IMPACT – A One Health collaboration on antibiotic resistance for sustainable change

PROJECT SUMMARY
ANTIBIOTIC RESISTANCE IN BACTERIA is a growing global challenge that affects human and animal health, whilst also threatening welfare, food-safety, productivity and development worldwide. The problem is shared and needs co-operation between countries through a One Health approach to create opportunities for sustainable change. Starting in 2014 with funding for five years, leading Chinese and Swedish researchers in human health, animal health and the environment are collaborating in a project on antibiotic resistance, called IMPACT.

Main areas included in the IMPACT research collaboration are:

- knowledge, attitudes and practice concerning human and animal antibiotic use
- distribution of resistant bacteria and genetic elements within the human, animal, environmental and health care sectors
- design, implementation and evaluation of strategies to promote rational use of antibiotics and to limit the spread of antibiotic resistance in all sectors.

ABOUT THE PROJECT
IMPACT – a One Health collaboration on antibiotic resistance for sustainable change

Partner organisations
The Sino-Swedish integrated multi-sectoral partnership for antibiotic resistance containment (IMPACT) funded from 2014 to 2018 by the Swedish Research Council (VR) and National Natural Science Foundation of China (NSFC).

China
Zhejiang University (PI)
China Agricultural University (co-PI)
Shandong University (co-PI)
Shandong Academy of Agricultural Sciences
Shandong Center for Disease Control and Prevention

Sweden
Public Health Agency of Sweden (PI)
Karolinska Institutet (co-PI)
Linköping University (co-PI)
Swedish National Food Agency
Swedish National Veterinary Institute
THIS MIXED METHODS PROJECT aims to deliver a deeper understanding of the interaction and the overlap of antibiotic resistant bacteria between humans, animals and the environment. The project also investigates interventions that may lead to sustainable behavioural change for the purpose of informing national and international policies.
One world – One health

ANTIBIOTIC RESISTANCE IS AN AREA where a ‘one health – one world’ approach is needed to fully understand and deal with the problem. Much is still unknown regarding the emergence of antibiotic resistance and how the spread can be mitigated. Cooperation between countries, between veterinary and human medicine, as well as the environmental sector opens up for new opportunities for sustainable change.

“The collaborative effort of multiple disciplines – working locally, nationally, and globally – to attain optimal health for people, animals and the environment.

(AVMA, 2008)
Main components and their relationships

Data collection I
Analyses I
Intervention
Data collection II
Analyses II

Samples from humans
Samples from pigs
Samples from environment
FGD:s Questionnaires

Microbiological analyses
Residue analyses
Molecular analyses
WGS
Data analyses

Identify previous successful interventions
Define set of interventions
Implement set of interventions
Process evaluation

Samples from humans
Samples from pigs
FGD:s Questionnaires

Microbiological analyses
Molecular analyses
WGS

Joint analyses
Comparisons between preintervention and postintervention

Antibiotic consumption humans and pigs
Prescriptions humans

July 2015
August 2015 – August 2017
August 2016 – July 2017
August 2017
September 2017 –

FGDs, focus group discussions; WGS, whole genome sequencing.
Collaboration between sectors and countries to achieve a common goal.
Timeline

Planning phase

- Establishing specific research questions and methods
- Development of study tools
- Selection of study sites and basic data collection
- Capacity building through workshops

2014

Baseline cross-sectional data collection

Household questionnaires
Rural residents in 769 households were asked about their knowledge, attitudes and practices regarding antibiotic use and resistance for humans and pigs, and about their health seeking behaviours.

Microbiology sampling
- Commensal samples were taken at households from humans and from pigs. Analyses focus on carriage of MRSA and ESBL- and Carbapenemase-producing Enterobacteriaceae.
- Environmental samples were also taken from drinking water sources, rivers, wastewater, vegetables and soil.

2015

Clinical isolates
Collected at the town hospital (MRSA and ESBL- and Carbapenemase-producing Enterobacteriaceae)

Continuous data collection

- Six focus group discussions with village residents
- Semi-structured interviews with village clinic doctors

Qualitative data collection
Continuous data collection

- Village clinic prescriptions
  - 600 prescriptions per year at each clinic

- Household antibiotic use
  - Antibiotic consumption for humans and pigs monitored at 200 households for 15 months

2016

Pilot intervention

- Six intervention villages
- Six control villages
- One year intervention period

For rural residents

- Information on antibiotics and aspects about antibiotic use and antibiotic resistance in humans, animals and environment:
  - Audiotapes (three times a week on village speakers)
  - One lecture every three months
  - Booklets and poster

For healthcare practitioners

- Training programmes for veterinarians and village clinic doctors, once every three months on:
  - Rational antibiotic use
  - Infection prevention and control

