The DAShED (Diagnosis of Aortic Syndrome in the ED) Study Training

What is Acute Aortic Syndrome (AAS)?

- AAS is a group of potentially life-threatening diseases involving the aorta, the largest blood vessel in the body.
- AAS includes:
  - Aortic dissection
  - Aortic intramural haematoma
  - Penetrating aortic ulcer

Rationale for Trial

AAS affects approximately 4,000 people each year in the UK

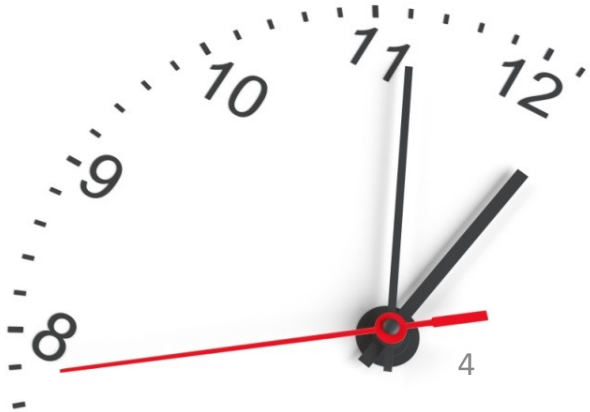
Chest pain (80%), back pain and abdominal pain are the most common presenting symptoms of AAS

These symptoms account for 2 million ED attendances per year in the UK due to other illnesses and disease

This creates a substantial diagnostic challenge

Rationale for Trial Continued

- Prognosis of AAS is best when patients are treated early.
- **Mortality increases 2% per hour of delay**
- The misdiagnosis rate during patients initial ED attendance is estimated between 1-3% to 1-7%. This leads to worse outcomes.



Diagnosing AAS

- Computed Tomography Angiography (CTA) has a high sensitivity for AAS.
- However, CTA over testing leads to diagnostic yield **as low as 2-3%.**
- Unrestricted use of CTA's incurs significant costs, has resource implications and leads to potentially avoidable exposure to ionising radiation.
- Chest x-ray, D-dimer and scoring systems are some tools clinicians use to help decide whether a patient needs a CTA.

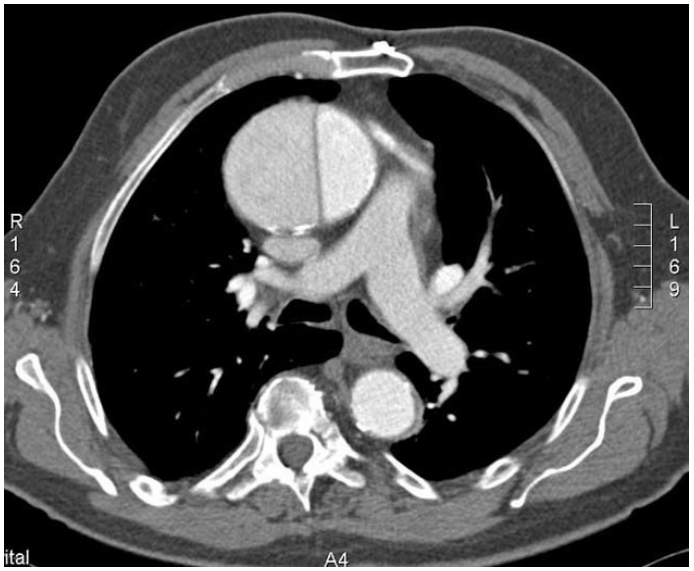


Image taken from Radiopedia: https://radiopaedia.org/articles/aortic-dissection?lang=gb

Clinical Decision Making Scoring System

ADD-RS

Canadian clinical practice guideline clinical decision aid

AORTAs score

Sheffield score

Trial Design

What? A multi-centre observational cohort study of people attending the ED with symptoms of Acute Aortic syndrome (AAS). It is a waived consent study

How? Prospective + retrospective data collection

When? 4 weeks recruitment across September – October 2022

Who? >5000 patients across 20 UK sites

Where? Recruitment location – Emergency Department

The study aims to collect data on patients presenting with possible AAS, to begin to evaluate the effectiveness of different diagnostic strategies, and how they impact the clinicians' decisions to use CTA scans. This will enable us to inform future research and guidelines.

