14-15 September 2022

Assessment of animal diseases caused by bacteria resistant to antimicrobials

Ad-hoc method of assessment and groups of animal species covered.

Standing Committee on Plants, Animals, Food and Feed

Section Animal Health and Welfare

Trusted science for safe food

efsa
European Food Safety Authority

Terms of reference

1.Global state of play as regards resistant bacterial animal pathogens that cause transmissible animal diseases

ToR1

1.Summarize the situation in the EU and identify the most relevant bacteria in the EU

ToR2

1.Listing and categorisation of the bacteria that are relevant in the EU in the framework of the Animal Health Law

ToR3

ToR 1

EFSA should perform a **literature review** as follows:

1. **Review AMR-related aspects of any bacteria** responsible for transmissible animal diseases for which **AMR concerns** are described both at EU level and globally
2. Target animal species should include **terrestrial and aquatic** food-producing farmed animals, but also include **companion animals**, as there is a lack of data on AMR in those species
3. Bacteria covered by **Directive 2003/99/EC** should be **excluded**
4. Describe the **occurrence** and **prevalence** of AMR in such bacteria, the most relevant **antibiotics** against which resistance has developed and may also include other aspects (**molecular mechanisms**)
5. **Uncertainties and data gaps** also identified and described

ToR 2

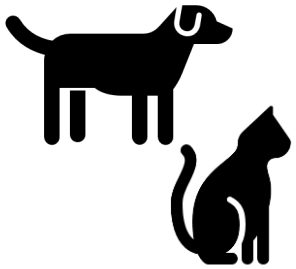
1. **Summarize the situation in the EU** in terms of the actual or potential **impact on animal health** of the **most relevant bacteria in the EU**, indicating those for which sufficient data exists and those for which data is not sufficient
2. EU **relevance** is to be understood on the basis of **practical considerations**, such as actual presence in the EU or presence elsewhere but in animal species, age groups or production systems which are widely used in the EU, or similar elements

EFSA published 8 Scientific Opinion:
https://storymaps.arcgis.com/collections/8bd9466e00f040ac91769480c70e891e?item=2

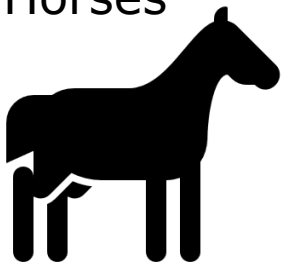
Scope of the Extensive literature review (ELR)

- **Animal (host) species** of interest

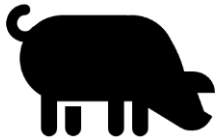
Cats and dogs



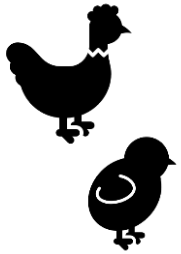
Horses



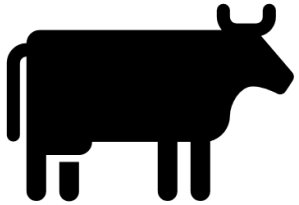
Swine



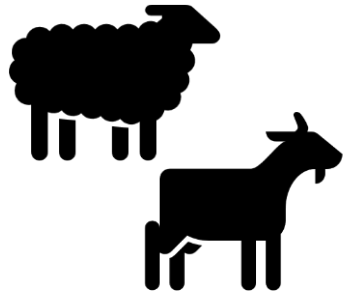
Poultry



Cattle



Goat and sheep



Rabbits

Aquatic animals

Chicken, turkey, duck, goose, game birds and ratites

Atlantic salmon, carp, rainbow trout, sea bream, tilapia

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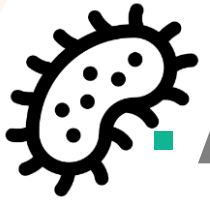
Scope of the Extensive literature review (ELR)



- **AMR Bacterial species** causing relevant diseases → excluded if:
  1. rarely cause disease or production losses considering the global situation*
  2. Its presence never or rarely leads to antimicrobial treatment*
  3. never or rarely cause antimicrobial treatment failure due to the existence of acquired antimicrobial resistance*

*as determined by EO

- Additionally, excluded if:
  - Already included in Directive 2003/99/EC
  - Intracellular pathogens (lack of data)
- Initial inclusion of 12-16 pathogens per (main) host
  - Rabbits: 5
  - Aquatic species: 4

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Scope of the literature review (ELR)

- **Antimicrobials considered**: B,C,D AMEG groups (guidelines, EO)

- Collection of data via procurement (Univ. Copenhagen)
- Data sources:
  - Scientific literature (EN): PubMed and Embase (>2010)
  - National AMR monitoring programs (EN, DE)
- Exclusion criteria (17): Main
  - Non-clinical (non-representative: MDR) isolates
  - N<50 (*E. coli*, *S. aureus*), N<10 (others)
  - Raw non-interpreted MIC data

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Assessment of (EU) relevance

- "Presence in the EU or elsewhere in animal species/age groups/ production systems widely used in the EU"
- **Clinical relevance**: importance of the disease caused by the pathogen/ amount of evidence available (publications/isolates) /geographic distribution
- **Availability of (other) therapeutic options** (number of alternatives in case of AMR) and classification (considering their AMEG category)

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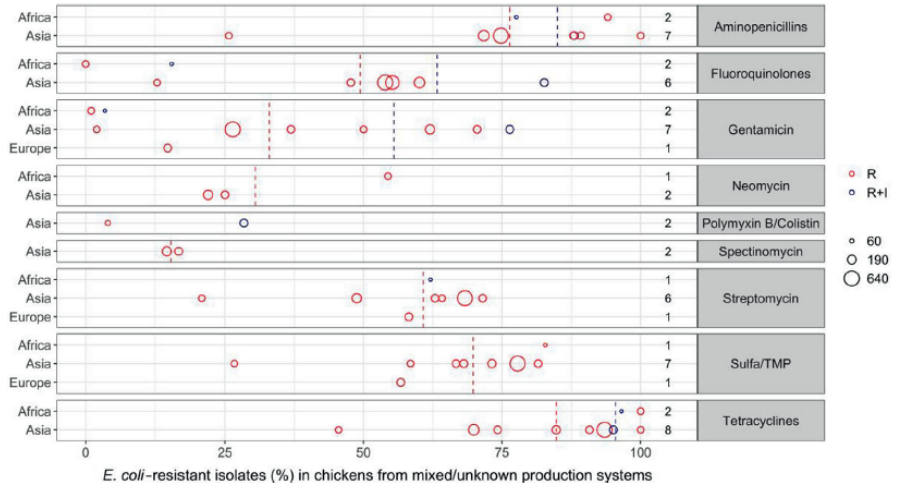
Content of scientific opinions

