CLINICAL STUDY PROTOCOL
ALTITUDE VERSION 1.2

18 JUNE 2025
VERSION 1.2

Multi-centre, Observational, Post-Market, Real World Registry to Assess Outcomes of Patients Treated with the Altura™ Endograft System for Endovascular Abdominal Aortic Aneurysm Repair

Altura Post-Market Registry Study: Altitude

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List of Attachments

1) **Instructions for Use (Sample)**
2) **Informed Consent Form (Template)**
3) **Case Report Forms (Template)**

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INVESTIGATOR SIGNATURE PAGE

I agree to conduct the study as detailed in this Clinical Investigational Plan and in accordance with all applicable regional laws and regulations. In addition, I agree to provide all the information requested in the case report forms presented to me by the sponsor in a manner to assure completeness, legibility and accuracy.

I agree to actively enroll patients into this study and confirm that I do not have any material conflicts including participation in any clinical investigations for competing products.

I will provide copies of this registry protocol and all necessary information about this registry to the registry staff under my supervision. I will discuss this material with them and ensure they are fully informed about the device under investigation as well as all aspects concerning the conduct of this registry.

I also agree that all information provided to me by the sponsor, including pre-clinical data, protocols, case report forms, and any verbal and written information, will be kept strictly confidential and confined to the clinical personnel involved in conducting the registry. It is recognized that this information may be relayed in confidence to the Ethics Committee or Institutional Review Board or to regulatory authorities.

In addition, no reports or information about the study or its progress will be provided to anyone not involved in the registry other than the sponsor, the Ethics Committee(s) or Institutional Review Board(s), or the independent medical reviewers. Any such submission will indicate that the material is confidential.

I will supervise the conduct of the clinical investigation to be performed in compliance with the clinical investigational plan, Good Clinical Practice (GCP)/ICH, the Declaration of Helsinki, ISO 14155:2011 and all applicable regulatory and ethical requirements.

_____ _____

Investigator Signature Date

_____

Investigator Printed Name

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2. STUDY CONTACT PERSONNEL

2.1. SPONSOR

EU GENERAL SPONSOR CONTACT
Anne Woodman **Clincal Programmes Coordinator** Tel: +44 793496083 Fax: +44 1235 879 Lombard Medical Ltd Lombard Medical House 4 Trident Park Didcot Oxfordshire OX11 7HJ United Kingdom Email : anne.woodman@endovastec-lm.com

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3. PROTOCOL SYNOPSIS

Title of the Registry	**Altitude Registry** **Multi-centre, Observational, Post-Market, Real World Registry to Assess Outcomes of Patients Treated with the Altura® System for Endovascular Abdominal Aortic Aneurysm Repair"**
Study Device	Altura Endograft System (Altura®-System)
Study Sponsor	Lombard Medical Ltd (Referred to herein as 'Lombard') Lombard Medical House 4 Trident Park Didcot Oxfordshire OX11 7HJ United Kingdom
Objectives	Post-market registry study to assess the clinical outcomes of the Altura® System in an all-comers, real world patient population with subjects receiving endovascular treatment for their Abdominal Aortic or aortoiliac Aneurysm (AAA)
Study Design	Multi-centre, single arm, open label, post-market registry study with consecutive, eligible patient enrollment at each site. All subjects undergoing treatment with the Altura®-System. Subjects will be followed procedurally to discharge, and as per institutional standard of care thereafter through to 5 years (total follow-up commitment).
Investigational Sites	Up to 80 global investigational sites with experience in the utilization of the Altura® System for the endovascular treatment of Abdominal Aortic Aneurysms (AAA). Product training will be conducted by Lombard personnel. Clinical sites will be directly supervised in initial registry cases by a Lombard trainer or a certified Proctor until a *minimum* of five study cases is completed over at least two implant days. This training period may be extended at the discretion of Lombard, or request of the implanting team.
Subject Population	Up to 1000 patients diagnosed with AAA who are considered candidates for Endovascular Repair, who meet the study eligibility criteria and sign the Informed Consent Form may be subsequently enrolled in the study main study. Data on up to a further 200 patients may be captured in centres undertaking their first 5 cases, in order to understand the learning curve associated with using the device.
Study Procedures	Treatment of the AAA with the Altura® System will be performed according to the standard of care at each registry site.

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Data capture	An eCRF will be used for data collection. Internet access is required for data entry (no further system- / computer-requirements).
Monitoring	Source data verification will be performed by means of intermittent on-site and/or off-site monitoring.
Study Timelines	Expected study start: December 2016 Expected enrollment duration: 24 months Expected total study duration: Open-ended until final subject has reached 5 years follow up.
Independent Event Review	An independent Clinician committee will adjudicate all Unanticipated Adverse Device Effects (UADE) and Serious Unanticipated Adverse Device Effects (SUADE) reported by sites within this registry, plus Major Adverse Events (MAE). The independent Clinician committee will complete the eCRF data capture form for the adjudications.
Imaging Assessment	Where the implanting physician determines that there has been a clinically significant device related event, the images datasets relating to that patient will be reviewed by a group of independent Clinician assessors. The independent Clinician(s) will complete the eCRF data capture form for the evaluations.
Inclusion Criteria	1. Male or female at least 60 years' old 2. Subject has signed informed consent for data and image release 3. Subjects with AAA and eligible for endovascular repair
Exclusion Criteria	1. Currently participating in another related study where primary endpoint has not been reached yet 2. Mycotic or infected aneurysms 3. Aneurysms associated with a known connective tissue disorder 4. Occluded iliac access vessels 5. Ruptured AAA 6. Patients deemed by the investigator to lie outside the Instructions for Use of the Altura®-System 7. Life expectancy less than 2 years 8. Known allergy to any of the device components 9. Pregnancy or breastfeeding or any plan to become pregnant during the study