Criteria

Inclusion criteria

- People presenting to ED with **ANY** symptoms of AAS
- Symptoms of AAS defined as: new-onset chest, back or abdominal pain, syncope or symptoms related to malperfusion.
- The clinician **does not** need to suspect AAS to enroll patient

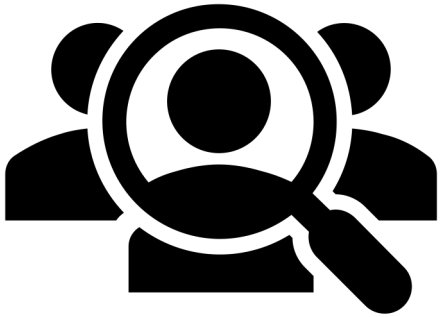
Exclusion criteria

- Patients presenting to ED with no symptoms of AAS

Trial Objectives

Primary

- To establish data characteristics of four clinical decision tools (ADD-RS, Canadian Clinical Practice Guideline, AORTAs score and Sheffield score) in patients presenting to the ED with any symptoms potentially attributable to AAS.



Trial Objectives

Secondary

- Patient characteristics
- Potential CTA rates with different clinical decision tools
- Patient enrolment rates at participating sites

Prospective Screening

We will prospectively identify people attending the ED with symptoms of AAS through a variety of methods including but not limited to:

- Reception staff and triage teams placing a focused paper Case Report Form (CRF) in the patient notes
- Local clinical staff advertising and recruitment campaigns
- Appointment of local champions
- Utilization of local TERN networks through the adoption of DAShED as a TERN Supported Project
- Use of medical students (where they are part of the direct clinical team) identifying potential patients and alerting the treating clinician

Prospective Data Collection

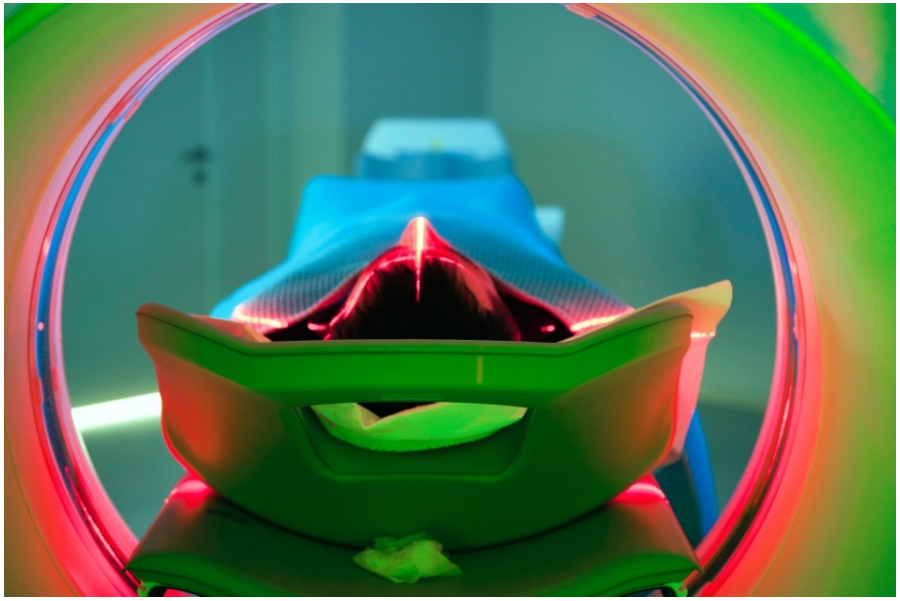
The CRF will include:

- Demographic data
- Information from history taking and examination.
- Any relevant imaging
- Suspected diagnosis from clinician

This can either be completed directly onto the eCRF or on a paper CRF and then later transferred to the eCRF by the local study team.

Retrospective Screening & Data Collection

- The local research team will perform daily searches of Radiology-ordering EPRs to identify all patients undergoing CTA in the ED.
- The local research team will perform daily searches on Trak for any patients who presented to ED that meet the inclusion criteria who may have been at presentation.



