The third JPIAMR joint call Transmission Dynamics - 2016

The third JPIAMR call, published in 2016, has awarded 28.3 M EUR to 19 research projects to bridge the knowledge gap on AMR transmission mechanisms.

The JPIAMR joint co-funded call “To unravel the dynamics of transmission and selection of antimicrobial resistance (AMR) at genetic, bacterial, animal, human, societal, and environmental levels, in order to design and evaluate preventive and intervening measures for controlling resistance” closed in July 2016 and received 83 applications. The call was conducted simultaneously by 22 participating funding organisations from 18 countries and the European Commission within the JPI-EC-AMR ERA-Net Cofund grant no 681055.

In total 19 project consortia with a total of 96 research groups from 16 countries applying for 28.3 M EUR for 3 years of research were recommended for funding by the JPIAMR Call Steering Group for the co-funded Call. The final funding decision will depend on national regulations and inspection of the formal proposals to be submitted to the national funding organisations. Each national funding agency will then take a formal decision on the projects to be supported.

The MRC provided funding for the UK partners of successful proposals (x11)

Links:
http://www.jpiamr.eu/
http://www.jpiamr.eu/fundedprojects/

JPIAMR 3rd Joint Call: Transmission Dynamics

Project Coordinator	Institution	Title of Award
Frank Schreiber	Federal Institute for Material Research and Testing, Germany	BEAT-AMR: Partnership against Biofilm associated Expression, Acquisition and Transmission of AMR

Project Partners	Summary
Qun Zulian Ren, Empa. Materials Science and Technology, Switzerland Henny van der Mei, University Medical Center Groningen, Netherlands **Jeremy Webb, University of Southampton, United Kingdom** **Saul Faust, University Hospital Southampton NHS Foundation Trust, United Kingdom**	A relatively recent advance in microbiology is the finding that the majority of infections are caused by bacterial biofilms. Biofilms are structured communities of bacteria found on surfaces that become embedded within a self-produced extracellular polymeric matrix. Biofilms can form on tissues or on biomedical surfaces, such as blood catheters or implants, where they act as a reservoir of potential healthcare associated infection. Bacteria living in biofilms can tolerate much higher antibiotic concentrations compared to planktonic bacteria and survive long enough to evolve antimicrobial resistance (AMR). They form persistent, hard to treat infections and exhibit an intrinsic biology that promotes the development and transmission of AMR. The goal of our consortium is to determine how bacteria adapt to antimicrobials during biofilm formation on surfaces coated with antimicrobials, how AMR mutations are acquired and evolve within mature biofilms, and how population dynamics within biofilms affect the transmission of AMR. We address the hypothesis that understanding the contribution of biofilms to AMR acquisition and spread will lead to the development of novel antimicrobial strategies and medical devices that are more effective in preventing biofilm-associated infection and AMR. Our team provides facilities and clinical research governance for experimental and translational medicine. Our synergy of leading laboratory, clinical and translational research across Europe will ensure the best chance to develop novel and successful interventions and therapeutic outcomes.

JPIAMR 3rd Joint Call: Transmission Dynamics

Project Coordinator	Institution	Title of Award
Birgitta Henriques-Normark	Karolinska Institutet, Sweden	PNEUMOSPREAD: Mechanisms for acquisition and transmission of successful antibiotic resistant pneumococcal clones pre- and postvaccination

Project Partners	Summary
Aras Kadioglu, University of Liverpool, United Kingdom Tim Sparwasser, Twincore, Germany Jens Lagergren, Royal Institute of Technology, Sweden	AMR in Streptococcus pneumoniae is spread globally by a limited number of clones. PCV vaccination has decreased AMR among vaccine-type strains. AMR now emerges by expansion of non-PCV types. The project focuses on genetic/functional properties of AMR clones with the goal to target their success and transmission in the carrier population. The goals are to: 1) Perform whole genome based analyses on emerging AMR after PCV introduction, comparing with pre-PCV. Sequence data will be correlated to host factors including clinical patient information. Phylogenetic and general machine learning methods will be applied and a data base will be created to identify microbial traits that link success of AMR to transmission, colonization and ability to cause invasive disease 2) A set of animal models will be used to study transmission, colonization and disease capability of AMR clones. Different endogenous and environmental cues will be applied to these studies by altering host immune defense, by sensitizing with influenza A virus, by exposure to long term antibiotics, and by affecting physical or chemical parameters in the environment 3) Drivers affecting transmission/colonization/invasive disease will be identified using appropriate mutants, and monitoring the influence of the host microbiome using germ free mice 4) Resistance transfer and role of competence pili, conjugative transfer and lack of CRISPR/Cas9 interference will be studied in the presence and absence of a respiratory microbiome 5) Clonal elimination will be attempted in mice models using antigens targeting AMR clones and by generating a CRISPR/Cas9 delivery system for interference of AMR clones during carriage.

