STAR Study

ShorT stay Aneurysm Repair (STAR): A 23-hour endovascular abdominal aortic aneurysm repair pathway with evaluation of eligibility, uptake, viability, acceptability, safety and cost.

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Protocol authorised by:

Name & Role	**Date**	**Signature**
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This protocol describes the STAR study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the UK Policy Framework for Health and Social Care Research. It will be conducted in compliance with the protocol, the Data Protection Act, and other regulatory requirements as appropriate.

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GLOSSARY OF ABBREVIATIONS

AAA	Abdominal aortic aneurysm
AE	Adverse Event
AneurysmDQoL	Aneurysm-Dependent Quality of Life measure
AneurysmSRQ	Aneurysm Symptom Rating Questionnaire
AneurysmTSQ	Aneurysm Treatment Satisfaction Questionnaire
CHP	Centre for Health Policy
COVID-19	Coronavirus Disease of 2019
EVAR	Endovascular aneurysm repair
GIRFT	Get It Right First Time
GP	General Practitioner
HAP	Hospital Acquired Pneumonia
HDU	High Dependency Unit
ICMJE	International Committee of Medical Journal Editors
ITU	Intensive Care unit
LOT-R	Life Orientation Test – Revised
MDT	Multidisciplinary team meeting
MET	Metabolic equivalents
MI	Myocardial Infarction
NIHR	National Institute for Health Research
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NVR	National Vascular Registry
POPS	Proactive care for Older Patient undergoing Surgery
PROMS	Patient Reported Outcome Measures
PSSRU	Unit costs for health and social care
STAR	ShorT stay Aneurysm Repair (detailed in this protocol)
UTI	Urinary Tract Infection

KEYWORDS

Abdominal aortic aneurysm; Day case; Endovascular aneurysm repair; Short stay.

STUDY SUMMARY

TITLE ShorT stay Aneurysm Repair (STAR): A 23-hour endovascular abdominal aortic aneurysm repair pathway with evaluation of eligibility, uptake, viability, acceptability, safety and cost.

DESIGN A prospective observational cohort study to assess the eligibility, uptake, viability, acceptability, safety and cost of a ShorT stay (23-hour) Aneurysm Repair (STAR) pathway. Outcomes will be collected up to 1 year.

AIMS This study aims to build on previous experience and background studies to formally assess a ShorT stay Aneurysm Repair (STAR) pathway accommodating patient, organizational, community, and social needs to ensure patient safety.

OUTCOME MEASURES Formal assessment of the short-stay pathway will report on:

1. Proportion of patients suitable for a short stay pathway (eligibility)
2. Proportion of patients who will accept admission to this pathway (uptake)
3. Proportion of patients admitted to the short-stay pathway that can be discharged at 23-hours (viability)
4. Patients' treatment satisfaction, quality of life (QoL) and the impact of AAA and its treatment on QoL after the short stay pathway at 30 days, 3 and 6 months.
5. Rate of device-related and other adverse events, readmission, mortality (at 30, 90 days 6 and 12 months) of patients.
6. Costs up to 6 months.
7. Qualitative data will also be collected describing the experiences, worries and concerns of patients, families and GPs; the key barriers and drivers to implementation of a 23-hour pathway.
8. Finally, a 'tool-kit', which may be used for implementation of a short-stay pathway in a wider

	group will be produced if there are a significant proportion eligible and accepting the pathway and the pathway is viable without perceived safety issues.
POPULATION	All patients with an infrarenal abdominal aortic aneurysm in at least five sites will be assessed for inclusion into the study. This is expected to be over 200 patients in five high-volume sites. From these patients we will be able to enrol suitable patients for the STAR pathway. We expect approximately 100 patients to be enrolled from the five centres.
ELIGIBILITY	Patients with an infrarenal AAA and iliac artery aneurysm are eligible for screening for participation in the study. Patients who meet all the Inclusion Criteria and none of the Exclusion Criteria will be eligible and offered AAA repair using the STAR pathway. Those who accept admission to this pathway will be enrolled.
DURATION	12-month enrolment and active follow up for a minimum of 6-months (with permission to collect routine clinical data for a period of 15 months from consent).

1. INTRODUCTION

1.1. BACKGROUND

Abdominal Aortic Aneurysms (AAAs) are common and present a significant risk of rupture and mortality when greater than 55 mm in size. For those patients where the risk of rupture outweighs the operative risks, repair is offered. At present, most patients in the UK are offered a minimally invasive endovascular approach.

EVAR is now established as a safe and acceptable alternative to open repair in suitable patients. In 2004 the EVAR-1 trial demonstrated a significant reduction in 30-day mortality from 4.6 to 1.6% and in-hospital mortality from 6.0 to 1.6% in patients receiving EVAR [1]. Since then, mortality and complication rates have fallen further. Recent reports from the National Vascular Registry (NVR) document 0.7% mortality and a 5.1% morbidity for the 2870 endovascular repairs across the UK in 2017 [2].

However, the estimated cost of the procedure is £12,000 [3], which is not cost-effective when compared to open repair – the cost of endografts and the increased burden of follow-up means that costs are greater overall [1, 3, 4]. The draft guidelines for aneurysm repair from the National Institute for Health and Care Excellence (NICE) published in 2018 (https://www.nice.org.uk/guidance/indevelopment/gid-cgwave0769/consultation/html-content) included a detailed cost analysis based on trial data which concluded EVAR is not cost effective, recommending EVAR is not used in fit or unfit, non-ruptured aneurysm patients. After unprecedented stakeholder opinion and intervention from NICE, changing the guideline committees final recommendations, the guidelines were finally published (https://www.nice.org.uk/news/article/nice-publishes-its-guideline-on-the-diagnosis-and-management-of-abdominal-aortic-aneurysms). The guidelines state that “where open surgical repair can’t be carried out – for example because of medical or anaesthetic risks – EVAR can be considered”. However, cost-effectiveness is clearly an important issue that will be ever more important in years to come, given increasing healthcare costs and studies to attempt to find cost effective improvements are needed.