Waived consent strategy

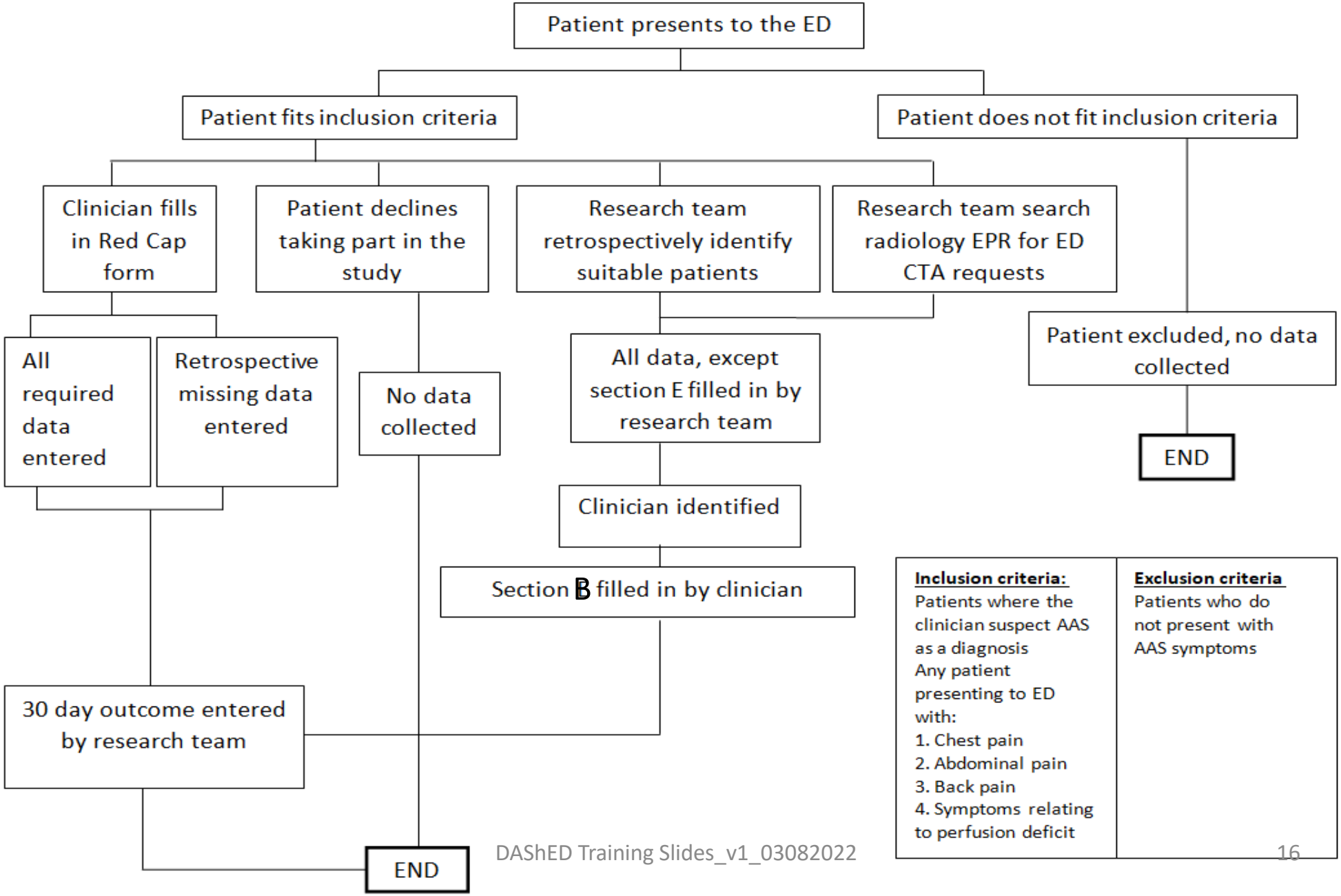
- We will be adopting a waived consent strategy.
- No personal information will be collected on the redcap database, so data will remain fully anonymised.
- All access to data before anonymisation will be undertaken by the direct care team.
- Patient information sheets (PIS) will be available to participants upon request.
- Details on withdrawing from the study will be on the PIS

Follow up

Patients enrolled will be followed up at 30 days by the clinical team using **routinely collected EPR data** to collect the following:

- Is the patient alive at 30-days?
- Has AAS been diagnosed?
- What is the patient's final hospital diagnosis?

Study Overview flow Chart



Endpoints (1)

Enrolment rate at each participating site
Proportion of patients in whom the ED clinician thinks AAS is a possible differential who have confirmed AAS
Proportion of patients in whom ED clinician considers AAS NOT a possible differential who had confirmed AAS
Number of AAS patients not enrolled due to lack of clinical/research support
CTA ordering and positivity rate

Endpoints (2)

Test characteristics of clinical acumen, ADD-RS score, AORTA score, Canadian guideline score and Sheffield AAS decision rule, and D-dimer (separately and in combination)
Median time from hospital presentation to imaging diagnosis and median time from symptom onset to hospital presentation (hours)
30-day mortality in proven AAS
Proportion of alternative diagnoses found on CTA and final hospital diagnosis
Identification of barriers to enrolment

Redcap database - Training

- QR code
- Link to website
- No patient-identifiable data will be inputted in Redcap, leave the local NHS Trust, or be viewed outside the clinical team.

https://redcap.cir.ed.ac.uk/surveys/

Redcap database - STUDY

- QR code
- Link to website
- No patient-identifiable data will be inputted in Redcap, leave the local NHS Trust, or be viewed outside the clinical team.

https://redcap.usher.ed.ac.uk/surveys/

Redcap database

09:53
◀ Camera
4G

Case Report Form

A A A

Please complete the DAShED Case Report Form, thanks.