JPIAMR 3rd Joint Call: Transmission Dynamics

Project Coordinator	Institution	Title of Award
Stephen Bentley	Wellcome Trust Sanger Institute, United Kingdom	Restrict-Pneumo-AMR: Prevention and Restriction of Antimicrobial Resistance in Pneumococci by Multi-Level Modelling

Project Partners	Summary
Nahuel Fittipaldi, University of Toronto, Canada James Kellner, University of Calgary, Canada Bernd Schmeck, Philipps-University Marburg, Germany **Paul Turner, University of Oxford, United Kingdom** Tom van der Poll, University of Amsterdam, Netherlands	Streptococcus pneumoniae is a major health threat in industrialized and developing countries. The pathogen affects both young and old people, immune-competent as well as immunocompromised individuals. By genetic recombination within diverse populations, individual strains are not only able to evade vaccination but also able to acquire antimicrobial resistance (AMR), which can then be transmitted onwards. This proposal aims to understand the mechanisms and distribution of this pneumococcal AMR repertoire at the genetic, bacterial, host and population levels to layout new strategies for risk assessment, prevention and reduction of AMR. In particular, the environmental, immunological and pharmacological drivers of resistance emergence and selection, the genetic population dynamics, as well as the fitness of the new traits in different host conditions will be analysed and modelled. To this end, a multinational consortium of researchers with complementary expertise has been formed. Available to the consortium are clinically important and newly emerged pneumococcal AMR strains, together with related patient metadata (clinical, genetic and transcriptomic) from clinical cohorts as well as highly detailed carriage sampling from a Thai cohort. Consortium members have proven expertise in microbiology, bacterial genetics, bioinformatics, in vivo/in vitro models while others are clinicians expert in the treatment of pneumococcal infections in both paediatric and adult patients. In a concerted effort, this consortium will develop countermeasures against antimicrobial resistance in a major health threat by multi-level modelling of its resistance emergence, selection, and transmission in diverse environments.

JPIAMR 3rd Joint Call: Transmission Dynamics

Project Coordinator	Institution	Title of Award
Jonas Warringer	University of Gothenburg, Sweden	TransPred : Predicting cell-cell horizontal transmission of antibiotics resistance from genome and phenome

Project Partners	Summary
Jonas Warringer, University of Gothenburg, Sweden Edward Moore, University of Gothenburg, Sweden Gianni Liti, University of Nice, France **Leopold Parts, Wellcome Trust Sanger Institute, United Kingdom** Jan Michiels, University of Leuven, Belgium	We propose to disclose candidate drug targets controlling the horizontal cell-cell transmission of antimicrobial resistance (AMR) and to predict AMR and its transmission dynamics from bacterial genome composition. We will integrate leading expertise from bacteriology, -omics and mathematical biology in the development of an integrated theoretical-empirical framework of plasmid borne transmission of AMR cassettes. We will employ massive-scale experimental evolution of Escherichia coli and Salmonella enterica gene deletion and overexpression collections, where adaptation requires transfer of AMR carrying conjugative plasmids. In addition, we will select for, identify and functionally dissect de novo mutations that promote horizontal transmission during long-term experimental evolution. Both approaches will disclose cellular functions controlling horizontal AMR transmission that are candidate targets for helper drugs delaying AMR development and spread. Second, we will sequence vast swaths of the genotype space inhabited by clinical bacterial isolates and disclose variants likely to alter transmission properties. DNA sequence data will be complemented by data on transcriptome, proteome and antibiotics resistance, allowing causally cohesive reconstruction of the history of antibiotics resistance. Third, we will integrate the omics data into a mathematical framework capable of predicting AMR transmission in clinical isolates, thereby laying the foundations for a future personalized medicine that tailors antibiotic choice to infection.