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Primary Study Evaluations	1. Immediate procedural technical success 2. Freedom from aneurysm rupture 3. Freedom from conversion to open surgical repair through to five years 4. Endoleak of any type, apart from type 2, through to five years 5. Clinically significant migration, requiring intervention or an increased frequency of surveillance through to five years 6. Aneurysm enlargement (>5mm) through to five years 7. Aneurysm regression (>5mm) through to five years 8. Secondary endovascular procedures of any type through to five years 9. Secondary vascular and/or endovascular procedures for resolution of: o Endoleak of any type o Device occlusion (due to thrombus or other causes) o Device migration leading to AAA sac expansion (>5mm diameter increase) o Device defect 10. Assessment Peri-operative Safety Parameters (up to 30 days post-procedure): o Procedural Blood loss >1,000mL o Mortality (all-cause) o Bowel Ischemia o Paraplegia o Renal Failure o Myocardial Infarction o Respiratory Failure o Stroke
Additional Evaluations	a) Device Patency and Integrity throughout the study b) Incidence of distal thrombosis, embolization and iliac stenosis c) Procedural and in-hospital evaluations: o Total intervention time (skin-skin) o Total theatre use time (including anaesthesia) o Fluoroscopy time o Contrast volume used o Estimated blood loss o Incidence of transfusion o Time in ICU o Time to hospital discharge o Proportion of patients where a decision is made by the surgical team that the patient is fit to be discharged from the

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	hospital <24h post procedure o Readmissions for access site complications o Readmissions for other complications
Statistical Considerations	Statistical analysis for recorded endpoints will consist of providing descriptive reporting, with bilateral confidence intervals at the 95% level. Additionally, Kaplan Meier analyses with survival estimates will be performed. Primary population will consist of the ITT population, defined as enrolled subjects, for procedural and safety endpoints. Moreover, effectiveness parameters will be reported for subjects in whom the Altura® System introduction into the body is successful. Some pre-specified subgroups are defined, but not limited to: - Elective AAA subjects treated having anatomical characteristics within and outside current company IFU, if any - Subjects treated with the Altura® System for revision of previous attempts at AAA repair, both with conventional grafts and endografts - Subjects requiring concomitant or secondary procedures for endovascular device placement - Treatment times for patients treated as part of the run-in cohort as compared to the formal registry component - Total fluoroscopy time for each case
Schedule of Tests	Patient eligibility will be assessed by the Investigator per institutional standard of care pre-procedural imaging. Blood tests and physical examination will also be collected as per routine schedule at each institution. Following Ethics committee/IRB approval and patient written informed consent, the patient will be screened for eligibility. Subjects will be followed procedurally and to hospital discharge and as per institutional standard of care thereafter through to 5 years (total follow-up commitment). The following table outlines a typical site follow-up schedule which will be altered to meet standard of care at individual sites.

Suggested Schedule of Tests:	**Screening/ Baseline**	**Procedure**	**Pre-Discharge**	**Days 1 and 7 post-discharge**	**FUP 1 1 month**	**FUP 2 6 month**	**FUP 3 1 Year**	**FUP yearly to 5 Years**
Inclusion/Exclusion	X							
Demographics/Medical History	X							
Physical Examination†	X		x		X	X	x	X
Blood Tests‡	X		x		X		x	X
Contrast-enhanced CT scan or alternate	x¥				x*		x*	x*

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Groin Ultrasound if discharge within 24 hours of procedure			X					
Procedural Information		x						
EQ5d Quality of life and Pain score				X				
Adverse Events		x	X		X	X	x	X

†The physical examination includes overall health, physical assessment, and vital signs.

‡Blood tests include serum creatinine and hemoglobin, if collected.

¥High resolution, contrast-enhanced CT scan is preferred up to 3 months prior to the scheduled procedure.

*If the institutions standard of care for EVAR involves another imaging modality e.g. US and abdominal x-ray, that modality may be collected as an alternative to CT.

4. STUDY OVERVIEW

4.1. OBJECTIVE

This registry is designed to assess the clinical outcomes of the Altura® Endograft System for endovascular repair of infra-renal abdominal aortic aneurysms (AAA) in a real-world patient population. Multiple clinical centres will be involved in the study to include a broad range of experience, and in a range of geographical territories.