In addition, waiting times are increasing - the NVR report 2017 stated “The median delay at the majority of vascular units tended to fall within the range of 60 to 90 days. Nonetheless, the upper limit of the interquartile ranges shows that, at 16% of the vascular units (12 of 75), 25% of patients operated on in 2017 waited more than 140 days.” For aneurysm repair patients were cancelled, for a variety of reasons, but lack of facilities and hospital beds were among the prime reasons for cancellation.

The average hospital stay for elective EVAR is 2 days (Interquartile range 1-4 days) [3]. There is a need for a more efficient care pathway. There is a focus on shorter stays and readmissions in the “Getting It Right First Time” (GIRFT) agenda, which is a Nationwide report of vascular surgery performance. The variation in practice is clearly demonstrated in this work. Research into the potential of shorter stay pathways is very much needed, to include patient acceptability.

Short Stay Aneurysm Repair (STAR) is certainly achievable. The results of papers on this subject have recently been synthesized in a systematic review. [5] The patients involved are selected according to fitness, social and anatomical criteria. There is wide variation in reported rates of short stay EVAR compared to the overall volume of patients from 23-79% of the cohort. There is also significant variation in terms of the success in discharging patients after a short stay (from 70-96%).

One report describes a select group of 27 patients in Cambridge who received EVAR, discharged the day after surgery [6]. There were no safety issues detected and the perceived costs of a short stay EVAR were less in a rudimentary cost analysis. The highly specialized vascular centre in Zurich, Switzerland has published results for day case EVAR, to demonstrate feasibility [7]. A protocol involving many elements of a fast-track programme and low-profile devices in the USA has shown that in selected patients, it is possible to perform next day discharge, with a low complication rate, mortality and readmission rate of 1.6% [8]. Despite these reports, which are now more than five years old, the concept of short stay aneurysm repair has not been adopted into practice. Some of the reasons for this are highlighted in the papers.

The Cambridge study suggested only 33% of patients are suitable for discharge the day after surgery, achieved in 81% of cases and even for these patients concluded that “an established pathway is required in order for [the potential benefits of next day discharge after EVAR] to be realized” as patents were not adequately prepared. Since this paper examined the utility of next day discharge (two bed day occupancy rather than less than 24 hours), this would seem to be vital before widespread adoption. The Swiss paper, and the more recent US study describe good outcomes for short stay EVAR but have not considered the costs and outcomes relevant to the National Health Service (NHS) and the selection and follow-up of these patients is not documented.

The success of short stay or day case surgery programmes has been demonstrated for many conditions such as coronary angiographic procedures and laparoscopic cholecystectomy where there is now evidence that day case procedures are feasible, acceptable, and safe [10, 11]. There have been many successful case histories of reducing length of stay in various specialties, which are vitally important to understanding implementation strategies. From study of these detailed case histories there have been several tools to empower units to introduce short stay pathways and release capacity in the health system. These include diagnosis, process mapping and problem-solving tools as well as strategies for staff involvement and reducing waste. Crucial to the success of these pathways appears to be design with a patient-centred approach [12]. Evidence synthesis from a publication from the National Institute for Health Research (NIHR) Health Service and Delivery Research programme has highlighted a consistent reduction in the length of stay of 0.5-3.5 days compared with conventional care without increasing post-operative complication rate, readmissions or reducing patient outcomes [13]. Given that a large proportion of patients at present are sent home at 2-4 days using current pathways [2] it would seem reasonable to suggest that a short stay, 23-hour pathway could become the norm for most patients undergoing elective EVAR.

Investigation has been conducted by the study team specifically to understand how a 23-hour pathway may be best designed to overcome organizational and personal barriers to implementation, including detailed discussions with patients and their families, a 38-patient audit in four sites to demonstrate organizational, procedure and patient factors affecting discharge.

These preparatory investigations have highlighted some of the necessary pre-operative and follow-up arrangements that will have to be in place to support patients, such as patient information, pre-booked telephone calls and appointments and placed a primary emphasis on social discharge planning, hence the need to incorporate a design phase in the research plan.

1.2. RATIONALE FOR CURRENT STUDY

It seems that the potential benefits of short stay EVAR could include increased satisfaction and care for recovery in a home environment, reduced adverse event rates from hospital care and a vital reduction in utilization of hospital services perhaps translating into a reduced cost. In addition, the option of a safe short-stay EVAR procedure could allow many urgent patients to be treated in short stay wards away from the general ward which may be overrun with COVID. There are, however, many barriers to implementation including patient, carer, and General Practitioner (GP) concerns regarding late recognition of and being away from immediate medical care for major complications and an increased burden on the family unit, GPs & community health and social care.

On a nationwide basis, we do not know the proportion of patients who would be suitable for, or accept 23-hour EVAR, whether this leads to unreported major adverse events or readmissions, unrecognized complications and most importantly whether patients, their families and family practitioners are satisfied with this approach, outcomes highlighted in the NHS outcomes framework 2013/14 [9]. Equally we do not know how institutions across the NHS would take up this approach.

