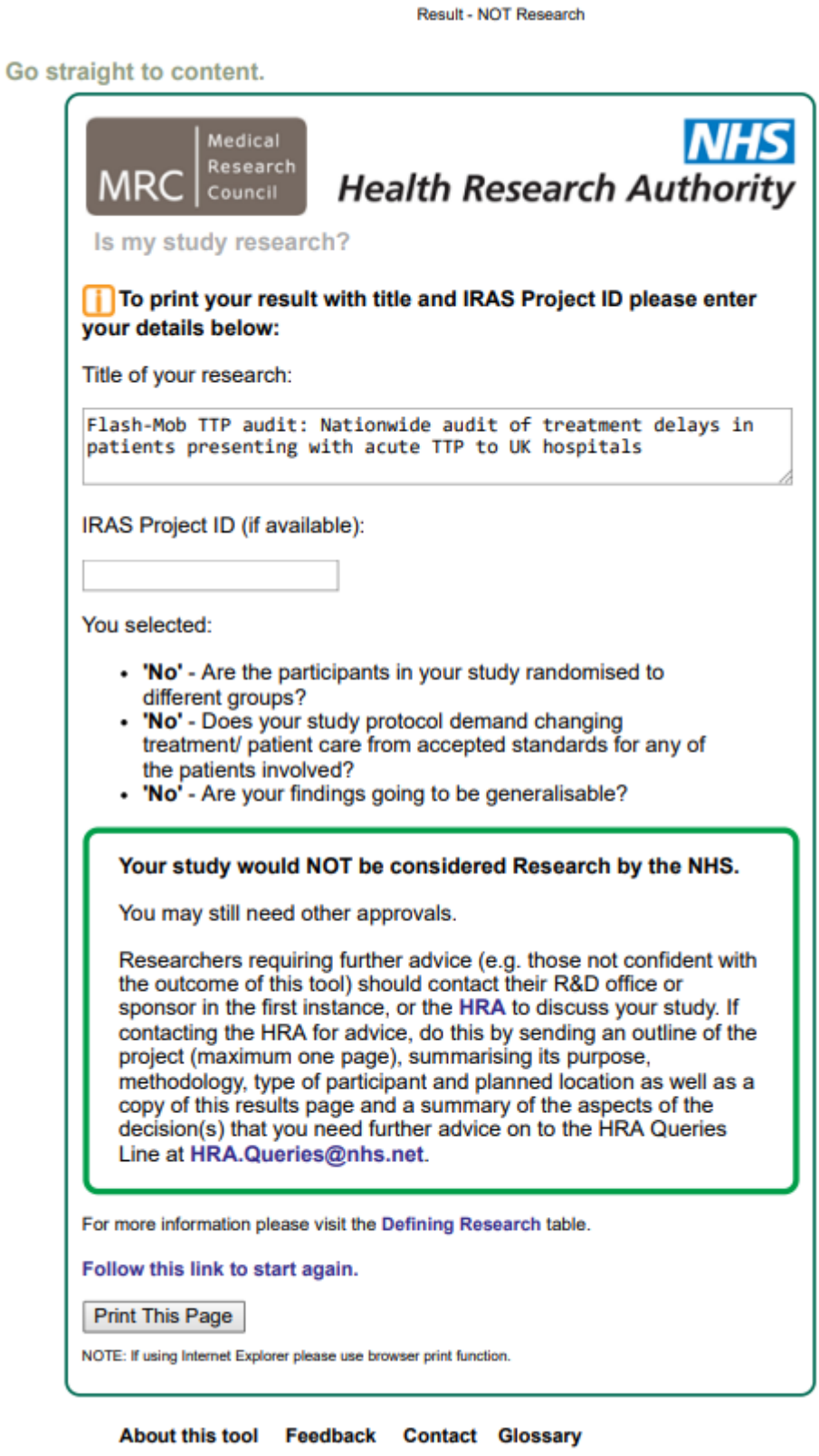
Treatment	
Date and time of admission	DD/MM/YYYY 00:00 (electronic record)
Site transferred from	Free text
Were concerns documented in notes regarding delay in hospital transfer?	Yes/No If "Yes" please describe issues
Troponin checked within 24 hours of admission to this hospital?	Y/N
Troponin raised above upper limit of normal range?	Y/N
Date of first steroids at this hospital (time if available)	DD/MM/YYYY 00:00 (provide dropdown option: "not given")
Date of central line insertion (time if available)	DD/MM/YYYY 00:00 (provide dropdown option: "Inserted at referral site"/"Not done")
Was patient intubated at this hospital prior to plasma exchange?	Yes/No/Intubated prior to arrival at this hospital/Unknown
Did patient commence plasma exchange on this admission?	Y/N – if No for explanation free text.
▪ Ward where plasma exchange administered	Renal unit/Haematology unit/ICU/Other/Unknown

