ISRCTN16665769 https://doi.org/10.1186/ISRCTN16665769

The role of cerebral embolic protection in preventing strokes and improving other health outcomes in patients receiving a replacement heart valve

Submission date
26/02/2020

Recruitment status
No longer recruiting

Registration date
23/06/2020

Overall study status
Ongoing

Last Edited
16/04/2025

Condition category
Circulatory System

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Transcatheter Aortic Valve Implementation (TAVI) is a standard treatment for Aortic Stenosis (AS), a condition where blood flow out of the heart is restricted by narrowing of the aortic valve. In a TAVI procedure, the aortic valve is replaced by placing a new valve delivered to the heart through a tube (catheter) placed in an artery. One risk associated with TAVI is stroke. During the TAVI procedure, debris (made up of parts of the diseased aortic valve and the surrounding tissue) can be released into the bloodstream. Most strokes occurring at the time of TAVI are due to this debris blocking part of the blood supply in the brain. Devices have been developed that capture some of the debris released and stop this reaching the brain, these are called Cerebral Embolic Protection (CEP) devices.
The purpose of this study is to assess whether using a Cerebral Embolic Protection (CEP) device during Transcatheter Aortic Valve Replacement (TAVI) can reduce the chance of a patient having a stroke. The study will also determine whether it improves the quality of life for patients and how the use of CEP impacts the NHS in terms of cost and service use.

Who can participate?
Patients aged 18 years or above, with aortic stenosis planned for treatment by TAVI.

What does the study involve?
In this study, patients who agree to take part (this means given written consent) receiving TAVI will be randomly assigned to receive CEP during TAVI or to the current standard of care without CEP. Potential participants will be approached prior to their TAVI procedure to discuss the trial.

What are the possible benefits and risks of participating?
We have no evidence that there are significant risks associated with using the CEP device. There are small risks associated with putting a device within an artery. These risks are less than 1% and include bleeding, infection or damage to the artery. The additional risks from the device are small.

The risks of a TAVI procedure itself include a 2-3% risk of stroke or death and a 10% risk of bleeding. You will be attended to and cared for by the standard care and clinical team throughout the procedure and your recovery.
If you take part in this study you will have a heart valve replacement procedure as part of your routine care. For some participants the procedure will be extended by about 10 minutes to place a cerebral embolic protection device. This time and procedure are extra to what you would have if you did not take part.
There is a small chance that patients in the TAVI with CEP arm will have to receive an small additional dose of X-ray contrast associated with the use of the CEP device. This could cause an injury to the kidney, however there are no reported cases of this happening to date.
The operation you are having uses ionising radiation to form images of your body. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. Dose levels are monitored carefully during your intervention.
We are all at risk of developing cancer during our lifetime. The normal risk is that this will happen to about 50% of people at some point in their life. Having this procedure might increase the chances of this happening to you from 50% to 50.13%. If you are in the group receiving CEP, the time for this radiation would be extended by 10 minutes.

Where is the study run from?
This study is run by University of Oxford (UK) in collaboration with the London School of Hygiene and Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
April 2020 to October 2025

Who is funding the study?
1. British Heart Foundation (UK)
2. Boston Scientific Corporation (USA)

Who is the main contact?
Zahra Jamal, bhfprotect-tavi@LSHTM.ac.uk

Study website
https://www.lshtm.ac.uk/research/centres-projects-groups/bhfprotect-tavi

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
276396

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
PID14772-SP001-AC001, IRAS 276396

Study information

Scientific Title
British Heart Foundation Randomised Trial of Routine Cerebral Embolic Protection in Transcatheter Aortic Valve Implantation

Acronym
BHF PROTECT-TAVI

Study objectives
Does the routine use of the Sentinel Cerebral Embolic Protection device during TAVI reduce stroke incidence?

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 23/04/2020, Wales Research Ethics Committee 5 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 (0)7970 422139; wales.rec5@wales.nhs.uk), ref: 20/WA/0121

Study design
Prospective multicentre randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
https://www.lshtm.ac.uk/research/centres-projects-groups/bhfprotect-tavi#resources

Health condition(s) or problem(s) studied
Aortic stenosis

Interventions
Current interventions as of 04/10/2024:

The study is an RCT evaluating use of the cerebral embolic protection device (Sentinel, Boston Scientific) in participants with aortic valve stenosis planned for treatment by Transcatheter Aortic Valve Implantation (TAVI).

Participants will be randomised 1:1 into a treatment cohort using the cerebral embolic protection device (Sentinel, Boston Scientific) or a control cohort with no cerebral protection system. Enrolled participants will be followed through 72 hours (or hospital discharge), whichever comes first, and assessed for the primary outcome.