4.2. BACKGROUND

Abdominal aortic aneurysm (AAA) is a common vascular pathology with a very significant mortality rate if the aneurysm ruptures.[1,2,3,4,5,6,7] with a sizable number of patients dying before a diagnosis is made. Just over 30,000 patients are newly diagnosed with AAA and around 44,000 repair procedures are performed in the US every year. It is estimated that up to 2,000,000 subjects are living with an undiagnosed AAA with an increase of AAA incidence in the elderly population >65 years. Risk factors include smoking, hypertension, hypercholesterolaemia, gender (men/women ratio 5:1) and family history (15-20% increased risk amongst first decree relatives). The rupture risk increases with age and concomitant hypertension as well as current tobacco use and presence of other cardio-respiratory diseases.

AAA is defined clinically as a focal dilatation of the aorta causing a diameter increase of >50% of the expected normal diameter.[4]

The principal risk related to aneurysms is rupture. Aneurysms slowly and continually increase in size, potentially to the point where it bursts or ruptures. The larger an aneurysm becomes, the higher the

[1]Semenciew R, Morrison H, Wigle D, et al. Recent trends in morbidity and mortality rates for abdominal aortic aneurysms. Rev Canadien Santé Publique 1992;83:274-6.

[2]Lelienfeld DE, Gurdenson PD, Sprafka JM, et al. Epidemiology of aortic aneurysms: Mortality trends in the United States 1951-1981. Atherosclerosis 1987;7:637-43.

[3]Fowkes FRG, Macintyre CCA, Rucjerley CV. Increasing incidence of aortic aneurysms in England and Wales. Brit Med J 1989;298:33-5.

[4]Hallett JW Jr. Diseases of the aorta and its branches – aneurysms. Merck Manual, Online Medical Manual (2008). Retrieved on 19March2010 from http://www.merck.com/mmpe/sec07/ch079/ch079b.html.

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likelihood of eventual rupture. The risk of rupture is weighed against the risk of perioperative morbidity. The United Kingdom Small Aneurysm trial (UKSAT) reported 103 aneurysm ruptures in 2,257 subjects over a period of seven years, with an annual rupture rate of 2.2%.[5] The decision to treat a patient that presents with an asymptomatic aneurysm is primarily dependent upon the size of the aneurysm. Current Society for Vascular Surgery (SVS) practice guidelines recommend surveillance for most subjects with a fusiform AAA in the range of 4.0 to 5.4cm in maximum diameter; therefore, surgical repair of abdominal aneurysms of 5.5 cm or greater in diameter is recommended in healthy male subjects, as is repair of saccular aneurysms. In females, the native aorta is smaller and accordingly intervention is suggested at a threshold of 5cm. Both male and female patients with a rapidly expanding AAA (typically >5mm in a 6-month period) are recommended to consider repair of their AAA.

Most current endografts have an aortic component, which contains a flow divider and which is connected to a pair of limb components which are usually attached by means of modular connections. Most devices have limited or no ability to reposition the implant once released from the delivery catheter and most devices require cannulating a 'gate' or contralateral stump, or using a pre-placed wire and snare in order to gain access to the contralateral limb of the implant. These factors demand high levels of skill, can create high levels of stress for the clinical team and can lead to unpredictably long procedure times. The patient can be exposed to high quantities of contrast agent and the patient and clinical team can be exposed to high levels of radiation.

4.3. STUDY DEVICE

The Altura System was designed to simplify EVAR procedures. The endografts are constructed from braided Nitinol which is covered by ribbed polyester graft fabric. There are a pair of aortic components that have a 'D'-shaped cross section that sit with their flat faces adjacent to each other in the centre of the aorta. This arrangement creates a circular cross section with a mid-line septum, and each part connects with its own modularly-attached limb. There is no need for cannulation, while the braided construction allows each graft component to be expanded or collapsed at will, allowing the placement in the aorta to be repositioned and adjusted.

Delivery catheters have a 14F outside diameter which is much smaller than many conventional devices and reduces the potential for injury to the access vessels during introduction of the device.

For more details on the device and intended use please refer to the attached Instructions of Use (IFU, Attachment 1).

4.4. STUDY DESIGN

This is a post-market, multicentre, open label, single arm, real world post-market registry study with consecutive, eligible patient enrollment at each site. All subjects undergoing treatment with the Altura® System will be followed procedurally to discharge, and as per institutional standard of care thereafter through to 5 years following implant. This registry of the CE-Marked Altura System in a "real world" patient population treated in a multi-centre setting will provide an assessment of the generalizability of the approach *and* system.

[5]Mortality results for randomized controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms Lancet 1998; 352:1649-55.

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After this protocol and the patient informed consent form are reviewed and approved by national, regional or local Ethics Committee (EC), potential subjects having infrarenal AAA will be offered participation in the study. This will be accomplished through the patient's reading of the informed consent form in the patient's native language and discussion of the study with the patient by the Principal Investigator (PI) and site personnel. Agreement to participate and to attend all standard of care follow-up visit will be documented with the patient's signature on the informed consent form, with appropriate signatures of the PI and the subject.

