Aggiornamenti nella sorveglianza dell'antibioticoresistenza in Italia nel settore animale

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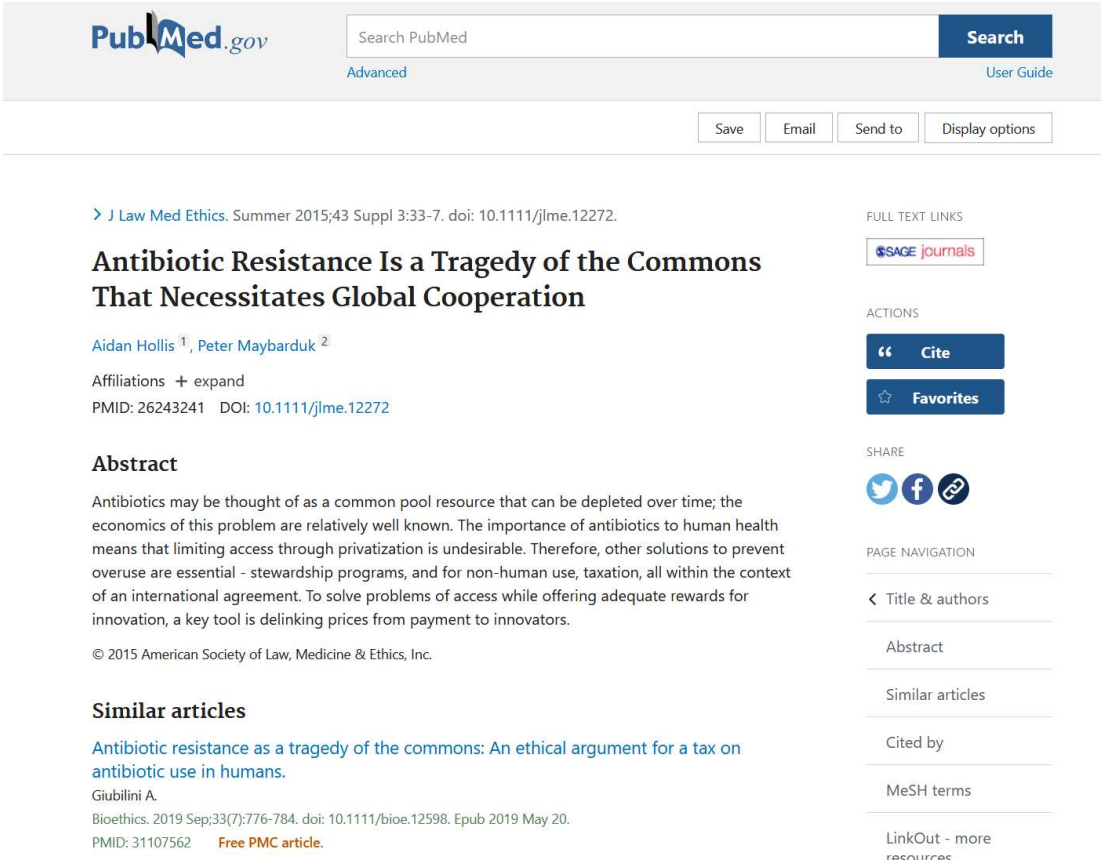
I Centri ed i Laboratori di Referenza Nazionali nell'ottica One Health
Ministero Salute – Roma, 6 dicembre 2023

Antimicrobial resistance as an example of «Tragedy of the Commons»



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J Law Med Ethics. Summer 2015;43 Suppl 3:33-7. doi: 10.1111/jlme.12272.

Antibiotic Resistance Is a Tragedy of the Commons That Necessitates Global Cooperation

Aidan Hollis [1], Peter Maybarduk [2]

Affiliations + expand

PMID: 26243241 DOI: 10.1111/jlme.12272

Abstract

Antibiotics may be thought of as a common pool resource that can be depleted over time; the economics of this problem are relatively well known. The importance of antibiotics to human health means that limiting access through privatization is undesirable. Therefore, other solutions to prevent overuse are essential - stewardship programs, and for non-human use, taxation, all within the context of an international agreement. To solve problems of access while offering adequate rewards for innovation, a key tool is delinking prices from payment to innovators.

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Tragedy of the Commons

From Wikipedia, the free encyclopedia

In economic science, the **tragedy of the commons** is a situation in which individual users, who have open access to a resource unhampered by shared social structures or formal rules that govern access and use,[1][2] act independently according to their own self-interest and, contrary to the common good of all users, cause depletion of the resource through their uncoordinated action.[3] The concept originated in an essay written in 1833 by the British economist William Forster Lloyd,[4] who used a hypothetical example of the effects of unregulated grazing on common land (also known as a "common") in Great Britain and Ireland.[5] The concept became widely known as the "tragedy of the commons" over a century later after an article written by Garrett Hardin in 1968.[6]

Ministero della Salute

Resistenza agli antimicrobici dei batteri zoonotici e commensali negli animali destinati alla produzione di alimenti e nelle carni derivate, 2014 – 2021 (DGSAF – DGISAN - IZSLT NRL-AR & CRN-AR)

Report presentato in anteprima al

Workshop Annuale del Laboratorio Nazionale di riferimento per l'Antimicrobicoresistenza e del Centro di Referenza Nazionale per l'Antibioticoresistenza, 23-24 novembre 2023

Reporting AMR

Data on AMR in **food- producing animals** and **derived meat**

- *Salmonella*
- *Campylobacter*
- *Indicator E.Coli*
- *E.coli* ESBL/AmpC/CP

- *Salmonella*
- *Campylobacter*
- *MRSA*
- *Indicator E.Coli*

Data on AMR in **Humans**

- *Salmonella*
- *Campylobacter*

Ireland

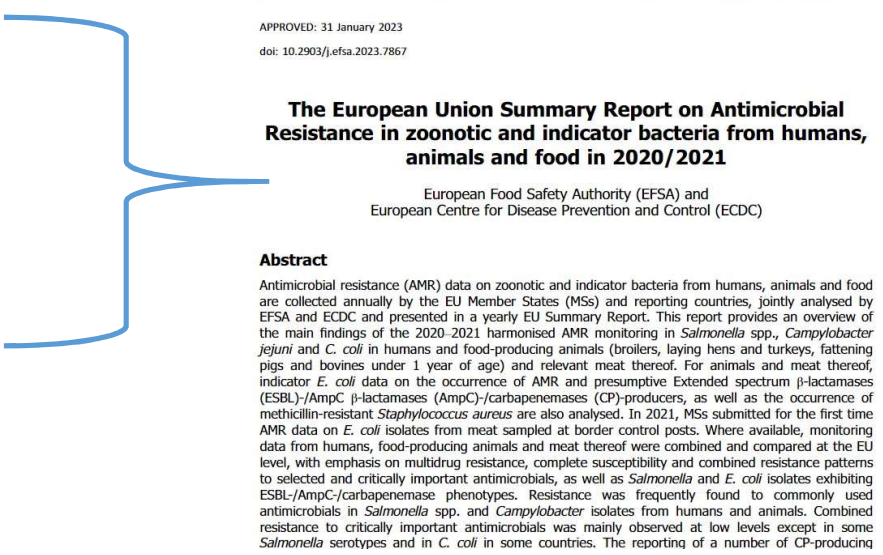
2021 2020 2019 2018 2017 2016 2015 2014 2013 2012
2011 2010 2009 2008 2007 2006 2005 2004

Italy

2021 2020 2019 2018 2017 2016 2015 2014 2013 2012
2011 2010 2009 2008 2007 2006 2005 2004

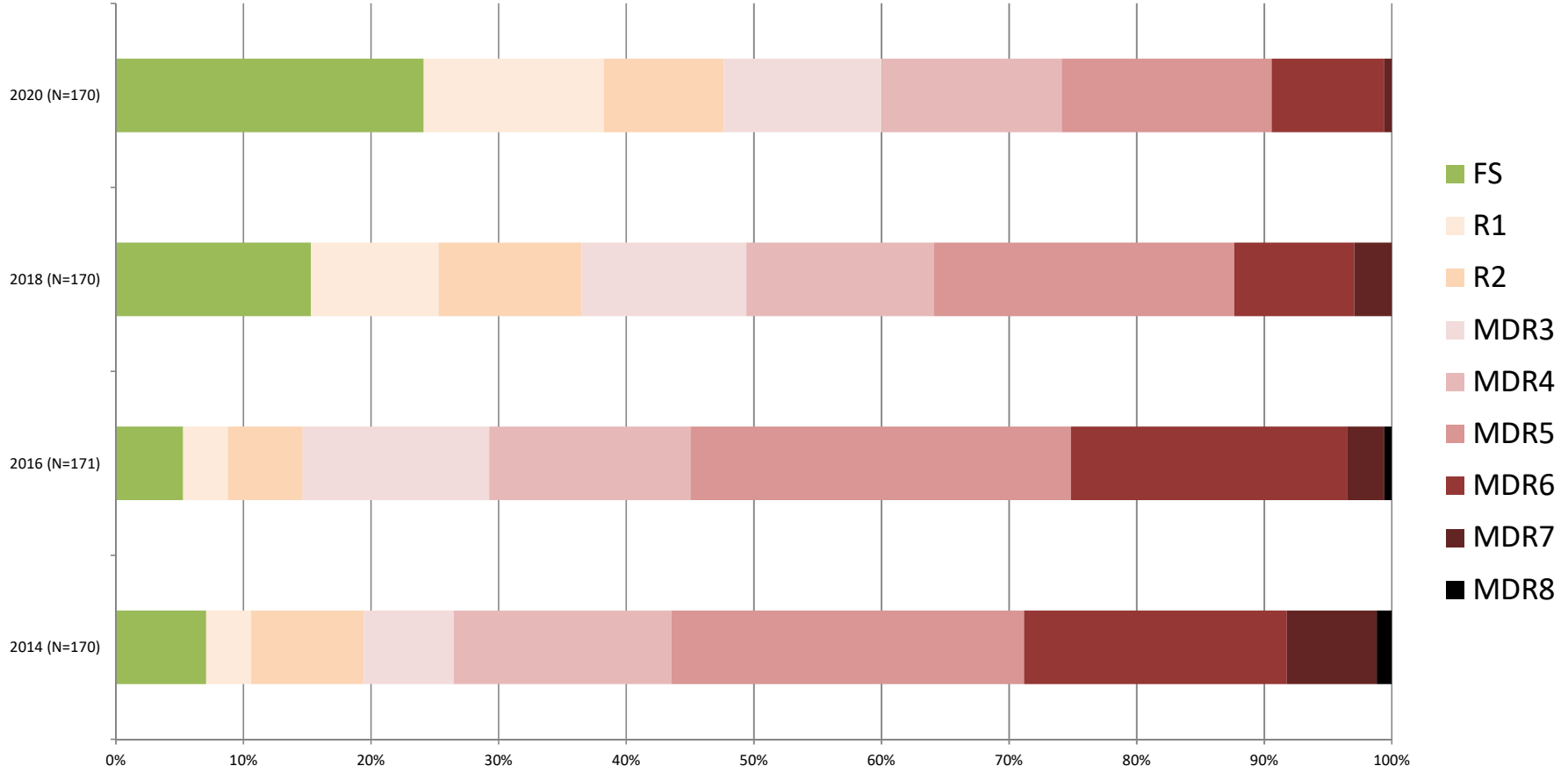
Latvia

2021 2020 2019 2018 2017 2016 2015 2014 2013 2012
2011 2010 2009 2008 2007 2006 2005 2004