Study Site

* must provide value

Please confirm the patient meets study Inclusion criteria i.e. Attended the ED with new-onset chest, back or abdominal pain, syncope, symptoms related to malperfusion or any other symptom of Acute Aortic Syndrome?

* must provide value

Yes

No

reset

SECTION A: Demographics

Recruiting ED Clinician name

* must provide value

Date and time of ED attendance

* must provide value

Now D-M-Y H:M

Symptom onset date and time (nearest hour)

Now D-M-Y H:M

Sex

* must provide value

Age

* must provide value

Patient initials only

* must provide value

Redcap database

SECTION B: ED clinician suspicion of AAS

Acute aortic syndrome/dissection a possible diagnosis according to treating clinician?

* must provide value

- Yes
- No
- Unknown

reset

ED clinician rating as to likelihood of AAS before confirmatory testing (from 0=not likely to 10=almost definitely; 99 if not available)

* must provide value

- 0
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10
- unknown

reset

Acute aortic syndrome/dissection the most likely diagnosis according to treating clinician?

- Yes
- No
- Unknown

reset

Suspicion for an alternative more likely diagnosis?

* must provide value

- Yes
- No
- Unknown

Redcap database

SECTION C: History of presenting episode

Chest pain?
* must provide value
- Yes
- No
- Unknown

reset

Back pain?
* must provide value
- Yes
- No
- Unknown

reset

Abdominal pain?
* must provide value
- Yes
- No
- Unknown

reset

Malperfusion (i.e. central nervous system, cardiac, mesenteric, limb)?
* must provide value
- Yes
- No
- Unknown

reset

Neurology: paraparesis, hemiparesis/acute confusion (can be transient)?
* must provide value
- Yes
- No
- Unknown

reset

Pain severe intensity or worst ever?
* must provide value
- Yes
- No
- Unknown

reset

Pain thunderclap/abrupt onset (including worst when awoke)?
* must provide value
- Yes
- No
- Unknown

reset

Pain tearing or ripping?
* must provide value
- Yes
- No
- Unknown

reset

Pain migrating or radiating?
* must provide value
- Yes
- No
- Unknown

reset

Pregnant?
- Yes
- No
- Unknown

reset

Recent significant trauma / high speed deceleration injury?
* must provide value
- Yes
- No
- Unknown

reset

Recent recreational drugs including cocaine, crack or other sympathomimetics?
* must provide value
- Yes
- No
- Unknown

reset

Redcap database

SECTION D: Past Medical History

Known Marfan syndrome/Connective tissue disease / Ehler Danlos / Giant cell arteritis?

* must provide value

Yes

No

Unknown

reset

Known or family history of aortic dissection/syndrome, aortic disease/Coarcation?

* must provide value

Yes

No

Unknown

reset

Known Aortic valve disease (Bicuspid /Dilated aortic root)?

* must provide value

Yes

No

Unknown

reset

Recent aortic manipulation / Instrumentation (within last year)?

* must provide value

Yes

No

Unknown

reset

Known Thoracic Aortic Aneurysm?

* must provide value

Yes

No

Unknown

reset

Known Abdominal Aortic Aneurysm?

* must provide value

Yes

No

Unknown

reset

Redcap database

SECTION E: Physical Examination findings

Pulse deficit (i.e. absence of one or more upper limb or femoral pulse)?

* must provide value

Yes

No

Unknown

reset

Systolic BP differential (>20mHg difference in SBP between arms at anytime during ED stay)?

* must provide value

Yes

No

Unknown

reset

Focal Neurological deficit?

* must provide value

Yes

No

Unknown

reset

New Aortic Regurgitation murmur (i.e. not previously documented)?

* must provide value

Yes

No

Unknown

reset

Hypotension (SBP < 90mmHg) or shock or pericardial effusion?

* must provide value

Yes

No

Unknown

reset

Hypertension (SBP >140 and DBP> 90) documented at any point during ED stay

* must provide value

Yes

No

Unknown

reset

Redcap database

SECTION F: Investigations

D-Dimer performed?

* must provide value

Yes

No

Unknown

reset

CXR performed in ED?

* must provide value

Yes

No

Unknown

reset

CT chest performed?

* must provide value

Yes

No

Unknown

reset

Camera 16:39 72%

redcap.cir.ed.ac.uk

Unknown

reset

SECTION G: Follow up to be completed at 30 days

Confirmed Acute Aortic Syndrome?

