# Introduction

Occupational exposure to antimicrobial-resistant bacteria poses a critical public health concern, particularly in industries such as poultry farming. Numerous studies in the literature have highlighted the occupational risks of extended-spectrum β-lactamase (ESBL) transmission among professionals working in pig farms, slaughterhouses or poultry abattoirs. A ‘top-down’ source attribution study by Mughini-Gras et al. (2019) analyzed the community-acquired ESBL-EC and pAmpC-EC in the Netherlands during 2005-2017 revealing 1,220 occurrences in humans and 6,275 in non-human sources, mainly farm animals and food.

**Evidence of occupational exposure:** Several studies in the literature provide evidence of the occupational exposure of farm and slaughterhouse workers to antimicrobial-resistant bacteria. Most of these studies were based on fecal sample analysis and detailed questionnaires to assess personal and occupational exposure. Price et al. (2007) explore the impact of antimicrobial use in food-animal production on resistant enteric bacteria. Their study finds that poultry workers in the Delmarva region have 32 times the odds of carrying gentamicin-resistant Escherichia coli and a higher risk of multidrug-resistant strains compared to community members. These results suggest that occupational exposure from live-animal contact in the broiler chicken industry significantly contributes to the spread of antimicrobial resistance in the community. Oguttu et al. (2008) investigated antimicrobial resistance in Escherichia coli from broilers and poultry abattoir workers. The study found high resistance levels in broilers, particularly to antimicrobials used on farms, and higher resistance levels in abattoir workers compared to controls. Another study by Huijbers et al. (2014) found high rates of ESBL- and AmpC-producing E. coli on Dutch broiler farms, with 96.4% prevalence in broilers and 19.1% in humans, particularly among those with frequent broiler contact. Genetic analysis revealed both clonal transmission and horizontal gene transfer, highlighting significant human-animal transmission risks. Dohmen et al. (2015) examined the prevalence of ESBL-producing Enterobacteriaceae in pig farmers and found a 6% carriage rate in humans, showing that ESBL genes in human isolates were often identical to those found in pigs. This established a strong link between the number of hours spent working on the farm and ESBL carriage, reinforcing the role of occupational exposure in AMR transmission. Later Dohmen et al. (2017) investigated the prevalence of ESBL carriage in pig slaughterhouse workers, finding a 4.8% prevalence rate among 334 workers and they identified specific job tasks, such as removing animal organs, as associated with higher ESBL carriage rates. This suggests that direct contact with animal products significantly increases the risk of ESBL transmission. These findings indicated a substantial association between job exposure and ESBL carriage, with higher prevalence in tasks involving direct animal contact compared to roles like refrigeration and packaging. Another study by Van Gompel et al. (2020) used shotgun metagenomics to analyze the fecal resistomes and microbiomes of pig and poultry farmers, slaughterhouse workers, and controls. It found higher ARG abundances in pig farmers and slaughterhouse workers compared to broiler farmers and controls. Differences in resistome and microbiome composition were observed based on occupational exposure, with significant correlations between on-farm working hours and ARG carriage. Another similar study in Europe by Wadepohl et al. (2020) examine the prevalence of ESBL-producing E. coli among poultry slaughterhouse workers, finding it in 5.1% of 99 fecal samples. Workers with higher exposure had a colonization rate of 10%, compared to 2.9% for those with lower exposure. None the less Fastl et al. (2023) conducted a systematic review to evaluate how animals contribute to human antimicrobial resistance (AMR). Analyzing 31 studies from 2012 to 2022, primarily from Europe and North America, they found that plenty of studies focused on AMR from chickens, cattle, and pigs, using diverse methodologies.

**Quantification of occupational exposure:** Although many studies focus on assessing occupational exposure, a robust framework for rigorously quantifying the exposure and transmission of ESBL *E. coli* from broiler production is currently lacking. Opatowski et al. (2021) proposes a stochastic quantitative risk assessment model to quantify the impacts of environmental, animal, and human sources from a One-Health perspective. This is a much more generalized and macro-analysis framework that evaluates AMR colonization in humans from five sources: water, food, livestock contact, and interhuman contacts. Another recent work by Lu et al. (2024) proposes a One Health-based quantitative microbial risk assessment (QMRA) framework, that emphasizes more in micro-analysis of the occupational exposure in order to manage health risks associated with tetracycline-resistant Aeromonas hydrophila in aquaculture. A more related work in the context of ESBL *E. coli* to poultry farm and slaughterhouse workers, is produced by De Freitas Costa et al. (2022), where the authors proposed a multidirectional dynamic risk model for ESBL *E. coli* transmission among broiler flocks, broiler farmers, and the open community in the Netherlands. Their work was more focused on

the dynamics of the clonal spread of ESBL *E. coli* among the different populations and was based on the estimated prevalence rates by Huijbers et al. (2014). However, to the best of our knowledge, no quantitative risk assessment model has been proposed dedicated to the modeling of the exposure and transmission of ESBL  *E. coli* in a farm to fork framework, that performs a micro- analysis to model the evolution of the AMR bacteria starting from the broiler farms to the professionals and consumers.