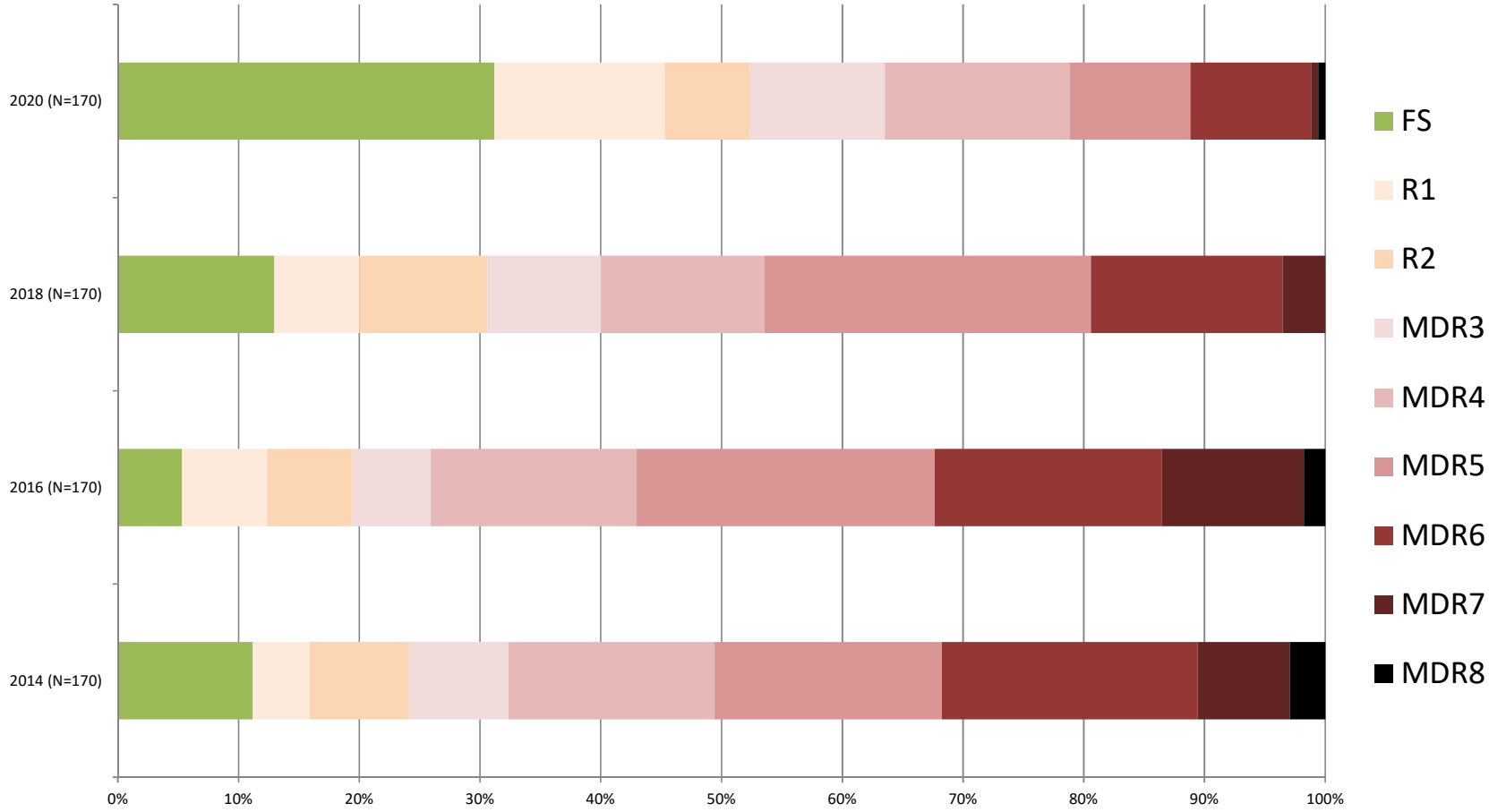


- **National Zoonoses country reports:** https://www.efsa.europa.eu/en/data-report/biological-hazards-reports
- **European Union Summary Report on Antimicrobial Resistance in zoonotic and indicator bacteria from humans, animals and food (EU Summary report AMR)**: https://www.efsa.europa.eu/en/news/bacteria-resistant-commonly-used-antimicrobials-still-frequently-found-humans-and-animals

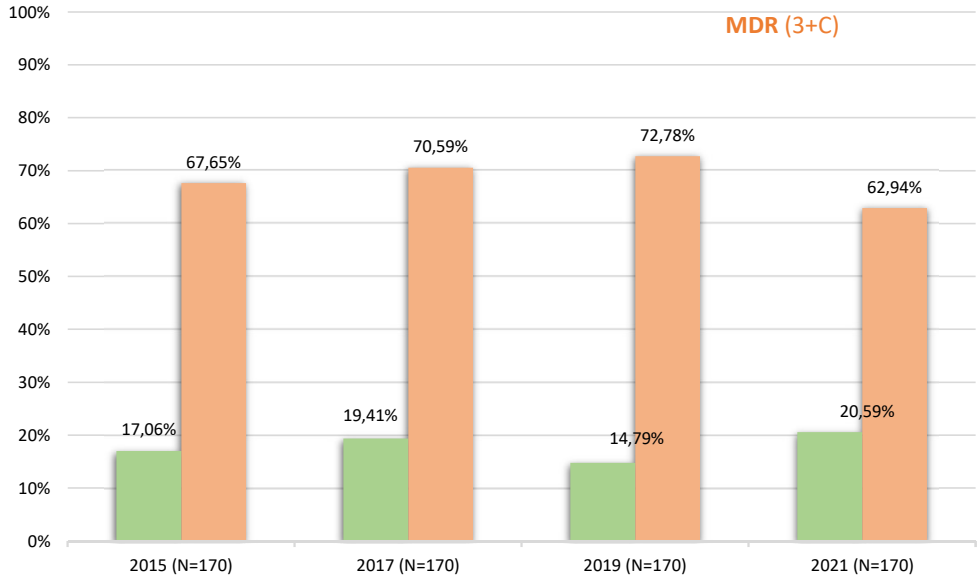
Distribuzione della suscettibilità antimicrobica e della multiresistenza (MDR, 3+C)
***E. coli* indicatore commensale - pollo da carne, contenuto intestinale**



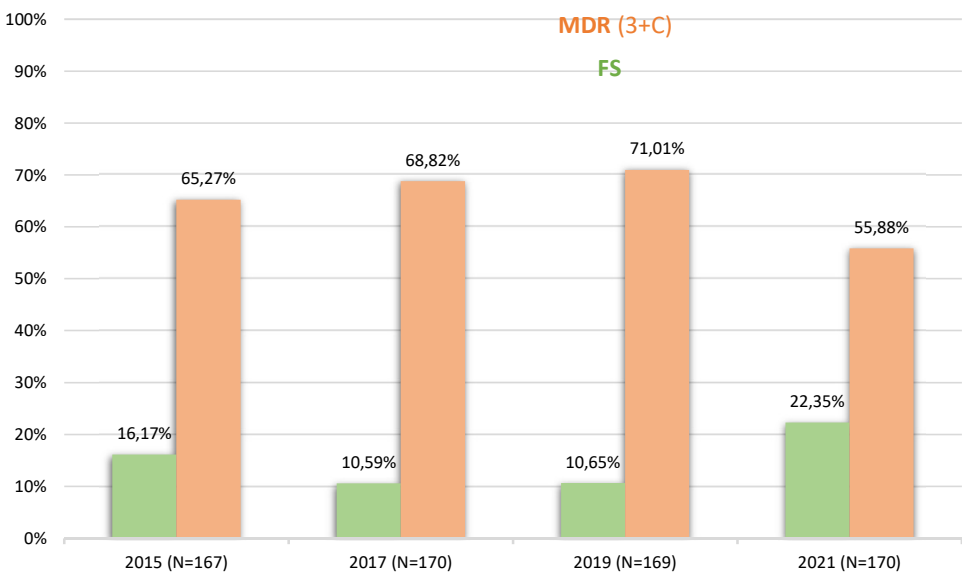
Distribuzione della suscettibilità antimicrobica e della multiresistenza (MDR, 3+C)
***E. coli* indicatore commensale - tacchino da ingrasso, contenuto intestinale**



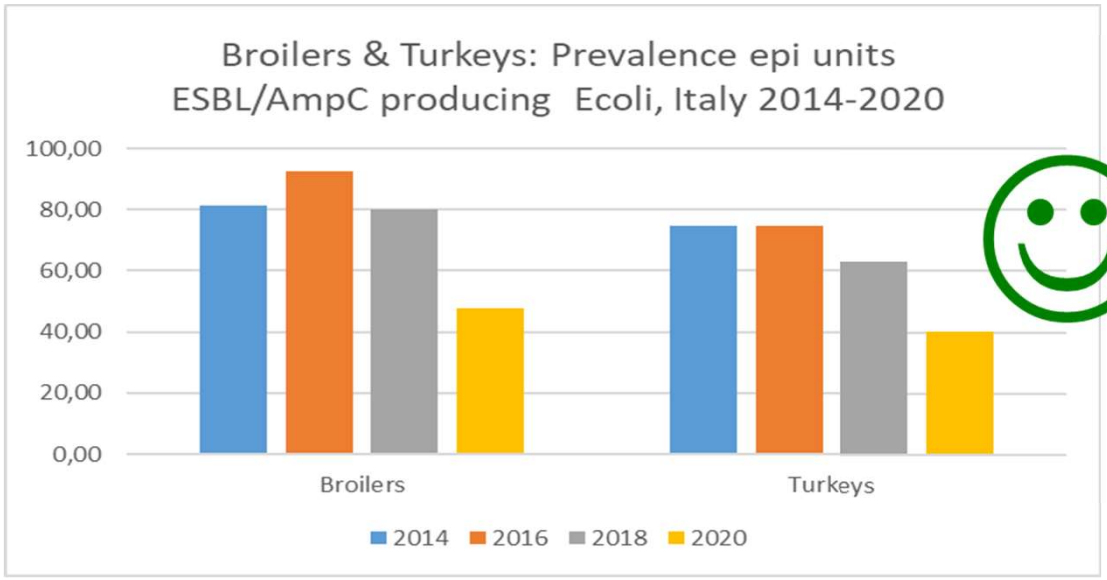
Completa suscettibilità (FS) e multiresistenza (MDR, 3+C)
***E. coli* indicatore commensale – bovino <12m, contenuto intestinale**



