Project Details	
Project Code	MRCNMH24Ex Caramaschi
Title	Using molecular and clinical data to predict outcomes to treatments for depression
Research Theme	Neuroscience & Mental Health
Summary	Up to 50% of people with depression do not benefit from the pharmacological and psychosocial treatments initially prescribed. This often results in the need to switch treatments several times before finding the optimal therapy. In this project you will develop and compare markers for antidepressant treatment efficacy focussing on integrating clinical, demographic, genetic and epigenetic characteristics using machine learning across studies and outcomes.
Description	People with depressive symptoms often need to switch antidepressant medications several times and combine those treatments with psychological therapies because of lack of effectiveness. The evidence so far on the link between patient's characteristics (e.g. sociodemographic or genetic) and response to treatment is not sufficient to be usefully implemented clinically. The project aims at exploring potential biomarkers for antidepressant treatment efficacy using machine learning to ultimately better inform clinicians and people with depression on the choice of therapy. The project will focus on DNA methylation in peripheral blood initially as it is both under the influence of genetic predispositions and environmental factors, while being stable and easily measurable. To achieve a large-scale study, we will use DNA methylation data from a variety of existing human studies across population studies and clinical trials. DNA methylation data obtained via microarrays will be integrated with other clinical, sociodemographic and genetic characteristics using a range of statistical and computational methods to predict antidepressants efficacy across studies and outcomes. Over the course of the studentship and depending on the interests of the student, they will have the opportunity to: 1) Identify patterns in DNA methylation that are linked to improvement in depressive symptoms in response to pharmacological treatments. 2) Develop and test a DNA methylation biomarker that predicts symptoms improvement in response to pharmacological treatments. 3) Combine the DNA methylation biomarker with other data (e.g. severity of symptoms) and compare its effectiveness in predicting reduced depressive symptoms. 4) Compare the predictive validity of biomarker across ages (e.g. childhood vs adulthood). 5) Develop and test a clinical marker to predict improvement in response to psychological therapies (e.g. CBT). 6) Investigate the acceptability and utility of predictive markers for mental health treatments from service providers and users via stakeholder meetings. The work will be carried out on unique existing datasets from richly phenotyped longitudinal population studies (e.g. Avon Longitudinal Study of Parents and Children and Generation Scotland), clinical trials (e.g. GENDEP trial) and health records from Improved Access to Psychological Therapies (IAPT) across Devon and Plymouth and from a digital clinical trial on cognitive-behavioural therapy. The project has elements of bioinformatics, clinical and qualitative work and is interdisciplinary in working with a supervisory team that consists of biologists, clinical psychologists and computational

	scientists. The student will be able to steer their project towards one of these components as the main aspect of their project. They will also have agency in the chronological order of the aims and activities to be undertaken. For instance, aims 5 and 6 can be independently achieved before 1-4. Within each aim, there is scope to expand certain areas, rather than others, for instance the work could focus on the clinical trials rather than the population studies or vice versa, with greater depth in specific predictive symptoms.
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