* must provide value

Yes

No

Unknown

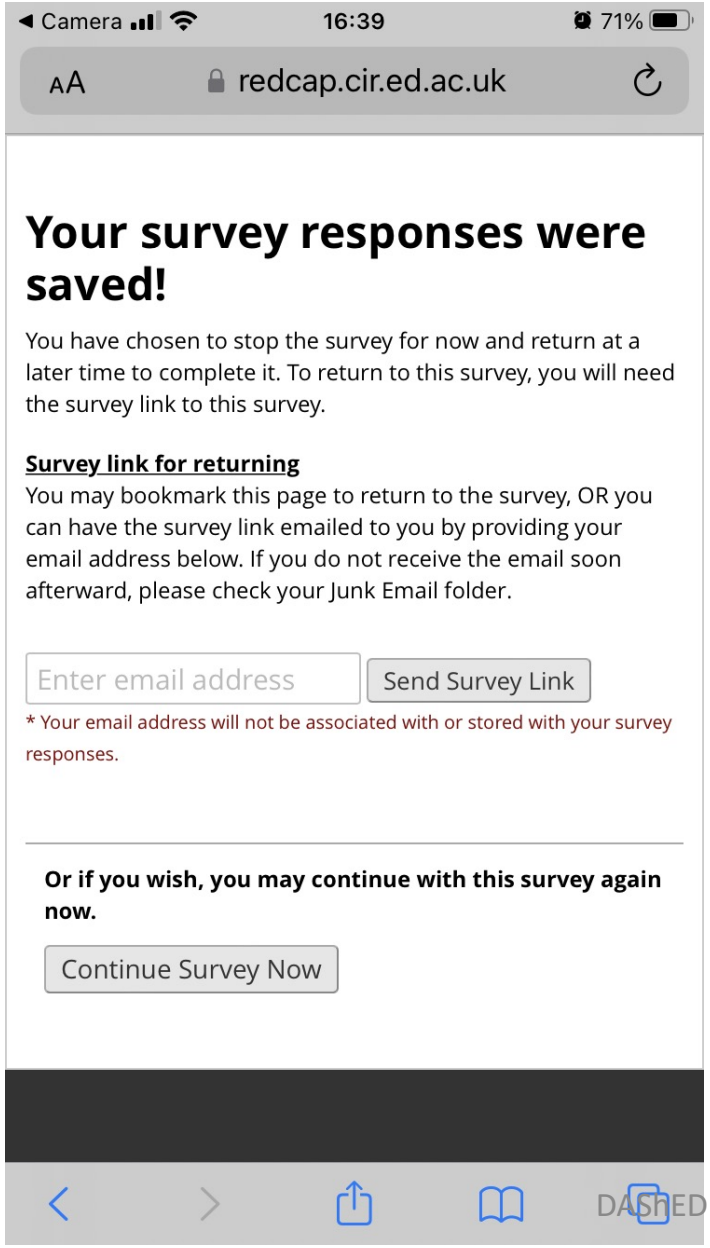
reset

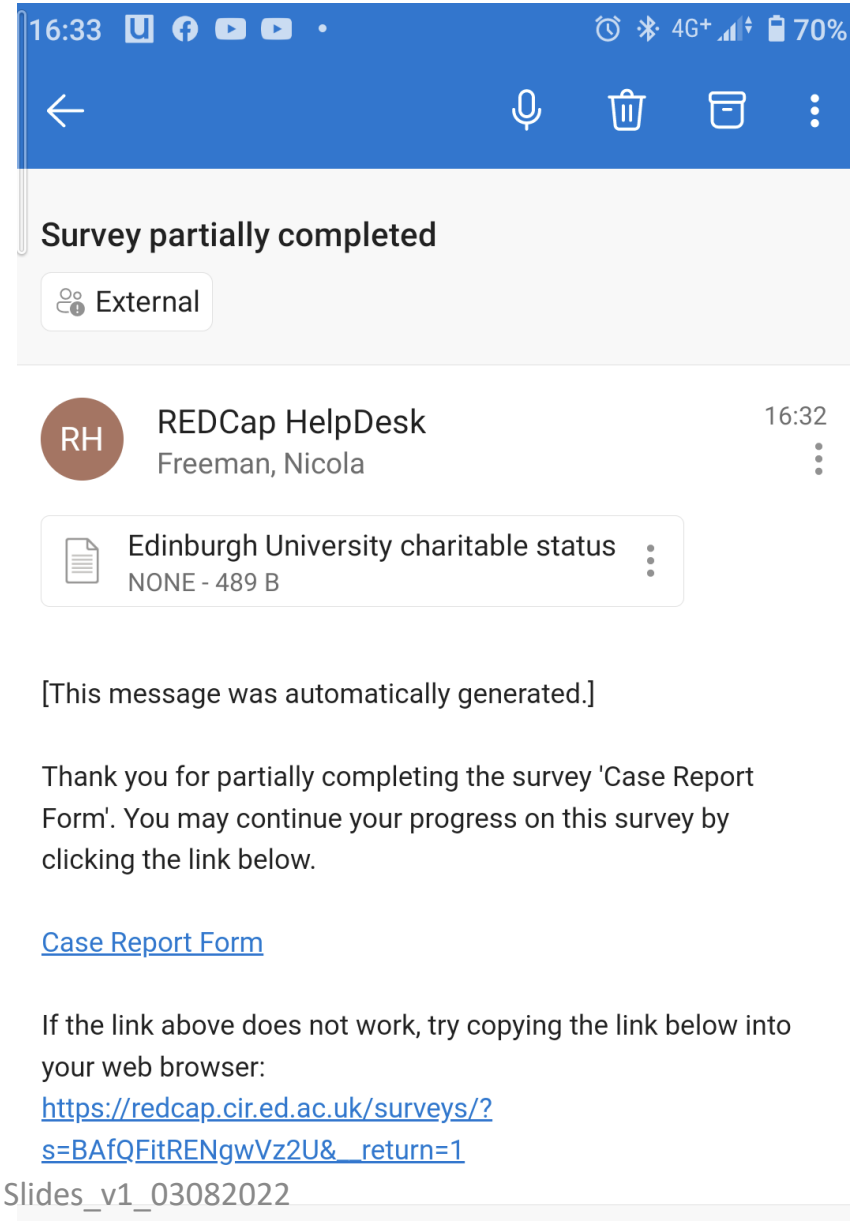
Final hospital discharge diagnosis (99 if unknown)