- Results of ELR:
  - Number of publications/AMR results
  - Coverage of National AMR monitoring programs
  - %R per bacteria/study
  - Data gaps/limitations
- Identification of most relevant AMR pathogens

Table 3: Data from last published versions of the national AMR monitoring programmes included in the literature review

Programme	FINRES-Vet	GERM-Vet	RESAPATH	SWEDRES-Svarm	UK-VARSS
Country	Finland	Germany	France	Sweden	United Kingdom
Laboratory method	Broth microdilution	Broth microdilution	Disk diffusion	Broth microdilution	Disk diffusion
AST interpretation	ECOFFs/CBPs	ECOFFs/CBPs	ECOFFs	ECOFFs	CBPs
E. coli	Yes	Yes	Yes	Yes	No
Origin (number of isolates)	Broiler (colibacillosis) 17–27/year	Broilers, young hens and laying hens, turkey (255–473)	Broiler, laying hen, duck, turkey 108–4,262/year	Laying hen 100 (overall)	
Years covered	2016–2019	2014–2018	2014–2018	2017–2018	
S. aureus	Yes	Yes	Yes	No	Yes
Origin (number of isolates)	Broiler (tenosynovitis) 8–26/year	Broilers, young and laying hens, turkeys	Laying hen and broiler 144–457/year		Chicken 26–33 (overall)
Years covered	2016–2019	2014–2018	2014–2018		2015–2019
E. cecorum	No	No	Yes	No	No
Origin (number of isolates)			Laying hen and broiler 124–445/year		
Years covered			2014–2018		



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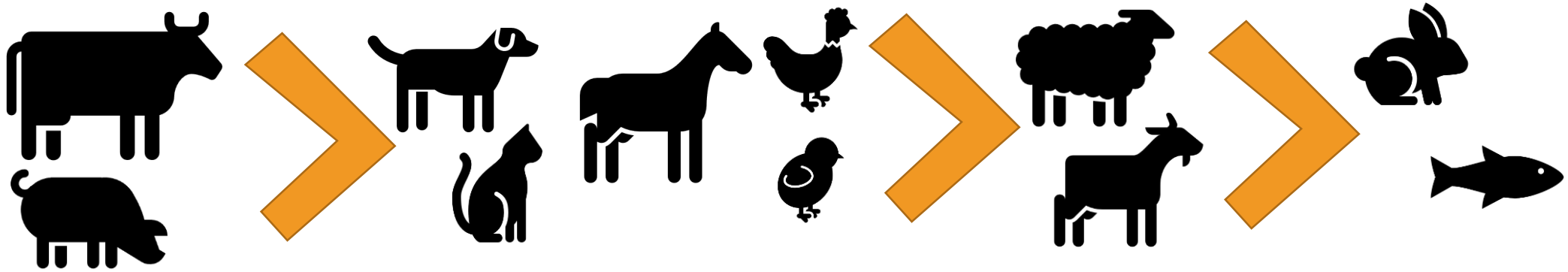
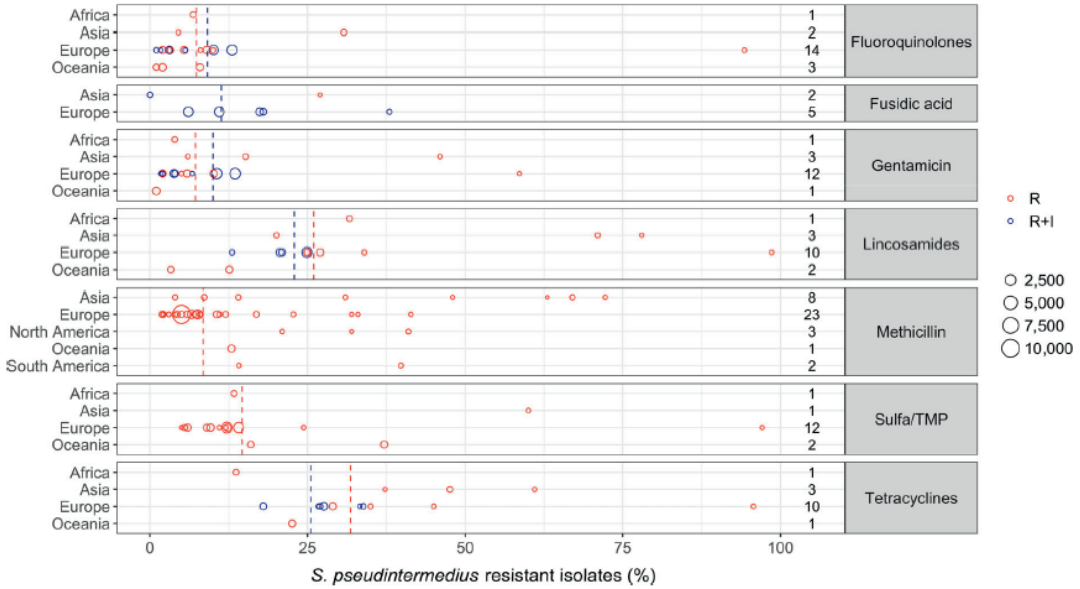
Assessment: Evidence available



- Not always related with clinical relevance (methodological challenges)