5. STUDY POPULATION AND PROCEDURES

Up to 80 global sites and up to 1000 subjects will participate in the main registry section of this study (hereafter, called "the registry"). Up to 200 additional patients will be evaluated in centres undergoing their initial training in the use of Altura to capture the ease, or difficulty, of learning to use the new system (hereafter called the "run in cohort"). Following investigator training, each PI will commence patient screening and enrollment under commercial approval (CE Mark). Clinicians will be directly supervised in each case by trained Lombard staff. To enroll patients into the registry each centre must have previously implanted at least 5 devices to enroll to the study. Individual clinicians with an experience of less than 5 devices must be directly supervised by a colleague with this level of experience, or direct support from a Lombard Clinical Specialist.
The intention is to capture data on a consecutive cohort of patients treated within the IFU of the Altura® - system. An enrolling site would be expected to capture data on all patients treated with the Altura® - system, except where the patient is being treated outside the IFU, or where the patient refuses consent to enter the study.

5.1 INCLUSION CRITERIA

A patient who meets all of the following criteria may be considered potential study subjects:

1. Male or female at least 60 years old
2. Subject has signed informed consent for data and image release
3. Subjects with AAA and eligible for endovascular repair

5.2 EXCLUSION CRITERIA

A patient who does not meet any of the following criteria may be considered potential study subjects:

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1. Currently participating in another related study where primary endpoint has not been reached yet
2. Mycotic or infected aneurysms
3. Aneurysms associated with a known connective tissue disorder
4. Occluded iliac access vessels
5. Ruptured AAA
6. Patients deemed by the investigator to lie outside the Instructions for Use of the Altura®-System
7. Life expectancy less than 2 years
8. Known allergy to any of the device components
9. Pregnant (females of childbearing potential only)

5.3 ENROLLMENT CRITERIA

Patients who fulfill all eligibility criteria, sign the Informed Consent and undergo endovascular intervention with the Altura®-System, will be considered to be enrolled in the registry, or run in cohort as appropriate. A patient must also consent to have his or her data used after treatment with the Altura®-System. There is no incremental risk and data will be collected anonymously.

5.4 PATIENT INFORMED CONSENT

Written informed consent, documented on the informed consent form (ICF) in accordance with Good Clinical Practice standards and study centre and national regulations, shall be obtained from each patient. The PI will retain a copy of the signed informed consent document in each patient's record, and provide a copy to the patient. A patient may also withdraw consent to have his or her data, or radiological images, used after treatment with the Altura®-System at any time without needing to justify their decision or have it affect their subsequent treatment. The data will be collected anonymously, with each patient in the study allocated a unique study site and patient code. All consenting patients entering the study will have an anonymized set of their pre-operative CT images lodged with the sponsor, in addition to sets of images relating to clinically significant events or re-interventions. The key to the study codes will be held securely by the PI at each site.

5.5 ENROLLMENT

Patient enrollment into this study is based on the site evaluation of patient conformance with the protocol-specified selection criteria (§5.1 and §5.2), and the Clinicians' assessment of suitability for treatment with the Altura®-System, as determined by institutional standard of care pre-procedural imaging such as high resolution contrast-enhanced CT scans (slice thickness *maximum* <3mm with axial, coronary, sagittal views). The CT scan will ideally have been performed within 3 months of the planned implantation date. Blood tests and physical examination will also be collected as standard of care at each institution.

A consenting patient is considered enrolled upon introduction of the selected delivery system into the patient.

5.6 IMPLANTATION PROCEDURE

The Altura procedure is performed according to institutional standard of care. Patient sedation, vascular access and procedural techniques will be handled at the discretion of the Investigator. For

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detailed information on the Altura delivery and deployment procedural steps please refer to the attached Instructions of Use (IFU, Attachment 1).

5.7 FOLLOW-UP REQUIREMENTS

Subjects will be followed procedurally, to hospital discharge and thereafter through to 5 years (total follow-up commitment) as per institutional standard of care.

The following table outlines a suggested follow-up schedule which may be altered to meet standard of care at individual sites.

Suggested Schedule of Tests:	**Screening / Baseline**	**Procedure**	**Pre-Discharge**	**Days 1 and 7 post-discharge**	**FUP 1 1 month**	**FUP 2 6 Month**	**FUP 3 1 Year**	**FUP yearly through to 5 Years**
Inclusion/Exclusion	X							
Demographics/Medical History	X							
Physical Examination†	X		X		X			
Blood Tests‡	X		X		X			
Contrast-enhanced CT scan	x¥				x*		x*	x*
Groin ultrasound if discharge within 24 hours			X					
Procedural Information		x						
EQ5d Quality of Life and Pain scores				X				
Adverse Events		x	X		X	x	x	X

†The physical examination includes overall health, physical assessment, and vital signs.

‡Blood tests include serum creatinine and hemoglobin, if collected

¥High resolution, contrast-enhanced CT scan is preferred up to 3 months prior to the scheduled procedure.

*If the institution's standard of care for EVAR subjects involves another imaging modality eg US and/or x-ray, that modality may be collected alternatively.