Submit

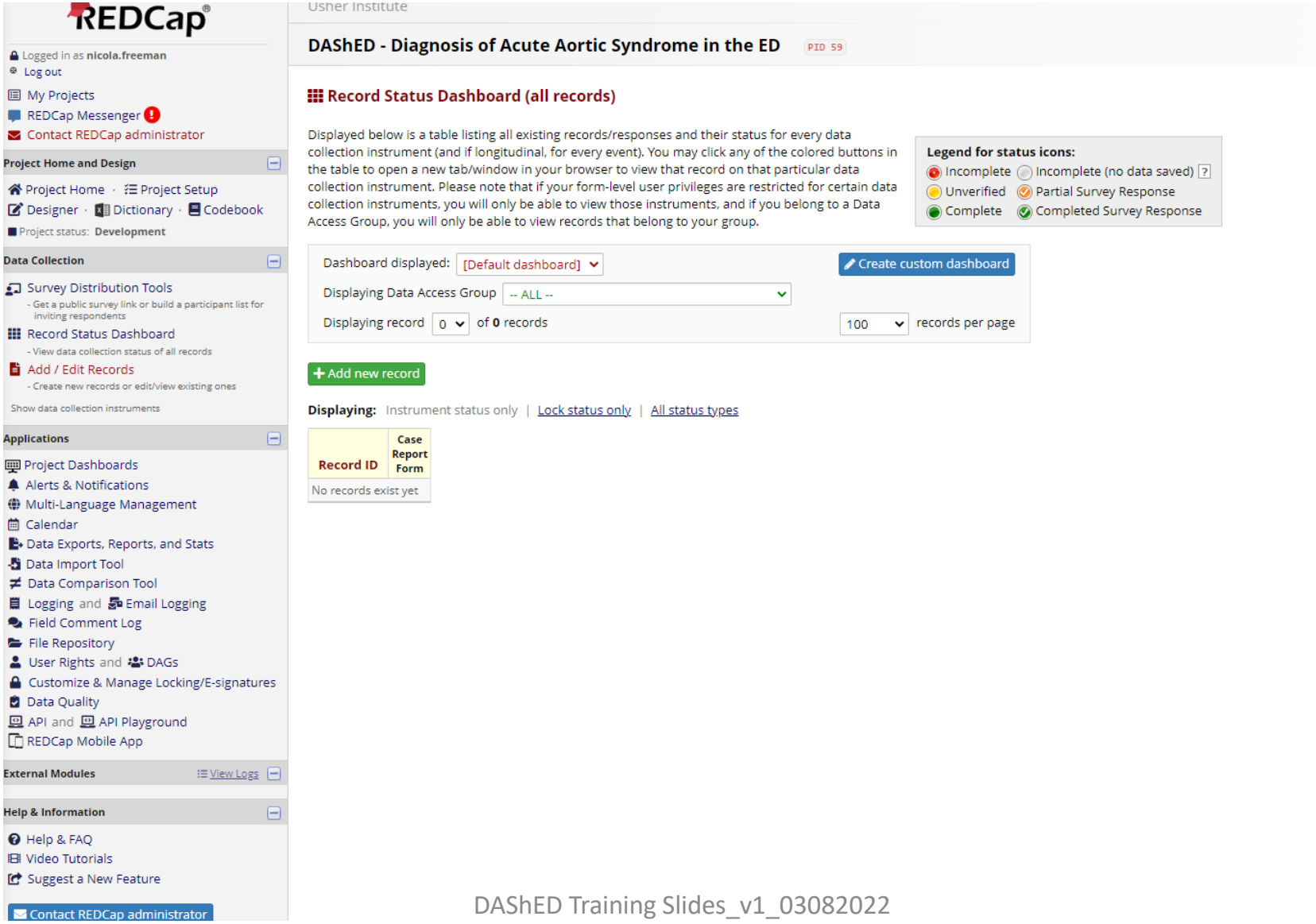
Save & Return Later

Redcap database





Redcap database



DAShED Study

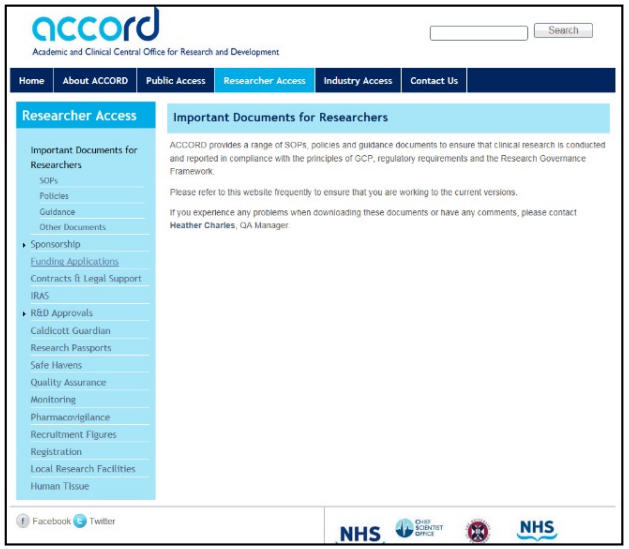
Sponsor SOP Training

[Based on sponsor template slides V5.0 02Dec2020]

ACCORD Training Resources

All ACCORD training material (SOPs, Forms, Policies, Guidance etc) can be found on *http://www.accord.scot*

Researcher Access → Important Documents for Researchers → SOPs/Policies/Guidance /Training



PI Responsibilities

- PI – is responsible for the conduct of the study at a specific site. The PI is responsible for the team at the site and must provide appropriate medical oversight.
- Please advise us if you wish to change PI at any point in the study.

Some PI tasks may be delegated to appropriately trained staff using the delegation log.

Delegation log - SOP CR007

- Tasks must be delegated appropriately for study role – study role should be noted rather than clinical role
- Staff members must be signed off by the PI before undertaking tasks. PI must only complete sign off and date boxes once staff member added to log – cannot pre-fill boxes