JPIAMR 3rd Joint Call: Transmission Dynamics

Project Coordinator	Institution	Title of Award
Constance Schultsz	University of Amsterdam, Netherlands	HECTOR: The impact of Host restriction of Escherichia coli on Transmission dynamics and spread of antimicrobial Resistance

Project Partners	Summary
Christian Menge, Friedrich Loeffler Institut, Germany Torsten Semmler, Robert Koch Institute, Germany **Roberto Marcello La Ragione, University of Surrey, United Kingdom** Lucas Domínguez Rodríguez, Universidad Complutense Madrid, Spain **NgoThi Hoa, University of Oxford, United Kingdom**	The prevalence of antimicrobial resistance (AMR) is increasing rapidly worldwide, including in bacteria colonizing healthy human and animal populations. The recent reports of plasmid mediated colistin resistance, potentially associated with colistin usage in agriculture, further raise fears of infections that have become untreatable due to AMR. The commensal flora of humans and animals is a reservoir of AMR encoding genes and Escherichia coli in particular can carry multiple AMR determinants. Antimicrobial resistance transmission within E. coli appears dominated by certain lineages. To what extent these are restricted to certain host species is unknown. Such host restriction may be an important determinant of the likelihood of transmission of resistant E. coli between different reservoirs, such as between animal and human hosts. The identification of determinants that allow disentanglement of the different modes of resistance transmission (i.e. bacteria vs mobile genetic elements such as plasmids) is crucial for a more targeted design of interventions to prevent and reduce transmission of resistance. The proposed research aims to identify determinants of host restriction of E. coli and their potential association with antimicrobial resistance transmission and prevalence. We propose a One Health approach using mixed methods, including whole genome sequencing of a large collection of E. coli isolates from human, animal and environmental sources in different geographic areas across Europe and in Vietnam, experimental models to study the role of host restriction determinants in transmission and bacterial fitness, and mathematical modelling.

JPIAMR 3rd Joint Call: Transmission Dynamics

Project Coordinator	Institution	Title of Award
Margreet Vos	Erasmus University Medical Center, Netherlands	MACOTRA: Combating MRSA; increasing our understanding of transmission success will lead to better control of MRSA

Project Partners	Summary
Jodi Lindsay, St George's, University of London, United Kingdom **Gwenan Knight, Imperial College London, United Kingdom** Leo Schouls, National Institute for Public Health and the Environment, Netherlands Gerard Lina, Universite Claude Bernard Lyon 1, France	The primary aims of the MACOTRA project are three-fold 1.To develop and provide a framework for evaluating differences in transmission of MRSA. 2. To unravel the different contributions to MRSA clonal success on a genetic and population level. 3. To develop a mathematical model which predicts and unravels the rise and shine of clones. Study material will be epidemiologically well-defined isolates from international collections, and microbiomes from patients. Study questions are from the bacterial point of view; • To delineate factors for unsuccessful and successful (epidemic) clonal MRSA, from both livestock and human isolates from the Netherlands, UK and France From the human point of view; • To study the role of MRSA carriage in relation to microbiome of nose and skin. From the interaction between the host and bacteria • To develop in-vitro models to study differences in strain survival and transmission in the host and in response to decolonisation, antibiotics, disinfectants and microbiome. Skin, plasma and microbiome models will be used. • To develop deterministic and individual-based mathematical models of bacterial dynamics, including survival, within human hosts, as well as on transmission dynamics between human hosts. MACOTRA study results and data from decolonisation and other intervention strategies, risk groups and antibiotic/disinfectants usage in the Netherlands, UK and France will serve as input to the mathematical models. The consortium exists of (molecular) microbiologists, medical doctors and mathematical modellers, all very successful and well-known in the MRSA and / or infectious disease field; from basic research to clinical (intervention) studies.