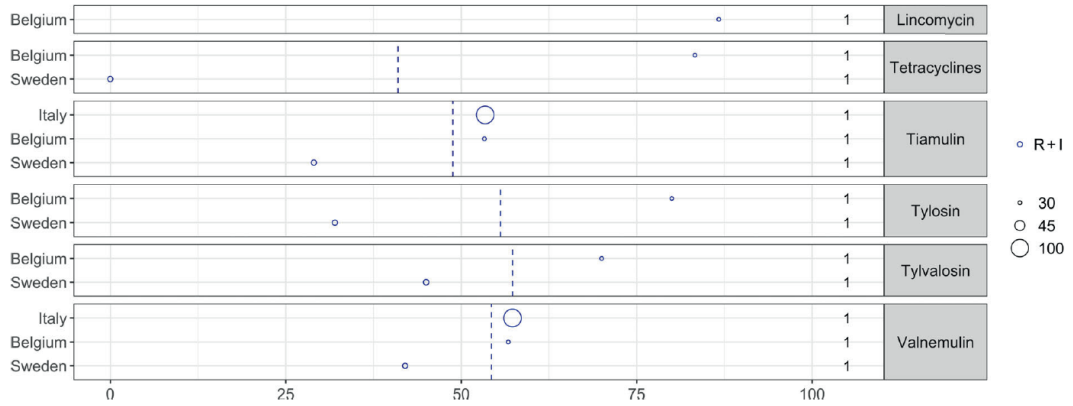


Figure 33: *Brachyspira hyodysenteriae* resistance data for each included study sorted by country

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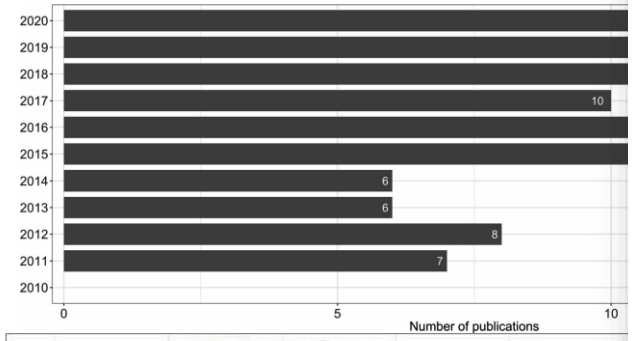
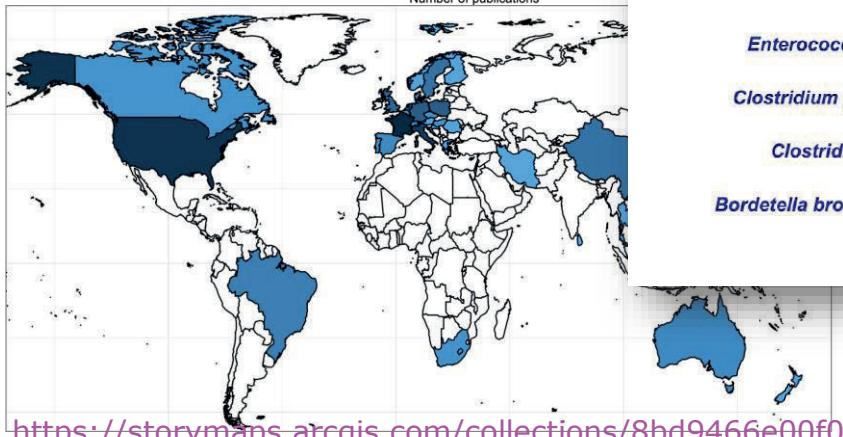
Assessment

Bacterial species	Number of eligible studies for data extraction (n = 98)*
Staphylococcus pseudintermedius	44
Escherichia coli	37
Pseudomonas aeruginosa	20
Staphylococcus aureus	14
Proteus spp.	10
Klebsiella spp.	7
Staphylococcus schleiferi	4
Enterococcus spp.	
Enterobacter spp.	
Bordetella bronchiseptica	
Clostridium perfringens	
Clostridioides difficile	