We hypothesise that with appropriate multi stakeholder co-design of a short stay aneurysm pathway, there is a significant cohort (greater than 50%) of EVAR patients who would be eligible and accept to undergo STAR, be discharged within 23 hours without any increase in complications or mortality and without a decrease in patient satisfaction or excessive burden on community resources. Consequently, we hypothesize that the cost effectiveness of EVAR can be significantly improved.

2. STUDY OBJECTIVES

The primary research objectives are:

1. To test this designed pathway (STAR) within a cohort of patients undergoing Endovascular Aortic Aneurysm Repair (EVAR) who are representative of the UK caseload, enrolled over 12-months and each followed-up for a minimum of 6 months
2. To report the eligibility, uptake, viability, acceptability and safety of a 23-hour pathway for this cohort.
3. Provide detailed costs of the pathway

The secondary research objectives include:

1. To provide generalisable strategies for implementation of STAR across the National Health Service.
2. Creation of a “tool-kit” to facilitate implementation across the National Health Service.

3. STUDY DESIGN

SUMMARY:

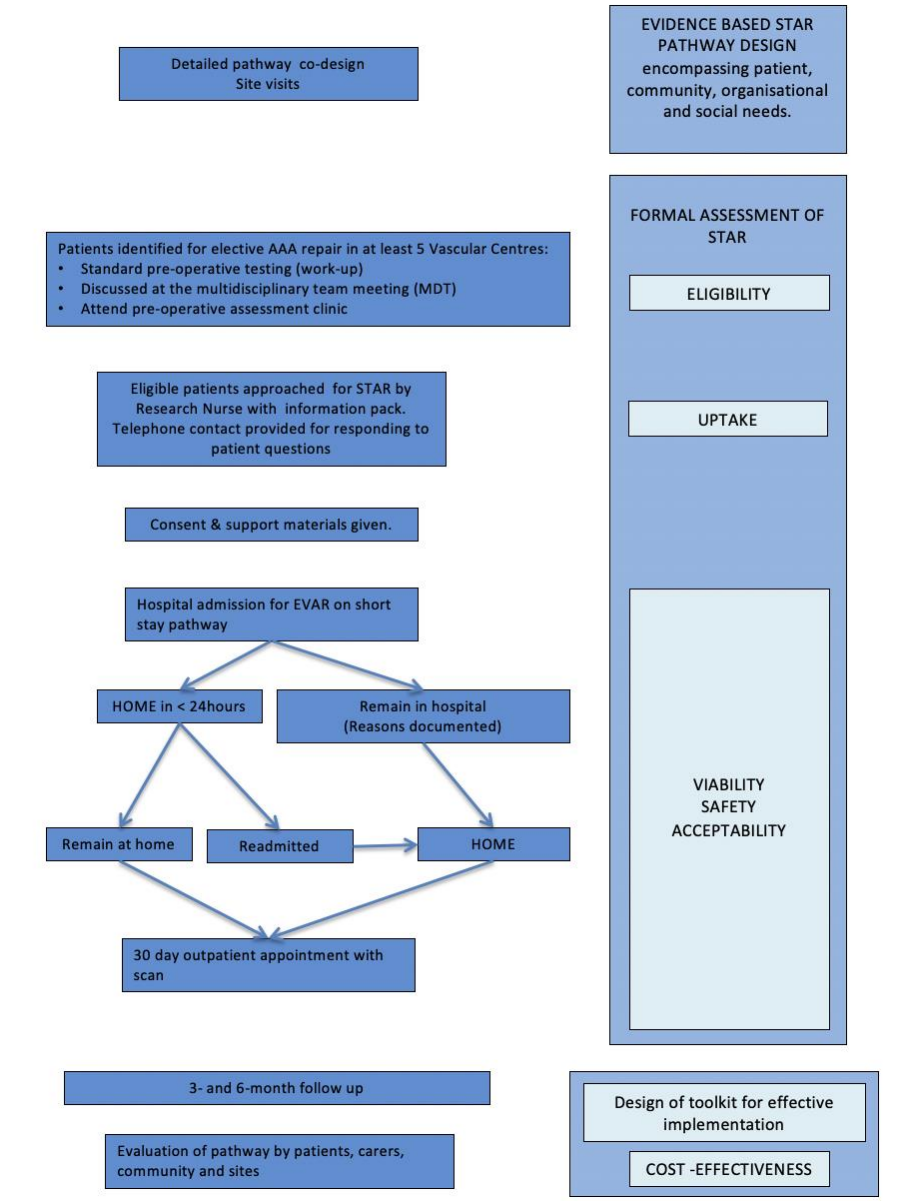
The STAR study is a prospective multicentre observational cohort study to assess the eligibility, uptake, viability, acceptability, safety and cost of a short stay (23-hour) aneurysm pathway for infrarenal AAA patients.

The study will take place in at least five sites in the United Kingdom. Over a 12-month recruitment period, all patients with AAA referred to or diagnosed at each of the units will be assessed for inclusion in the STAR pathway if suitable for EVAR.

We anticipate assessment of over 200 AAA patients with an aim of recruiting up to 100 patients into the study to undergo EVAR using the STAR pathway.

Patients may be enrolled into the study to undergo EVAR using the STAR pathway provided all inclusion and no exclusion criteria are met as specified in Section 4. Subjects will be evaluated through to hospital discharge, receive a telephone call at 48 hours, return for follow-up visits at one month and telephone follow ups at three- and six-months post treatment. Patients recruited into the study will have their routine clinical data collected at 12 months when they return for follow-up visits.

Figure 1 shows the study outline:



SCREENING, ELLIGIBILITY AND UPTAKE:

Patients identified in or referred to the vascular unit with a CT- proven aneurysm which has reached threshold for intervention (i.e., over 55 mm in males and 50 mm in females OR a saccular aneurysm that the MDT deems necessary to repair OR a common iliac aneurysm that the MDT deems necessary to repair) will be screened.