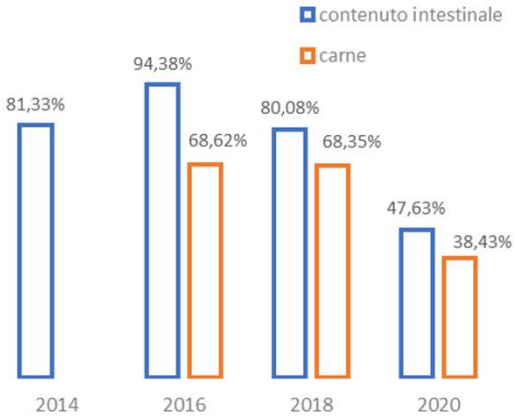
Completa suscettibilità (FS) e multiresistenza (MDR, 3+C)
***E. coli* indicatore commensale – suino da ingrasso, contenuto intestinale**



Eppur si muove…

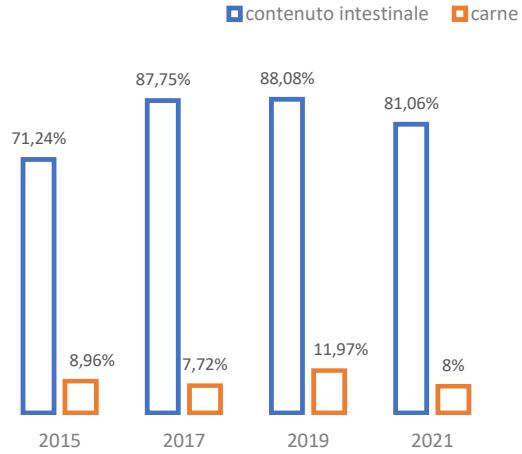


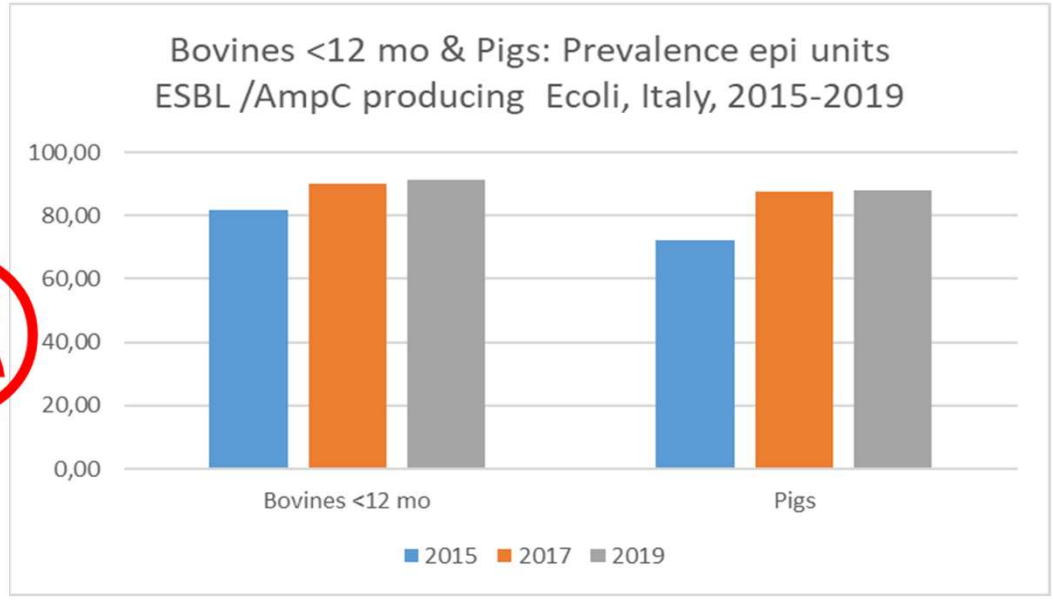
ESBL/AmpC producing E. coli in broilers and meat thereof, 2014-2021, Italy



A clue that the selection pressure by all antimicrobials and especially by beta-lactams has not decreased enough…

Prevalence ESBL/AmpC producing E. coli in pigs and meat thereof, 2014-2021, Italy





Carbapenemase-producing E. coli

Table 45: Prevalence of carbapenemase-producing *E. coli* from broilers and fattening turkeys collected within the specific carbapenemase-producing microorganisms monitoring in Italy in 2014

Poultry population	Number of caecal samples tested on selective culture media	Number of caecal samples tested positive for carbapenemase-producing *E. coli*	Prevalence (95% CI)
Broilers	300	0	0.0% (0.0, 1.2)
Fattening turkeys	300	0	0.0% (0.0, 1.2)

This study provides baseline information of utmost interest, as in Italy, CPE-R Enterobacteriaceae in humans are widespread and are currently considered a major burden among healthcare-associated infectious diseases.

Specific monitoring of ESBL-/AmpC-producing E. coli

ESC-R *E. coli* were confirmed as ESBL-/AmpC-producing *E. coli* by performing relevant Polymerase Chain Reaction (PCR) tests. Corresponding prevalence in broilers and fattening turkeys is shown in the table below.

ESBL-AmpC-producing E. coli

Table 46: Prevalence of ESBL-/AmpC-producing *E. coli* from broilers and fattening turkeys within the specific ESBL-/AmpC-producing *E. coli* monitoring in Italy in 2014

Poultry population	Number of caecal samples tested on selective culture media	Number of caecal samples tested positive for ESBL-/AmpC-producing *E. coli*	Prevalence (95% CI)
Broilers	300	244[a]	81.3% (76.5, 85.6)
Fattening turkeys	300	224[b]	74.7% (69.5, 79.5)

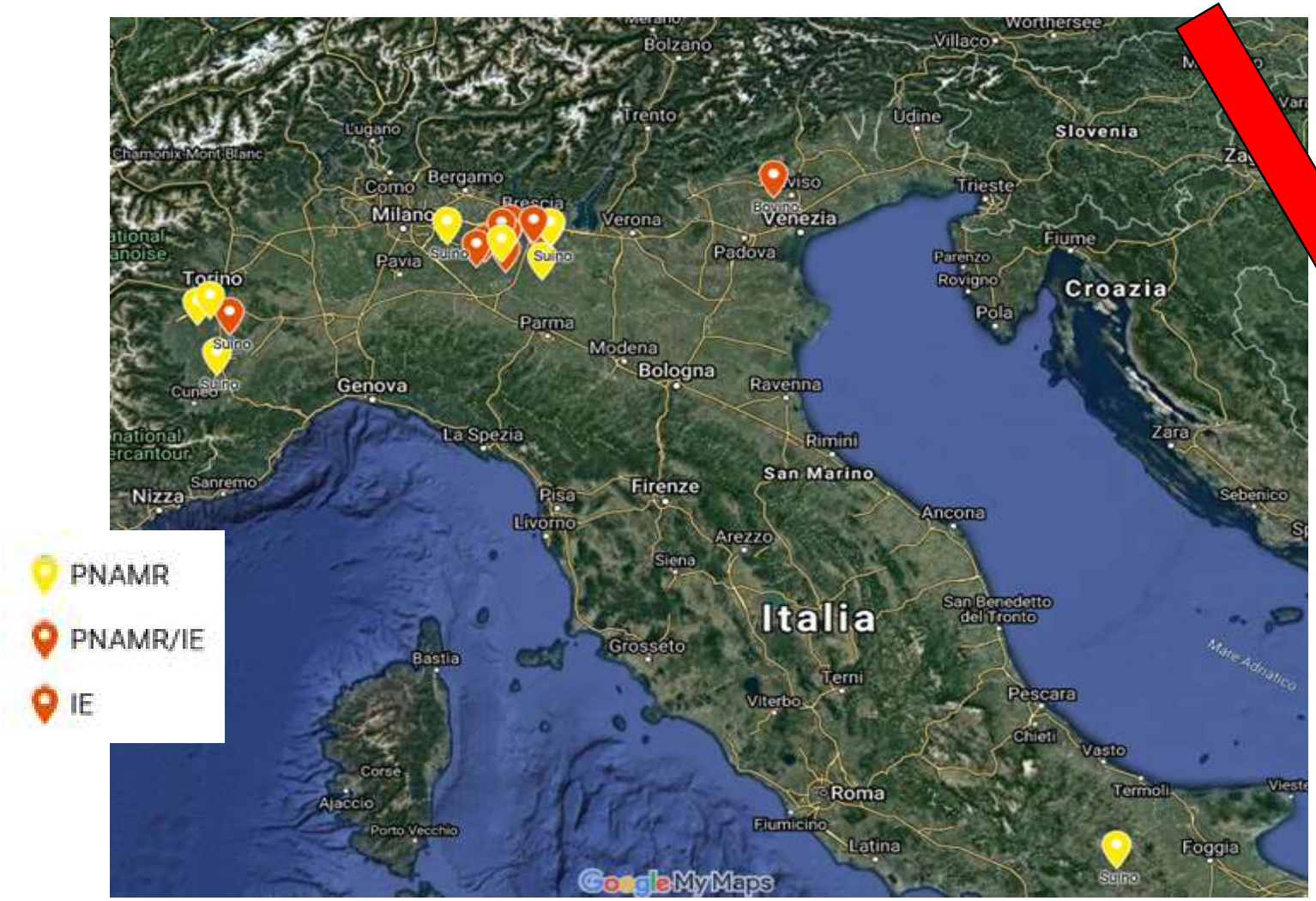
(a): Nearly 86% were ESBL-producing *E. coli*, with 69% harbouring genes of the CTX-M family (mostly encoding the enzyme CTX-M-1). Transferable AmpC genes, encoding CMY-2, were found in 13.1% of isolates. All isolates had MICs indicating clinical resistance to cefotaxime or ceftazidime. Among these ESC-R isolates, 95.1% were multi-drug resistant.

(b): Nearly 96% were ESBL-producing *E. coli*, with 73% harbouring genes of the CTX-M family (mostly encoding the enzyme CTX-M-1). Transferable AmpC genes, encoding CMY-2, were found in 2.7% of isolates. All isolates had MICs above the Ecoffs and all isolates, except two, had MICs also in the range of clinical resistance for cefotaxime or ceftazidime. Among these ESC-R isolates, 90.2% were multi-drug resistant.

