**Proposal to the ExCo of the ESVS**

# The European Research Hub

**Starting as an endorsement and network organization, which could later develop into an organisation applying for grants/sponsorship, awarding grants, and performing trials.**

*(Updated September 14, 2021, by the Task Force (TF).[1])*


---

**Suggested aims and organisation**

We suggest that that, at least initially, the ERH itself would not perform either randomised trials or prospective observational studies but work as an endorsement and network organization within the European Society for Vascular Surgery. The steering committee would then develop the following activities:

1) Evaluate research proposals from European researchers, preferably multicentre and multinational trials, according to a SOP to be developed, providing informed peer-review and endorsement to support external funding. Proposals can be initiated by individual researchers, groups, as well as by the ESVS Guidelines and Vascunet committees.

---

[1] Members of the Task Force who developed this proposal (in alphabetic order): Christian Behrendt, Martin Björck, Alison Halliday, Stavros Kakkos, Joakim Nordanstig, Janet Powell, Maarit Venermo

2) Facilitate the feasibility (information about access to regulator criteria in ESVS countries, participation, and recruitment) of good quality proposals.

3) Maintain, and update continuously, a list of interested researchers/institutions that can be invited to participate when a proposal for multicentre research is endorsed.

4) Maintain a contact list of experienced epidemiologists, biostatisticians, and other experts that can be consulted when a trial is designed.

5) Facilitate contact with established research facilities. This can be helpful when the trial is conducted, such as data management, randomisation, production of placebo tablets, etc.

6) Organize educational activities during ESVS and other meetings.

The advantage of starting by giving this kind of support, rather than performing trials, are the following:

1) The project could start earlier.

2) The financial needs are much less, and would not constitute any limitation.

3) With this start the potential of the ERH can be evaluated. If it turns out to be successful, ERH could develop into a more “active” organisation after some years

4) Evidence of a successful start, could facilitate industrial sponsorship for moving forward to running trials in the future.

5) Members of the Task Force have identified three trials that could serve as pilot projects for this first phase (Appendix).

## Time line and suggested activities

**October 2021-January 2022**: Communication between the ExCo and the TF regarding the details of the proposal. Work within the TF to develop the three pilot projects continues in parallel, please see the appendix.

**November 2021**: Budget proposal for 2022. 10-15.000 Euro? It would need to cover the expense of the kick-off meeting in November 2022, see below.

**February 2022**: strategic meeting of the ExCo: Final decision if to proceed with the project.

**March 2022**: Announcement of applications to become members of the ERH committee. Deadline for applications April 30.

**May 2022**: Decision by the ExCo to nominate 5-9 members of the committee (the number may depend on the strength of the applications).

**May – September 2022**: Monthly TC to develop the organisation of the ERH committee and the three pilot projects identified by the TF.

**September 2022**: First FtF meeting of the committee during the ESVS meeting in Rome.

**November 2022**: First 2-day kick-off meeting (brain-storming) similar to when a Guidelines committee starts to work. The aims are to:

a) Define the short and long term aims of the ERH.

b) Identify the steps of the application and endorsement process.

c) Identify the clinically relevant research gaps and trials, after contact with the chairs of the different Guidelines writing committees and the GLC.

d) Identify the steps how to receive national and international funding in the short and long term perspective.

e) Plan the activities and apply for the budget for 2023.

# Appendix:

Description of the three multinational trials that were identified by the TF. They are meant as pilot projects to be developed in parallel with the creation of the ERH, to gain more experience in organising multinational trials, endorsed - but not financed - by the ESVS.

**1) Small aneurysm trial for women**

Although it has been shown by the UKSAT and the ADAM trials that watchful waiting is as efficient as early surgery for patients with AAA in the interval 4.0-5.5 cm, that is not necessarily true for women. They have a higher rupture risk, but also a higher perioperative mortality, compared to men. It has been estimated that the rupture risk of a 4.2 cm AAA in women is the same as that of a 5.5 cm AAA in men. The endovascular shift may also affect men and women differently. There were only 188 women of 1.090 patients (17%) in the UKSAT, and 9 of 1136 (0.8%) in the US ADAM trial (both published in the NEJM 2002, a long time ago). There were similar sex ratios in the PIVOTAL and CAESAR trials of EVAR vs surveillance respectively. The plan is to randomise women with an AAA in the interval of 4.0-5.9 cm between immediate and delayed surgery, with AAA-related mortality as a primary outcome and AAA-related events and quality of life as secondary outcomes. The numbers required demand a multinational study.

**2) The optimal antithrombotic treatment after endovascular infrainguinal revascularisation**

The CAPRIE study, performed twenty years ago, demonstrated a MACE prevention benefit for clopidogrel monotherapy over aspirin monotherapy in patients with peripheral arterial disease. It has also become a common practise to offer a period of dual antiplatelet therapy (DAPT) following lower limb revascularisation despite a relative lack of evidence for this practise among PAD patients. More recently, benefits in terms of composite endpoints including MALE and MACE outcomes have been demonstrated in both stable PAD patients and in PAD patient undergoing open or endovascular infrainguinal revascularisation; when combining low dose rivaroxaban with aspirin (dual pathway inhibition, DPI), as compared to aspirin monotherapy (COMPASS and VOYAGER PAD trials). In the setting of endovascular revascularisation, the question however remains which of the currently used and evidence-based antithrombotic treatment regimens that translate to the most pronounced patient benefit while at the same time causes least bleeding side effects.

The aim of this three-armed open-label RCT study proposal is to determine the efficacy and safety of DPI versus DAPT versus clopidogrel monotherapy on hard endpoints of treatment efficacy (MACE and MALE endpoints) following infrainguinal endovascular revascularisation.

**3) EVAR vs open surgical repair in AAA patients with a hostile neck**

EVAR in AAA patients with a “hostile” neck, treated outside the IFU of conventional devices is associated with suboptimal results (endoleak, AAA rupture and patient survival). Results are compared with standard EVAR performed in patients with a AAA neck that has favourable characteristics allowing endograft placement within the IFU of the various devices. Typically, a hostile (infrarenal) neck is described as a short neck with a length of less that 10mm in length, an angulated neck with a suprarenal angle $>60^0$, or a neck with a non-cylinder morphology (tapered or

reverse tapered), often in combination. Occasionally, the presence of a focal neck bulge prevents IFU EVAR. Recently inside IFU EVAR for large infrarenal necks has also been shown to be associated with a high frequency of EVAR complications. Unfortunately, outside the IFU EVAR is a worldwide practice, particularly for patients deemed to be at high risk for open surgical repair (e.g. patients with inflammatory AAAs, high age, multiple or severe comorbidities).

The advent of fourth generation endografts (Endurant IIs, Aorfix, Ovation/Alto, Treovance and Gore conformable) has potentially solved the problem of the hostile neck in most cases. There is no trial evidence, however, that they are better than open surgical repair, and no long-term follow-up data.

The aim of this RCT is to compare open surgical repair with EVAR using a fourth generation device (Endurant IIs, Alto and Gore conformable) in patients with a AAA and a hostile neck, suitable for both procedure types (inside IFU). This will be a non-inferiority trial, and randomisation will be stratified by the particular “hostile” neck anatomy, as described above.