**Applicant PI:** 17351 Professor Jeremy Guggenheim

**Applicant Institution:** Cardiff University, School of Optometry & Vision Sciences, Maindy Road, Cardiff CF24 4LU. United Kingdom.

**Application Number / Title:** 17351 - Genetic risk factors for refractive error

**Lead Collaborators:** 1) Cathy Williams

**Collaborating Institutions and Addresses:** 1) University of Bristol, Social and Community Medicine, Oakfield House, Oakfield Grove, Bristol BS8 2BN. United Kingdom.

**Keywords provided by the Applicant PI to describe the research project:** Myopia, Refractive error, Genetics, Genomic prediction

**Application Lay Summary:**

**1a**: Vision loss seriously impairs the independence and quality of life of those affected, and incurs high healthcare costs. Refractive error is a leading cause of untreatable visual impairment in the UK.
We will study the genetic information of UK Biobank participants in order to discover why certain individuals are more likely than others to develop refractive errors. Stringent safeguards will ensure the anonymity of participants.
We anticipate making discoveries that will improve ongoing research into new treatments and allow personalized treatments to be formulated, so that the most effective treatments can be administered to those individuals who will benefit most.

**1b:** (1) The findings of this research project will help prevent future patients from developing untreatable, visually-impairing eye disease by allowing the detection of individuals at very high risk of refractive error due to genetic factors, at a young age. These individuals can be offered treatment to reduce refractive progression (e.g. orthokeratology for myopia), which will reduce their risk of sight loss in adulthood.
(2) By discovering genetic risk factors for refractive error, we will generate new avenues for treating refractive error and its associated eye disease.

**1c:** We will examine whether naturally-occurring genetic variants that differ from person-to-person are risk factors for refractive errors such as myopia (short-

sightedness). With millions of genetic variants contained in the human genome, this requires high-performance "clusters" of computers to carry out the analyses. We will also use statistical methods to design predictive mathematic models for detecting individuals at-risk of developing short-sightedness. These mathematical models will be tested in separate (independent) cohorts of patients to evaluate whether they are effective in a clinical setting.

**1d:** Genetic analyses will be carried out after stratifying by ancestry, to avoid false-positives from population stratification. We will use the maximum sample size available for traits, after excluding outliers. For a minority of traits (e.g. #2217, "Age started wearing glasses") there will be approximately 400,000 participants of European ancestry with valid responses. However, most traits of interests will require information obtained during the ophthalmic assessment: in prior work we derived a variable "refractive error" in which valid measurements were available for 89,120 self-reported White European participants (JAMA Ophthalmology 2015; doi: 10.1001/jamaophthalmol.2015.3556).