Patients will be assessed as standard of care at the sites from a cardiorespiratory function and social circumstances perspective, according to local standard protocols.

Each patient will be discussed at the multidisciplinary team meeting (MDT) which we suggest should comprise of a Vascular Surgeon, Radiologist, Vascular Nurse Specialist, Anaesthetist and Peri-operative physician. The number of patients undergoing open repair, complex EVAR or EVAR not suitable for STAR will be collected and documented in a screening log. Those treated conservatively and reasons for this will also be documented in the screening log.

No identifiable data will be passed to the central study team in the screening log (age, sex and aneurysm size and reasons for non-inclusion will be reported). All identifiers will be removed from screening logs when data is submitted for analysis.

Patients potentially suitable for STAR, will be contacted by post, telephone or approached at routine clinic visits. Patients will also have the opportunity to get familiar with the study taking place by reading the study Poster, that is to be displayed in the departmental waiting rooms. Potentially suitable patients will be able to approach medical professionals during their clinic appointments or contact the coordinating study team by email, to see if they meet the eligibility criteria for STAR pathway. They will receive patient information packs, explaining the STAR pathway. For the patients, this will:

- Involve patients in their care by allowing them to share their own experiences with healthcare professionals, carers, and other patients in a similar position, via patient focus groups.
- Recognize and counter any fears about complications; provide assurance of their safety and what they can expect when recovering at home.
- Include information about the process and their expectations, “what is normal, and what constitutes an emergency”
- Set expectations for support at home (follow-up conversations and emergency helplines).

This will aid in understanding the process involved in STAR, highlight the similarities and differences compared to the traditional EVAR repair pathway, address frequently asked questions and reduce concerns patients may have prior to their admission.

All elective EVAR patients will be assessed at routine surgical or anaesthetic pre-assessment clinics. Patients will be assessed for their eligibility for the 23-hour pathway using a standardized assessment tool based on the inclusion and exclusion criteria given above and discussion at the MDT.

Those eligible for study entry who have been provided with information about the STAR study, will be given an opportunity to discuss this with members of the vascular team and the project co-ordinator, and will be asked whether they will take part and sign a consent form. The number of patients undergoing EVAR suitable for the STAR pathway but refusing to take part in the study and the reasons (e.g. patient choice, fears over 23 hour EVAR etc) will be documented in the screening log. The uptake rate will therefore be assessed.

INTERVENTION:

GPs will be informed of the study and sent site specific information after each patient is recruited.

This will aid in understanding the process involved in STAR, highlighting the similarities and differences compared to the traditional EVAR repair pathway. We will aim to address frequently asked questions and concerns patients and their GPs may have, as they arise.

Pre-operative COVID-19 preparations for surgery will be adhered to according to local protocol. An opportunity for pre-habilitation whilst waiting for surgery will be utilised. Detailed advice including exercise, psychological preparation and breathing exercises with virtual support from nursing teams will be available.

The detailed pathway protocol for care, developed by the multidisciplinary team, will be agreed by all sites in the set-up phase of the study, and include relevant site specific modifications.

On the day of the planned EVAR, each site may differ in arrangements, but a suggested pathway is that patients will arrive at hospital (time zero) 2 hours before their procedure (Day 0). The patient will undergo a standard EVAR procedure either under general, regional or local anaesthesia with percutaneous or open cut down access.

Following the procedure on day 0 the patient will be nursed in recovery before returning to the ward. Existing standard of care practice for monitoring of EVAR patients will be continued at each site.

A protocol-driven pathway for post-operative care will be used to encourage early rehabilitation – early mobilization on the evening of the operative day; early removal of intravenous/arterial lines and catheter if placed; eating and drinking in evening of day 0; discharge summaries and medication routinely available (with pre-packs from pharmacy) from early morning day 1; and adequate analgesia.

The following morning (day 1), assuming there are no complications from surgery, the patient will be deemed medically fit for discharge. Standard patient specific post-operative investigations will be undertaken. The Vascular Nurse specialist or member of the clinical team who is to follow-up the patient will ensure discharge plans are in place utilizing specifically agreed protocols. Discharging the patient before 24 hours will allow further short stay patients to be admitted into the same bed (perhaps allowing establishment of an EVAR bed and for patients to be treated in a short stay unit) to further improve efficiency of the pathway.

3.1. STUDY OUTCOME MEASURES

Primary Endpoints

This study will formally assess a short stay pathway for AAA repair with the aim of reporting the:

1. Proportion of infrarenal AAA patients suitable for EVAR using a short stay pathway (eligibility)
2. Proportion of these patients who will accept admission to undergo EVAR using STAR pathway (uptake)
3. Proportion of patients admitted to the short-stay pathway who are able to be discharged at 23-hours (viability)
4. Patient well-being (W-BQ16), treatment satisfaction (AneurysmTSQ), and EQ-5D-5L (quality of life) questionnaires will be administered at different points of the study including at baseline (prior to STAR), as well as at 2-4 days, 30 days, 3- and 6-months after STAR. (See Appendix 1 for questionnaire schedule).
5. Rate of device-related and other adverse events, readmission, mortality (at 30 days, 3-, 6- and 12-months) of patients.
6. Costs up to 6 months.

