Name of project	**Validation of AVAS classification by using machine learning in prediction of vascular access creation and in the prediction of uninterrupted use of the vascular access for dialysis**
Acronym of the project	**VAVASC trial** (**V**alidation of the **A**rterio **V**enous **A**ccess **S**tage **C**lassification) trial
Web page	**www.vavasc.com**
ClinicalTrial identifier	NCT04796558
Leader of the project	Balaz, P, O'Neill, S., Lawrie, K.,
Type of the study	Prospective, multi-centre, international, collaborative
Registration	None
Number of patients included	Minimum 500, optimal 1000
Start of the study	2021
Estimated end of the study	2023-2024
Ethics committee approval	Yes. This should be reviewed in each centre, and if necessary each centre should have approval of its own ethics committee. However, please note that this is an observational study that is collecting data from existing medical records. In many centres (e.g. those with routine ultrasound arteriovenous mapping) there will be no alteration to patient care. There is therefore unlikely to be a requirement for patient information or consent. If ethical approval is required in individual centres it could potentially be obtained from a Proportionate Review Service. If applicable, participating units should also register with local audit/clinical governance structures and gain permission from the Caldicott Guardian.
Informed consent	Depends on the centre and decision of the ethical board of each centre
Database (data storage)	Electronic database - eCRF (Waldauf, P.)
Statistic analysis	Predictive modelling by using machine learning (Waldauf, P., O'Neill, S.)
Financial support	No

Background	Ultrasound of upper limb vessels as a part of preoperative assessment of patients referred for arteriovenous access placement has been recommended repeatedly in several studies and guidelines. Each patient needing arterio-venous access (AVA) is unique and has different possibilities for fistula creation that depend on many factors as well the anatomical condition of inflow arteries and outflow veins, the so-called 'arteriovenous access map'. In 2020 we created, published and retrospectively evaluated the inter-rater reliability of the AVAS classification, which is a simplified way of sharing the information about suitability for access creation depending on vascular anatomy (doi: 10.1093/ckj/sfaa189). However, before routine use of the AVAS classification system in clinical practise it requires prospective validation and comparison with other clinical factors. Finally, whether the AVAS classification can be used for the prediction of vascular access function as defined by uninterrupted use of vascular access for dialysis without need for any access intervention/procedures (SONG-HD, doi: 10.1053/j.ajkd.2017.12.003) remains to be tested. This project has two main parts: 1. Validation of AVAS classification with and without combination with other factors using a predictive statistical model. 2. Validation of AVAS classification in terms of prediction of uninterrupted use of successfully created vascular access for dialysis. The data will be collected prospectively. Both parts of the project will be taking place simultaneously.
Working hypothesis	Part 1: AVAS classification with/without selective clinical parameters is a useful tool for sharing information about the type of AVA which will be created. Part 2: Increasing AVAS with/without selective clinical parameters is an accurate predictive tool for the prediction of the uninterrupted use of successfully created vascular access for dialysis.

Socio Economic aspect	Classification of vascular access is important for improving efficiency of communication across multi-disciplinary teams, which helps streamline care and avoids errors. At the individual patient level it is critical for communicating vascular access complexity and thus ensuring preservation of precious access. At a unit level, in the NHS best practice tariff criteria are based on national guidance and expert opinion that are intended to drive improvements in processes of care. The best practice tariff for haemodialysis is that 80% of patients on haemodialysis should receive dialysis via a functioning arteriovenous fistula. Individual units with complex vascular access populations may be unfairly penalised for not meeting this target. A classification system for vascular access would help define vascular access populations, leading to fairer comparison of unit performance and appropriate remuneration for the cost of care.
Methodology	Data will be collected prospectively (Belfast City Hospital, UK, University hospital Královské Vinohrady Prague CZ). Other centres around the world will be asked for cooperation (announcement will be posted via scientific societies, Twitter, ResearchGate, LinkedIn, Facebook, Kidney Academy etc.) in March 2021. The data collected will be the parameters of the vessels on the upper limb, in order to be able to evaluate AVAS (VAVASC FORM). Along with anatomical dispositions of the patients, other parameters will be collected. Obligatory parameters (parameters A): - Side of the arm: Left Right - Dominant hand: Left Right - Allen's test: Positive Negative (A negative Allen's test is demonstration of a complete palmar arch and intact collateral blood flow to the hand) - Sex: M F - Age: ……