2017

Analyses and dissemination

- Data are analysed and results published continuously

2018

Post-intervention cross-sectional data collection

- Following the same pattern as the baseline
**Key findings**

**TO ENABLE COLLABORATIVE** One Health work, time must be invested to develop shared conceptual and contextual frameworks among all researchers. Also allocate time for joint planning of the data collection which should link different data types together to allow for integrated analyses across sectors and instruments. [11]

**RURAL RESIDENTS GENERALLY** have low levels of knowledge about antibiotics (as with other studies in Asia and globally) and their self-reported attitudes and practices could lead to both overuse and underuse of antibiotics. Storage of antibiotics for both human use and pig use is common in households, however most residents are not aware that they are storing antibiotics. [3]

**THE ENVIRONMENT PLAYS** an important role in the emergence and dissemination of antibiotic resistant bacteria, however, the factors facilitating this development are not yet well understood. Putative transmission routes of CTX-M-producing *Escherichia coli* to different environmental matrices were evaluated by analysing the genetic relatedness of isolates from bird faeces, pig faeces, drinking water, river sediment, river water and wastewater. The analyses indicate that both plasmid and clonal expansion are important for the dissemination of CTX-M-genes and that wild birds may act as potential vectors across long distances. Regional dissemination between different environmental matrices of CTX-M-producing *E. coli* increases the exposure risk of humans and animals in the area. [1]

**ANTIBIOTIC RESIDUES ARE** present in various compartments of the environment. The concentration levels of fluoroquinolones in wastewater are estimated to pose biological risks for development and selection of antibiotic resistance in bacteria. The concentration of antibiotics in drinking-water and vegetables are estimated to pose no appreciable direct risk to human health through consumption, but might still pose an important indirect risk through contribution to resistance development. [7]

**EXTENDED SPECTRUM ß-LACTAMASE (ESBL)** producing bacteria carrying genes encoding resistance to last-resort antibiotics carbapenems and colistin are present in wells in rural China, indicating water as a potential source of antibiotic resistance. [10]

**KLEBSIELLA PNEUMONIAE** is associated with health-care associated infections and has a high capacity to acquire mobile genetic elements such as plasmids containing antibiotic resistance genes. However, data on the occurrence and characteristics of extended spectrum ß-lactamase (ESBL) producing *K. pneumoniae* in environmental sources are scarce. We show that clinically relevant strains of ESBL-producing *K. pneumoniae* are occurring in environmental sources. [2]
COMMUNITY-ASSOCIATED MRSA (Methicillin-resistant *Staphylococcus aureus*) and livestock-associated MRSA, belonging to ST59 and ST9, respectively, were identified in both humans and pigs. The genotypic and phenotypic comparison of isolates indicates that bidirectional transmission of MRSA has occurred between humans and pigs in the study area. [8]

A FIRST REPORT OF MCR-3 AND MCR-3.5 in *Escherichia coli* in backyard pig husbandry shows that mcr genes are not restricted to pigs from large-scale commercial farms, but also occur in pigs from small-scale backyard holdings. Adequate measures, such as raised awareness of rational use of antibiotics in both animals and humans, prudent use of colistin in pigs for disease treatment and prevention, and good management and hygiene of backyard farming, should be considered to limit the spread of *mcr* genes. [5]

WE PRESENT A FIRST REPORT of the colistin resistance gene *mcr*-5 in an *Aeromonas hydrophila* isolate from the faeces of a backyard pig. The ColE-like replication primase in *mcr*-5-harbouring plasmid pI064-2, which is widely distributed among Enterobacteriaceae, *Pseudomonas* spp. and aeromonads, indicates that *mcr*-5 has the potential to disseminate among different bacterial species. [4]

OXAZOLIDINONES ARE SOME of the few remaining options for antimicrobial treatment of infections caused by multidrug resistant Gram-positive pathogens, including staphylococci. There is a wide distribution of oxazolidinone resistance genes *optrA* and *cfr* in household animals in the investigated rural villages, and the presence of *optrA* and *cfr* may be explained by co-selection by a number of unrelated antimicrobials. We identified a possibility of transmission of these pathogens between different households within the same village and even between different villages. Furthermore, a first identification of *optrA* in isolates of *Staphylococcus simulans* was made. [6]

WE USE A ONE HEALTH approach to address important research questions that individual discipline investigations are unable to. The results obtained should more closely reflect the world in which human health, animal health and the environment are inextricably and intimately interlinked. The data sources include before-after cross-sectional collection of biological samples, demographic information, questionnaires and focus group discussions; longitudinal sampling of prescriptions from village clinics and antibiotic use for pigs and humans in a subset of households; and process evaluation data from a pilot One Health intervention package. [9]
Publications


Conference abstracts

Dyar OJ, Yin J, Chen B, Nilsson M, Xuewen L, Ottoson J, Sun C, Yin H, Börjesson S on behalf of the IMPACT consortium. Risk factors for carriage of resistant bacteria in humans and pigs: a One Health study in rural China. Accepted at 29th European Congress of Clinical Microbiology and Infectious Diseases, 13-16 April 2019, Amsterdam, Netherlands.


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