▪ Date and time octaplas/plasma released from blood bank for first plasma exchange	DD/MM/YYYY 00:00 (electronic record)
Did patient receive rituximab during this hospital admission?	Y/N
▪ Date of first rituximab infusion	DD/MM/YYYY
Aftercare	
Was patient alive day +30 after admission to this hospital?	Y/N – if No days from admission to this hospital to death
Date discharged from hospital	DD/MM/YYYY or "Died"
Destination at discharge	Home/Rehab centre/Local hospital/Died/Other
PART D: Hospital transfer before diagnosis of TTP considered	
Baseline characteristics	
Date and time of hospital admission (electronic record)	DD/MM/YYYY 00:00
Site transferred from	Free text
Indication for hospital transfer	Manage presumed stroke/Manage presumed sepsis/Manage obstetric complication/Manage presumed cardiac event/Other "free text"
Date and time that admission full blood count received in laboratory (electronic record)	DD/MM/YYYY 00:00 (electronic record)
Platelet count (x 10^9/L)	Number
Haemoglobin (g/L)	Number *(automatic question if <20)*
Are Fragments or schistocytes reported in blood film?	Y/N/Blood film not reported
If no fragments on admission blood film ask subsequent question:	
Please document date and time (sample received in laboratory) of first blood film to report fragments or schistocytes during this hospital admission.	DD/MM/YYYY 00:00 Or "No blood film reporting fragments or schistocytes during admission"
When was a diagnosis of TTP first objectively considered in the notes?	DD/MM/YYYY 00:00 (if recorded)
Date and time ADAMTS13 activity assay received in laboratory	DD/MM/YYYY 00:00 (electronic record) "Not sent at this hospital"
Clinical symptoms to suggest CNS involvement within 48 hours of hospital admission?	Y/N/Unknown
Troponin checked within 24 hours of hospital admission?	Y/N
Was troponin raised above laboratory upper limit of normal?	Y/N/"Not done at this hospital"
Treatment	
Was patient treated actively for TTP with intention to start plasma exchange?	Yes No – too unwell No – diagnosis of TTP not considered during hospital stay No – other (provide free text)

Date of first steroids (time if available)	DD/MM/YYYY 00:00 (provide option "steroids not given)
Was an FFP transfusion given prior to starting PEX/hospital transfer?	Y/N
Were platelets transfused?	Y/N – If Yes "Did patient have life threatening haemorrhage?" Y/N
▪ Date of first platelet transfusion	DD/MM/YYYY
Date of central line insertion (time if available)	DD/MM/YYYY 00:00 (provide option "not done at this hospital"
Was patient intubated prior to plasma exchange?	Yes/No/Intubated prior to arrival at this hospital/Unknown
Did patient commence plasma exchange at this hospital?	Y/N (if no provide reason)
▪ Ward where first plasma exchange administered	Renal unit/Haematology unit/ICU/Other/Unknown
▪ Date and time octaplas (or plasma) released from blood bank for first plasma exchange	DD/MM/YYYY 00:00 (electronic record)
Did patient receive rituximab at this hospital?	Y/N
▪ Date of first rituximab infusion	DD/MM/YYYY
Aftercare	
Was patient alive day +30 after initial admission?	Y/N – if No "days from admission to this hospital to death"/Unknown
Date discharged from hospital	DD/MM/YYYY or Died
Destination at discharge	Hospital transfer/Home/Rehab centre/Died/Other
From review of clinical notes what do you feel were the most important contributory factors for delay in starting PEX or hospital transfer? (Rank up to 3 options considered significant, with 1. being the most important factor. If there were none then leave blank)	• Uncertainty of diagnosis • Unable to get central line inserted promptly • Difficulty co-ordinating hospital transfer (If select this "Please describe issues" free text) • Difficulty co-ordinating local plasma exchange • Other (free text)
Was plasma exchange delayed while an ADAMTS13 level was awaited?	• Yes/No/Unknown

16.2 Appendix 2: Confirmation that this is not research

http://www.hra-decisiontools.org.uk/research



Result - NOT Research

Go straight to content.

MRC Medical Research Council

NHS Health Research Authority

Is my study research?

To print your result with title and IRAS Project ID please enter your details below:

Title of your research:

Flash-Mob TTP audit: Nationwide audit of treatment delays in patients presenting with acute TTP to UK hospitals

IRAS Project ID (if available):

You selected:

- **'No'** - Are the participants in your study randomised to different groups?
- **'No'** - Does your study protocol demand changing treatment/ patient care from accepted standards for any of the patients involved?
- **'No'** - Are your findings going to be generalisable?

Your study would NOT be considered Research by the NHS.

You may still need other approvals.

Researchers requiring further advice (e.g. those not confident with the outcome of this tool) should contact their R&D office or sponsor in the first instance, or the HRA to discuss your study. If contacting the HRA for advice, do this by sending an outline of the project (maximum one page), summarising its purpose, methodology, type of participant and planned location as well as a copy of this results page and a summary of the aspects of the decision(s) that you need further advice on to the HRA Queries Line at HRA.Queries@nhs.net.