It should be noted that, when using selective culture methods, the occurrence of ESBL/AmpC-producing *E. coli* in broilers and fattening turkeys is assessed with much greater sensitivity than when using non-selective culture methods. Considering randomly selected isolates of indicator commensal *E. coli* (n=170) from the same caecal samples, cultured on non-selective media, the occurrence of

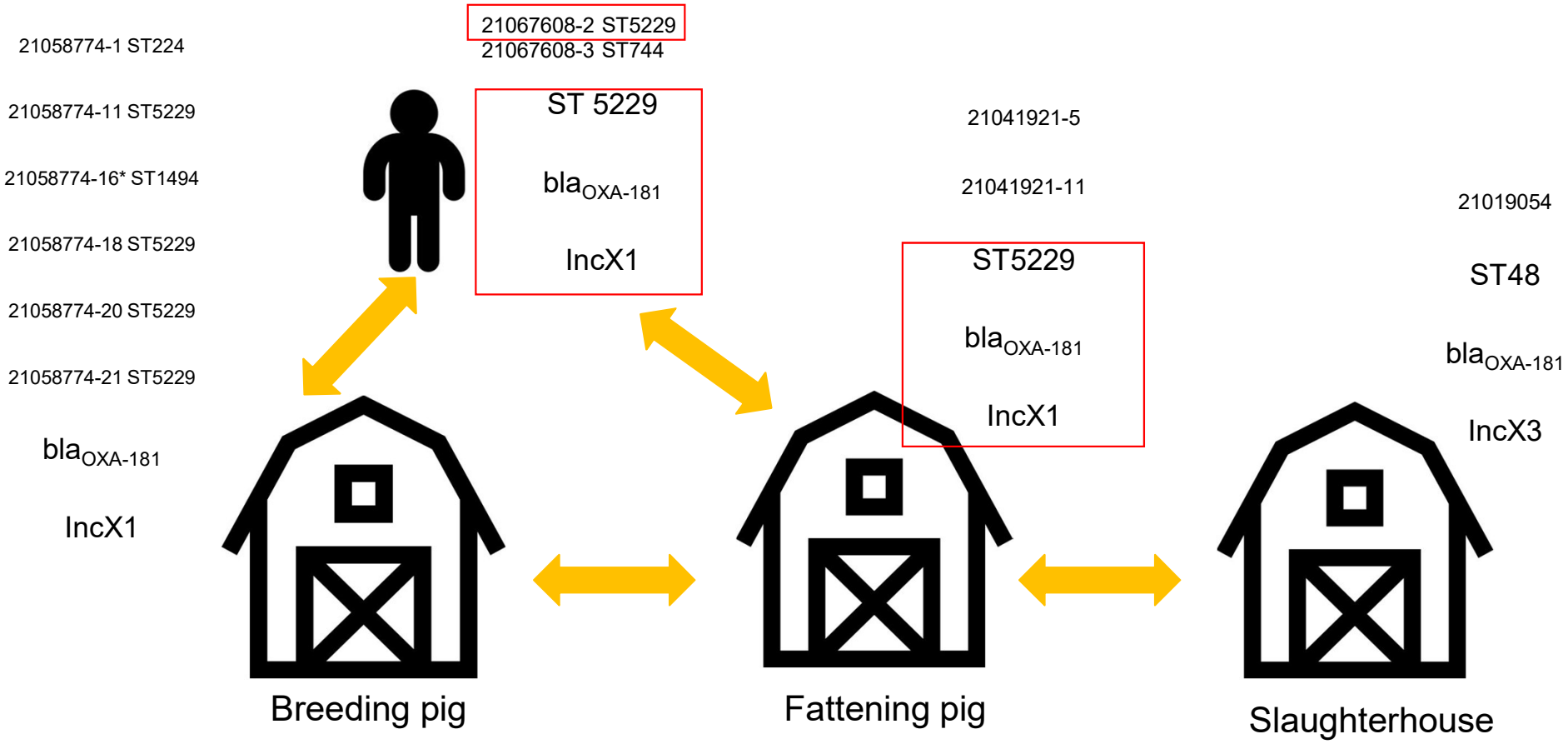
Da «The European Union Summary Report on AMR, 2014»

Update at December 2021 → **25 isolates** Oxa-48-like (24 OXA-181; 1 OXA-48) from EpiUnits sampled at slautherhouse (Dec (EU) 2020/1729) in 11 provinces (5 Regions)
n=21 from pigs (**6.98%**; 95% CI 4.37-10.47%; 21/301) **n=4** from bovines <12 months (**1.29%;** 95% CI 0.35–3.27%, 4/310)



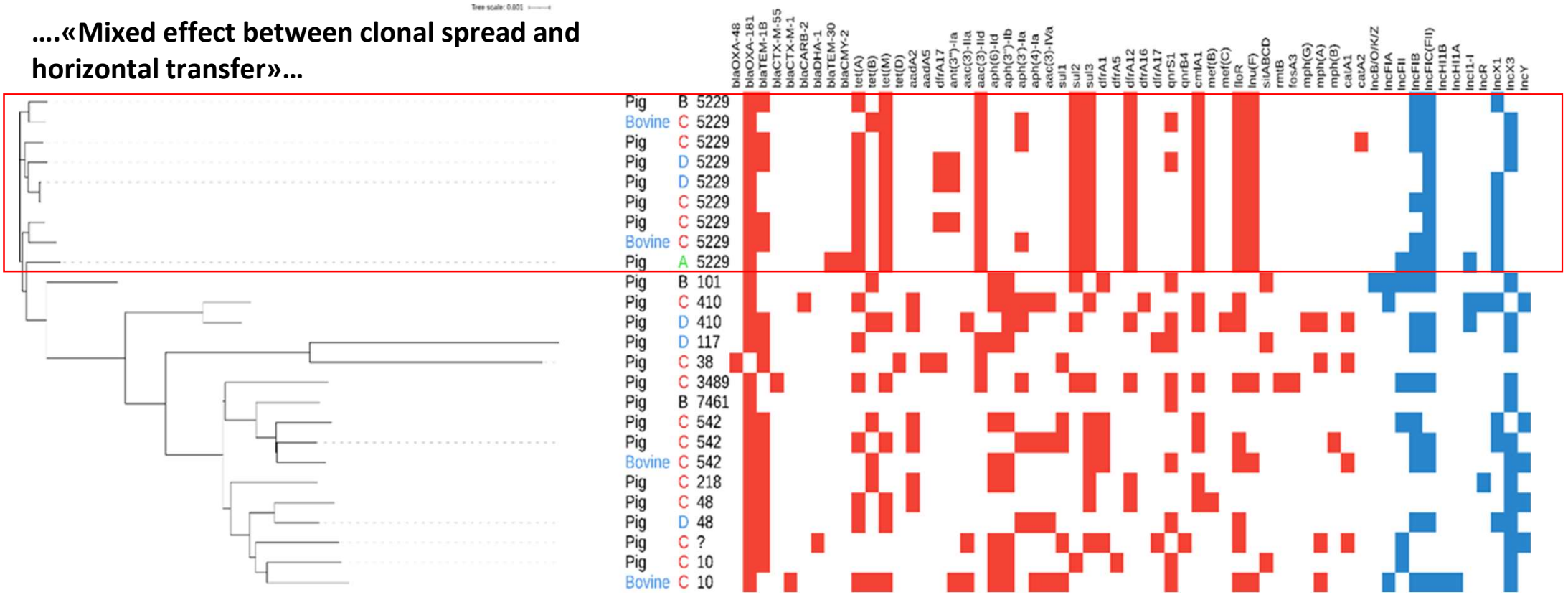
Epidemiological investigation: for >80% the positive (2021) EpiUnits that were **investigated and sampled at the farm of origin**, an OXA-48-like producing E. coli (OXA-181) **has been isolated**

Epidemiological Investigation: Case1 (Index case)



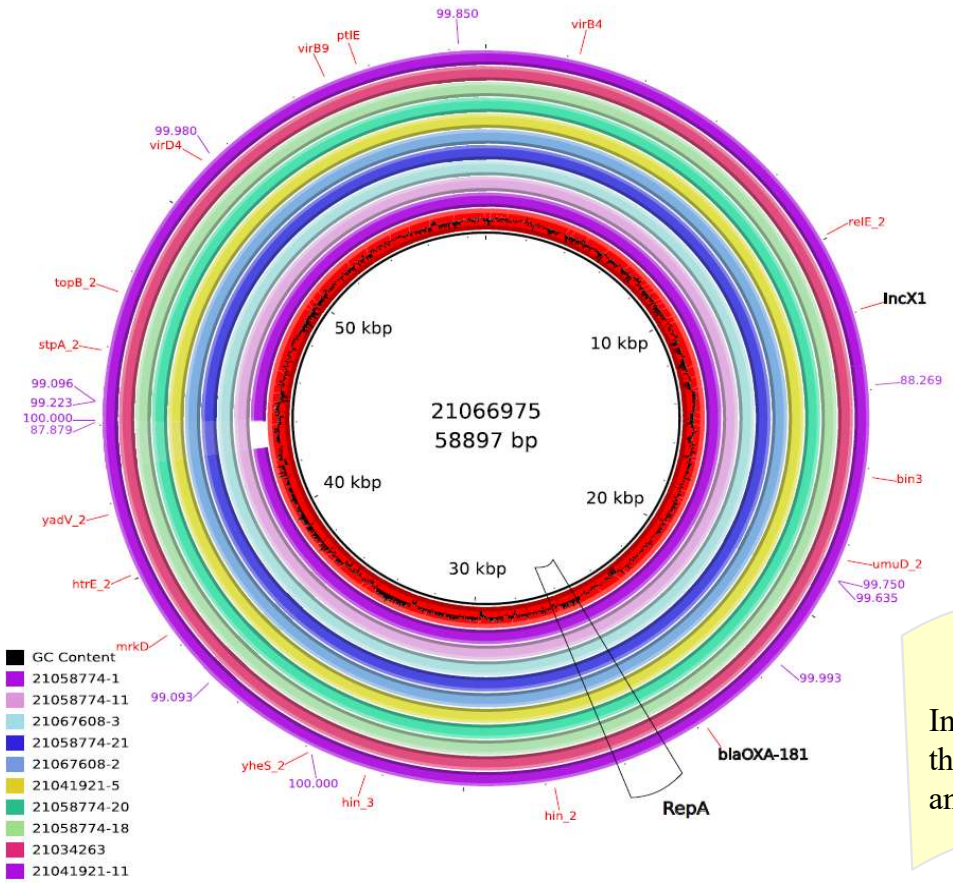
Results of the survey at slaughter (short-read): Mash clusterization of the WGS complete genome, resistome and plasmidome of the n=25 OXA181-producing Escherichia coli

….«Mixed effect between clonal spread and horizontal transfer»…



- A non-clonal population of OXA-48-like producing *E. coli* in the dataset analyzed. **However, …. (ST5229, 9/25, 36% isolates). IncX3, IncX1, (one IncF) the replicons most represented.**
- **IncX3 or IncX1 harboured the OXA-181 gene. No specific pathotype found.**
- The clusters were distributed according to the different Clonal Complexes (CCs) and STs.
- No clear region or host species correlation was observed.

