Introduction
Cardiovascular Disease (CVD) risk reduction is based on treating modifiable risk factors such as dyslipidaemia, hypertension, diabetes and smoking. Clustering of risk factors in individuals is often evident.

Evidence suggests this approach will lead to risk reduction. The reduction seen in RCTs may not be obtained in routine care. Currently there is no non-invasive method to study cumulative risk reduction when multifaceted risk reduction interventions are applied.

Vascular wall properties such as endothelial function, inflammation and smooth muscle proliferation are important in the pathogenesis of atherosclerosis (Fig 1).

Thus CVD risk and protective factors influence endothelial integrity. Endothelial dysfunction is considered to be reversible by risk factor modification.

Vascular flow patterns can be affected by characteristics of the arterial wall and endothelial dysfunction and vice versa (Fig 1).

Aim of the Study
To develop a robust method to study characteristics of vascular flow using ultrasound to assess endothelial function and vasodilatation. There are four stages:

1. To standardise and validate the methodology to enable computational risk flow data and other flow characteristics to be used clinically. (Current Study).

2. To study different patient groups to investigate associations between the derived vascular flow measurements and estimated risk.

3. To use prospective studies to establish if computational flow dynamic data can predict outcome following treatment in patient groups.

4. To conduct a clinical study to determine the impact of different patient groups on the measurement of plaque) was addressed in 2009 with the publication of the AHA guidelines (Fig 2).

Method
The common carotid artery is of significant pathological importance with respect to stenosis and flow prior to the bifurcation.

The lack of a coherent methodology protocol for ultrasound (to standardise the measurement of plaque) was addressed in 2009 with the publication of "Joint recommendations for reporting Carotid Ultrasound Investigations in the United Kingdom".

The following characteristics of vascular flow will be assessed by ultrasound measurements of velocities at peak systole and at end diastole at different locations in the carotid artery (82 individuals, 26 with HD and 26 healthy volunteers).

1. Velocity & Velocity Gradient
2. Dynamic Velocity Profiles
3. Wall Shear Stress
4. Dilation & Artery Stiffness

Velocity & Velocity Gradient Evaluation
Velocity will be measured at equidistant intervals across the vessel diameter. The flow will be measured in a line across the lumen in the direction of flow. This will begin at 90 degrees to the wall when no plaque is present.

Current limitations & difficulties:
- Minimum distance between measurement point ~ 0.5mm.
- Consistency of intervals operator dependent.
- Measurement line may not be perpendicular to vessel wall if plaque is present.

Wall Shear Stress Evaluation
Changes to the endothelial surface layer, the glycocalyx, are the precursor to vascular injury and atherosclerosis. Both typically develop at branches and bends in the arterial tree that are exposed to disturbed patterns of blood flow. The glycocalyx provides a barrier against leakage of fluid, proteins and lipids across the vascular wall. In addition it modulates the adhesion process of leukocytes to the vessel wall.

Vink et al have shown that glucose itself alters the structure of the glycocalyx. It is possible that glycocalyx modifications may provide valuable insight into the early stages of atherosclerosis.

Dynamic Velocity Profiles
The velocity profile in straight pipes at steady state is parabolic. Due to the pulsatile nature of blood flow velocity profiles are very different and indeed vary significantly over the cardiac cycle.

The membrane makes RBC behaviour more complicated than e.g. tumbling. A basic science approach to blood flow simulation using explicitly resolved cellular component avoids use of empirical models. It is the only way correctly to account for interaction with vessel boundary conditions. The fluid shear forces to which the endothelium is exposed and which is the trigger for the release of nitric oxide (NO).

Distensibility/Stiffness of Arteries
Arteries are known to become stiffer and lose flexibility as we age. This manifests itself in higher blood pressure values and higher pulse wave velocities (PWV) due to the pulse wave being less well-damped. Artery stiffness is determined noninvasively by measuring change in diameter by US and blood pressure measurement.

Studies using aortic PWV measurements found PWV to be significantly higher in hypertensive-diabetics compared to patients with diabetes or high blood pressure alone, and in turn, PWV in these patients were found to be higher than in healthy controls. Thus, the additive nature of hypertension and diabetes to cardiovascular risk is reflected by abnormalities in PWV measurements.

Bibliography
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