	- Height: …… - Weight: …….. - BMI: …….. - Diabetes: Yes No - CV line previous or current Yes No - Side of the CV line if place Left Right Non-obligatory parameters (parameters B): - Smoking history: Yes No - Hypertension: Yes No - Heart failure: Yes No - Ischemic heart disease: Yes No - Cancer (previous or current): Yes No In order to evaluate uninterrupted use of the vascular access for dialysis (part 2 of the study), we will follow the patients and do a time to event analysis of the arteriovenous accesses for one year after creation or up until the first intervention for maintaining patency has been performed. If the patient dies during follow up the date of death should be recorded. The data for this part will be collected prospectively (Belfast City Hospital, UK, University hospital Královské Vinohrady Prague, CZ and other centres). Predictive models will be used for validation of AVAS classification. The data will be registered via eCRF and analysed by Waldauf, P. and O'Neill, S.
Methodology step-by-step	1. Patient with need of AVA creation is assessed in outpatient clinic as usual. 2. To reduce bias all consecutive patients must be captured. 3. Each registered health care professional (HCP) in the participating centre in the VAVASC study has access to eCRF (electronic database). They can fill the collected data straight into the database or at a later date from the notes they usually take when recording arteriovenous mapping. If the HCP or centre prefers paper forms, a paper document (VAVASC FORM) can

	be used and researchers from each centre will put the data from the paper form into the eCRF regularly. Collection of data into eCRF primarily is the preferable approach. If the HCP examining the patient has access to eCRF, they do not have to fill the paper VAVASC FORM. 4. Patient is scanned using ultrasound and the vascular parameters are marked/registered (eCRF or VAVASC FORM). If the HCP wishes, they can evaluate the patient according to AVAS classification. The HCP can skip this step since the vascular parameters can be used to establish the AVAS by the VAVASC research group. 5. Patients' risk factors are also marked/registered. Only "obligatory parameters" (parameters A) are necessary to collect. The HCP can also collect the parameters B, that are voluntary. For centres using paper form (VAVASC FORM) - If the centre/individual HCP prefers paper forms only, VAVASC FORM is stored in a prepared box in each clinic in the hospital entitled as "VAVASC". - Researcher from each centre regularly collects the VAVASC FORM documents. - Researcher from each centre regularly enters obtained data from VAVASC FORM into the eCRF. - A similar approach may be used by centres that already record the information on the VASVASC form elsewhere (e.g. the medical records or centre specific arteriovenous maps) 6. Patient is indicated for AVA as usual (not necessarily as is indicated by AVAS) 7. Researcher from each centre regularly follows up the patients and enters type of AVA which was created into the eCRF. 8. Researcher from each centre regularly follows up the patients and enter data about the fate of AVA for one year or up until the first intervention for maintaining

	patency has been performed. If the patient dies during follow up the date of death should be recorded.
Statistic method	Predictive modelling using machine learning (O'Neill, S., Waldauf, P.)
Responsibilities of the research team	1. The centre lead registers interest with VAVASC research group, and will seek local ethical approval. 2. Centre lead is responsible for ensuring the required data is collected by HCPs in the clinic, and supervising the data collectors in their centre. 3. HCP in the clinic: Carries out arteriovenous mapping and records clinical data. 4. HCP in the clinic or data collector fills the paper VAVASC FORM/ or fills the data into eCRF (computer) database, approx. 10 minutes. 5. Data collector in each centre where eCRF is not used: may collect the VAVASC FORM and enter data into the eCRF, approx..1 hour/week 6. Centre lead or data collector in each center regularly checks the patient follow up, approx. 1 hour/week 7. Project leader of VAVASC group: regularly sends informative email about status of the study to all researchers (how many patients recruited, how many centres are active etc.). 8. VASVASC group will analyse results and prepare manuscript.
Authorship	Named author is a HCP who acts as a centre lead, and sets up the study in their centre including ethical approval. This HCP is also invited into the writing group, so they are able to participate in drafting and reviewing the final manuscript. Collaborator /collaborative author (also PubMed citable) is a HCP who collects patient data and enters the data in the eCRF or provides the data to the centre lead for entry. To reduce bias collaborators must capture consecutive patients. There is no minimum or maximum amount of consecutive patients that could be entered by a collaborator. However, each collaborator must collect data for patients who have

	gone onto have successful vascular access creation and these patients must be followed up for the full follow up period. Unfortunately, in some cases attempts at vascular creation will fail so collaborators are encouraged to recruit as many consecutive patients as they can. To avoid disadvantaging and excluding low volume centres (which would impact the generalizability of the study) no time limit will be set for recruitment of consecutive patients. However, the eCRF will close to further data entry on X.