Principal Investigator
Dr Alexandru Dregan

Address
King's College London, Primary Care and Public Health Sciences, Capital House, 42 Weston Street, London SE1 3QD. United Kingdom.

Summary of research
Arterial stiffness, Cardiovascular Disease, Biomarkers, Inflammation

Application Lay Summary:
1a: Our recent findings published in Circulation indicated an association between several inflammatory disorders with cardiovascular disease (CVD). The study used primary care data with incomplete information on traditional vascular risk factors (ie hypertension, cholesterol) and demographic characteristics. In this study we aim to explore the possibility that the prevalence of inflammatory disorders and their association with incident CVD and mortality events vary across different deprivation and ethnic groups. Secondly, in a subsample of participants (N=190,000) we will test the hypothesis that inflammatory biomarkers and regulatory factors are associated with markers of atherosclerosis (arterial stiffness) and clinical outcomes.

1b: Our research is funded by the NIHR Biomedical Research Centre at Guy’s and St Thomas’. We aim to develop our expertise to utilising and analysing the UK Biobank data. The planned analyses will provide new understanding about the role of inflammation in CVD risk across different population subgroups. These findings will help identify the need for more targeted preventative measures. The use of inflammatory and CVD biomarkers will highlight potential mechanisms through which these inflammatory conditions may impact on CVD.
risk. The findings will facilitate enhanced risk prediction modelling and identify potential therapeutic targets for inflammatory disease patients.

1c: In the full UK Biobank cohort, baseline data on inflammatory disorders will be used to assess their prevalence and relationship with subsequent risk of CVD and mortality in subgroups defined by their deprivation and ethnicity. Baseline vascular risk factors (ie smoking, hypertension, cholesterol, diabetes, BMI) will be used as covariates. Additionally, the relationships between inflammatory biomarkers (ie CRP, rheumatoid factor) with inflammatory disorders, as well as with CVD and CVD-related biomarkers (ie arterial stiffness) will be estimated to explore mechanisms through which inflammation influences CVD risk. The impact of genetic regulators of inflammation biomarkers (IRF-5) will be explored.

1d: The analyses of inflammatory disorders and risk of CVD and mortality events will be conducted on the full cohort, except those with established CVD at baseline. When available in 2016, the relationships between measured inflammatory biomarkers with CVD will be conducted on the full cohort, except those with established CVD at baseline. The relationships between measured inflammatory biomarkers with CVD-biomarkers will be conducted on the subsample of patients (N=190,000) with a measure of arterial stiffness. We would like to request access to the genotype and primary care data when available, to identify incident cases of disease.

“We plan to expand the scope of the investigation to consider the interaction between inflammation and mental health (e.g. depression and psychotic disorders) as a determinant of subsequent CVD morbidity and mortality. We plan to test the hypothesis that inflammation and depression have a synergistic impact on CVD incidence and mortality.”