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P338 -THe East and NoRth LOndon DIabetes Cohort Study (HEROIC): Rationale, Study Design and Outline Protocol

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Introduction

Diabetic kidney disease (DKD) is the commonest single reported cause of end-stage renal disease worldwide. Although the level of albuminuria has been shown to be a strong predictor of adverse renal and cardiovascular outcomes, there remains a high degree of heterogeneity in the clinical presentation, histopathology, rate of progression, and complications of disease. This is complicated further by: (i) the inclusion of patients with both chronic kidney disease and diabetes in studies without biopsy-confirmed DKD, despite the finding that up to 60% of renal biopises in patients with diabetes may demonstrate alternative and/or additional diagnoses, and (ii) studies of DKD have been conducted predominantly in white populations, despite other ethnicities having a higher prevalence of diabetes and often more severe disease.

East and North Central London is one of the most ethnically diverse and socially deprived areas of Europe with some of the highest rates of diabetes and associated complications.

We are undertaking the HEROIC study, which aims to:
1. Identify a multi-ethnic cohort of patients with an accepted and standardised histological diagnosis of DKD and moderate or high risk of progression;
2. Describe the pattern of decline in kidney function and development of complications over time;
3. Explore the relationship between progression and
i. histological parameters
ii. structural and functional imaging of the kidney, heart, blood vessels and retina using MRI and optical coherence tomography angiography (OCT-A);
4. Establish a tissue and biofluid resource for the investigation of novel markers and mediators of disease progression.

Methods

HEROIC is a secondary care-based, longitudinal study of patients with biopsy proven DKD. Patients at moderate or high-risk of progression according to eGFR and albuminuria criteria will be invited to participate (Figure).

Demographic, clinical, quality of life and laboratory measures will be assessed annually over 5 years. Biopsy material will be biobanked along with blood and urine samples collected at baseline and annually. Measured GFR, echocardiogram, renal and cardiovascular MRI, along with OCT-A will be performed at

baseline and twice more over the follow-up period. The primary outcome is death, renal replacement therapy or 30% decline in eGFR.

The study commenced in December 2018 and aims to recruit 500 participants. HEROIC is designed as a hypothesis generating observational study, but the sample size is based on 90% power to detect associations between histological and imaging parameters, and renal outcomes.

Value of Results and Summary

HEROIC represents a unique multi-ethnic longitudinal study of histologically characterised patients with DKD. This is the first study of its kind with standardised inclusion criteria and serial collection of clinical data, biological samples and imaging parameters. This work will not only provide a detailed description of risk factors for progression of disease, but also a bioresource with the potential to identify novel markers of renal decline, and uncover key mechanistic pathways underlying the pathogeneis of DKD.