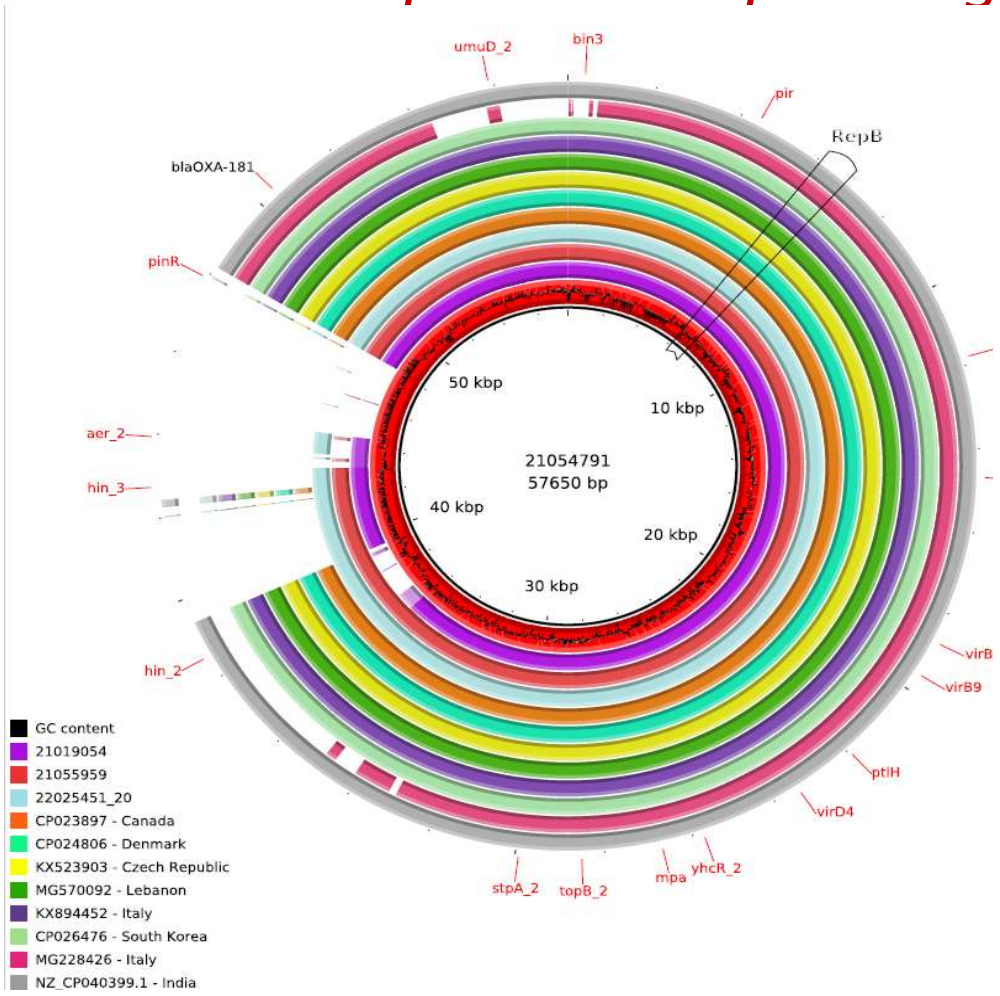
*Full plasmid sequencing: **IncX1** plasmids*



- ✓ All the 12 IncX1 resolved plasmids were almost identical with a 98-99% coverage and 99-100% sequence identity
- ✓ **Novelty: No similar IncX1 plasmids were found in public available databases (around 50% identity with other publicly available plasmids).**

IncX1 more stable than IncX3 because of the presence of the RelE/StbE toxin family and its antitoxin RelB?

Full plasmid sequencing: ***IncX3*** *plasmids*



- ✓ All three resolved plasmids IncX3 harboring $bla_{\text{OXA-181}}$ from *E.coli* were very similar with a 90-91% coverage and 100% identity
- ✓ They shared a similarity of 99% with 89% of the plasmid covered, when compared with publicly available IncX3 plasmids containing $bla_{\text{OXA-181}}$ (from *E. coli, C. freundii, K. pneumoniae*), from human cases
- ✓ 100% coverage and identity of the IncX3 plasmid from *E. coli* ID 21019054 with a $bla_{\text{OXA-181}}$-IncX3 plasmid of a *C. freundii* isolate (ID 22025451-20) from the same pig holding

Resistome

Resfinder
Abricate

Geni Resfinder	Mutation	PATTERN RESISTENZA
mdf(A)_1 tet(A)_6 dfrA12_8 aadA2_1 cmlA1_1 sul3_2 mef(B)_1 tet(M)_8 blaTEM-1B_1 blaOXA-181_1		AMP,CHL,SMX,TET,TMP,ETP,TRM
floR_2 cmlA1_1 tet(A)_6 sul2_2 sul3_2 tet(M)_8 aac(3)-IId_1 dfrA12_8 lnu(F)_1 mdf(A)_1 blaOXA-181_1	gyrA p.D87N parC p.S80I	AMP,CHL,CIP,GEN,NAL,SMX,TET,TMP,FEP,ETP,MER,TRM
blaOXA-181_1 mdf(A)_1 tet(A)_6 floR_2 sul3_2 lnu(F)_1 ant(3'')-Ia_1 sul2_2 aac(3)-IId_1 aph(3')-Ia_1	gyrA p.D87N parC p.S80I	AMP,FOT,TAZ,CHL,CIP,GEN,NAL,SMX,TET,TMP,FEP,TAZ,ETP,MER,TRM
blaOXA-181_1 tet(M)_8 cmlA1_1 aadA2_1 dfrA12_8 mdf(A)_1 blaCTX-M-1_1 mph(A)_2 floR_2 sul2_2 sul3_2	gyrA p.D87N parC p.S80I	AMP,AZI,FOT,TAZ,CHL,CIP,NAL,SMX,TMP,FEP,TAZ,ETP,MER,TRM
qnrS1_1 blaOXA-181_1 sitABCD_1 dfrA5_1 sul2_3 aph(3'')-Ib_5 aph(6)-Id_1 mdf(A)_1 blaTEM-1B_1		AMP,FOT,CIP,SMX,TMP,FEP,FOT,ETP,IMI,MER,TRM
mdf(A)_1 blaOXA-181_1 qnrS1_1 tet(M)_8 cmlA1_1 aadA2_1 dfrA12_8 blaTEM-1B_1 sul3_2 tet(A)_6 floR_2	gyrA p.D87N parC p.S80I	AMP,FOT,CHL,CIP,GEN,NAL,SMX,TET,TMP,FEP,FOX,ETP,IMI,MER,TRM
aph(3')-Ia_1 blaOXA-181_1 dfrA17_1 aadA5_1 sul1_5 armA_1 aph(4)-Ia_1 aac(3)-IVa_1 mph(G)_1 aac(3)-IIa_		AMP,AZI,GEN,SMX,TMP,FOT,ETP,MER,TRM
blaOXA-181_1 tet(A)_6 floR_2 mdf(A)_1 sul2_2 sul3_2 ant(3'')-Ia_1 lnu(F)_1 aac(3)-IId_1 aph(3')-Ia_1	gyrA p.D87N parC p.S80I	AMP,CHL,CIP,GEN,NAL,SMX,TET,ETP,MER,TRM
mdf(A)_1 tet(B)_1 floR_2 aac(3)-IId_1 tet(M)_8 sul3_2 dfrA12_8 lnu(F)_1 aadA2_1 blaOXA-181_1 blaTEM-1B		AMP,CHL,GEN,SMX,TET,TMP,FEP,FOT,ETP,MER,TRM
blaOXA-181_1 sul2_2 floR_2 tet(A)_6 sul3_2 mdf(A)_1 ant(3'')-Ia_1 lnu(F)_1 aac(3)-IId_1 aph(3')-Ia_1	gyrA p.D87N parC p.S80I	AMP,CHL,CIP,GEN,NAL,SMX,TET,ETP,MER,TRM
blaOXA-181_1 mdf(A)_1 blaTEM-1B_1 sul3_2 tet(A)_6 floR_2 sul2_2 lnu(F)_1 ant(3'')-Ia_1 aac(3)-IId_1 aph(	gyrA p.D87N parC p.S80I	AMP,FOT,CHL,CIP,GEN,NAL,SMX,TET,ETP,TRM
mdf(A)_1 blaOXA-181_1 blaTEM-1B_1 sul3_2 tet(A)_6 floR_2 sul2_2 ant(3'')-Ia_1 lnu(F)_1 aac(3)-IId_1 aph(	gyrA p.D87N parC p.S80I	AMP,CHL,CIP,GEN,NAL,SMX,TET,ETP,TRM
blaOXA-181_1 mdf(A)_1 cmlA1_1 tet(M)_8 sul3_2 blaTEM-1B_1 tet(A)_6 floR_2 sul2_2 aac(3)-IId_1 dfrA12_	gyrA p.D87N parC p.S80I	AMP,FOT,CHL,CIP,GEN,NAL,SMX,TET,TMP,FEP,ETP,MER,TRM
blaOXA-181_1 sul3_2 blaTEM-1B_1 mdf(A)_1 floR_2 sul2_2 ant(3'')-Ia_1 lnu(F)_1 aac(3)-IId_1 aph(3')-Ia_1	gyrA p.D87N parC p.A56T par	AMP,AZI,CHL,CIP,GEN,NAL,SMX,TET,TMP,FEP,ETP,MER,TRM
blaTEM-1B_1 mdf(A)_1 blaOXA-181_1 sul1_5 aadA5_1 dfrA17_1 catA1_1 floR_2 aac(3)-IId_1 aph(6)-Id_1 aph	gyrA p.D87N parC p.S80I	AMP,FOT,CHL,CIP,GEN,NAL,SMX,ETP,MER,TRM
blaOXA-181_1 mdf(A)_1 tet(A)_6 sul3_2 blaTEM-1B_1 floR_2 sul2_2 lnu(F)_1 ant(3'')-Ia_1 aac(3)-IId_1 aph(	gyrA p.D87N parC p.S80I	AMP,FOT,CHL,CIP,GEN,NAL,SMX,TET,ETP,MER,TRM
mdf(A)_1 blaOXA-181_1 qnrS1_1 tet(A)_6 tet(M)_8 floR_2 sul2_2 cmlA1_1 aac(3)-IId_1 dfrA12_8 lnu(F)_1	gyrA p.D87N parC p.S80I	AMP,CHL,CIP,GEN,NAL,SMX,TET,TMP,ETP,TRM
mdf(A)_1 blaOXA-181_1 tet(A)_6 aph(4)-Ia_1 aac(3)-IVa_1 blaTEM-1B_1 aph(3')-Ia_1		AMP,CHL,CIP,GEN,TET,ETP,TRM
blaTEM-1B_1 aac(3)-IIa_1 lnu(G)_1 mdf(A)_1 sul3_2 cmlA1_1 aadA2_1 dfrA12_8 blaOXA-181_1 tet(B)_2 floR_2		AMP,CHL,GEN,SMX,TET,TMP,ETP,MER,TRM
floR_2 aac(3)-IIa_1 blaTEM-1B_1 lnu(G)_1 mdf(A)_1 dfrA12_8 aadA2_1 cmlA1_1 sul3_2 blaOXA-181_1 tet(B)_2		AMP,CHL,GEN,SMX,TET,TMP,ETP,TRM
mdf(A)_1 blaTEM-1B_1 blaOXA-181_1 lnu(G)_1 tet(A)_6 dfrA1_10 sul3_2 floR_2 catA1_1		AMP,CHL,SMX,TET,TMP,ETP,MER,TRM
blaOXA-181_1 floR_2 dfrA12_8 aadA2_1 cmlA1_1 sul3_2 qnrS1_1 tet(A)_6 blaTEM-1B_1 mdf(A)_1		AMP,CHL,GEN,SMX,TET,TMP,ETP,MER,TRM
mdf(A)_1 blaOXA-181_1 aac(3)-IVa_1 aph(4)-Ia_1 floR_2 tet(A)_6 blaTEM-1B_1 aph(3')-Ia_1 qnrS1_1		AMP,CHL,CIP,GEN,NAL,SMX,TET,TMP,ETP,TRM
rmtB_1 mdf(A)_1 blaOXA-181_1 cmlA1_1 tet(M)_8 tet(A)_6 fosA3_1 floR_2 qnrS1_1 sul3_2 sul2_2 aac(3)-IIc	parC p.S80I	AMP,FOT,TAZ,CHL,CIP,GEN,NAL,SMX,TET,TMP,FEP,TAZ,ETP,MER,TRM
blaOXA-181_1 blaTEM-1A_1 tet(A)_6 aph(6)-Id_1 aph(3'')-Ib_5 dfrA1_8 aac(3)-IId_1 cmlA1_1 aadA2_1 mdf(		AMP,CHL,CIP,GEN,NAL,SMX,TET,TMP,ETP,TRM
dfrA12_8 aadA2_1 cmlA1_1 blaTEM-1B_1 qnrS1_1 tet(A)_6 blaOXA-181_1 mdf(A)_1 sul3_2		AMP,CHL,CIP,SMX,TET,TMP,ETP,MER,TRM
blaTEM-30_1 mdf(A)_1 blaOXA-181_1 qnrS1_1 tet(A)_6 cmlA1_1 aadA2_1 dfrA12_8		AMP,CHL,CIP,SMX,TET,TMP,ETP,MER,TRM
mdf(A)_1 blaOXA-181_1 floR_2 sul2_2 cmlA1_1 tet(M)_8 tet(A)_6 sul3_2 aac(3)-IId_1 dfrA12_8 lnu(F)_1	gyrA p.D87N parC p.S80I	AMP,FOT,CHL,CIP,GEN,NAL,SMX,TET,TMP,FEP,ETP,MER,TRM
blaOXA-181_1 mdf(A)_1 tet(A)_6 floR_2 sul2_2 sul3_2 ant(3'')-Ia_1 lnu(F)_1 aac(3)-IId_1 aph(3')-Ia_1	gyrA p.D87N parC p.S80I	AMP,FOT,CHL,CIP,GEN,NAL,SMX,TET,ETP,TRM
blaOXA-181_1 sul2_2 floR_2 mdf(A)_1 tet(A)_6 sul3_2 blaTEM-1B_1 lnu(F)_1 ant(3'')-Ia_1 aac(3)-IId_1 aph(	gyrA p.D87N parC p.S80I	AMP,FOT,CHL,CIP,GEN,NAL,SMX,TET,ETP,MER,TRM