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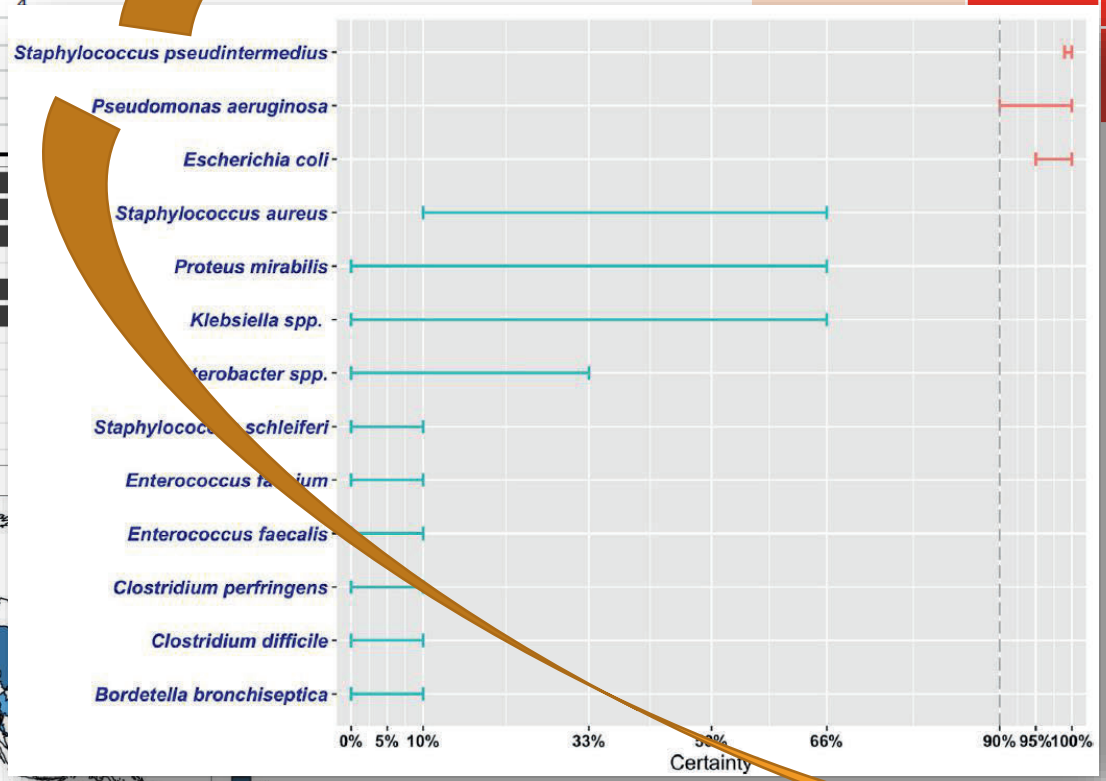
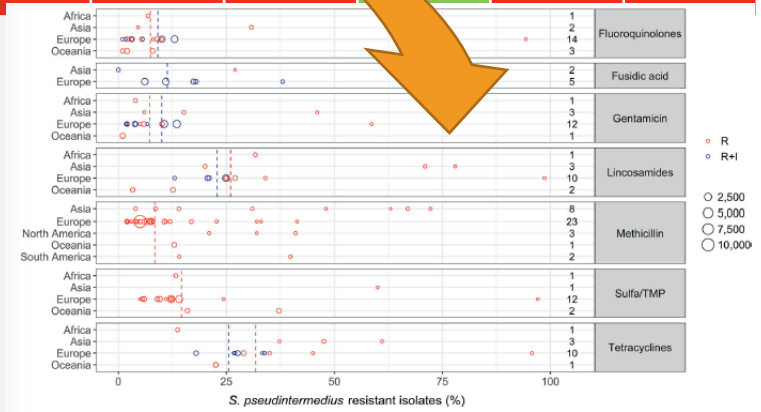
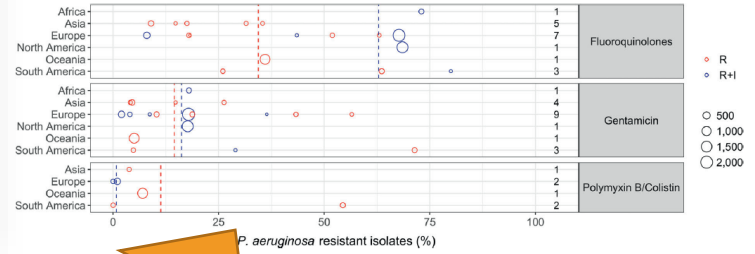
S. pseudo							
E. coli							
P. aerug							
S. schleiferi							
S. aureus							







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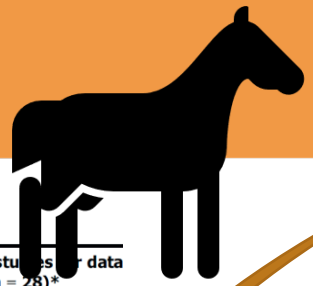
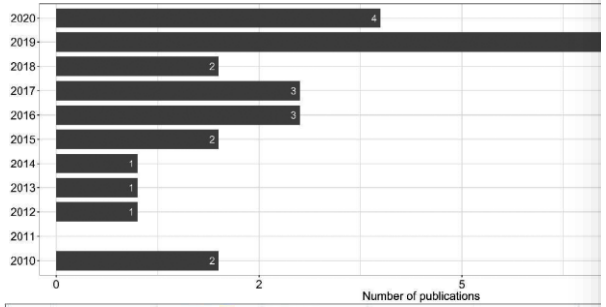
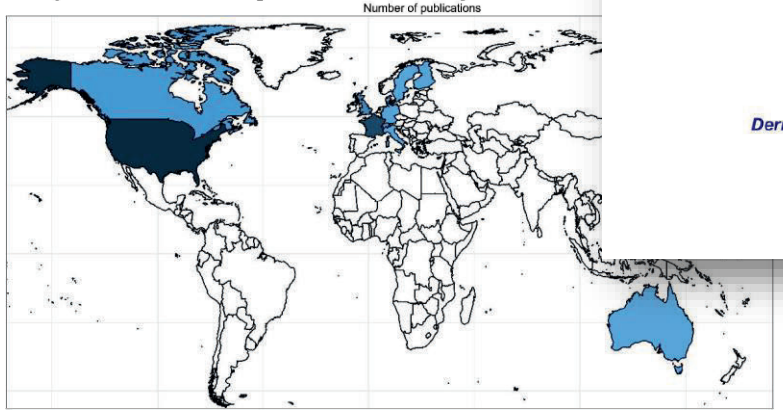
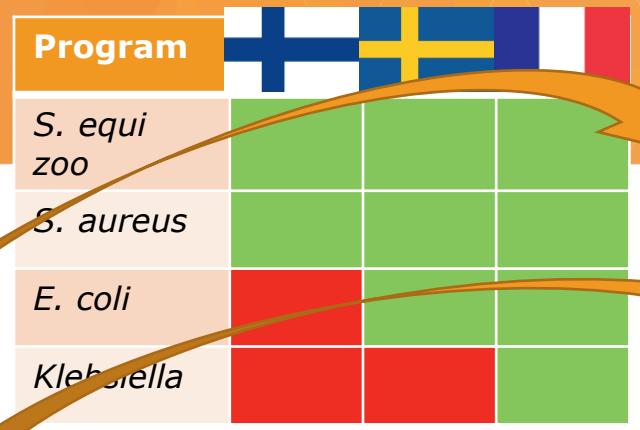
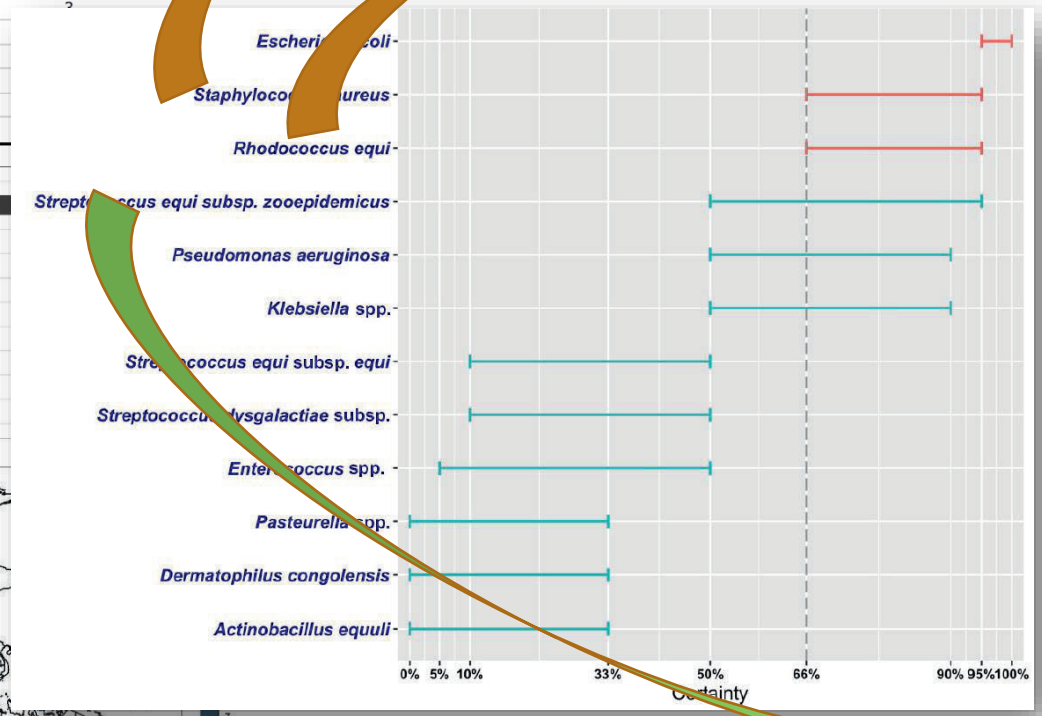