Therefore, within the context of the JPIAMR project ENVIRE, we propose the first farm-to-fork foodborne and occupational QMRA model that quantifies the risk of colonization of ESBL *E. coli* from broiler chickens to broiler meat consumers and to poultry professionals with a direct contact exposure. Cite Codex. The ultimate objective of this work is to integrate the newly proposed model to the One health framework to contribute to the reduction of the selection and the spread of antimicrobial resistant bacteria in broiler chickens and from chicken farms to the environment, and ultimately to humans.

# 2. Materials and methods 2.1 Model overview 2.2 Hazard identification The gut microbiota is a reservoir of antimicrobial resistance genes \cite{carlet12}. Among Enterobacteriaceae, Escherichia coli is becoming a major storehouse of ESBL genes, which impart resistance to a number of β-lactam antibiotics \cite{ny16}. ESBLs degrade oxyimino-cephalosporin (cefotaxime, ceftazidime) and they are defined as β-lactamases that confer resistance to bacteria against the penicillins, the first-generation, second-generation and third-generation generation cephalosporins and aztreonam by hydrolysing these antibiotics. They are inhibited by β-lactamase inhibitors \cite{chong11}. For example, ESBL-producing E. coli are resistant to many β-lactam antibiotics, including penicillins, aztreonam and most cephalosporins.ESBLs started to evolve as mutations outside the active site of β-lactamases in the 1980s and they are most often produced by members of the *Enterobacteriaceae*. The three β-lactamases TEM (named after the patient Temoneira), SHV (sulfhydryl reagent variable) and CTX-M (active on cefotaxime, first isolated at Munich) are the most important representatives of ESBLs in relation to *E. coli* colonizing and infecting poultry. Resistance to third-generation cephalosporins is most serious, since this group of antibiotics is currently used to treat highly dangerous human infections. ESBL E. coli can emerge in the human or animal gut following the use of antibiotics. Since the first ESBL was reported in the mid-1980s, a significant number of reports concerning not only ESBL but also plasmidic class C β-lactamases, like those of the CMY family from both human clinical and community isolates, have been published \cite{nordmann98, bradford01}. Initially, ESBL-production was mainly observed in hospital infections caused by Klebsiella pneumonia, but today it is also frequently associated with community-acquired infections, mostly urinary tract infections caused by E. coli \cite{livermore07, paterson05}.

# E. coli, a Gram-negative facultative anaerobe\cite{carlson04} whose primary habitat is the distal intestines of humans and animals, is the most common cause of urinary tract infections\cite{flores15} and urosepsis in humans. Acquisition of drug resistance genes by E. coli makes the treatment of these infections difficult.

# The intestinal carriage of ESBL E. coli is usually asymptomatic and persistent \cite{bar16}. However, many studies have shown the association of faecal carriage with ESBL E. coli infections \cite{ruppe13}. Many sytamatic rewiews \cite{bezabih21, woerther13} in the literature have provided evidence of worldwide prevalence of human ESBL E. coli carriage and its increasing trend.