Secondary Endpoints

7. Qualitative data will also be collected describing the experiences, worries and concerns of patients, families, and GPs; the key barriers and drivers to implementation of a 23-hour pathway; potential improvements to the proposed short-stay pathway; and an assessment of the key determinants of resource use, including those of nurse-led follow-up, to allow formal health economic analysis.
8. Lastly, if there are a significant proportion eligible and accepting the pathway and the pathway is viable without perceived safety issues. then work should

focus on widespread adoption. We will produce a 'tool-kit', which may be used for implementation of a short-stay pathway in a wider group. This will allow other units to take on STAR if this pathway proves effective.

4. PARTICIPANT ENTRY

4.1. PRE-REGISTRATION EVALUATIONS

Patients will receive imaging as standard of care. Those identified or referred to the vascular unit with a CT-proven aneurysm which has reached threshold for intervention (i.e., over 55 mm in males and 50 mm in females OR a saccular aneurysm that the MDT deems necessary to repair OR a common iliac aneurysm that the MDT deems necessary to repair) will be screened.

Each patient will undergo standard of care assessment at the sites from a cardiorespiratory function and social circumstances perspective, according to local standard protocols.

Patients will be discussed in the Multidisciplinary meeting at each site and be seen pre-operatively in a surgical or anaesthetic clinic.

Those patients who are eligible and who will accept admission to this pathway will be enrolled in the study.

The patient is considered enrolled when they have signed the consent form after agreeing to undergo EVAR using the STAR pathway.

4.2. INCLUSION CRITERIA

Patients may be included in the study and offered treatment using the STAR pathway if:

- They have been assessed as suitable for standard infrarenal EVAR within the manufacturer's "Instructions for Use" for the chosen endograft.
- Age over 55 (effectively excluding connective tissue disease)
- Fully independent at home or adequate provision for home care after discharge which would enable patients to perform basic activities of daily living including mobility, eating, drinking and bathing.
- Living with a partner or family member or having similar help available for the first 24-hours after discharge from hospital.
- Transport to attend the hospital in which they were treated within 1 hour for the first 24-hours after discharge. Should an ambulance not be readily available to attend hospital within this timeframe, patients must be made aware and agree to make their own transport arrangements.
- Capable of complying with Protocol requirements, including follow-up.
- An Informed Consent Form signed by the participant or legal representative.

4.3. EXCLUSION CRITERIA

Patients will be excluded from being offered treatment using the STAR pathway (with reasons carefully documented) if there is:

- Significant cardiac disease defined as one or more major predictors of increased perioperative cardiovascular risk according to the American College of Cardiology Cardiac Risk Classification (Appendix 3), which remain untreated at the time of surgery.
- Significant renal failure (pre-operative creatinine level of over 150 µmol/L or GFR less than 30mL/min/1.73m^2 indicating severe chronic kidney disease (stage IV).
- Significant respiratory disease needing increased post-operative care not available in the home environment (e.g., nebulisers or oxygen therapy which is not set-up at home).
- Any other condition, which in the opinion of the multidisciplinary team makes discharge within 23-hours unsafe.
- Patients who lack capacity to consent to 23-hour EVAR will be excluded from the study.
- There is concurrent enrolment in another drug or medical device study or have recently been involved in any research prior to recruitment

4.4. WITHDRAWAL CRITERIA

The patient will remain free to withdraw at any time from the protocol treatment and study follow-up without giving reasons and without prejudicing their future care and should notify the Investigator in this event – these patients will be treated from this time as patients that are undergoing standard EVAR. The Investigator may also withdraw the participant from the study at any time based on his / her medical judgment.

5. ADVERSE EVENTS

5.1. DEFINITIONS

Adverse Event (AE): any untoward medical occurrence in a patient or clinical study subject.

Serious Adverse Event (SAE): any untoward and unexpected medical occurrence or effect that:

- **Results in death**

- **Is life-threatening** – *refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.*
- **Requires hospitalisation, or prolongation of existing inpatient's hospitalisation**
- **Results in persistent or significant disability or incapacity**
- **Is a congenital anomaly or birth defect**

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

5.2. REPORTING PROCEDURES

All adverse events will be reported. Depending on the nature of the event the reporting procedures below should be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

Anticipated Adverse Events (AES) may occur as a result of treatment of an aneurysm. These would include general surgical complications and those associated with local, regional and general anaesthesia and events specific to EVAR such as bleeding, access vessel complications, endoleak and open conversion.

The adverse events listed below are anticipated device and procedure-related risks:

Device and Procedure Anticipated risks		
-Access vessel dissection or rupture -Amputation -Aortic rupture -Buttock claudication -Chest infection -Endoleak -Failure to manage at home -Falls -Graft infection	-Graft kinking -Graft migration -Graft limb thrombosis/stenosis/occlusion -Haemorrhage -Limb ischemia -Multiple organ failure -Myocardial infarction -Renal failure	-Respiratory failure -Spinal cord ischemia -Stroke -UTI -Unable to contact patient -Visceral ischemia -Wound infection

Risk-to-Benefit Rationale: The intervention aims to discharge patients within 23-hours after EVAR. With discharge at or before 23-hours there is a theoretical risk of missing complications that could be treated earlier in hospital. This risk is mitigated by early telephone/remote contact after discharge and careful selection of low-risk patients. The risk is low as the vast majority of major complications occur within 23-hours. Advantages to discharge at or before 23-hours could be that of increased patient satisfaction recovering at home, reduced hospital acquired complications

such as a urinary tract infections (UTI), hospital acquired pneumonia (HAP) and at present, reduced risk of COVID-19 infection and transmission.

5.2.1 Non serious AEs

All such events, whether expected or not and whether related to the study or not, will be recorded. Adverse events will include medical, social and psychological untoward events. These will be reported on the standard data collection forms at each data collection time point.

