

Project Details	
Project Code	MRCPHS26Br Taylor G
Title	What are the biological mechanisms underlying the association between smoking, smoking cessation and mental health: a triangulation approach
Research Theme	IIAR
Project Type	Dry lab
Summary	<p>What are the biological mechanisms underlying the association between smoking, smoking cessation, and mental health? A growing body of evidence supports smoking as a causal risk factor for poorer mental health, and there is evidence for long-term improvements in mental health following smoking cessation. However, less is known about the mechanisms underlying this association. This PhD project will examine hypothesized biological mechanisms, such as inflammation markers. The candidate will receive training in methodological approaches, including techniques from genetic epidemiology, advanced machine learning aligned with MRC's Foundations for Excellence, and innovative G-methods for causal inference to reduce residual and time-varying confounding.</p>
Description	<p>Background: The student will apply a triangulation approach, enhancing methodological rigor and interdisciplinary robustness, across their program of work to strengthen causal inference by comparing different approaches with assumed unrelated sources of bias. The student will work with multiple data sources from different populations (NHANES – United States; IMAGEN – multiple countries across Europe; UK Biobank – United Kingdom) and compare effect estimates derived from traditional modelling (e.g., regression, generalized linear models) to estimates from more sophisticated approaches, including innovative G-methods (e.g., marginal structural models), advanced machine learning techniques aligned with MRC's Foundations for Excellence, adjustment for genetic risk to exposure, and Mendelian Randomization, supporting data science priority skills.</p> <p>This triangulation approach not only leads to more robust conclusions but also provides an excellent training opportunity for the student across a variety of advanced methods.</p> <p>Key Research Question: What are the biological mechanisms that underlie the association between smoking, smoking cessation, and mental health?</p> <p>The student will undertake four main studies:</p> <p>Study 1: A systematic review and meta-analysis of studies examining causal biological mechanisms linking smoking, smoking cessation, and mental health (e.g., inflammation pathways).</p> <p>Study 2: A cross-sectional and longitudinal mediation and moderation analysis using pre-existing data from cohort studies (IMAGEN, UK Biobank, NHANES) to examine the relationship between smoking, cessation, and mental health, including potential mediators and moderators (e.g., inflammation markers such as cytokines, corticosteroids, neurotrophins). The student can also explore dose-response relationships, such as smoking heaviness.</p> <p>Study 3: Re-examination of longitudinal associations in Study 2 using IMAGEN and NHANES, employing methods to overcome residual and</p>

	<p>time-varying confounding, including innovative G-methods (e.g., inverse probability weighted marginal structural models, G estimation of structural nested models) and advanced machine learning techniques to explore temporal patterns, and outcome prediction.</p> <p>Study 4: Re-examination of the cross-sectional associations in Study 2 using UK Biobank, applying adjustment for genetic risk and Multivariable Mendelian Randomization to reduce confounding, supporting a data science skills-based approach.</p> <p>Student Ownership: The student will have the opportunity to take full ownership of both the methodological and theoretical aspects of the project. This type of project offers an extensive range of interdisciplinary research decisions involving data science, epidemiology, and mental health, such as selecting variables for analysis, choosing specific biomarkers, neurological systems, mental health outcomes, and time-varying confounders. Students will be empowered to explore various modelling approaches and select methods based on scientific rationale and training needs. They will choose from a variety of techniques, including innovative G-methods and advanced machine learning, tailoring their approach to best fit the project's objectives. Additionally, the student will have the opportunity to shape the patient and public involvement (PPI) component of the project, including selecting platforms and crafting messaging that align with their interests and career objectives.</p> <p>Skills Development: The student will develop core capabilities aligned with the MRC's Foundations for Excellence, particularly in causal inference, big data handling, and advanced analytics, while addressing Priority Skills Needs in data science, interdisciplinary thinking, and translational research. The project leverages the collective expertise and infrastructure across the GW4 alliance, enabling the student to benefit from joint supervision, cross-institutional training workshops, and exposure to distinct but complementary research cultures at Bath, Bristol, and Exeter. This supports GW4's commitment to collaborative doctoral training as a mechanism for developing future research leaders.</p> <p>International Impact: These findings will significantly improve our understanding of the mechanisms by which tobacco use affects mental health and whether such harms are reversible after cessation. The results will inform the development of bespoke individual-level and public health interventions (e.g., messaging around mental health benefits of quitting) for high-risk populations. This work also has important policy and healthcare implications both in the UK and internationally. The relevance of targeted messaging was recently highlighted in the UK Government's Khan Review, "Making Smoking Obsolete."</p> <p>PPI: PPI will be embedded throughout the project to ensure the research reflects the lived experiences of people affected by smoking and mental health issues. The student will work with existing lived experience panels at Bath, Bristol, Exeter, and policy partners, and across the GW4 network to refine research questions, interpret findings, and co-create dissemination materials. They will shape engagement activities based on their interests, such as focus groups or digital outreach.</p>
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Supervisory Team	
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