- PI is responsible for the overall conduct of ALL study tasks so only need complete the PI section at the top.
- Start date entered must be before staff member started conducting tasks
- PI on the log must have current CV and GCP certificate filed in eISF
- Ensure end dates are added for staff members who leave during study
- PI to sign off once site is closed

Site Signature & Delegation Log

Study Title	Sponsor/EudraCT Number	Site location
STUDY1	20xx-xxxxxx-xx	Royal Infirmary of Edinburgh

PI Name	PI Signature	PI Initials	Date From	Date To
JOHN SMITH	John Smith	J.S	12 AUG 2020	

Print name	Study role*	Signature	Initials	**Tasks Delegated	From	To	PI Signature	PI Date
GORDON ADAMS	RESEARCH NURSE	Gordon Adams	GA	1, 2, 4, 7, 8, 9, 10, 11, 12, 16, 17, 22	12 AUG 2020		John Smith	20 AUG 2020
JENNIFER PATEL	STUDY DOCTOR	Jennifer Patel	JP	1, 2, 3, 4, 5, 6, 14, 14, 18, 21	20 SEP 2020		John Smith	20 SEP 2020
ANGELA BELL	LEAD PHARMACIST	Angela Bell	AB	19, 20	30 OCT 2020		John Smith	30 OCT 2020

*Study roles can include but not limited to: Principal Investigator, Co-Investigator, Trial manager, Research Nurse, Lead Pharmacist, trial coordinator