5.2.2 Serious AEs

An SAE form will be completed and emailed to the Chief Investigator within 24 hours of the local team becoming aware. However, hospitalisations for elective treatment of a pre-existing condition will not need reporting as SAEs.

SAEs will be categorised into related or unrelated to the STAR intervention and anticipated or unexpected with EVAR and a full description of the event recorded.

All SAEs will be reported to the <name of REC> where in the opinion of the Chief Investigator, the event was:

- 'related', i.e., resulted from the administration of any of the research procedures; and
- 'unexpected', i.e., an event that is not listed in the protocol as an anticipated occurrence

Reports of related and unexpected SAEs will be submitted within 15 days of the Chief Investigator becoming aware of the event, using the NRES SAE form for non-investigational medicinal product (non-IMP) studies. The Chief Investigator will also notify the Sponsor of all related and unexpected SAEs.

Local investigators will report any SAEs as required by their Local Research Ethics Committee, Sponsor and/or Research & Development Office.

Adverse events (both expected and unexpected), will be subject to scrutiny by an independent safety committee chaired by Professor Rob Sayers, Professor of Vascular Surgery, University of Leicester and Past President of the Vascular Society and include a patient representative, an independent vascular nurse specialist and statistical input, to ensure the adverse event rate is within acceptable limits according to best current evidence.

Serious unexpected adverse events will be reported to the sponsor and ethics committee within 24 hours as standard protocol. The oversight committee will also have access to patient feedback from the focus groups.

Contact details for reporting SAEs

CI email (and contact details below)
Please send SAE forms to:
Colin Bicknell
Email: RGIT@imperial.ac.uk
Tel: 02033126072 (Mon to Fri 09.00 – 17.00)

6. ASSESSMENT AND FOLLOW-UP

DATA COLLECTION:

Source data will be collected in source documents which will be provided by the study co-ordinating centre. This data will then be transferred to a secure online database (REDCap). The research nurses at each site will be trained in their use

For each patient, baseline data will be collected by the research nurses at the routinely scheduled pre-operative clinic visit. This will include demographic data, morphological characteristics of the aneurysm, functional activity data and details pertaining to the patient's social set up at home. Baseline patient-reported data (PROMS) will also be registered. Overall, data logging at this stage should not exceed 30 minutes and should form part of routine pre-operative assessment. Any cancellations and/or rescheduling of patients will also be documented.

During the hospital stay the procedural details, use and specifics of post-operative and any high dependency care, date and time of discharge, reasons for delayed discharge and complications will be collected. Post-discharge, details of nurse consultation will be recorded, and any patient concerns documented.

At routine follow up visits and telephone appointments, complications, adverse events, readmissions and reinterventions will be recorded as set out in appendix 1. Participants will complete well-being and aneurysm specific quality of life questionnaires. Health resource use and EQ-5D-5L health status questionnaires will be administered to better delineate social and informal care needs, as set out in appendix 1.

At the midpoint and end of the study, patient focus groups, run by a research fellow and involving surgical and managerial input, will be convened to review their experience and seek suggestions for further improvement of the pathway.

Patient reported outcome measures (PROMs) have been developed and validated prior to this study in work involving one of the grant applicants (RH). With much evidence suggesting that disease-specific PROMs are more sensitive to change in surgical patients [18], a set of tools was developed to assess symptoms, quality of life and treatment satisfaction in patients with AAA, including those undergoing repair. [19-20]. These PROMS will form a cornerstone of patient outcome measures in this study.

Well-being (W-B16) questionnaires will be used to measure depressed and anxious mood, energy, positive well-being, and stress at baseline, at 2-4 days post-op and 30 days.

Similarly, the Aneurysm Treatment Satisfaction Questionnaire (AneurysmTSQ) will be recorded at baseline in patients who (a) have had active monitoring of their aneurysm for over 2 months prior to decision to undergo repair and/or patients who (b) have undergone assessment and treatment of their comorbidities as part of their work-up for AAA repair. Where this is not the case, AneurysmTSQ will be recorded at 30 days, 3 and 6 months.

EQ-5D-5L health status questionnaires will be administered at baseline, 3- and 6-months.

Data collection for health economics analysis: Resource use data will be collected to allow a microcosting approach, and accurate cost and cost-effectiveness analyses. This will include accurate measurement of hospital stay across HDU, ITU and other wards. A survey of standard equipment and consumables used for each patient intra- and post-operatively and patient contact with medical staff during the admission will be undertaken.

The unit costs of medical equipment and consumables will be taken from manufacturers' list prices and published sources. Staff salary costs will be taken from the PSSRU unit costs for health and social care. Costs related to hospital stay will be taken from published NHS reference costs.

Destination of discharge will be recorded. Following discharge, the time taken for follow up and number of consultations at GP surgery and hospital outpatients will be documented to allow calculation of the burden on healthcare services and an effective cost analysis.

Patients, families and carers will be asked to keep a record of medical care during the follow-up period after surgery allowing the patient and healthcare workers to complete details regarding readmission (with reasons, interventions and length of stay), GP visits and other health resource use (using similar case report forms to those developed as part of a recent trial for ruptured aneurysms – the IMPROVE trial, CI JTP). Details of care will be collected on specifically designed case record forms. This mechanism will also allow costing of direct and indirect costs in care given by friends and family, including time taken of work for initial care and hospital appointments.

FOLLOW UP:

The schedule for data collection is detailed in Appendix 1.

Data will be collected according to the schedule:

- at baseline
- in-hospital
- at a telephone appointment at 2-4 days after discharge from hospital

- at a routine follow-up appointment at 30-days (+/-14 days)
- at a telephone appointment at 3 months (+/-14 days)
- at a telephone appointment at 6 months (+/-14 days)
- from routine NHS data at 12 months after EVAR (+/- 3 months)*

*Collection of routine NHS follow-up data to include mortality, routine imaging, complications, readmission and reintervention data. Patients will be asked for permission to collect routine clinical data following their procedure.