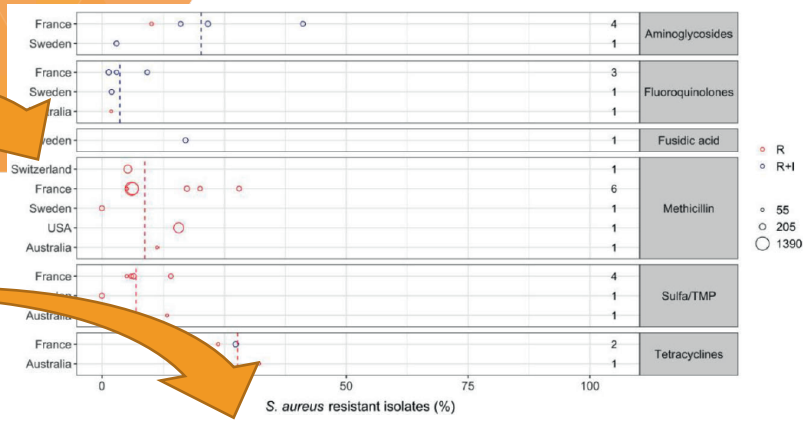
Bacteria species	Number of eligible studies for data extraction (n = 28)*
Escherichia coli	14
Staphylococcus aureus	10
Streptococcus equi subsp. *zooepidemicus*	9
Klebsiella spp.	6
Pseudomonas spp.	6
Rhodococcus equi	5
Streptococcus equi subsp. *equi*	3
Streptococcus dysgalactiae subsp. *dysgalactiae/equisimilis*	
Pasteurella spp.	
Enterococcus spp.	
Actinobacillus equuli	
Dermatophilus congolensis	

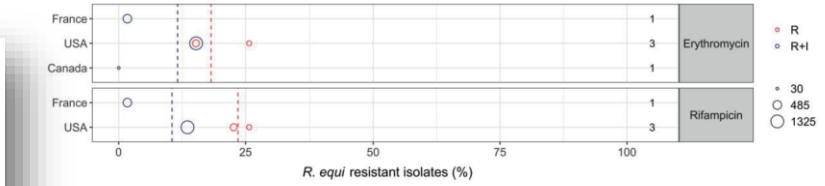






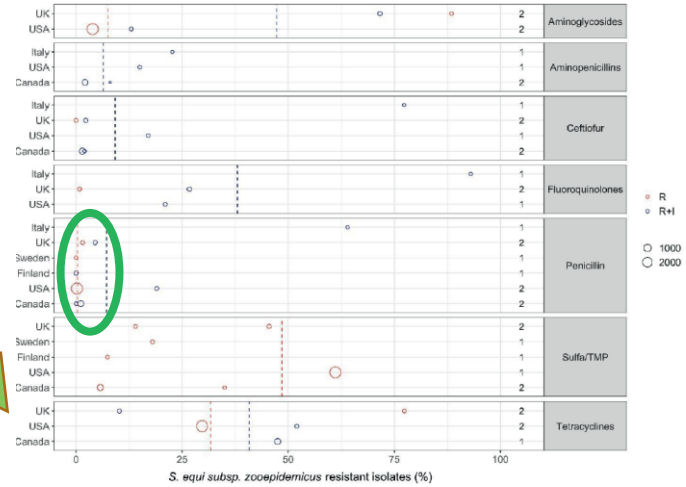






Spread of Multidrug-Resistant *Rhodococcus equi*, United States

Sonsiray Álvarez-Narváez, Steeve Giguère,[1] Noah Cohen, Nathan Slovis, José A. Vázquez-Boland



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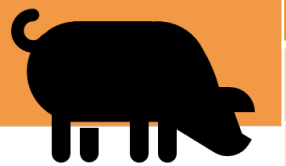
Assessment



Program						
E. coli						
A. pleurop						
S. suis						
P. multo						
B. hyo...						

