

# Quantifying human exposure to antimicrobial resistance from animals and food

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## Abstract

Antimicrobial resistance (AMR) is an emerging threat to global health, and a phenomenon where humans, animals (production and companion), food and the environment are all highly interrelated. Among other critical knowledge-gaps, the relative importance of each transmission pathway remains however widely unknown, making the decisions of those involved in the implementation of surveillance programs and related policy-making, challenging. Ecology from Farm to Fork of Microbial Drug Resistance and Transmission (EFFORT) is a five-year EU FP7 project, which has as one of its goals the estimation of the relative importance of different food and animal transmission routes for human exposure to AMR in the overall population. Our approach and framework for developing a comparative exposure assessment model to quantify human exposure to AMR is the focus for this paper. We hope that the results can support future political decisions and the prioritisation of risk management options along the food chain, thereby contributing to reducing human exposure to antimicrobial resistance. Furthermore, by producing and using results from whole community sequencing (WCS), the project may demonstrate the usefulness of metagenomics data for surveillance and source attribution, providing the framework for future related research.

**Keywords:** *antimicrobial resistance, exposure assessment, source attribution, modelling, food safety*

## Introduction

Antimicrobial resistance (AMR) is an emerging threat to global health (1) - threatening to undermine decades of progress in treatment of infectious diseases, as the number of effective antimicrobials declines. The main driver of AMR is antimicrobial usage in humans and animals, and resistant bacteria are found in humans, animals, food and the environment. Humans can consequently be exposed to AMR bacteria through different routes and sources, but the relative importance of each transmission pathway remains widely unknown. The debate has and still is centered on the importance of food-producing animals and food as a reservoir for human exposure (2).

Ecology from Farm to Fork Of microbial drug Resistance and Transmission (EFFORT) is a five-year EU FP7 project which focuses on understanding the eco-epidemiology of antimicrobial resistance (AMR) from animal origin and its transmission to humans. The EFFORT trans-disciplinary

consortium is made up of 20 partners from 10 European countries. The scientific research is divided in eight work packages (WP): (i) integrated evidence base, (ii) molecular ecology and epidemiology, (iii) ecology and transfer of resistance, (iv) integrated epidemiological analysis, (v) resistance and usage, (vi) intervention studies, (vii) exposure assessment and (viii) economic impact analysis. EFFORT's aim is to provide scientific evidence and high quality data to inform decision makers and the scientific community about the consequences of AMR in the food chain.

The objective of WP7 is to estimate the relative importance of different food and animal transmission routes for human exposure to AMR in the overall population. Our approach and framework for developing a comparative exposure assessment model to quantify human exposure to AMR is the focus for this paper.

## Materials and methods

Estimating human exposure to AMR is not as straightforward as traditional microbial exposure assessment, since antimicrobial resistance can be carried by many bacterial species, including commensals. Focusing on a single species is therefore likely to underestimate the exposure. In addition, genes coding for antimicrobial resistance are often located on plasmids that can be transferred between bacterial species, e.g. between Enterobacteriaceae, such as *E. coli* and *Salmonella* spp. For the comparative exposure assessment model, we therefore chose to focus on estimating human exposure to AMR determinants, i.e. resistance genes.

## Data

The data expected to become available from the EFFORT project that can be used as input for the comparative exposure assessment include data collected from:

- farms (pooled faecal and environmental samples from pig herds, broiler and turkey flocks, veal calves and trout farms),
- companion animals (dogs),
- wildlife (wild boars), and
- retail meat (pork, chicken, turkey meat, veal and trout).

Faecal samples from farm and companion animals and wildlife will be analysed using whole community sequencing (WCS), providing distributions of the occurrence of resistant genes, plasmids and bacterial species. In addition *E. coli* will be isolated, tested for susceptibility and sequenced. The occurrence of resistance genes in meat samples will be

determined by use of qPCR. Which genes to focus on will be decided based on the preliminary metagenomic results from the faecal samples. In total, more than 30,000 samples from nine countries are collected and analysed.

### Model

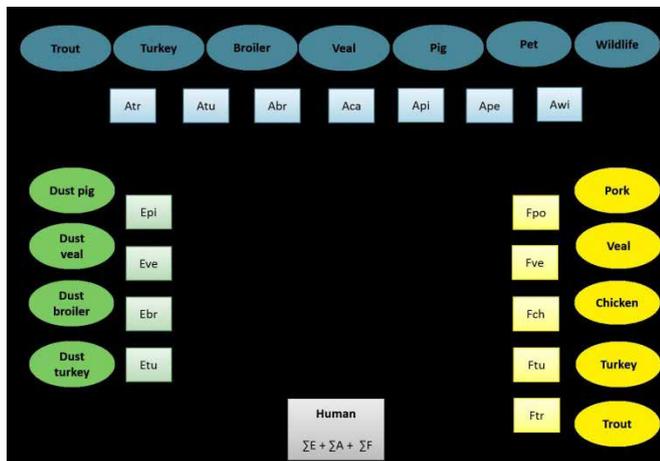
Approaches for quantifying the relative importance of specific sources and transmission routes for human illness have been gathered under the term ‘source attribution’ (3). Ideally, the source attribution model to be developed for addressing AMR should quantify the number of human infections with antimicrobial resistant bacteria resulting from exposure from each of the included transmission routes. However, due to the complexity and uncertainty of modelling e.g. the transfer of resistance from commensals to pathogens and from this estimating the risk of infection, we chose, at least in the first go, to focus only on human exposure to AMR determinants.

We hope that the results can support political decisions and the prioritisation of risk management options along the food chain, thereby contributing to reducing human exposure to antimicrobial resistance. Furthermore, by producing and using results from WCS, the project may demonstrate the usefulness of metagenomics data for surveillance and source attribution.

### References

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**Figure 1.** Illustrates the model concept including the transmission pathways included.



Transmission from direct contact with animals will be estimated using the following basic equation:

$$A = P_c * F_{rc} * P_i * F_i * P_r * C$$

Where A = exposure per person per day,  $P_c$  = probability of contact with animal,  $F_{rc}$  = contact frequency per person,  $P_i$  = probability of ingestion of faeces given contact,  $F_i$  = amount of faeces ingested per ingestion event,  $P_r$  = prevalence of AMR determinant, C = quantity of AMR determinant.

For food exposures, the equation becomes:

$$A = C_o * P_r * C * F_{cc}$$

Where A = exposure per person per day,  $C_o$  = consumption of food product per person per day,  $P_r$  = prevalence of products with AMR determinant at retail, C = quantity of AMR determinant in contaminated products,  $F_{cc}$  = fraction of cross contamination (depends on transference rate from product to environment ( $T_{rpe}$ ) and transference rate from environment to product ( $T_{rep}$ )).

### Expected results and discussion