A telephone consultation, at a booked time will be had between the nurse specialist and patient (involving the carers/family and including a telemedicine component if possible) between day 2 and 4. The aim of the follow-up consultation is to ensure expected recovery, no evidence of post-operative complications and further follow-up arrangements as well as discuss patient issues and worries/fears/concerns. Where there are specific concerns the telephone interview may be amended to discuss these issues.

An emergency contact line will also be established to ensure patients are safe during this study. This will be present on the ward to ensure 24-hour advice is available as a first point of contact. All staff on the vascular ward will be made aware of the study and protocols for escalation of queries and emergency calls from patients will be made available. The use of this contact number will be monitored during the study with a call log, and this will inform whether a helpline would be necessary during any further study/trial or during implementation.

In the case where a patient cannot be contacted during a scheduled telephone consultation or ‘does not attend’ a scheduled clinic visit, standard protocol driven strategies involving the next of kin will be used.

A participant has completed the active data collection section of the study after the 6-month follow up. Any participant that does not complete these requirements due to voluntary withdrawal, physician withdrawal, death, or any other reason will be considered a withdrawal. Participants will not be provided with any medical care by the Sponsor after study completion or withdrawal, although routine NHS clinical care will be continued.

In the event where incidental findings relating to the participant’s health become apparent, the immediate clinical team will ensure the participant, as well as their GP are informed and that appropriate follow up is organised with the appropriate team/specialist service.

LOCAL STUDY SITES:

The local principal investigators and clinical staff at the local study sites are responsible for:

- helping facilitate local management approval (aided by the Study Coordinating Centre)
- completing study training and adhering to regulatory requirements (GCP, use of study database etc)
- identification of potentially eligible patients
- conducting study procedures and follow-up according to study protocol and recording and reporting protocol deviations to the Chief Investigator
- prompt reporting of SAEs to the Chief Investigator (using the relevant form)
- dealing with routine enquiries from patients and their families
- obtaining appropriate information to confirm study endpoints as per the protocol
- The end of the study will be reached when the last enrolled (100^{th}) participant' medical notes are accessed at 12 months post their EVAR procedure. At this stage there will be a data lock, and preparations for analysis and dissemination of findings will take place.

7. STATISTICS AND DATA ANALYSIS

7.1 STATISTICS

SAMPLE SIZE ASSUMPTIONS

It is assumed that each of the centres will offer approximately 70% of patients presenting with an infrarenal AAA an EVAR procedure, based on the National rates from the NVR database. Of this group we assume that 70% of these patients are eligible for a short stay EVAR programme and an estimated 10% patient refusal rate based on our preparatory studies.

SAMPLE SIZE CALCULATION

The estimates of participants are calculated on a pragmatic basis. Each of the confirmed participating centres has significant experience in EVAR and treatment of patients with aneurysmal disease, performing 319 elective EVARs annually combined in 2018. We plan to assess over 200 patients for eligibility. We estimate that this will allow inclusion of approximately 100 patients in the STAR pathway in 12-months which should be achievable.

Analysis will occur at the end of the study. No Interim analysis is planned. A full analysis plan will be developed before database locks. The statistical analysis plan will be prepared by Dr Manuel Gomes, an Associate Professor in Health Economics, at University College London and Miss Anna Pouncey, senior clinical research fellow at Imperial College London. Overall, statistical analysis will be overlooked by Professor Janet Powel.

POPULATION TO BE ANALYSED

All patients with AAA with be analysed for eligibility and all patients eligible will be assessed for uptake. All patients enrolled in the study will be analysed in full, and the viability, safety and acceptability and cost will be calculated in full.

ANALYSIS

A formal statistical analysis plan will be determined before database lock. We will assess the proportion of patients suitable for and enrolling in STAR. The wider acceptability will be assessed in terms of responses to the PROMs and community health resources used. Viability of STAR will be assessed by reporting how many of the short stay admissions are discharged within 24 hours, without need for readmission or mortality (aneurysm related and all cause) within 30 days, 3, and 6-months of endograft placement. The safety of the pathway will be assessed from the number of adverse events reported within the same period and by analysing the clinical data from routine appointments at approximately 12-months. Data will be reported by tertiles of age and sex. The effect of age, sex and aneurysm diameter on eligibility, uptake, viability, acceptability and safety will be investigated by logistic regression analysis.

Current work consisting of a retrospective data collection of 36 patients undergoing elective infrarenal EVAR at a single institution with a view to explore the drivers of inpatient, outpatient and total costs of EVAR, and will form a basis for comparison.

The health economic analysis will take the perspective of the English NHS and Social Services. Informal care will also be accounted for. This will be led by Associate Professor, Dr Manuel Gomes.

Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

8. REGULATORY ISSUES

8.1. ETHICS APPROVAL

The Study Coordination Centre has obtained favourable opinion from the Bromley Research Ethics Committee (REC) and Health Research Authority (HRA). The study must also receive confirmation of capacity and capability from each participating NHS Trust before accepting participants into the study or any research activity is carried out. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

8.2. CONSENT

Consent to enter the study will be sought from each Participant only after a full explanation has been given, an information leaflet offered and time allowed (minimum twenty-fours) for consideration.

The Investigator will verify that all potential Subjects for this study are provided with a consent form describing this study and sufficient information to make an informed decision about their participation.