JPIAMR 3rd Joint Call: Transmission Dynamics		
Project Coordinator	**Institution**	**Title of Award**
Constança Ferreira Pomba	University of Lisbon, Portugal	PET-Risk: Risk of companion animal to human transmission of antimicrobial resistance during different types of animal infection
Project Partners	**Summary**	
Constança Ferreira Pomba, University of Lisbon, Portugal Stefan Schwarz, Friedrich Loeffler Institute, Germany Scott Weese, University of Guelph, Canada **Anette Loeffler, Royal Veterinary College, United Kingdom**	The close contact of pets with humans provides excellent opportunities for interspecies transmission of resistant bacteria and their resistance genes in either direction. Infections in humans due to antimicrobial resistant bacteria originating from pets are becoming a concern. While any animal-human contact offers a chance of transmission, it is generally accepted that a high bacterial burden and high antimicrobial resistance gene copy numbers are present during an active infection. There is a gap of knowledge on the dynamics of transmission and selection of antimicrobial resistance at the pet-human interface. Animals may exchange antimicrobial-resistant bacteria and resistance genes with humans, but the extent to which this happens is unknown. PET-Risk will evaluate the transfer of antimicrobial resistance between pets and household members during animal infections and determine which type of infection (skin and soft tissue vs. urinary tract infections) presents a higher risk of transmission to humans. Furthermore, in a longitudinal study we will collect samples of infected animals under antimicrobial treatment, and their household members at several time points, which will allow the assessment of critical control points at which interventions could substantially affect the spread of resistance. The causality and directionality of pet-human spread of resistance genes will be established by using state-of-the-art techniques in order to design and evaluate preventive and intervening measures for reducing the public health risks of antimicrobial resistance.	

JPIAMR 3rd Joint Call: Transmission Dynamics		
Project Coordinator	**Institution**	**Title of Award**
Edward Feil	University of Bath, United Kingdom	SpARK: The rates and routes of transmission of multidrug resistant Klebsiella clones and genes into the clinic from environmental sources
Project Partners	**Summary**	
Piero Marone, Fondazione IRCCS Policlinico San Matteo, Italy Sylvain Brisse, Institut Pasteur, France **Louise Matthews, University of Glasgow, United Kingdom** Jukka Corander, University of Oslo, Norway **Aanensen David Wellcome Trust Sanger Institute, United Kingdom**	Klebsiella pneumoniae (Kp) is a leading cause of multidrug resistant hospital-acquired infections globally, and is responsible for an increasing public health burden in the community. In order to control the spread of Kp through targeted surveillance and intervention policies it is necessary to identify the sources of emergent community and health-care associated infection from the interlinked and varied niches encompassing “the environment”. To address this, we will sample from multiple clinical, community, agricultural, veterinary and environmental settings in and around a single town, Pavia, in Northern Italy, and supplement these data with matched samples from France and elsewhere. We will use whole genome sequencing of community (mixed-colony) samples to assay accessory gene abundance and distribution. This contrasts with the more common approach based on phylogenetic analysis of single colonies, which would be of limited utility over broad environmental scales due to the complexity of transmission chains, environmental dormancy, and high rates of recombination. In contrast, our gene-centric approach provides a much more efficient means to understand ecological adaptation, the distribution of resistance and virulence genes, and to identify key environmental reservoirs from which clinical clones emerge. A key deliverable of this project will be the establishment of a pan-genome database (‘pangenomium’) that will integrate with both existing Kp genome community resources established by project partners (BIGSdb-kp, and wgsa.net).	

JPIAMR 3rd Joint Call: Transmission Dynamics		
Project Coordinator	**Institution**	**Title of Award**
Johann Pitout	University of Calgary, Canada	ST-131_transmission: Escherichia coli ST131: a model for high-risk transmission dynamics of antimicrobial resistance
Project Partners	**Summary**	
Neil Woodford, Public Health England, United Kingdom Fernando Baquero, Ramón y Cajal Institute for Health Research, Spain Marie-Hélène Nicolas-Chanoine, Paris VII University, France Laurent Poirel, University of Fribourg, Switzerland Alvaro Pascual, Fundación Púbica para la Gestión de la Investigación de Salud en Sevilla, Spain	This project will connect a large number of transnational academic resources to investigate the transmission success of Escherichia coli ST131 clone. E. coli is the most common cause of urinary tract and bloodstream infections worldwide. A recent WHO report states that resistance to one of the most widely used antibiotics (fluoroquinolones [FQs]) is very widespread. In many parts of the world, FQs are now ineffective in more than half of patients. A single E. coli clone, ST131, is predominantly responsible for this global FQ-R and cephalosporin-R pandemic causing millions of antibioticresistant infections annually. It remains unclear which features of ST131 had resulted in the biggest antimicrobial resistance success of the 2000s. We propose a combined European-Canadian consortium that will investigate the transmission dynamics of ST131. This study will explore the vertical and horizontal transmission of resistance and virulence genes and how they contributed to the transmission success of ST131 among humans, animals and different environments. The broad goal is to improve human health by better understanding managing infections due to multidrug resistant E. coli. The study will explore explanations for the high transmission rates and success of ST131. A famous quote from Stephen Hawking; “Intelligence is the ability to adapt to change”. ST131 adapted rapidly to environmental changes; we need to know why and how. This project will serve as a model to predict what can possibly happen in the future with the continuing emergence of multidrug resistant clones among bacteria	