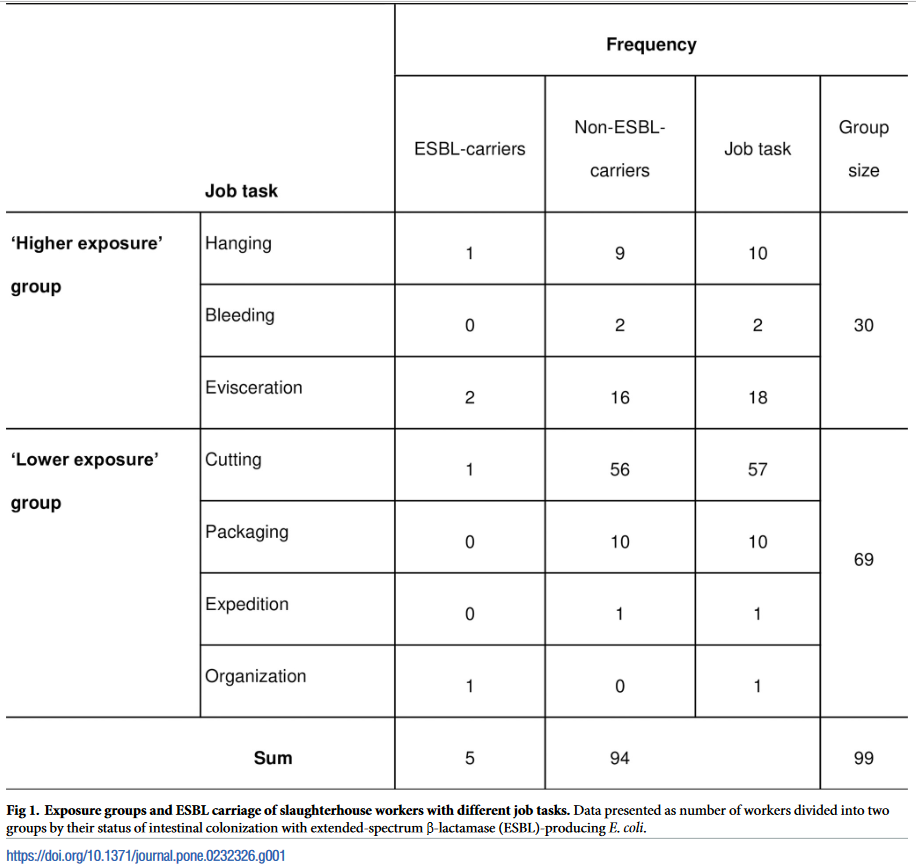
# 2.3 Hazard characterization dose response 2.4 Exposure assessment Defining the different modules and tables of parameters 2.5 Risk characterization Defining the risk of ESBL carriage, average risk computation for foodborne pathway 2.6 Sensitivity analysis

**3. Results**  
**3.1 Baseline simulations  
3.2 Effect of bio security practices**Bio-security and hygiene practices DEFINE  
**3.2.1 Literature study:** Several studies have assessed various hygiene and biosecurity protocols implemented in farms and slaughterhouses. Racicot et al. (2013) evaluated the effectiveness of various hand sanitization protocols for heavily contaminated hands among catching crew members. They compare water and soap, degreasing cream, hand wipes, and alcohol-based gel for neutralizing Salmonella on hands of workers. Mo et al. (2016) studied 27 Norwegian broiler farms to identify risk factors for cephalosporin-resistant Escherichia coli, finding resistance in 13.8% of parent flocks and 22.5% of broiler flocks. Key risk factors include previous flock status, the number of parent flocks supplying chicks, disinfection routines, and access for transport personnel. The study by Franceschini et al. (2019) specifically evaluated turkey farmers' exposure to antimicrobial-resistant (AMR) bacteria to rank farm practices in Northern Italy. Through a literature review and interviews with veterinarians, the study identified high-risk practices, such as direct contact during vaccination and litter management, which elevate exposure to methicillin-resistant Staphylococcus aureus (MRSA) and extended-spectrum beta-lactamase (ESBL). Youssef et al. (2021) provides a systematic literature review of 14 studies on farm-level biosecurity measures to reduce zoonotic bacterial transmission from livestock to humans. They find mixed effects on infection risks, with most studies showing medium risk of bias.   
**3.2.3 Bio security practices   
3.2.2 Effect of bio security practices**

**4. Discussions  
4.1 Model validation**  
Wadepohl et al. (2020) comparison with empirical proportion of colonized workers.  
**4.2 Model limitations and perspectives**  
**4.2.1 Model assumptions:** only direct contact based, transmission rates,  **4.2.2 Airborne transmission:** The possibility of airborne transmission of ESBL was explored by Dohmen et al. (2017). The study involved 131 individuals from 32 pig farms, analyzing stool, pig rectal swabs, and dust samples. Results showed a significant presence of CTX-M-group 1 ESBL in both human and dust samples, suggesting that inhalation of contaminated air could be an additional transmission route. This study highlighted that occupational exposure to airborne dust in pig farms could contribute to ESBL carriage in humans. Luiken et al. (2020) provided insights into the resistomes and bacterial microbiomes of farm dust from 35 broiler and 44 pig farms. The study used shotgun metagenomic analysis to reveal a rich variety of antimicrobial resistance genes (ARGs) in farm dust, more extensive than in animal feces. It demonstrated that farm dust resistomes were significantly associated with animal feces resistomes and influenced by antimicrobial usage on farms. This study suggests that dust is a critical vector for ARG transmission, posing risks to both animals and humans.