The formal consent of a Participant using the approved consent form, will be obtained by the local PI (or designated colleague detailed in the delegation log) before EVAR and study data will not be collected until informed consent has been obtained.

Any significant, new information which emerges while the study is in progress that may influence a Subject's willingness to continue to take part in the study will be provided to the Subject.

The Investigator shall verify that documentation of the acquisition of informed consent is recorded in each Subject's records in accordance with applicable regulations.

The right of the participant to refuse to participate without giving reasons will be respected. After the participant has entered the study, the clinician remains free to give alternative treatment to that specified in the protocol at any stage if he/she feels it is in the participant's best interest, but the reasons for doing so should be recorded. In these cases, the participants remain within the study for the purposes of follow-up and data analysis. All participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment.

8.3. CONFIDENTIALITY

All Subject records will be kept confidential to the extent provided by applicable laws and regulations. The study monitors and other authorized representatives of the Sponsor may inspect all documents and records required to be maintained by the Investigator, including but not limited to medical records. Such records may also be reviewed by the Site's Ethics Committee. The Investigator will inform the Subjects that their records will be reviewed.

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.

Each participant will be pseudonymised by being given a unique study ID. Data that is non-identifiable will be transferred to the study team for analysis. Password protected NHS and Imperial College London computers will be used to temporarily store, collate and analyse pseudonymised data. RedCap (a secure web application) will be used to build and manage the database.

Non-identifiable data will be transferred to Imperial College London for analysis.

8.4. INDEMNITY

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study

8.5. SPONSOR

Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

8.6. FUNDING

W. L. Gore & Associates (UK) Ltd and Medtronic Limited are funding this study.

Participants and individual researchers will not receive any payments, reimbursement of expenses or any other benefits or incentives, nor receive any personal payment over and above normal salary for taking part in this research.

8.7. AUDITS

The study may be subject to audit by Imperial College London under their remit as Sponsor and other regulatory bodies to ensure adherence to GCP and the UK Policy Frame Work for Health and Social Care Research.

9. STUDY MANAGEMENT

The day-to-day management of the study will be co-ordinated through Pinar Ulug (project manager) and Maria Nicola (clinical research fellow).

10. PUBLICATION POLICY

On completion, we will produce an executive summary of our findings to be distributed to relevant policymakers, organized in conjunction with the Centre for Health Policy at Imperial College London.

We will present the results from the study and discuss the role of accelerated discharge pathways in minimally invasive vascular surgery. to the National screening committee and the Vascular Society. We will aim to publish the findings of the study in widely disseminated high impact academic journals. We will make our intervention methodology and results available through presentations, workshops, conferences, the website, working papers and journal articles. We will provide an interactive framework on a web-based platform to facilitate the adoption of our model and methodology in other fields. The dissemination strategy for our findings will be aimed at reaching the largest possible stakeholder audiences. We will maintain and develop the study internet site, initially used as a public and participant information tool, to disseminate our findings, and to facilitate the adoption of our model and methodology in other fields.

It is the intent that the multicenter results of this study will be submitted for publication (in a peer reviewed journal). A publications committee consisting of representatives for the study investigators will be established to review the multicenter results and develop publications at the completion of the study. The publication will be approved by the companies funding the trial before publication.

For Patients/Public, we will produce a short, easy to understand summary of our research findings that will be available from our website or that can be sent to interested persons, GPs, nurses, and screening providers. The information available to patients who attend for surgery will also be amended as a result of the experience gained in this study

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Appendix 1. Schedule of data collection for the formal assessment of STAR

	Baseline (Routine) pre-op clinic	In hospital	2-4 days after discharge	30 Days	3 and 6 months	12 months (from routine F/U data)
Demographic profile	x					
Aneurysm characteristics	x					
Duke Activity Status Index	x					
Procedural details		x				
Admission, in-hospital, and discharge details and cancellations		x				
Details of routine surveillance imaging				x		x
Complications		x	x	x	x	x
Reinterventions		x	x	x	x	x
Adverse events		x	x	x	x	x
Readmission			x	x	x	x
Health resource use		x	x	x	x	
PROMS						
EQ-5D-5L	x				x	

Well-being Questionnaire	x		x	x	x	
AneurysmTSQ	x			x	x	

Appendix 3: American College of Cardiology Cardiac Risk Classification

Clinical Predictors of Increased Perioperative Cardiovascular Risk
MAJOR RISK
UNSTABLE CORONARY SYNDROMES
• Acute or recent MI with evidence of important ischemic risk by clinical symptoms or non-invasive study • Unstable or severe angina (Canadian Class III or IV) • Decompensated CHF
SIGNIFICANT ARRHYTHMIAS
• High-grade atrioventricular block • Symptomatic ventricular arrhythmias in the presence of underlying heart disease • Supraventricular arrhythmias with uncontrolled ventricular rate
SEVERE VALVULAR DISEASE
INTERMEDIATE RISK
MILD ANGINA PECTORIS (Canadian Class I or II)
PREVIOUS MI (by history or pathological Q waves)
COMPENSATED (or prior) CHF
DIABETES MELLITUS (especially insulin-dependent type)
MINOR RISKS
ADVANCED AGE
ABNORMAL ECG (e.g., left ventricular hypertrophy, left bundle branch block, ST-T abnormalities)
RHYTHM OTHER THAN SINUS (e.g., atrial fibrillation)
LOW FUNCTIONAL RESIDUAL CAPACITY (e.g., inability to climb one flight of stairs with a bag of groceries)
HISTORY OF STROKE
UNCONTROLLED SYSTEMIC HYPERTENSION

ECG, electrocardiogram; MI, myocardial infarction; CHF, congestive heart failure