6. STUDY EVALUATIONS

6.1. PRIMARY STUDY EVALUATIONS

The primary effectiveness evaluation is an assessment of the following:

1. Immediate procedural technical success
2. Freedom from aneurysm rupture
3. Freedom from conversion to open surgical repair through to five years
4. Endoleak of any type, apart from type 2, through to five years
5. Clinically significant migration requiring intervention or an increased frequency of surveillance through to five years

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6. Aneurysm enlargement (>5mm) through to five years
7. Aneurysm regression (>5mm) through to five years
8. Secondary endovascular procedures of any type through to five years
9. Secondary vascular and/or endovascular procedures for resolution of:
    - Endoleak of any type
    - Device occlusion (due to thrombus or other causes)
    - Device migration AAA sac expansion (>5mm diameter increase)
    - Device defect

1. Assessment Peri-operative Safety Parameters (up to 30 days post-procedure):
    - Procedural Blood loss >1,000mL
    - Mortality (all-cause)
    - Bowel Ischemia
    - Paraplegia
    - Renal Failure
    - Myocardial Infarction
    - Respiratory Failure
    - Stroke

6.2. ADDITIONAL EVALUATIONS

Additional evaluations include, but are not limited to:

1. Device Patency and Integrity throughout the study
2. Incidence of distal thrombosis, embolization and iliac stenosis
3. Procedural and in-hospital evaluations:
    - Total intervention time (skin-skin)
    - Total theatre use time (including anaesthesia)
    - Fluoroscopy time and radiation dose
    - Contrast volume used
    - Estimated blood loss
    - Incidence of transfusion
    - Time in ICU
    - Time to hospital discharge
    - Proportion of patients where a decision is made by the surgical team that the patient is fit to be discharged from the hospital <24h post procedure completion
    - Readmissions for access site complications
    - Readmissions for other complications

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7. ELECTRONIC CRF

The registry will utilize an electronic case report form (eCRF) system for data collection. All site staff will be trained on correct eCRF completion during the initiation visit at each site. Only trained personnel will receive access and be able to enter data in the eCRF. All eCRF pages will be electronically signed by the investigator at each site. Each subject will be anonymized and given a specific registry number in the eCRF. Please refer to Attachment 3 for a detailed version of the eCRF.

8. DATA MANAGEMENT

The data required for the registry will be entered by the investigation sites into electronic case report forms. Detailed edit checks will ensure a high-quality standard of the data entered in the database. Additionally, data management will review the collected data and issue possible queries. Queries should be resolved by the investigation site on an ongoing basis. When all registry data is complete, the database will be locked and data analyzed.

9. STATISTICAL CONSIDERATIONS

9.1 STUDY POPULATIONS

Two study populations will be considered for data analysis.

ITT population: all subjects who have signed the ICF, fulfilled all eligibility criteria, and undergone endovascular intervention with the Altura®-System.

Effectiveness population: all subjects from ITT population for whom the Altura® System has been successfully implanted.

9.2 GENERAL CONSIDERATIONS

Statistical analyses will be done using SAS System®, Version 9.2 or further.

All safety endpoints will be analyzed on the ITT population. The number of successful device implantation and procedure measurements will be reported on the ITT population.
For all end points which are not safety outcomes, the statistical reporting will be done on the effectiveness population.

9.3 STATISTICAL METHODS

Quantitative parameters will be described using the following summary descriptive statistics: number of collected values, mean, standard deviation, median, first and third quartiles, and minimum and maximum values.
Qualitative parameters will be described using frequencies and percentages. Percentages will be calculated on the number of collected observations.
In all cases, the number of missing values will be specified.

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All confidence intervals will be two-sided and performed at the 0.05 significance level.

Exact bilateral confidence intervals at the 95% level will be presented.

For all binary parameters recorded in time, specifically safety endpoints, Kaplan-Meier analyses with survival estimates will be performed.

The rate of Major Adverse Events (MAEs) will be assessed at 1 year and subsequent time points. The events to be analyzed will be:

All-cause death,
Stroke (excludes transient ischemic attack),
Myocardial infarction,
Renal failure (excludes renal insufficiency),
Respiratory failure (excludes chronic obstructive pulmonary disease or pulmonary complications),
Paralysis (excludes paraparesis)
Procedural blood loss > 1000mL

A full analysis of all safety endpoints will be presented, and in particular these data will be presented and analyzed as follows:
- Total number of serious adverse events (SAE) reported
- Total number of unanticipated adverse device (UADE) effects
- Total number of unanticipated serious adverse device (SUADE) effects
- Total number of adverse events (AE) reported
- Number and percentage of subjects with at least one SAE reported
- Number and percentage of subjects with at least one UADE reported
- Number and percentage of subjects with at least one SUADE reported
- Number and percentage of subjects with at least one AE reported

9.4 DISTRIBUTION OF THE PATIENTS

The number of patients in the ITT and in the Effectiveness population, as well as the distribution by site will be presented.
The reasons for interruption of patient follow-up will be listed and the average time of patient follow-up will be given.
Descriptive statistical data will be used to draw up the characteristics of subjects at the time of enrollment (demographics, baseline data).