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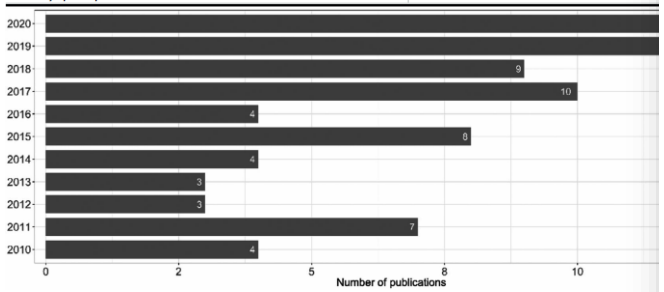
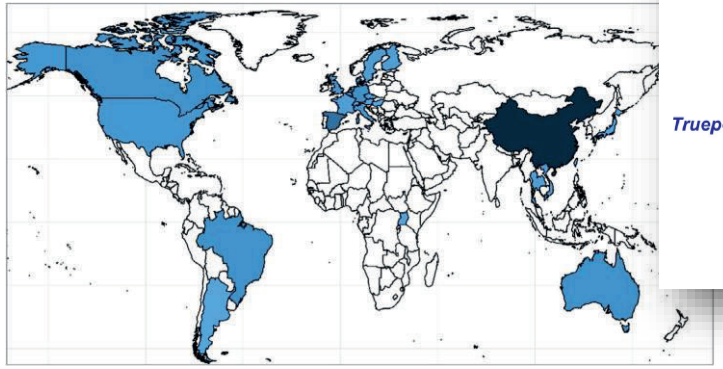
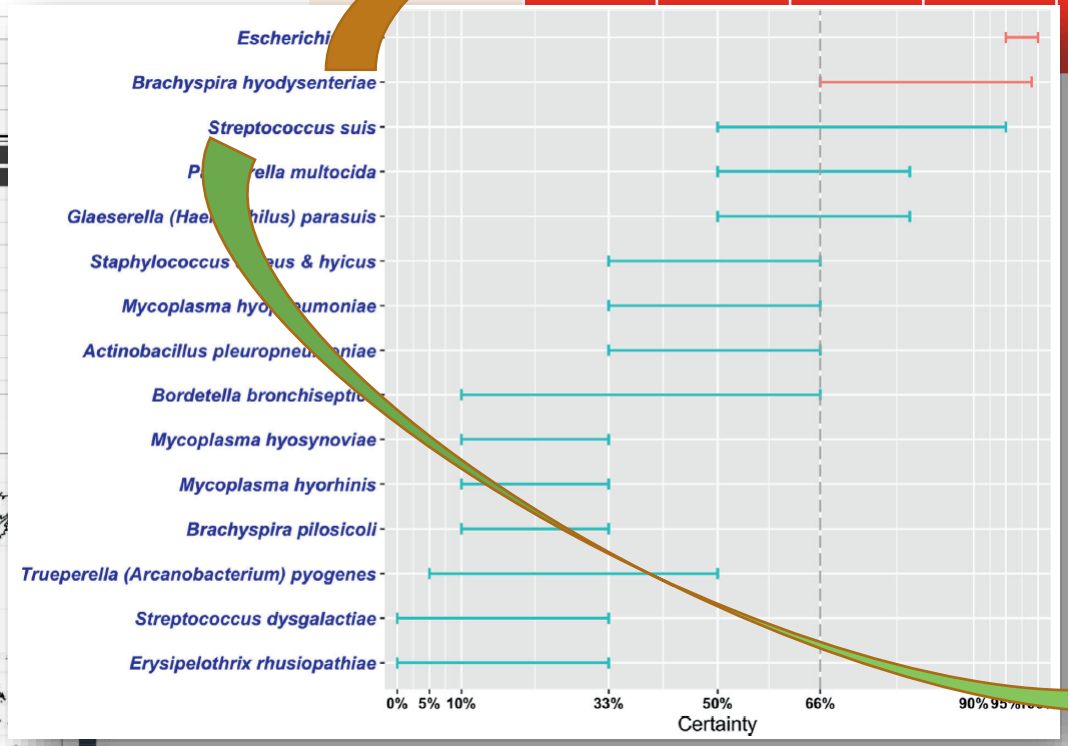
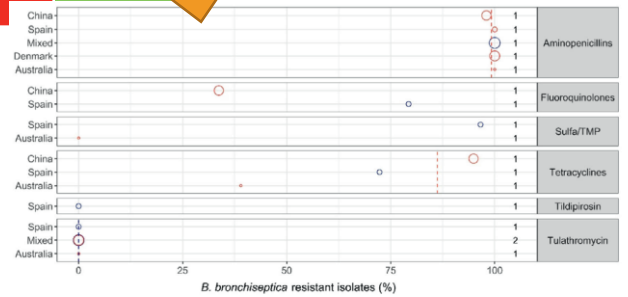
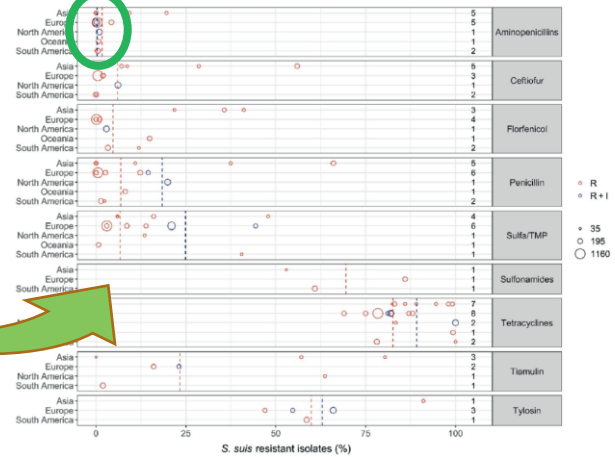
Bacteria species	Number of eligible studies for data extraction (n = 77)*
Escherichia coli	34
Streptococcus suis	20
Actinobacillus pleuropneumoniae	17
Pasteurella multocida	16
Glaesserella (Haemophilus) parasuis	8
Bordetella bronchiseptica	6
Staphylococcus aureus/S. hyicus	3
Brachyspira hyodysenteriae	3
Trueperella (Arcanobacterium) pyogenes	1
Erysipelothrix rhusiopathiae	1
Streptococcus dysgalactiae	0
Mycoplasma hyosynoviae	0
Mycoplasma hyorhinis	0
Mycoplasma hyopneumoniae	0
Brachyspira pilosicoli	0