ORIGINAL RESEARCH article

Front. Microbiol., 17 November 2022
Sec. Infectious Agents and Disease
Volume 13 - 2022 | https://doi.org/10.3389/fmicb.2022.1016895

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The hazard of carbapenemase (OXA-181)-producing *Escherichia coli* spreading in pig and veal calf holdings in Italy in the genomics era: Risk of spill over and spill back between humans and animals

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Carbapenemase-producing Enterobacterales (CPE) are considered a major public health issue. In the frame of the EU Harmonized AMR Monitoring program conducted in Italy in 2021, 21 epidemiological units of fattening pigs (6.98%; 95% CI 4.37–10.47%; 21/301) and four epidemiological units of bovines <12 months (1.29%; 95% CI 0.35–3.27%, 4/310) resulted positive to OXA-48-like-producing *E. coli* ($n = 24$ OXA-181, $n = 1$ OXA-48). Whole Genome Sequencing (WGS) for in-depth characterization, genomics and cluster analysis of OXA-181-(and one OXA-48) producing *E. coli* isolated, was performed. Tracing-back activities at: (a) the fattening holding of origin of one positive slaughter batch, (b) the breeding holding, and (c) one epidemiologically related dairy cattle holding, allowed detection of OXA-48-like-producing *E. coli* in different units and comparison of further human isolates from fecal samples of farm workers. The OXA-181-producing isolates were multidrug resistant (MDR), belonged to different Sequence Types (STs), harbored the IncX and IncF plasmid replicons and multiple virulence genes. Bioinformatics analysis of combined Oxford Nanopore Technologies (ONT) long reads and Illumina short reads identified $bla_{OXA-181}$ as part of a transposon in IncX1, IncX3, and IncFII fully resolved plasmids from 16 selected *E. coli,* mostly belonging to ST5229, isolated during the survey at slaughter and tracing-back activities. Although human source could be the most likely cause for the introduction of the $bla_{OXA-181}$-carrying IncX1 plasmid in the breeding holding, concerns arise from carbapenemase OXA-48-like-producing *E. coli* spreading in 2021 in Italian fattening pigs and, to a lesser extent, in veal calf holdings.

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Isolation rates (prevalence) from caecal samples according to the National Monitoring Programme on AMR, Dec (EU) 2020/1729, Italy 2021-2023

- 2021

Species	Samples cultured	Samples positive	%	95% CI
Pigs	301	21	6,98%	4,37-10,47%
Bovines <12m	310	4	1,29%	0,35–3,27%

- 2022

Species	Samples cultured	Samples positive	%	95% CI
Broiler chicken	479	1	0,21%	0,01-1,16%
Turkey	397	1	0,25%	0,01-1,40%

- 2023

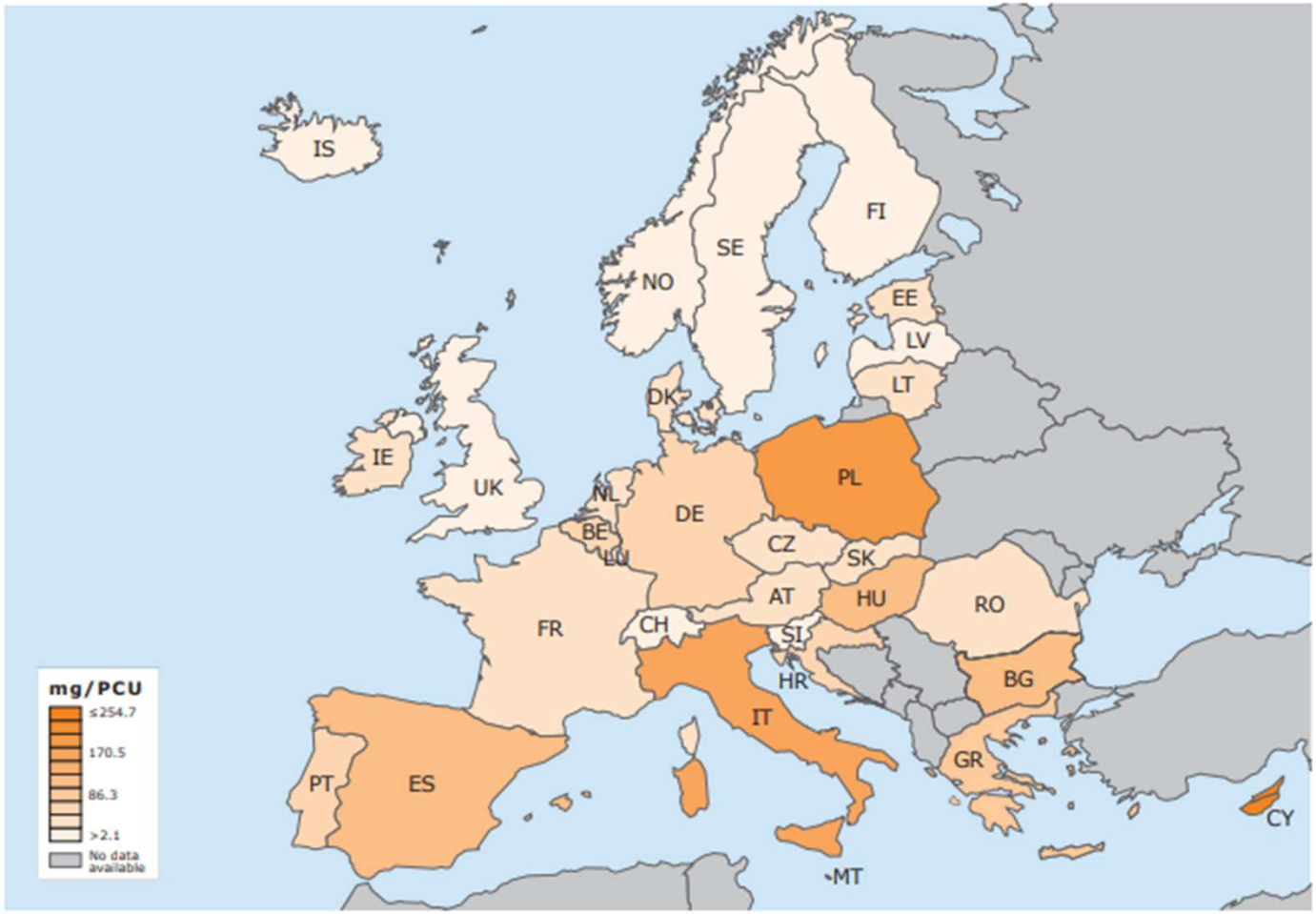
Species	Samples culture	Samples positive	%	95% CI
Pigs	184	17	9,24%	5,47-14,38%
Bovines <12m	201	4	1,99%	0,54-5,02%

Update: 15 October 2023

Mean EU 31 Countries:
73.9 mg/PCU

Italy
157.5 mg/PCU

Figure 2. Spatial distribution of overall sales, in mg/PCU, of antibiotic VMPs for food-producing animals in 31 European countries in 2022[1]



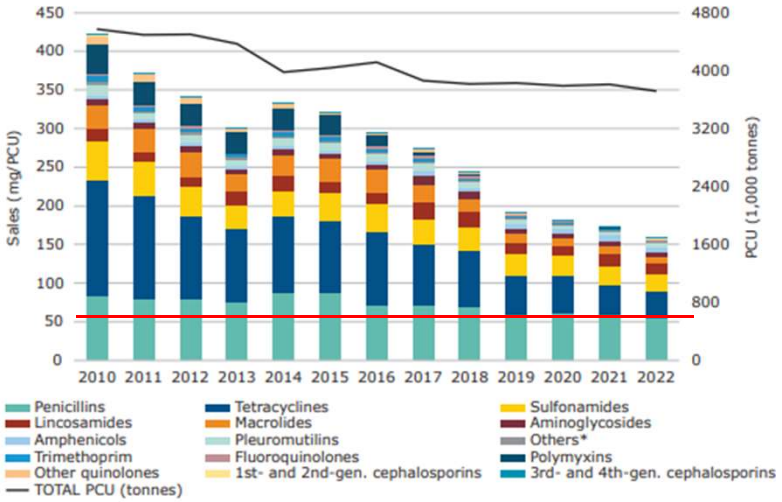
[1] ESVAC-participating countries' codes according to ISO 3166 — Codes for the representation of names of countries and their subdivisions.