**4.2.3 Sensitivity analysis results**

# Wadepohl et al. (2020) Association of intestinal colonization of ESBL-producing *Enterobacteriaceae* in poultry slaughterhouse workers with occupational exposure—A German pilot study This study is the first of its kind to collect data on the occupational exposure of slaughter house workers to ESBL-producing Enterobacteriaceae in Europe.



Adhikari et al. (2020) Quantitation of Risk Reduction of E. coli Transmission after Using Antimicrobial Hand Soap.

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Chen et al. (2001) Quantification and Variability Analysis of Bacterial Cross-Contamination Rates in Common Food Service Tasks Transfer rate from chicken to finger tips: the normal distributions in log percent transfer rate from chicken to hand (0.94 +- 0.68). These turns out to be lognormal parameters.

# Lopez et al. (2013) Transfer Efficiency of Bacteria and Viruses from Porous and Nonporous Fomites to Fingers under Different Relative Humidity Conditions Transfer rate form cutting board/knife to finger tips

Gibson et al. (2002) Quantitative assessment of risk reduction from hand washing with antibacterial soaps Transfer rate from finger tips to lips

Depoorter et al. (2012) Assessment of human exposure to 3rd generation cephalosporin resistant E. coli (CREC) through consumption of broiler meat in Belgium QMRA farm to fork, with meat to hand transfer rate from the following paper, assuming *Salmonella* and *E. coli* has same attaching properties

Montville et al. (2000) Glove barriers to bacterial cross-contamination between hands to food chicken to hand transfer rate (%) through gloves, gamma (5.91, 0.40, -5) and chicken to bare hand, normal (0.71, 0.42); for *Salmonella* substitute

Leonas et al. (2003) The Relationship of Fabric Properties and Bacterial Filtration Efficiency for Selected Surgical Face Masks Average over the 6 different Bacterial Filtration Efficiency (BFT) was used as the q\_mask parameter in the model

# King et al. (2020) Bacterial transfer to fingertips during sequential surface contacts with and without gloves Although previous studies have investigated the transfer efficiency of various microorganisms during a single contact from fomite to finger[18](https://onlinelibrary.wiley.com/doi/full/10.1111/ina.12682#ina12682-bib-0018), [19](https://onlinelibrary.wiley.com/doi/full/10.1111/ina.12682#ina12682-bib-0019), [23](https://onlinelibrary.wiley.com/doi/full/10.1111/ina.12682#ina12682-bib-0023) and finger to fomite,[23](https://onlinelibrary.wiley.com/doi/full/10.1111/ina.12682#ina12682-bib-0023)-[25](https://onlinelibrary.wiley.com/doi/full/10.1111/ina.12682#ina12682-bib-0025) only a small number of studies have considered more than one surface contact.[21](https://onlinelibrary.wiley.com/doi/full/10.1111/ina.12682#ina12682-bib-0021), [26](https://onlinelibrary.wiley.com/doi/full/10.1111/ina.12682#ina12682-bib-0026) Repeated contact with a surface covered in fluorescent powder shows that skin became saturated after six contacts,[27](https://onlinelibrary.wiley.com/doi/full/10.1111/ina.12682#ina12682-bib-0027) while a separate study using fluorescent particles found an equilibrium after five contacts.

Julian et al. (2009) A Model of Exposure to Rotavirus from Nondietary Ingestion Iterated by Simulated Intermittent Contacts stochastic-mechanistic model of exposure to rotavirus from nondietary ingestion iterated by simulated intermittent fomes-mouth, hand-mouth, and hand-fomes contacts typical of a child.   
The transfer is assumed to occur instantaneously and uniformly, and the duration of contact is assumed to not affect transfer. The latter is based on the work of Cohen-Hubal et al., who found that duration does not increase the amount of both lipophilic uvitex and nonlipophilic riboflavin tracer residues transferred between surfaces on contact.(25) It is assumed that, after transfer, virus is distributed evenly over the en tire surface.

### [An Examination of Broiler Growth](https://getd.libs.uga.edu/pdfs/morris_jonathan_a_201505_ms.pdf) gives the constant for the Meeh’s formula used to compute the broilers surface area from its weight.

Explanation of ECDF at hanging stage:

For hanging stage we use the foodborne module output C\_prod as the concentration on the birds. The sudden peak is due to very low sd for the negatve flocks.