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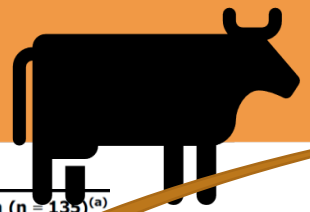
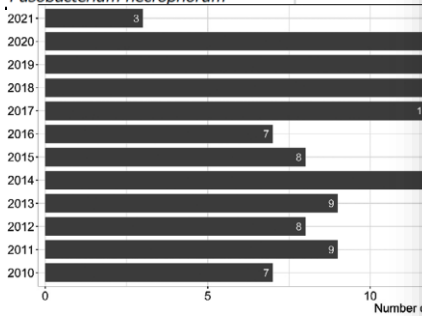
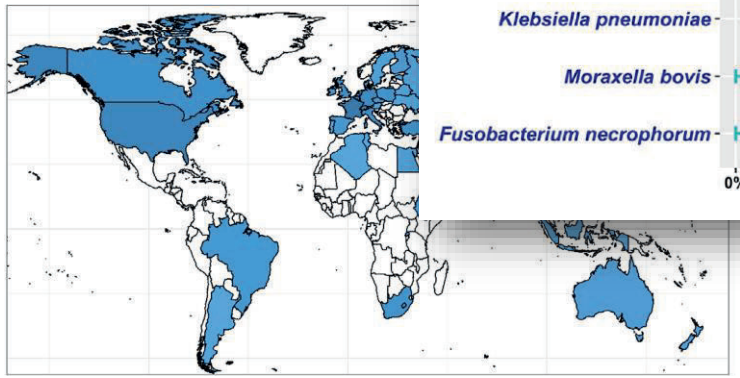
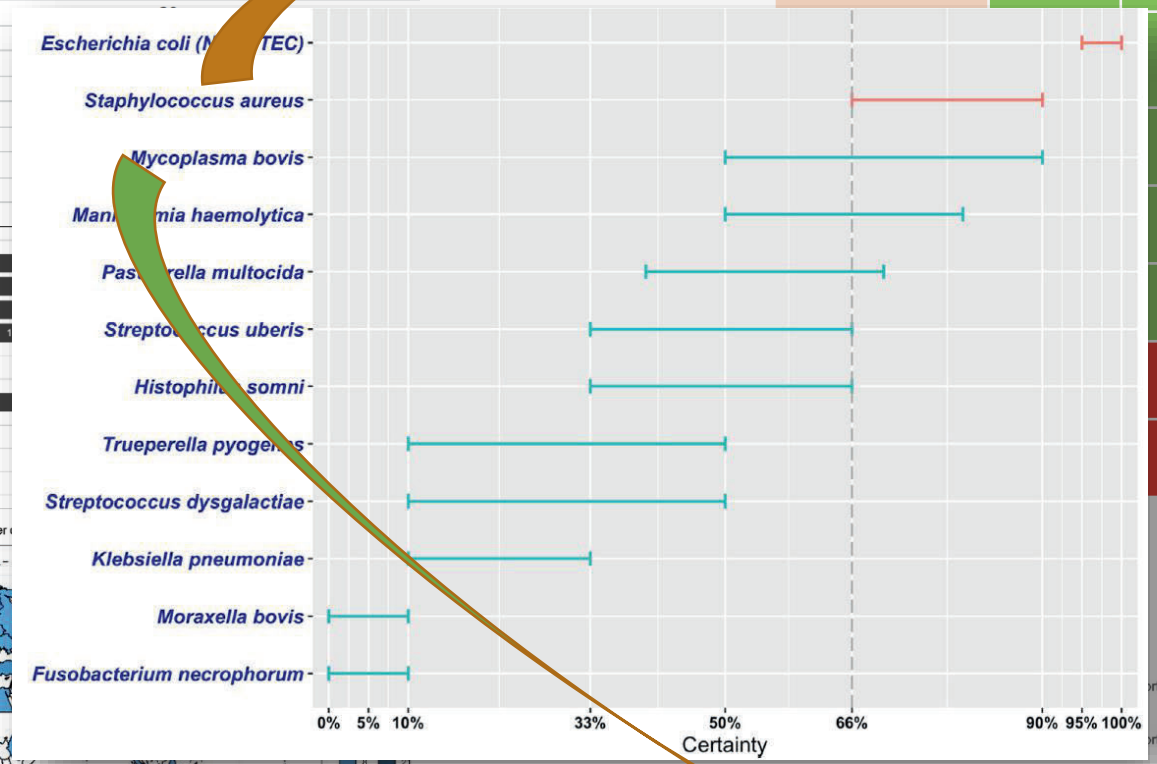


Bacterial species	Number of eligible studies for data extraction (n = 135)[a]
Staphylococcus aureus	66
Escherichia coli	37
Pasteurella multocida	23
Mannheimia haemolytica	
Streptococcus uberis	
Streptococcus dysgalactiae	
Histophilus somni	
Trueperella pyogenes	
Mycoplasma bovis	
Klebsiella pneumoniae	
Moraxella bovis	
Fusobacterium necrophorum	