JPIAMR 3rd Joint Call: Transmission Dynamics		
Project Coordinator	**Institution**	**Title of Award**
Willem van Schaik	University Medical Center, Utrecht, Netherlands	STARCS: Selection and Transmission of Antimicrobial Resistance in Complex Systems
Project Partners	**Summary**	
Dik Mevius, Wageningen University, Netherlands Dan Andersson, University of Uppsala, Sweden Teresa Coque, Ramón y Cajal University Hospital, Spain Romain Koszul, Institut Pasteur, France **Mark Woolhouse, University of Edinburgh, United Kingdom** Surbhi Malhotra-Kumar, University of Antwerp, Belgium	Selection and transmission are key determinants for the dissemination of antimicrobial resistance (AMR) across the planet. These determinants of AMR are frequently studied in laboratory settings while in reality they occur in complex systems, e.g. in microbial communities that colonize human and animal guts or in environmental ecosystems. The central aim of STARCS (Selection and Transmission of Antimicrobial Resistance in Complex Systems) is to characterize and quantify the processes of selection and transmission of AMR genes and drug-resistant bacteria in complex (eco)systems from a ‘One Health’ perspective and to integrate these elements into predictive mathematical models, which will be used to inform policy development. To reach this goal, the consortium will (i) develop and implement innovative metagenomics methodologies to map the expression of AMR genes and their linkage to bacterial hosts and mobile genetic elements in human, animal and environmental samples, (ii) use relevant animal models (using mice and ducks) and observational studies (in hospitals and in dogs and their owners) to analyse and quantify the processes of selection and transmission of drug-resistant Enterobacteriaceae (specifically Extended Spectrum Beta-Lactamase producing Escherichia coli) and (iii) implement state-of-the-art epidemiological modelling to quantify the spread of ESBL-producing E. coli between humans and animals. STARCS will develop technological breakthroughs to assess selection and transmission dynamics on the level of the resistance gene, the mobile genetic element, the bacterium, the human/animal/environment interface and in clinical settings. This project will deliver important knowledge into selection and transmission of AMR, will provide the scientific community with novel tools to study selection and transfer of AMR in complex systems and will result in much-needed guidance towards policy decisions by international and national institutions. Ultimately the results from STARCS will form an evidence-based foundation for the development of new regulations, aimed at curbing the spread of AMR.	

JPIAMR 3rd Joint Call: Transmission Dynamics		
Project Coordinator	**Institution**	**Title of Award**
Patrick Boerlin	University of Guelph, Canada	TransComp-ESC-R: Genomic approach to transmission and compartmentalization of extended-spectrum cephalosporin resistance in Enterobacteriaceae from animals and humans
Project Partners	**Summary**	
Richard Bonnet, Université d'Auvergne, France Jean-Yves Madec, French Agency for Food, Environmental and Occupational Health Safety, France Michael Mulvey, University of Manitoba, Canada Stefan Schwarz, Friedrich-Loeffler-Institut, Germany **James Wood, University of Cambridge, United Kingdom**	Resistance to extended-spectrum cephalosporins (ESC) in Enterobacteriaceae is a major challenge for public health worldwide. Its international presence in almost every ecological niche and biological compartment with still ongoing dynamic expansion makes it an ideal target to study the spread of AMR. This project intends to use genomic, evolutionary, transcriptomics, proteomics and experimental approaches to assess the similarities between a variety of ecological niches and biological compartments formed by Enterobacteriaceae species, host species/source (humans, dogs, cattle, swine, chicken, meat products) and geography (Europe: Germany and France, and North America: Canada). These similarities will serve as a basis to identify and focus further on clonal lineages and plasmids able to spread across compartments, using whole genome and plasmid sequencing. A combination of phylogenetic and epidemiologic analyses will allow an assessment of the directionality of transmission between compartments. These analyses will be complemented by series of experiments on transmission of ESC resistance plasmids in vivo in two animal models (chicken and cattle) and on effects of ESC resistance plasmids on the bacterial transcriptome and proteome and its association with plasmid maintenance. These experiments will help to identify major transmission pathways between animals and humans and potential new intervention targets for the control of ESC resistance. The team assembled for this project consists of experienced researchers with a wide spectrum of expertise ideal for the successful completion of a study of antimicrobial resistance in the context of One Health.	