9.5 HANDLING MISSING VALUES

In order to provide unbiased and informative findings, no replacement of missing values is planned for any parameters. In all applicable cases, reported analysis will mention the number of missing values for each outcome relatively to the considered analysis set (ITT, Effectiveness).

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9.6 SUBGROUP ANALYSIS

In addition to the analysis of recorded evaluations on the ITT and Effectiveness populations, several subgroups are pre-specified, although not limited to:

1. Elective AAA subjects treated having anatomical characteristics within and outside current company IFU, if any
2. Subjects treated with the Altura® System for revision of previous attempts at AAA repair, both with conventional grafts and endografts
3. Subjects requiring concomitant or secondary procedures for endovascular device placement
4. Treatment times for patients treated as part of the run-in cohort as compared to the formal registry component
5. Total fluoroscopy times in the run-in cohort as well as the formal registry

For these subgroups, all parameters will be assessed using the same statistical methods than described in section 9.3, as appropriate.

10. ADVERSE EVENT REPORTING

The safety of the device will be monitored throughout the registry by assessment of unanticipated adverse device effects (UADE), serious unanticipated adverse device effects (SUADE) and serious adverse events (SAE). All unanticipated adverse device effects and serious unanticipated adverse devise effects will be reported in the electronic CRF system and will be assessed by an independent safety review in order to comply with vigilance reporting. Other adverse events will not be considered in this registry (Definitions according to ISO 14155:2011(E)).

10.1 UNANTICIPATED ADVERSE EVENT DEFINITIONS[6]

UADE

UADE are (non-serious) adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device as well as any event resulting from user error or from intentional misuse of the investigational medical device.

USADE

An USADE is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. An USADE is a serious adverse device effect which by its nature, incidence, severity or outcome **has not been** identified in the current version of the risk analysis report.

Serious Adverse Event (SAE)

An SAE is a serious adverse event that

[6] Clinical investigation of medical devices for human subjects, good clinical practice. ISO 14155:2011.

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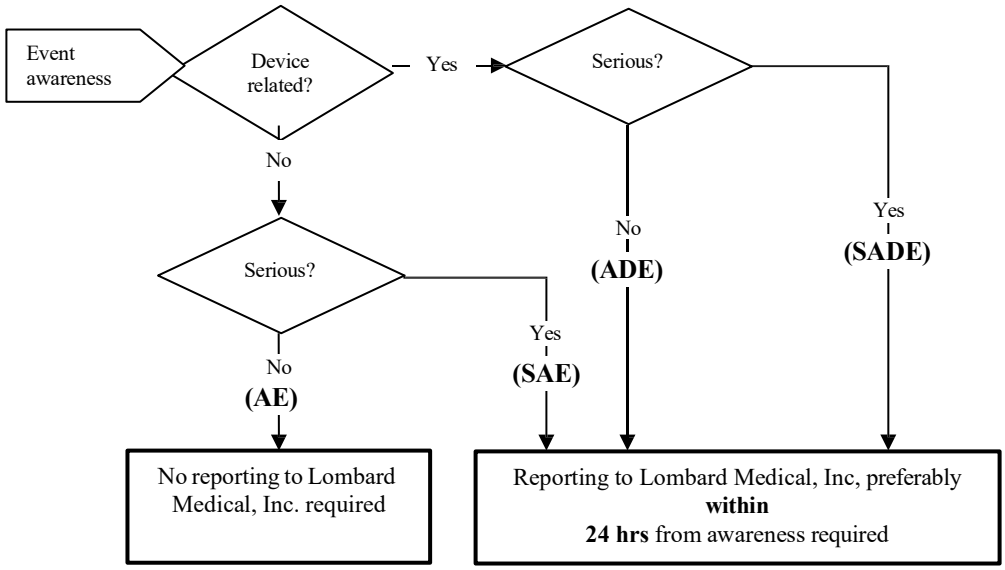
a) led to death
b) led to serious deterioration in the health of the subject, that either resulted in
    1) a life-threatening illness or injury, or
    2) a permanent impairment of a body structure or a body function, or
    3) in-patient or prolonged hospitalization, or
    4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
c) led to fetal distress, fetal death or a congenital abnormality or birth defect

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered an SAE.

10.2 ADVERSE EVENT REPORTING

The **relation to the investigational device** is classified by the investigator as either:

- Related or
- Not related
- The investigator must report any UADE, SAE and SUADE **in the eCRF** to Lombard as soon as possible when he becomes aware of the event, preferably **within 24 hours of awareness** of the event. The decision tree for the event reporting looks as follows:



10.3 ADVERSE EVENT DEFINITIONS

The following event definitions will be applied during this study.

- *Death*: Any death occurring during the study period, regardless of cause.
- *Aneurysm-related death* is defined as any death occurring within 30 days from the date of

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the procedure, regardless of cause, and death due to aneurysm rupture or following any procedure intended to treat the aneurysm.