Consented patients will be randomised at a 1:1 ratio to either the control or intervention arm before their TAVI procedure. This will be done using a secure online randomisation service.

The intervention group will have TAVI performed with CEP. The Claret Sentinel dual-filter device (Boston Scientific, MA, USA) is a single use, embolic protection catheter inserted into the right radial or brachial artery. This is the only device currently approved for clinical use in both Europe and the USA. The device employs two filters (nitinol frames with 140-micron pores polyurethane film), one delivered to the brachiocephalic artery (Proximal Filter), and one to the left common carotid artery (Distal Filter) before TAVI. Following the TAVI procedure the system is removed.

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Previous interventions:

The study is an RCT evaluating use of the cerebral embolic protection device (Sentinel, Boston Scientific) in participants with aortic valve stenosis planned for treatment by Transcatheter Aortic Valve Implantation (TAVI).

Participants will be randomised 1:1 into a treatment cohort using the cerebral embolic protection device (Sentinel, Boston Scientific) or a control cohort with no cerebral protection system. Enrolled participants will be followed through 72 hours (or hospital discharge), whichever comes first, and assessed for the primary outcome.

Consented patients will be randomised at a 1:1 ratio to either the control or intervention arm at the time of the their TAVI procedure. This will be done using a secure online randomisation service.

The intervention group will have TAVI performed with CEP. The Claret Sentinel dual-filter device (Boston Scientific, MA, USA) is a single use, embolic protection catheter inserted into the right radial or brachial artery. This is the only device currently approved for clinical use in both Europe and the USA. The device employs two filters (nitinol frames with 140-micron pores polyurethane film), one delivered to the brachiocephalic artery (Proximal Filter), and one to the left common carotid artery (Distal Filter) before TAVI. Following the TAVI procedure the system is removed.

Intervention Type
Device

Phase
Phase III

Drug/device/biological/vaccine name(s)
Cerebral embolic protection device (Sentinel, Boston Scientific)

Primary outcome measure
Current primary outcome measure as of 20/02/2025:

The incidence of stroke at 72 hours post-TAVI, or hospital discharge (if sooner). Events will be validated by an independent clinical events committee blinded to trial treatment.

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Previous primary outcome measure as of 04/11/2021:

The incidence of stroke at 72 hours post-TAVI, or hospital discharge (if sooner). Events will be assessed by the local stroke team and validated by an independent clinical events committee blinded to trial treatment.

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Previous primary outcome measure:

The incidence of all stroke within 72 hours (or hospital discharge) of the TAVI procedure, measured using patient records

Secondary outcome measures
Current secondary outcome measures as of 04/10/2024:

1.Combined incidence of all-cause mortality or non-fatal stroke at 72 hours post-TAVI or hospital discharge (if sooner)
2. Combined incidence of all-cause mortality, non-fatal stroke or transient ischaemic attack at 72 hours post-TAVI or hospital discharge (if sooner).
3. Incidence of all-cause mortality at 72 hours post-TAVI or hospital discharge (if sooner)
4. Win ratio for all-cause mortality, disabling stroke and non-disabling stroke at 72 hours post-TAVI, or hospital discharge (if sooner)
5.Incidence of all-cause mortality at 12 months post-TAVI.
6. Incidence of all-cause mortality up to the end of the trial. This will use trial data up to 12 months, and centrally held NHS data from 12 months to the end of the trial
7. Incidence of stroke as defined by centrally held NHS data between 72 hours post-TAVI or hospital discharge (if sooner) and 30-days post-TAVI.
8. Incidence of stroke as defined by centrally held NHS data between 30-days post-TAVI and the end of the trial.
9. Stroke Severity: Assessed using the National Institutes of Health Stroke Scale (NIHSS) in participants who have had a stroke within 72-hours post-TAVI or hospital discharge (if sooner)
10. Disability Outcome Assessed using the Simple Modified Rankin Scale questionnaire (smRSq) up to 12 months post-TAVI in participants who have had a stroke within 72-hours post-TAVI or

hospital discharge (if sooner)
11. Cognitive Outcome Assessed using the standardised Montreal Cognitive Assessment (MoCA) up to 12-months post-TAVI.
12. Vascular access site related complications (VARC-2 criteria) at 72-hours post-TAVI or hospital discharge (if sooner) and between 6-8 weeks post-TAVI
13. Cost-effectiveness analysis at 12 months

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Previous secondary outcome measures as of 05/01/2024:

1. Combined incidence of all-cause mortality or non-fatal stroke at 72 hours post-TAVI, or hospital discharge (if sooner)
2. Combined incidence of all-cause mortality, non-fatal stroke and transient ischaemic attack at 72 hours post-TAVI or hospital discharge (if sooner)
3. Incidence of all-cause mortality at 72 hours and 12 months post-TAVI
4. Incidence of stroke as defined by centrally held NHS data between 72 hours post-TAVI (or discharge from hospital, if sooner) and 30-days post-TAVI
5. Incidence of stroke as defined by centrally held NHS data between 30-days post-TAVI and the end of the study
6. Stroke severity assessment in participants who have had a stroke within 72-hours post-TAVI or hospital discharge (if sooner) measured using NIHSS
7. Cognitive outcomes measured using the Montreal Cognitive Assessment up to 12 months post-TAVI
8. Disability outcomes in participants who have had a stroke up to 72 hours post-TAVI or discharge if sooner measured using simple modified Rankin Scale questionnaire up to 12 months post-TAVI
9. Vascular access site and access related complications according to standard criteria defined by the Valve Academic Research Consortium (VARC-2) at 72-hours post-TAVI or hospital discharge (if sooner) and between 6-8 weeks post-TAVI
10. Cost-effectiveness analysis using the EQ-5D-5L and data on resource utilisation at 12 months post-TAVI

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Previous secondary outcome measures as of 29/11/2022:

1. Combined incidence of all-cause mortality or non-fatal stroke at 72 hours post-TAVI, or hospital discharge (if sooner)
2. Incidence of all-cause mortality at 72 hours and 12 months post-TAVI
3. Incidence of stroke as defined by centrally held NHS data between 72 hours post-TAVI (or discharge from hospital, if sooner) and 30-days post-TAVI
4. Incidence of stroke as defined by centrally held NHS data between 30-days post-TAVI and the end of the study
5. Stroke severity assessment in participants who have had a stroke within 72-hours post-TAVI or hospital discharge (if sooner) measured using NIHSS
5. Cognitive outcomes measured using the Montreal Cognitive Assessment up to 12 months post-TAVI
6. Disability outcomes in participants who have had a stroke up to 72 hours post-TAVI or discharge if sooner measured using simple modified Rankin Scale questionnaire up to 12 months post-TAVI
7. Vascular access site and access related complications according to standard criteria defined by

the Valve Academic Research Consortium (VARC-2) at 72-hours post-TAVI or hospital discharge (if sooner) and between 6-8 weeks post-TAVI
8. Cost-effectiveness analysis using the EQ-5D-5L and data on resource utilisation at 12 months post-TAVI

Previous secondary outcome measures as of 04/11/2021:

1. Combined incidence of all-cause mortality or non-fatal stroke at 72 hours post-TAVI, or hospital discharge (if sooner)
2. Incidence of all-cause mortality at 72 hours and 12 months post-TAVI
3. Incidence of stroke as defined by centrally held NHS data between 72 hours post-TAVI (or discharge from hospital, if sooner) and 30-days post-TAVI
4. Incidence of stroke as defined by centrally held NHS data between 30-days post-TAVI and the end of the study
5. Cognitive/disability outcomes measured using the Montreal Cognitive Assessment and simple modified Rankin Scale questionnaire at 72-hours post-TAVI or at hospital discharge (if sooner), and up to 12 months post-TAVI
6. Vascular access site and access related complications according to standard criteria defined by the Valve Academic Research Consortium (VARC-2) at 72-hours post-TAVI or hospital discharge (if sooner) and between 6-8 weeks post-TAVI
7. Cost-effectiveness analysis using the EQ-5D-5L and data on resource utilisation at 12 months post-TAVI

Previous secondary outcome measures:

Measured using patient records:
1. Combined incidence of all-cause mortality and stroke up to 12 months
2. Incidence of all-cause mortality up to 12 months
3. Cognitive outcomes up to 12 months
4. Vascular access site injury between 6-8 weeks post-TAVI
5. Acute kidney injury between 6-8 weeks post-TAVI
6. Cost-effectiveness analysis

Overall study start date
01/04/2020

Completion date
09/10/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 04/11/2021:
1. Participant is willing and able to give informed consent for participation in the trial
2. Aged 18 years or above
3. Considered to be candidates for TAVI by the clinical team (via any access route where CEP may be used)

4. Participant is suitable for treatment with the cerebral embolic protection device in the opinion of the treating physician

Previous inclusion criteria:
1. Willing and able to give informed consent for participation in the trial.
2. Aged 18 years or above
3. Diagnosed with aortic stenosis (including bioprosthetic valve dysfunction)
4. Planned transfemoral TAVI

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
9,712

Total final enrolment
7635

Key exclusion criteria
Current exclusion criteria as of 04/11/2021:

No specific exclusion criteria.
Participants involved in observational studies will be eligible for this study. As this is an all-comer design, current or previous participation in other ongoing randomised trials will not be disqualifying for recruitment to this study unless treatment is expected to impact the effect of using a CEP device on stroke.