PI Signature: (Sign once site closed): _____ Date: _____

** Tasks delegated *(change to study specific as necessary – tasks in **Bold** should not be removed unless otherwise agreed with Senior Clinical Trial Monitor or designee)*		
1. Obtain informed consent	**10. Completion of final CRF signature**	**19. IMP dispensing**
2. Obtain medical history	11. Data QC check	**20. IMP accountability**
3. Perform physical examination (clinician only)	**12. Data query completion**	21. IMP Administration
4. Perform inclusion and exclusion assessments	**13. Assessment of AEs (clinician only)**	**22. Set up and maintenance of ISF**
5. Confirm eligibility (clinician only)	**14. Assessment of SAEs (clinician only)**	23. *Other (please list)*
6. Medical oversight of participant care (clinician only)	**15. Pharmacovigilance reporting to Sponsor**	24.
7. Collection of study specific samples	**16. Record deviations/violations**	25.
8. Processing of study specific samples	**17. Report deviations/violations to Sponsor**	26.
9. Completion of CRFs	**18. IMP prescribing** (clinician only)	27.

Page ___ of ___
CR007-T12 v3.0

Training Log - SOP CR007

- All study specific training should be documented on the training log.
- All study team members listed on delegation log must have evidence of protocol and SOP training.
- The PI is responsible for ensuring that the research team are fully informed of the protocol and study specific procedures
- A new protocol training log should be completed following implementation of a protocol amendment

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Study Specific Training Record

Study Title	Site Location	Study Ref #	Principal Investigator
STUDY1	Royal Infirmary of Edinburgh	XXXX/XXXX	JOHN SMITH

Training title	Training provider	Date	Name of attendee	Signature
SIV: Protocol v1.0 01AUG2020 and Sponsor SOPs	John Smith (PI) and Lisa Jones (Monitor)	12 Aug 2020	John Smith	John Smith
SIV: Protocol v1.0 01AUG2020 and Sponsor SOPs	John Smith (PI) and Lisa Jones (Monitor)	12 Aug 2020	Gordon Adams	Gordon Adams

Study Specific Training Record

Study Title	Site Location	Study Ref #	Principal Investigator
STUDY1	Royal Infirmary of Edinburgh	XXXX/XXXX	JOHN SMITH

Training title	Training provider	Date	Name of attendee	Signature
SIV Training Slides: Protocol v1.0 01AUG2020	Slides sent via email	20 Sep 2020	Jennifer Patel	Jennifer Patel
SIV Training Slides: Protocol v1.0 01AUG2020	Slides sent via email	30 Oct 2020	Angela Bell	Angela Bell

Recruitment Reporting

- It's important to report your recruits on the CPMS database each month
- Contact your R&D team or emailed DAShED study team if you are unsure how to do this
- Support funding to your R&D relies on recruitment records and project performance therefore it is important accurate recruitment figures are reported monthly
- The CI or delegate is responsible for checking the recruitment figures uploaded onto CPMS are correct and up to date.

Trial Data - SOP CR004

- Study data will be recorded on source documents and eCRF by PI or delegate
- **Source data** - all information necessary for the reconstruction and evaluation of the trial, in their original record or certified copy of original record.
- **Source document -** the original record where source data are recorded for the first time
- Study data should be recorded directly into the eCRF where possible

Waived Consent Process

- We will be adopting a waived consent strategy.
- No personal information will be collected, and data will remain fully anonymised.
- All access to data before anonymisation will be undertaken by the direct care team.
- Patient information sheets (PIS) will be available to participants upon request.
- Details on withdrawing from the study will be on the PIS

Suspected Research Misconduct – SOP CR014

Unacceptable conduct including fabrication, falsification, plagiarism, misrepresentation, breach of duty of care and improper dealing with allegations of misconduct*

- If you suspect a case of misconduct contact ACCORD in person, via telephone or email QA@accord.scot
  - Do not inform the individual suspected of misconduct
- ACCORD QA will investigate and escalate as required
  - Minor instances of misconduct may be resolved informally

Study Closure – SOP CR009

- End of Study: last patient last visit
- Closeout visits will be carried out remotely
- PI to ensure local R&D are informed of end of study
- Duration of archiving – All study documentation will be kept for a minimum of *3* years from the protocol defined end of study point
- All close out actions must be completed before archiving can start

More information & Contacts

- EMERGE/DAShED study team
  - **Email: dashedstudy@gmail.com**
- ACCORD website www.accord.scot
  - All ACCORD SOPs listed in presentation available:
    - CR003 Suspected Serious Breaches
    - CR004 Recording and Reporting Study Data
    - CR007 Study documents
    - CR014 Suspected Research Misconduct
- ACCORD QA address:
  - qa@accord.scot

Thank you!