- *Cardiac-related death* is defined as death due to arrhythmia, heart failure (including cardiogenic shock), or myocardial infarction
- *Clinically significant migration* is defined as distal stent movement more than 10 mm from the original implant location relative to the centre of the distal renal artery requiring intervention or causing complications
- *Pulmonary-related death* is defined as death due to due to pulmonary edema, respiratory failure, or pulmonary embolism
- *Vascular-related death* is defined as death due to stroke, cerebral hemorrhage, or other clear vascular event that is not categorized as cardiac-related or pulmonary-related
- *Other* is to be used to identify a death due to any event that cannot be clearly categorized as above, but where some information is available.
- *Unknown* is to be used to identify a death where no information is available.
- *Procedural Technical Failure* is defined as a failure of the Altura® System to be delivered and deployed, such that the procedure is not completed, or the device failure results in a serious complication, or a residual endoleak occurs that cannot be resolved during the index procedure.
- *Major Adverse Event:* An event occurring during the study that meets one of the following criteria:
    - *All-Cause Death* (see above).
    - *Bowel Ischemia*: the lack of adequate blood flow to the intestines that requires intensification of medical therapy or surgical/endovascular intervention.
    - *Myocardial Infarction:* increase of one or more cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit (URL) together with evidence of myocardial ischemia with at least one of the following: myocardial ischemia; ECG changes indicative to new ischemia (new ST-T changes or left bundle branch block (LBBB)); development of pathological Q-waves in the ECG; imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
    - *Paraplegia*: Paralysis of the lower extremities inclusive of the lower trunk, excluding paraparesis;
    - *Renal failure*: GFR < 15 ml/min, permanent dialysis, renal transplant, or death due to renal dysfunction.
    - *Respiratory Failure*: pneumonia or respiratory failure requiring ventilator support beyond 24 hours post-procedure
    - *Stroke*: a sudden development of neurological deficit due to vascular lesions of the brain such as hemorrhage, embolism, or thrombosis that persists for >24 hours;
    - *Procedural Blood Loss >1,000mL*: Estimated blood loss during the index procedure >1,000mL.

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10.4 OTHER DEFINITIONS

- *Aneurysm Sac Enlargement*: Aneurysm sac diameter increase of >5mm in late follow-up as compared to the initial post-operative measurement.
- *Aneurysm Rupture*: bleeding or leaking of blood from the aneurysm subsequent to the index procedure.
- *Conversion to Open Repair*: open surgical repair of the abdominal aortic aneurysm due to unsuccessful delivery or deployment of the stent graft, due to complications or other clinical situations that precluded successful endovascular treatment, or at any time following initial successful endovascular treatment for any reason.
- *Luminal Thrombus Requiring Intervention*: any endovascular surgical intervention after completion of the Altura® System implantation for resolution of endograft thrombosis. Excludes 100% occluded vessels.
- *Distal Ischemia*: New onset of compromised peripheral blood flow resulting in femoral or peripheral arterial occlusion or stenosis (attributable to the index procedure and not related to natural progression of atherosclerotic disease) causing a threat to the viability of the limb and requiring surgical or percutaneous intervention; or stent graft occlusion requiring any intervention.
- *Endoleak*: Clear evidence of contrast outside the fabric of one or both endografts which communicates with the aneurysm sac originating proximally at the infrarenal segment (Type IA), distally (Type IB); between components, if an extender is used (Type III); trans-device (Type IV); or from a patent collateral vessel (Type II: e.g., lumbar artery; inferior mesenteric artery, accessory renal artery). Contrast outside of the braided stent but contained within the graft fabric, that does not communicate with the aneurysm sac is not to be reported as an endoleak.
- *Migration*: Reported stent distal movement >10mm from the original implant location relative to the centre of the distal renal artery.
- *Occlusion requiring intervention*: Intervention for stent occlusion. Excludes vessels which are not 100% occluded.
- *Renal Dysfunction – sustained decrease in estimated GFR after treatment by > 30 % negative change from baseline (minimum 2-follow-up intervals)*
- *Secondary Endovascular Procedure*: any non-diagnostic intervention after the index procedure intended to correct or repair an endoleak, device obstruction or occlusion, migration, aneurysm sac expansion and/or a device defect (including infection);
- *Successful Implantation*: Successful delivery and deployment of the device.

11 RESPONSIBILITIES

11.1 SPONSOR RESPONSIBILITIES

This registry is conducted under the responsibility of Lombard Medical Ltd. Only Lombard staff and designees approved by Lombard will participate in this registry. Lombard is responsible as the Sponsor to ensure:

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- Proper site and investigator selection.
- Availability of signed investigator agreements prior to study initiation.
- Availability of regulatory and EC approval prior to the initiation of the study at any site.
- Appropriate insurance policies are obtained and maintained for the study.
- That the Study is managed and monitored with special attention to verification of all clinical requirements, adherence to protocol, good clinical practices and compliance with applicable government and institutional regulations.
- Proper regulatory approvals are obtained, and reporting to regulatory authorities per applicable regulations is performed.
- That sites are supported and adequately trained on the device.
- That specially trained Lombard staff and designees approved by Lombard will support the sites during the application of the system in operating theatres, hybrid rooms etc.