JPIAMR 3rd Joint Call: Transmission Dynamics		
Project Coordinator	**Institution**	**Title of Award**
Barth F Smets	Technical University of Danmark, Denmark	DARWIN: Dynamics of Antimicrobial Resistance in the Urban Water Cycle in Europe
Project Partners	**Summary**	
Søren Johannes Sørensen, University of Copenhagen, Denmark **David Graham, Newcastle University, United Kingdom** **Jan-Ulrich Kreft, University of Birmingham, United Kingdom** Jesús Romalde, Universidade de Santiago de Compostela, Spain Carlos García-Riestra, University Hospital Complex of Santiago de Compostela, Spain Mical Paul, Technion Israel Institute of Technology, Israel	While therapeutic antibiotic use directly impacts the evolution of AntiMicrobial Resistance (AMR), it has become increasingly clear that the environmental dimension of AMR is also of great importance. We postulate that urban water systems (UWS), which are our receptacle for excreted antimicrobials, AMR organisms and AMR genes, are central conduits of AMR to and from pathogens and environmental strains. This is because of high microbial densities and the co-mingling of different wastes, which promotes accelerated AMR gene transfer (HGT) and multi-resistance due to the cooccurrence of antibiotics, biocides, metals and microbes. In DARWIN, we will undertake a never-previously-performed pan-European examination of the fate of key AMR organisms and genetic determinants in UWSs resulting from discharged hospital and community wastes, including transmission mechanisms in different stages of sewer catchments and receiving waters. We focus on the spread of AMR genes encoding clinically relevant extended spectrum β-lactam (ESBL) and carbapenem resistance in three countries with differing AMR profiles and sewage management practices. We postulate that AMR genes readily transmit in UWSs from pathogens and commensal hosts in human wastes (after antibiotic use) to environmental strains better adapted to migrate through the sewer environment, which is driven by local ecologies, conjugal plasmid transfer and phage-mediated transduction. Hence, we will, for the first time, determine specific bacterial hosts that carry AMR genes across UWSs, and identify where key HGT events occur with the ultimate goal of assessing the relative risk of AMR genes returning back to humans due to environmental exposure. To guide risk assessments, a predictive dynamic mathematical model for UWSs will bedeveloped to assist in health and sewage management decisions.	

JPIAMR 3rd Joint Call: Transmission Dynamics		
Project Coordinator	**Institution**	**Title of Award**
Jesus Rodriguez-Banõ	Servicio Andaluz de Salud, Spain	MODERN: Understanding and modelling reservoirs, vehicles and transmission of ESBL-producing Enterobacteriaceae in the community and long term care facilities
Project Partners	**Summary**	
Evelina Tacconelli, University Hospital of Tübingen, Germany Stephan Harbarth, University of Geneva, Switzerland Jan Kluytmans, University Medical Center Utrecht, Netherlands Didier Hocquet, University Hospital Besançon, France **Ben Cooper, University of Oxford, United Kingdom**	The continuing spread of extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBLPE) is among the most important problems in antimicrobial resistance. It is also a good model to investigate the epidemiological complexity of resistance in Enterobacteriaceae. Available data on the transmission determinants of ESBL-PE in community settings are scarce, methodologically limited and mostly based on single centre studies. A comprehensive investigation using present typing and modelling techniques is warranted to develop a sound quantitative understanding of the interactions involved. A consortium of investigators with diverse expertise from countries with high and low endemicity of ESBL-EP has been created. Transmission and persistence of ESBL-PE within households and longterm care facilities will be studied. Individual and group-level determinants for transmission and persistence will be quantified, together with other ecological variables including environmental, food and wastewater contamination. Advanced molecular typing techniques and state of the art analytical methods will be used. Data generated in this project will directly inform a suite of mathematical models which, in addition to encapsulating current understanding of the processes, will be used to explore the potential effectiveness of different interventions to control ESBL-PE spread. The expected outputs are a comprehensive characterisation of ESBL-PE transmission considering bacterial clones and mobile genetic elements, as well as individual and ecologic-level factors in different settings, to inform public health authorities about interventions that should be prioritised to control transmission of these organisms.	