Project Details	
Project Code	MRCPHS25Br Siviter
Title	Quantifying the impact of chronic pesticide exposure on disease susceptibility
Research Theme	Population Health Sciences
Summary	Humanity has endured several outbreaks of infectious diseases that threaten population health. Environmental factors can influence disease susceptibility, but quantifying the impact of specific stressors is extremely challenging. Humanity regularly consumes pesticides at low concentrations. While risk-assessments ensure that consumers do not consume 'dangerous' levels of pesticides, the long-term impact of chronic exposure to multiple pesticides is difficult to quantify. Here, the candidate will explore the impact of chronic pesticide exposure on disease susceptibility and health, using bumblebees as a model system. The candidate will develop skills in experimental design, molecular techniques, and meta-analysis.
Description	In the 21st century, humanity has endured several outbreaks of infectious diseases that threaten population health and prosperity. Disease outbreaks can result in direct mortality and can also have long-lasting sublethal impacts on health. Importantly, the impact of diseases are not evenly distributed across population demographics. Environmental factors, that shape individual health, can contribute towards disease susceptibility. However, disentangling the interactions between individual health, and disease susceptibility, is extremely challenging due to the complexities arising around social-economics, and genetics. Identifying specific environmental factors that influence disease susceptibility is vital for improving population health. Intensive farming practices mean that humanity regularly consume pesticides at low concentrations. While, risk-assessments, ensure that we as consumers are not exposed to 'dangerous' levels of pesticides in the short-term, the long-term impact of chronic pesticide exposure is difficult to quantify. Furthermore, risk-assessment is focused on the impact of one specific pesticide, but food products will typically contain several agrochemicals. Consequently, in any given meal, we routinely consume a cocktail of different pesticides. For example, in a recent survey conducted by the European Food Safety Authority, 84% of participants contained at least 2 pesticides. The same report also concluded that while it is 'not yet possible to derive estimates of the burden of disease from pesticides in Europe… strong links have been established between exposure to pesticides and increased risk of several chronic diseases including cancers, Parkinson and Alzheimer's diseases'. To understand the relationship between pesticides, and disease susceptibility, highly controlled experiments are required that identify (i) specific pesticides that may contribute towards disease susceptibility and (ii) attempt to identify the molecular markers underpinning these interactions. Here, we will explore the impact of chronic pesticide exposure in a highly replicable, and trackable insect system. Bumblebees (Bombus terrestris) are a eusocial species which are routinely exposed to a cocktail of agrochemicals, as well as other environmental stressors, including pathogens. We will develop this model system and establish to what

	extent long-term pesticide exposure influences disease susceptibility of bumblebees to the pathogen Vairimorpha bombi. V. bombi is an infectious disease which can impair bumblebee behaviour, physiology and health, but the relationship between pesticide consumption and V. bombi susceptibility is poorly understood. While the candidate will lead, and design their own project around this question, we anticipate they will answer four key research questions. 1. How does chronic exposure to individual pesticides influence bumblebee disease susceptibility and health: Here, the candidate will identify pesticides that influence disease susceptibility and health. There are hundreds of different pesticides used in agriculture (e.g. insecticides, herbicides, fungicides) which humanity regularly consume through food. Here, the candidate will test how six pesticides (imidacloprid, thiamethoxam sulfoxaflor, flupyradifurone, glyphosate, pyraclostrobin), influence disease susceptibility, and individual health. Using a highly replicated, microcolony design, the candidate will inoculate bumblebees with V. bombi and record pathogen development and intensity. They will also record the impact on bumblebee behaviour, physiology, and health. 2. How does chronic exposure to multiple pesticides influence bumblebee disease susceptibility and health: Here, the candidate will quantify the interaction effects between multiple pesticides and bumblebee disease susceptibility. The candidate will expose bumblebees to multiple pesticides, in a fully crossed experimental design. The specific pesticide used will be decided based on the data obtained during Q1. The candidate will quantify both individual, and combined impacts of pesticides on disease intensity and will use novel statistical approaches to investigate the nature of the interactions (e.g. synergistic, additive or antagonistic). 3. Identify the molecular determinants driving interactions between pesticides and disease susceptibility: Here the candidate will investigate the molecular markers that result in some pesticides influencing disease susceptibility. The student will expose bumblebees to insecticides selected from data derived from addressing Q1 and Q2, and then conduct transcriptome profiling by RNA sequencing where the transcriptional response to insecticide exposure will be compared between insecticide exposed and unexposed bees. State-of-the art bioinformatic tools will be used to intersect phenotypic information generated in Q1 and Q2 with transcriptional signatures observed in treated versus untreated bees and identify key genes and gene regulatory networks putatively involved in pesticide-mediated changes in disease susceptibility. A selection of these candidate genes will be functionally validated using reverse genetic approaches such as RNA interference. 4. How does chronic pesticide exposure influence disease susceptibility and health: a meta-analysis: Finally, the candidate will conduct and meta-analysis, across all animal taxa, to ascertain the relationship between pesticide exposure and disease susceptibility. They will source data from both experimental and correlative data to (i) identify specific chemicals associated with disease susceptibility, (ii) determine the relationship between toxicity and disease susceptibility and (iii) quantify interaction effects between multiple pesticides.

	Outcome: The ultimate aim of this project is to identify pesticides that can influence disease susceptibility in bumblebees as a foundation for further investigation of their impact on human health.
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