11.2 INVESTIGATOR RESPONSIBILITIES

It's the **investigator's** and **investigation site staff's** responsibility to conduct this registry in accordance with relevant rules and regulations, including but not limited to, this registry protocol, the signed investigator agreement, Good Clinical Practices, all applicable laws and regulations and any conditions or restrictions imposed by the reviewing EC. This includes compliance with requirements related to EC approval and reporting, and proper patient informed consent prior to participation in the study. The investigator is also responsible for protecting the rights, safety, and welfare of the subjects under his/her care.

- Each investigator, or designated sub-investigator, is responsible for supervising all procedures conducted under this protocol at his/her institution.
- Furthermore, the investigator is responsible for ensuring that data are completely, accurately, and promptly recorded on each patient's eCRFs and related documents are available to verify the accuracy of the eCRFs, and for ensuring the clinical monitor has access to all necessary records to ensure the integrity of the data
- The investigator is also responsible for providing anonymized pre-operative CT scan images, identified with the patient study code, to the sponsor. In addition, they will also be required to provide images in the advent of a clinically significant event or re-intervention.

In order to be considered for the participation in the registry the investigator must:

- Provide the sponsor with a complete signed registry contract
- Acquire and provide all applicable approvals, including but not limited to, the ethics committee (where appropriate) and/or the hospital board.
- **The investigator must complete the above process and start enrollment within 3 months from the date he/she receives the needed regulatory documents for the registry. If this deadline cannot be met the investigator and his/her team will not be able to participate in this registry.**

In addition, all local regulations must be adhered to, in particular, those which afford greater protection to the safety of registry subjects. Suitably qualified and trained clinical personnel of the investigation site must ensure compliance with the protocol, adherence to ethical and regulatory obligations and proper maintenance of registry records.

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By signing the protocol signature page, the investigator agrees to conduct the registry according to protocol.

11.3 INDEPENDENT IMAGE ANALYSIS

Where the implanting physician determines that there has been a clinically significant device related event, the images datasets relating to that patient will be reviewed by a group of independent Clinician assessors. The independent Clinician(s) will complete the eCRF data capture form for the evaluations.

12 CONFIDENTIALITY AND PATIENT RIGHTS

12.1 CONFIDENTIALITY

Registry subjects will be identified only by a unique subject number used in all correspondence and the registry database. The investigator and the investigation site team shall maintain patient confidentiality during all site audits and inspections and in all documentation. The investigator will keep a list containing the names of all patients along with their assigned subject number.

All information provided to the investigator relevant to the device, as well as information obtained during the course of the registry, will be regarded as confidential. The investigator and all members of his or her registry team agree not to disclose or publish such information in any way to any third party without prior written permission from Lombard which will not be unreasonably withheld, except as required by law. The Investigator will take all measures to ensure patient confidentiality is maintained at all times. All subject data must be anonymized before retrieval from the clinical site.

12.2 PATIENT RIGHTS

The subject has the right to withdraw from the registry at any time and without reason.
Upon early withdrawal from the registry, the electronic case report forms (eCRFs) should be completed as far as possible and the reasons for withdrawal should be documented if possible.

13 ETHICAL CONSIDERATIONS

The registry will be performed with a CE-marked device. No data identifying the subject and no other confidential data will be recorded. No procedures and examinations are required in addition to those that are standard of care in each participating site. The knowledge gained from this registry might provide information to improve the treatment of patients with AAA eligible for endovascular treatment and/or the device.

This registry is performed in accordance with the Declaration of Helsinki and the parts of ISO 14155:2011(E) applicable for registries.

14 MONITORING

The eCRF will **not** be considered as source document.

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Source data verification will be performed by means of intermittent on-site and/or off-site monitoring. Details will be outlined in the monitoring plan.

15 STUDY TERMINATION

The registry can be terminated or suspended prematurely at a specific investigation site or in total due to low compliance to the CIP, lack of enrolled subjects or that it becomes apparent that the registry can no longer fulfill its aims. Lombard can do so at its own discretion without having any further obligations to the registry site(s).

16 PUBLICATION

Lombard intends to publish the results of this registry. Lombard reserves the right to include the report of this registry in any regulatory documentation or submission or in any informational materials prepared for the medical profession. The ownership of the data shall at all times be held by Lombard. Only Investigators from centres with high protocol compliance, fast enrollment and high quality data sets from follow-up visits will be considered as authors on publications.

Any single centre within the registry is not permitted to publish its own separate registry data prior to the publication of the multi-centre data at any time throughout the study, without the express permission of Lombard Medical.

Lombard agrees that after publication of multi-centre data investigators shall be permitted to present at symposia, national or regional professional meetings, and to publish in journals, theses or dissertations, or otherwise of their own choosing, methods and results of the registry. Any prior publication in any way or form is not permitted, unless approved in writing by Lombard.

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ATTACHMENT 1

Instructions for Use (IFUs)

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ATTACHMENT 2

Informed Consent Form (Template)

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ATTACHMENT 3

Case Report Forms (Template)

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