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Previous exclusion criteria:

1. Anatomically unsuitable for treatment with the cerebral embolic protection device in the opinion of the treating physician
2. Clinical contra-indications to the use of the CEP device in the opinion of the treating physician

Date of first enrolment
29/10/2020

Date of final enrolment
09/10/2024

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
John Radcliffe Hopsital
Oxford University Hospitals NHS Trust
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Leeds General Infirmary
Great George Street
Leeds
United Kingdom
LS1 3EX

Study participating centre
Royal Sussex County Hospital
Eastern Road
Brighton
United Kingdom
BN2 5BE

Study participating centre
New Cross Hospital Royal Wolverhampton
Wolverhampton Road
Heath Town
Wolverhampton
United Kingdom
WV10 0QP

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Morriston Hospital
Heol Maes Eglwys
Cwmrhydyceirw
Swansea
United Kingdom
SA6 6NL

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Crescent
Old Dalkeith Road
Edinburgh
Lothian
United Kingdom
EH16 4SA

Study participating centre
St. Bartholomews Hospital
West Smithfield
London
United Kingdom
EC1A 7BE

Study participating centre
Kings College Hospital
Mapother House
De Crespigny Park
Denmark Hill
London
United Kingdom
SE5 8AB

Study participating centre
Royal Victoria Hospital
274 Grosvenor Road
Belfast
United Kingdom
BT12 6BA

Study participating centre
Guy's and St Thomas' NHS Foundation Trust
St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
Basildon and Thurrock University Hospitals NHS Foundation Trust
Basildon Hospital
Nethermayne
Basildon
United Kingdom
SS16 5NL

Study participating centre
Liverpool Heart & Chest Hospital
Broadgreen Hospital
Thomas Drive
Liverpool
United Kingdom
L14 3PE

Study participating centre
Derriford Hospital
Derriford Road
Crownhill
Plymouth
United Kingdom
PL6 8DH

Study participating centre

Southampton General Hospital
University of Southampton and University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Golden Jubilee National Hospital
Agamemnon Street
Clydebank
United Kingdom
G81 4DY

Study participating centre
Royal Papworth Hospital
Papworth Road
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0AY

Study participating centre
St Georges Hospital
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
Victoria Hospital (blackpool)
Whinney Heys Road
Blackpool
United Kingdom
FY3 8NR

Study participating centre
Bristol Heart Institute
Lower Maudlin Street

Bristol
United Kingdom
BS1 2LX

Study participating centre
Nottingham City Hospital NHS Trust
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Hammersmith Hospitals NHS Trust
Hammersmith Hospital
Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
Freeman Road Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9LT

Study participating centre
Castle Hill Hospital
Castle Road
Cottingham
United Kingdom
HU16 5JX

Study participating centre
The James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Sheffield Teaching Hospitals NHS Foundation Trust
Northern General Hospital
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
United Kingdom
AB25 2ZN

Study participating centre
Royal Stoke University Hospital
Newcastle Road
Stoke-on-trent
United Kingdom
ST4 6QG

Study participating centre
University Hospitals Coventry and Warwickshire NHS Trust
Walsgrave General Hospital
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
Cleveland Clinic
33 Grosvenor Place
London
United Kingdom
SW1X 7HY

Sponsor information

Organisation
University of Oxford

Sponsor details
Clinical Trials and Research Governance
Joint Research Office
1st floor, Boundary Brook House
Churchill Drive
Headington
Oxford
England
United Kingdom
OX3 7GB
+44 (0)1865 616480
ctrg@admin.ox.ac.uk

Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Funder Name
Boston Scientific Corporation

Alternative Name(s)
Boston Scientific, Boston Scientific Corp., BSC

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in major international scientific journals and present them at academic conferences. Lay results for patients will be available upon request through our trial website and via their local hospital.

Intention to publish date
31/07/2026

Individual participant data (IPD) sharing plan
The current data sharing plans for this study are unknown and will be available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v1.0	16/03/2020	23/06/2020	No	Yes
Protocol file	version 4.0	17/10/2022	29/11/2022	No	No
Participant information sheet	version 7	29/07/2024	04/10/2024	No	Yes
Protocol file	version 6	29/07/2024	04/10/2024	No	No
Other files	Communication from the BHF PROTECT-TAVI Trial Steering Committee	25/10/2024	28/10/2024	No	No
Protocol (other)			16/04/2025	Yes	No
Results article		30/03/2025	16/04/2025	Yes	No
Statistical Analysis Plan			16/04/2025	Yes	No