Project Details	
Project Code	MRC22IIARBa Feil
Title	The spread of antimicrobial resistance plasmids in humans, animals and the environment
Research Theme	Infection, Immunity, Antimicrobial Resistance & Repair
Summary	Mitigating the global impact of antimicrobial resistance (AMR) requires targeted surveillance and intervention within different clinical, community, animal and environmental settings. This project will help to prioritise such approaches by examining how the adaptation of bacterial strains to different niches impacts on the spread of any AMR plasmids they carry. This interdisciplinary approach will involve bioinformatics, modelling and competition experiments.
Description	The emergence of bacterial pathogens that are increasingly resistant to antibiotics is a pressing global public health crisis. In order to tackle this problem, it is important to consider not just hospitals and human communities, but also the wider environment; a perspective captured in the "One-Health" framework. Antibiotic resistant bacteria (ARB) and antibiotic resistance genes (ARGs) are commonly isolated from environmental settings due to a number of key drivers. One possibility is direct pollution from human communities via wastewater or some other route. Alternatively, new resistant strains may evolve de novo within the environment either through mutation or through the acquisition of ARGs via plasmid conjugation or other form of horizontal transfer. The release of antibiotics into the environment, either through their use in agriculture or directly from human communities, might subsequently select for any ARBs that are present. ARGs are often carried on plasmids that are highly mobile between strains, and even different species of bacteria. This means that AMR plasmids, and the ARGs they carry, can potentially transmit and spread independently of their host bacteria. This project will focus on the dynamics of AMR plasmid transmission between strains adapted to different ecological niches. Recent work by the Feil group (https://www.biorxiv.org/content/10.1101/2021.08.05.455249v2), and others, has suggested that ARB typically do not spread unimpeded from one setting to another, despite there being multiple opportunities for transfer. The most likely explanation is that different strains are adapted to different niches, which makes it more difficult for strains to invade a niche that is different from the one to which it is adapted. For example, there is good evidence that the strains of Escherichia coli and Klebsiella pneumoniae commonly isolated from humans are mostly distinct from those isolated from cows, other livestock or wild animals. On the one hand then, ARGs are carried on highly mobile plasmids that can spread between strains and species, but on the other the strains that harbour these plasmids tend to be ecologically restricted. This project will address this contrasting dynamic using multiple approaches. First, the project will exploit large genomics datasets for K. pneumoniae and E. coli from multiple clinical and non-clinical sources which have been generated by the SpARK and Oh-DART consortia, as well as other projects. These data sets consist of short-read data for thousands of isolates, and long-read data for hundreds of isolates. Bioinformatics approaches combined with transmission network analysis will be used to

	contrast the distributions of bacterial strains and plasmids (which will be assembled and categorised using the existing long-read data). Mathematical modelling and computer simulation will be used to identify the conditions under which AMR plasmids and/or their host strains will spread. We will consider multiple parameters including differing levels of ecological structuring of the host strains, a range of plasmid mobility and promiscuity, fitness cost of plasmid carriage and presence of antibiotic. The modelling and bioinformatics approaches will be complemented by competition and conjugation experiments designed to identify the conditions under which a niche adapted antibiotic susceptible strain can capture beneficial AMR plasmids from strains that are otherwise poorly competitive. The mathematical modelling will take the recent work by Ueda et al (https://doi.org/10.1371/journal.pone.0183120) as a starting point. The experiments will incorporate realistic antibiotic concentrations as measured directly in the field.
Supervisory Team	
Lead Supervisor	
Name	Professor Edward Feil
Affiliation	Bath
College/Faculty	Science
Department/School	Biology and Biochemistry
Email Address	e.feil@bath.ac.uk
Co-Supervisor 1	
Name	Dr Tiffany Taylor
Affiliation	Bath
College/Faculty	Science
Department/School	Biology and Biochemistry
Co-Supervisor 2	
Name	Professor Barbara Kasprzyk-Hordern
Affiliation	Bath
College/Faculty	Science
Department/School	Chemistry
Co-Supervisor 3	
Name	Dr Ben Adams
Affiliation	Bath
College/Faculty	Science
Department/School	Mathematical Sciences
Co-Supervisor 4	
Name	Dr Aimee Murray
Affiliation	Exeter
College/Faculty	College of Medicine and Health
Department/School	European Centre for Environment and Human Health, Environment and Sustainability Institute