«Penicillins»,
Che significa in realtà
«Oral amoxicillin» e «Oral clav+ amoxicillin»

ITALY

Sales trends (mg/PCU) of antibiotic VMPs for food-producing animals

Sales trends by antibiotic class (mg/PCU) from 2010 to 2022[1]

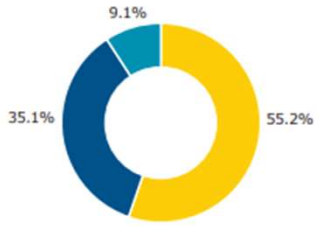


[1] Sales data sorted from highest to lowest in 2022.
* The class 'Others' includes sales of the following sub-classes: imidazole derivatives (metronidazole), nitrofuran derivatives (furazolidone) and other antibacterials (bacitracin, furaltadone, rifaximin, spectinomycin). Of note is that some of the sales could be for non-food-producing animals.

Since 2011:

- 57.5% overall annual sales (from 371.0 mg/PCU to 157.5 mg/PCU in 2022)
- 76.2% 3rd- and 4th-generation cephalosporin sales (from 0.36 mg/PCU to 0.09 mg/PCU in 2022)
- 59.0% fluoroquinolone sales (from 2.2 mg/PCU to 0.90 mg/PCU in 2022)
- 95.9% other quinolone sales (from 9.1 mg/PCU to 0.38 mg/PCU in 2022)
- 98.1% polymyxin sales (from 30.7 mg/PCU to 0.58 mg/PCU in 2022)
- PCU decreased by 17.4% between 2011 and 2022

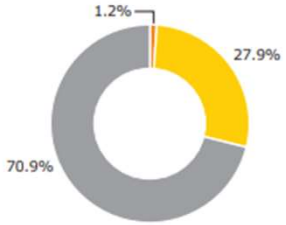
Proportion of sales (mg/PCU) by product form in 2022[1]



Sales of oral powders, oral solutions and premixes accounted for 90.5% of total sales in 2022.

[1] The sales of oral powders and other forms (intramammary, intrauterine, bolus and oral paste products) are not represented in this figure and represent 0.2% and 0.4% of total sales, respectively.

Proportion of sales (mg/PCU) by AMEG categories in 2022

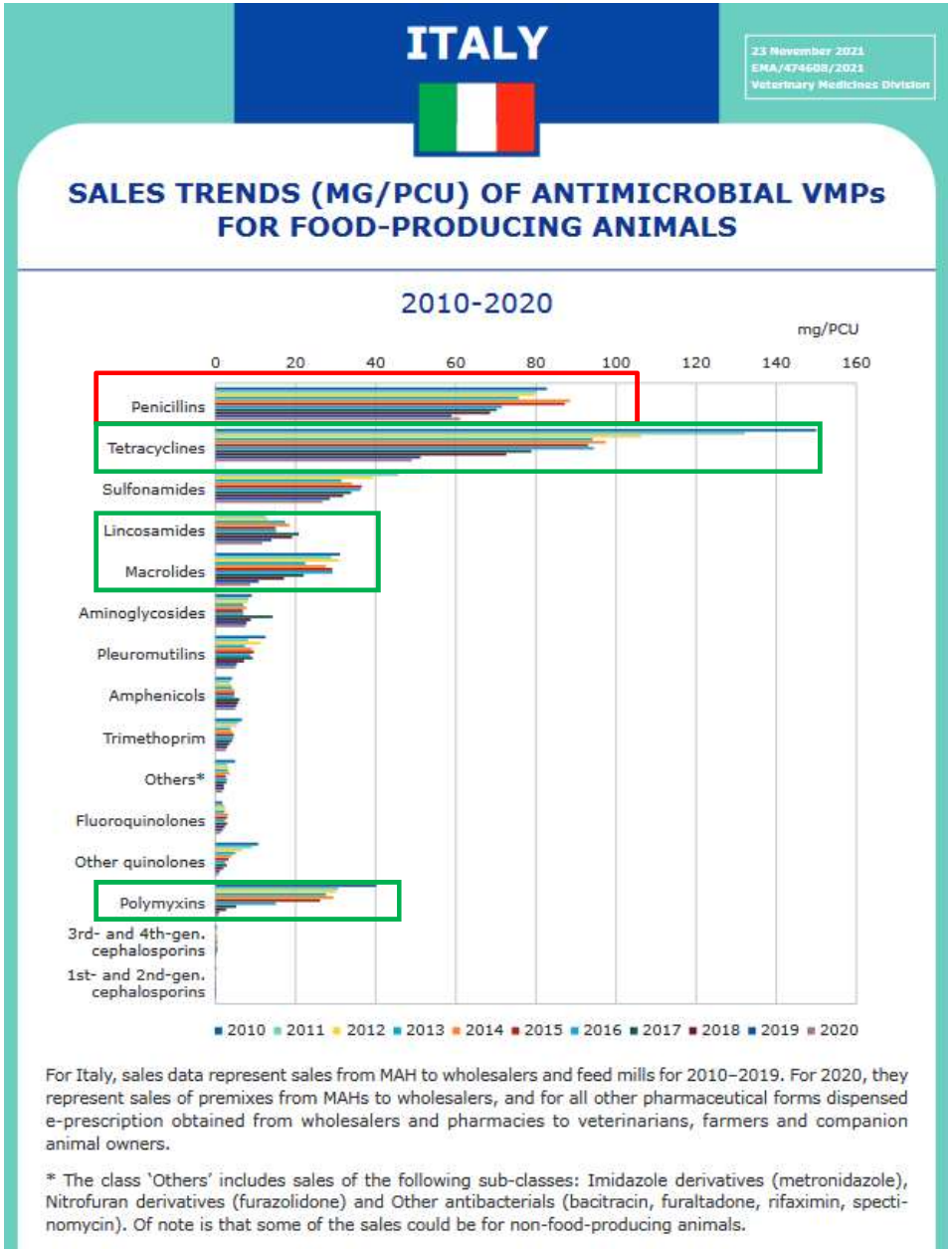


The majority of antibiotic VMP sales in 2022 belonged to the AMEG category D (Prudence), accounting for 70.9% of total sales.

2022 sales data

In 2022, overall sales decreased by 9.2% in comparison to 2021 (from 173.6 mg/PCU to 157.5 mg/PCU). The three highest selling antibiotic classes were penicillins, tetracyclines and sulfonamides, which accounted for 34.6%, 22.6% and 13.8% of total sales, respectively.

ESVAC Report Italy:
from 427 mg/PCU in 2010
to 181 mg/PCU in 2020
to 174 mg/PCU in 2021
to 158 mg/PCU in 2022



«Penicillins» in EU e IT, negli animali produttori di alimenti, significa «amoxicillina per uso orale» e «clav+amoxicillina per uso orale» (suini).

Somministrazione di gruppo

In Italia, in 2020 e 2021 le vendite di «penicillins» rappresentano circa 1/3 di tutte le vendite in mg/PCU per gli animali produttori di alimenti

AMINOPENICILLINE (Amoxicillina per uso orale) e uso negli Animali : ALCUNI FATTI…

- LE AMINOPENICILLINE ESERCITANO PRESSIONE DI SELEZIONE PER IL MANTENIMENTO E LA DIFFUSIONE DELLA RESISTENZA ALLE CEFALOSPORINE DI 3 ° -4 ° GENERAZIONE
- LE AMINOPENICILLINE NON SONO BETA-LATTAMICI DI PRIMA LINEA per LA GRAN PARTE DEI PRINCIPALI PATOGENI VETERINARI GRAM-POSITIVI E GRAM-NEGATIVI
- I BETA-LATTAMICI DI PRIMA LINEA per patogeni veterinari Gram +ve e Gram –ve (Actinobacillus pleuropneumoniae, Pasteurella multocida, Mannheimia hemolytica ecc.) SONO PENICILLINE A SPETTRO RISTRETTO (ovvero penicillina G (iniezione), penicillina V (orale), penetamato (intramammaria) ...)
- Le aminopenicilline sono da considerarsi BETA-LATTAMICI DI PRIMA LINEA SOLO PER: Salmonella spp. (quando la somministrazione di antibiotici è clinicamente appropriata o autorizzata dalla legislazione dell'UE), Yersinia pseudotuberculosis, Proteus mirabilis ...
- Era vero anche per E. coli, ma la prevalenza di R acquisita è alta, quindi è raccomandato effettuare sempre prima un test di sensibilità.
- **Altre Enterobacteriaceae di rilevanza clinica sono TUTTE intrinsecamente resistenti ...**

Obiettivi di riduzione antibiotici nel settore veterinario PNCAR 2022-2025

- Riduzione ≥30% del consumo totale di antibiotici totali (mg/PCU) nel 2025 rispetto al 2020 **(cioè da circa 182 mg/PCU ad almeno 128 mg/PCU, almeno -6,5% in media anno)**
- Riduzione ≥ 20% del consumo di antibiotici autorizzati in formulazioni farmaceutiche per via orale (premiscele, polveri e soluzioni orali) nel 2025 rispetto al 2020.
- Mantenimento a livelli sotto la soglia dell'1 mg/PCU dei consumi (mg/PCU) delle polimixine.
- Mantenimento a livelli sotto la soglia europea dei consumi (mg/PCU) delle classi di antibiotici considerati critici per l'uomo.
- Riduzione ≥ 10% del numero totale delle prescrizioni veterinarie di antimicrobici HPCIAs per animali da compagnia/deroga

Improving Knowledge; Risk Management (& Control) Options provided to the Central Competent Authority (IT MoH, DGSAF) at the end of 2021

To: The Directorate General for Animal Health and Veterinary Medicinal Products

-Descriptive epidemiology,
-main genomics, and provisional clustering results
-perspectives of possible RMOs
Discussed during the NRL-AR Italy annual Workshop (Nov 2021)
RMOs further discussed in a One Health perspective with the CAs in the Regions involved

Istituto Zooprofilattico Sperimentale del Lazio e della Toscana *M. Aleandri*

Direzione Operativa Diagnostica Generale

Centro di Referenza Nazionale per l'Antibioticoresistenza (D. M. 4 ottobre 1999)

National Reference Laboratory for Antimicrobial Resistance (Reg.(EC) 2004/882 - Reg.(EU) 2017/625)

Roma, 29/09/2021

A: Ministero Salute
-DG Sanità Animale e Farmaci Veterinari
Via G. Ribotta 5, 00144;
ROMA

Prot.
All.

Oggetto: E. coli produttori di carbapenemasi e Piano Nazionale AMR: Proposta di protocollo generale per attività di approfondimento negli allevamenti di origine delle Unità Epidemiologiche positive al macello, e di opzioni di risk managament.

