Application number/Title: 18532 - An epidemiological and genome-wide association approach to coeliac disease

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

CoeliacDisease, IrritableBowelSyndrome, Environment, Lifestyle, Genetics,

Comorbidities

Application Lay Summary:

1a: Coeliac disease (CD) is an autoimmune condition of the digestive system characterised by an adverse reaction to gluten. CD prevalence is estimated at 1% in Europe and North America, but may be as high as 8-10%, whilst UK CD incidence has increased fourfold between 1990 and 2011, likely due to increased diagnostic testing. The current proposal has two main aims: firstly, to investigate the association between a wide range of sociodemographic, environmental and lifestyle in association with prevalent and incident CD; secondly, to perform a genome-wide association study (GWAS) in order to identify genetic variants associated with CD.

1b: CD consists of a range of debilitating gastrointestinal and non-gastrointestinal symptoms. Whilst avoidance of gluten can ameliorate these symptoms, evidence suggests that CD is underdiagnosed or often misdiagnosed as other conditions such as irritable bowel syndrome (IBS). Furthermore, apart from the presence of HLA-DQ2 or HLA-DQ8 genotypes, there is a lack of established factors that increase the risk of CD or exacerbate the condition. This research project into the lifestyle, sociodemographic and genetic determinants and distribution of CD will ultimately provide novel insights that will inform the

prevention, treatment and diagnosis of the condition.
1c: We will investigate the epidemiology of CD through exploring how it varies by environmental and sociodemographic characteristics, such as smoking, alcohol, diet, early-life exposure etc., and biochemical markers. We will undertake a GWAS in order to identify variants associated with CD which will provide an insight into potential mechanisms. A key aspect of our research is establishing the characteristics that distinguish CD from conditions with similar symptomatology. Therefore, we will also perform the same analyses investigating the association between lifestyle, environmental and genetic factors with those with IBS and those on a gluten-free diet.
1d: The full cohort (approx. 500,000 participants) will be included.