



**Application number/Title:** 30439 - Unravelling environmental and genetic drivers of gallstone disease

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**Keywords provided by the Applicant PI to describe the research project:**

Gallstones, Cholelithiasis, Cholecodolithiasis, Gallbladder, Cardiovascular disease

**Application Lay Summary:**

**1a:** Gallstones are a common condition which affect up to 15% of adults in the developed world. Gallstones are typically found in the gallbladder, under the liver. Whilst in the gall bladder they may cause pain and discomfort, however, if gallstones migrate through the bile ducts (tubes joining the liver and gall bladder to bowel) they can cause people to become very unwell. The presence of gallstones has been linked to the development of other diseases, such as heart disease. This study will identify risk factors for developing gallstones and establish which people go on to develop gallstone related diseases.

**1b:** This study will identify genetic variants associated with the development of gallstone disease and how these variants interact with environmental factors. Gallstone disease is a major health burden in developed countries. Based on this study, it may be possible to prevent gallstone disease, treat recurrent disease or identify future therapeutic targets. This is of particular concern in patients who are unfit for biliary tree surgery. Furthermore, it has been demonstrated that gallstone disease is associated with future heart disease. By identifying at risk groups, it may be possible to implement interventions which will allow prevention of cardiovascular disease or cancer.

**1c:** UK Biobank clinical data on gallstone disease, gallbladder operations, blood tests and genetics will be collated. We will then compare patients who have

gallstones to those who do not, this will allow use to identify genetic changes which lead to the development of gallstone disease. Once these changes are identified we will see if patients with these changes have gallstones earlier in their lives. We will then assess the impact of diet, exercise and other environmental factors on the development of gallstones. Finally we will identify genetic changes associated with the development of heart disease or cancer after gallstones.

**1d:** We would like the full cohort of patients who have data available on the development of gallstones and environmental factors, including diet, exercise and sociodemographic factors. We would also like access to participants who have been genotyped in order to identify genetic variants associated with the development of gallstone disease.