For more information please visit the Defining Research table.

Follow this link to start again.

Print This Page

NOTE: If using Internet Explorer please use browser print function.

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16.3 Appendix 3: Regional audit leads contact details

Region	Lead	email
Central London	Zara Sayar Ferras Alwan	zara.sayar@nhs.net ferras.alwan@nhs.net
East Midlands	Emily Millen Harshita Goradia	emily.millen@nhs.net harshita.goradia@nuh.nhs.uk
East of England	Tom Bull	tombull@nhs.net
Greater Manchester	Luke Carter	lukecarter@nhs.net
Kent, Surrey and Sussex	James Clark Caroline Grist	james.clark@nhs.net carolinegrist@nhs.net
North East and N. Cumbria	Keir Pickard Alex Langridge	k.pickard2@nhs.net alexander.langridge@nhs.net
Northern Ireland	Claire Corrigan	claire.corrigan@belfasttrust.hscni.net
North Thames	Sophie Todd	sophie.todd2@nhs.net
North West Coast	Rebecca Shaw	r.shaw3@nhs.net
North West London	Chris Bailey	chrisbailey1@nhs.net
Scotland	Lyndsay McLeod-Kennedy	lyndsay.mcleod-kennedy1@nhs.net
South London	Andrew Doyle	andrew.doyle@gstt.nhs.uk
South West Peninsula	Rory McCulloch	rmcculloch1@nhs.net
South Yorkshire	Claire Mapplebeck	claire.mapplebeck@nhs.net
Thames Valley	Alex Rampotas	alexandros.rampotas@ouh.nhs.uk
Wales	Vicki Ware Astrid Etherington	victoria.ware@wales.nhs.uk astrid.etherington@wales.nhs.uk
West Midlands	Richard Buka	richard.buka@nhs.net
Wessex	Izabela James Udi Reddy	izabela.james@uhs.nhs.uk udaya.reddy2@nhs.net
West of England	Amy Knott	amy.knott@nhs.net
Yorkshire and Humber	Alexandra Pike	alexandra.pike@nhs.net

16.4: Appendix 4: Letter to Trust Audit Officer

24/09/2019

Dear Audit Officer,

Re: Flash-Mob TTP Audit

I am writing to ask if your Trust can participate in the Flash-Mob TTP Audit, led by HaemSTAR, a national network of trainees promoting research in non-malignant haematology. The Senior Investigator is Prof. Marie Scully at University College London and data management is co-ordinated by the University of Birmingham. The protocol is attached and key points are summarised in the discussion below.

This is a nationwide audit designed to assess early management of patients presenting with acute thrombotic thrombocytopenic purpura (TTP) to UK hospitals against the audit standard set out in the British Society of Haematology guideline (Scully et al, 2012). The audit outcomes aim to provide insights into acute TTP care that will help shape and improve future national care models.

The audit aims to open in over 40 sites across the UK, including both regional tertiary TTP centres and non-specialist centres. Most tertiary sites will contribute over 15 patients, and non-specialist centres will recruit 2 to 5 patients. Total recruitment target is 200 patients.

We recognise that TTP is a very rare disease and as such have taken great care to protect patient anonymity within the audit design. As only minimal patient demographics are recorded only local data contributors, who work at the centres where the patients were treated, will be able to identify patients. The data manager and management committee, who will have central access to data, will not be able to identify patients. Submitted data will be stored online through a secure and encrypted server running the Research Electronic Data Capture (REDCap) web application hosted by the University of Birmingham.

Patient outcomes will only be published/presented collectively and no individual patient will be identifiable within the results analysis. The performance of specific hospitals will not be disclosed within any public presentation of results. No third parties will have access to data.

The audit protocol has been independently reviewed by the Manager of Information Governance at University Hospitals Birmingham NHS Foundation Trust and the Caldicott Guardian at University Hospitals Plymouth NHS Trust and audit and data management plans have been reviewed by the Directors of Birmingham Surgical Trials Consortium, University of Birmingham. All are satisfied that the protocol is an audit and does not compromise patient anonymity. As such, a data sharing agreement between trusts is not necessary.

To ensure the perspective of patients was included the TTP Network, the largest UK charity for patients with TTP, were involved in audit design. Feedback was supportive of the audit's aims and no concerns regarding patient anonymity were raised.

We hope that these assurances are helpful and we hope that your site will be able to contribute data.

If you require any further information that may aid your decision process, I would be happy to be contacted directly. My email address is rmcculloch1@nhs.net. Thank you for considering this audit in your portfolio.

Yours sincerely,

Dr. Rory McCulloch
Lead Investigator & Vice chair of HaemSTAR
On behalf of the Management Committee for Flash-Mob TTP Audit