Si rimette uno schema generale, relativo alle modalità ed azioni in materia di approfondimento epidemiologico della rilevazione delle positività eventualmente riscontrate nelle unità epidemiologiche prelevate al macello ai sensi della Dec. (EU) 2020/1729.

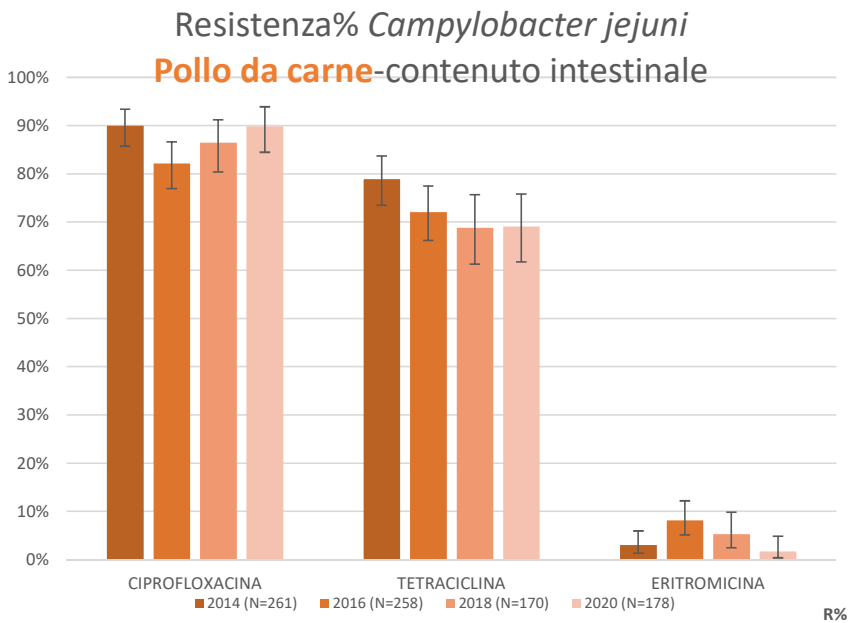
Conclusions

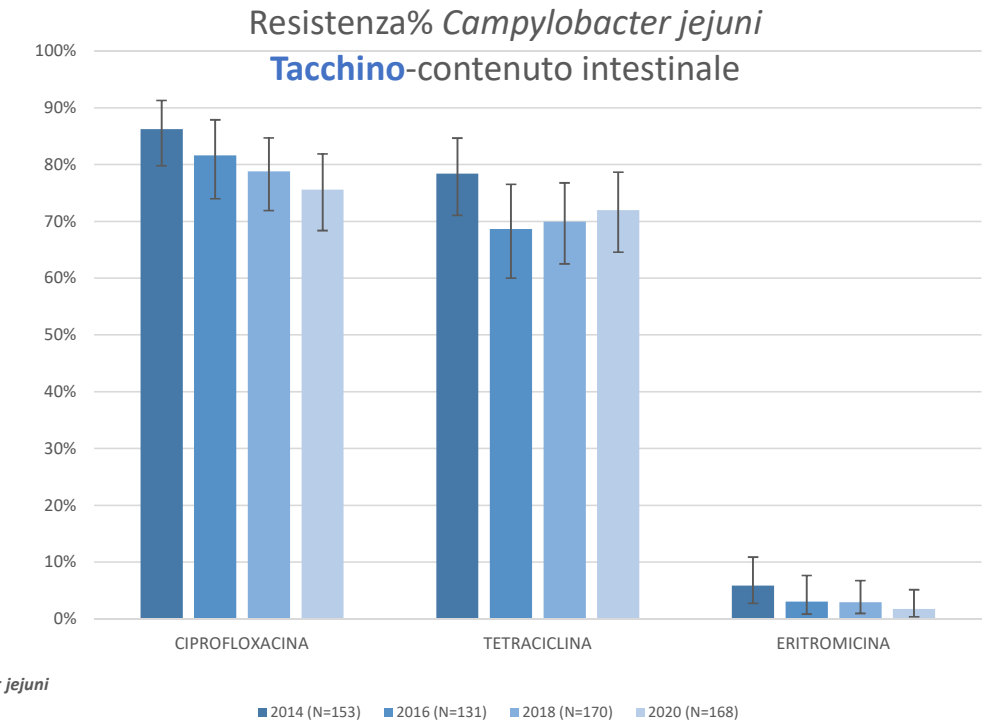
- Whatever the initial source (most likely: humans), we have provided evidence that these CPE have been amplified within the intensive animal production systems, especially in pigs in Italy;
- **And they still persist especially in pig holdings, after two years**;

-There is evidence for keeping mandatory the specific methods for all the CPE and OXA-48-like across all MSs:
-to allow comparability across MSs is an important aim of the AMR monitoring legislation

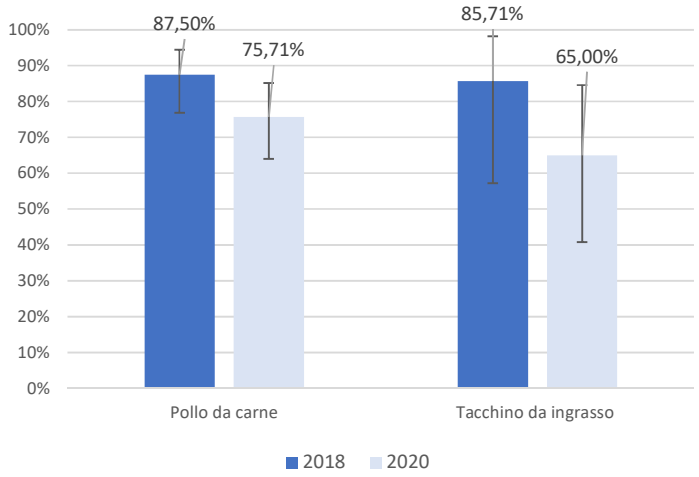
Esempi di resistenza ad HPCIAs in Italia (ed in EU) con evoluzione diversa nel tempo

- L'evoluzione della situazione epidemiologica in caso di emergenza e diffusone di resistenze e co-resistenze ad HPCIAs ha sempre margini di incertezza ed imprevedibilità: considerazioni a posteriori (sui trend)
- third-fourth gen cephalosporin resistance: ESBL/AmpC (si è già detto)
- fluoroquinolone resistance
- colistin resistance
- (per tacere di macrolide resistance)



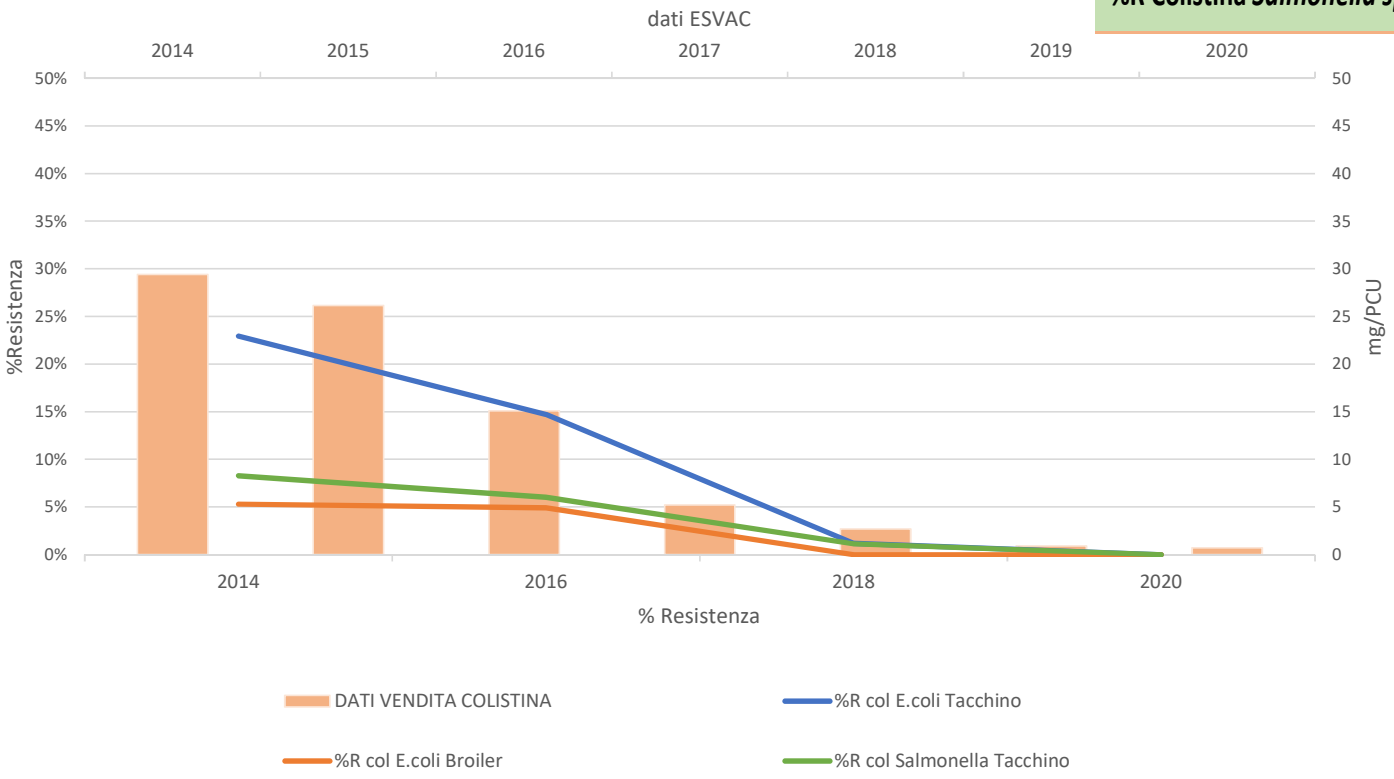


R% Ciprofloxacina- *Campylobacter jejuni* carne al dettaglio



Dati di vendita ESVAC e % resistenza alla colistina

	2014	2016	2018	2020
%R Colistina *E. coli* Tacchino	22,94%	14,71%	1,2%	0%
%R Colistina *E. coli* Pollo da carne	5,3%	4,9%	0%	0%
%R Colistina *Salmonella spp.* Tacchino	8,28%	6,02%	1,15%	0%



Argomento di riflessione generale in SPV

- «Lasciar correre» la diffusione di agenti biologici, di genomi accessori o di determinanti virulenza e AMR, può non avere gli esiti attesi in termini di riduzione, e di tempestività ed efficacia di effetto di interventi, allorché si decide di intervenire soltanto a distanza di tempo…

**Thanks to all personnel at IZSLT,
and to all the people at the
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Tamara Cerci	Fiorentino Stravino
Gessica Cordaro	Tiziana Brancaccio
Elena dell'Aira	Ilaria Congiu
	Daniele Smedile

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per l'Antibioticoresistenza

https://www.izslt.it/crab/