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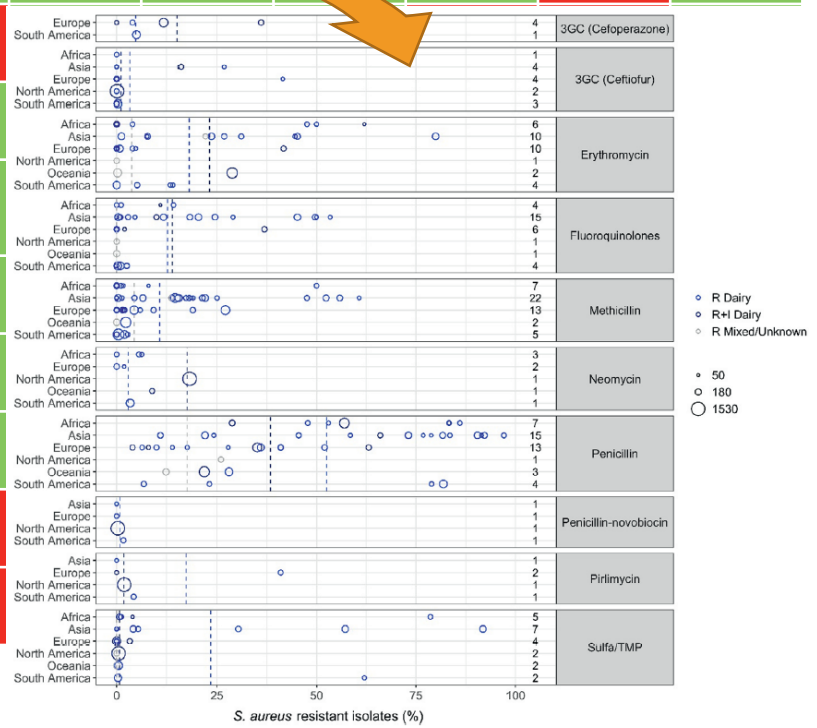
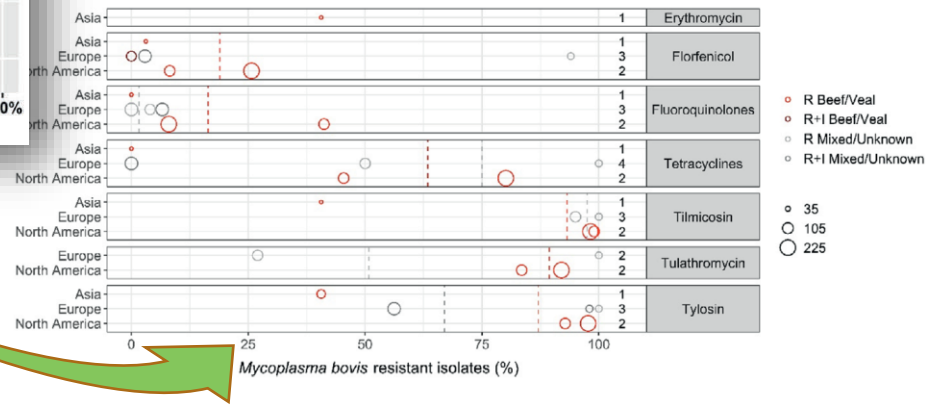
S. aureus									
S. uberis									





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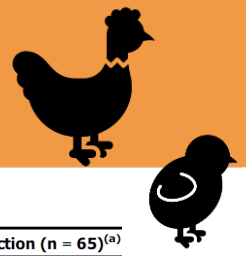

Program					
E. coli					
S. aureus					
E cecorum					

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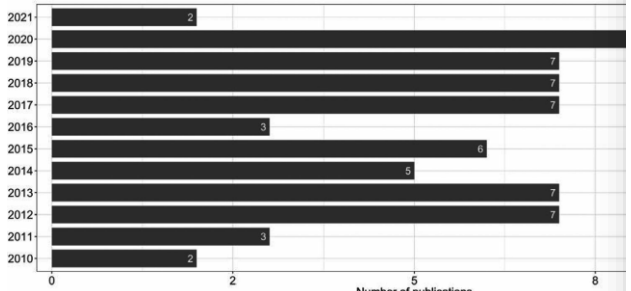
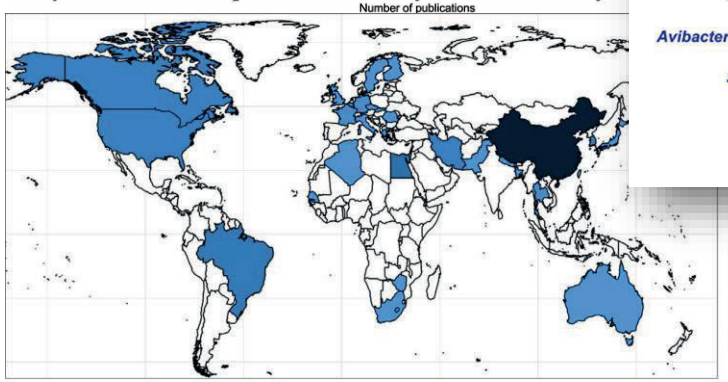
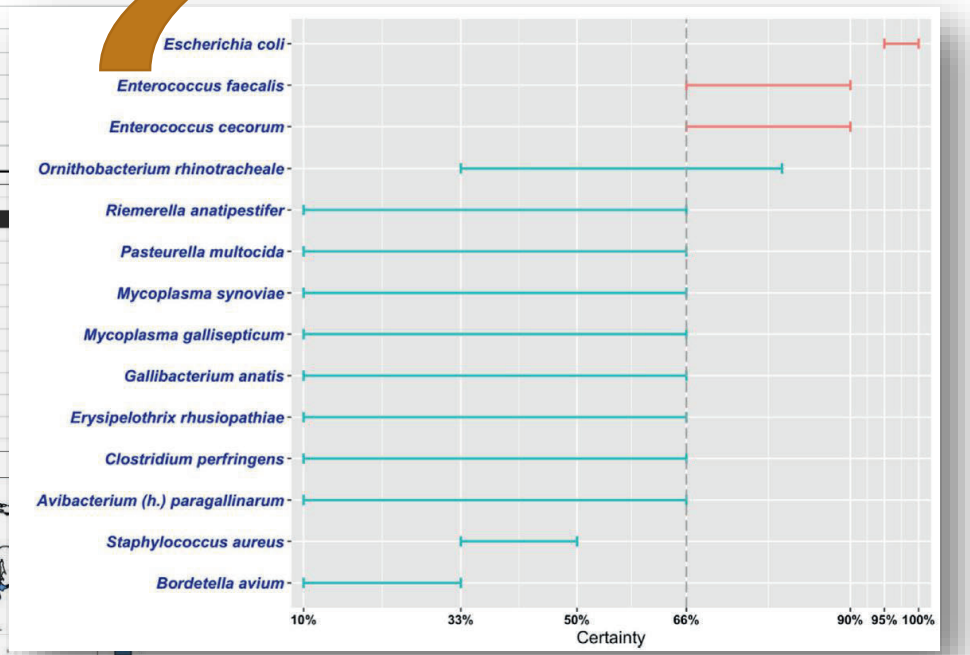
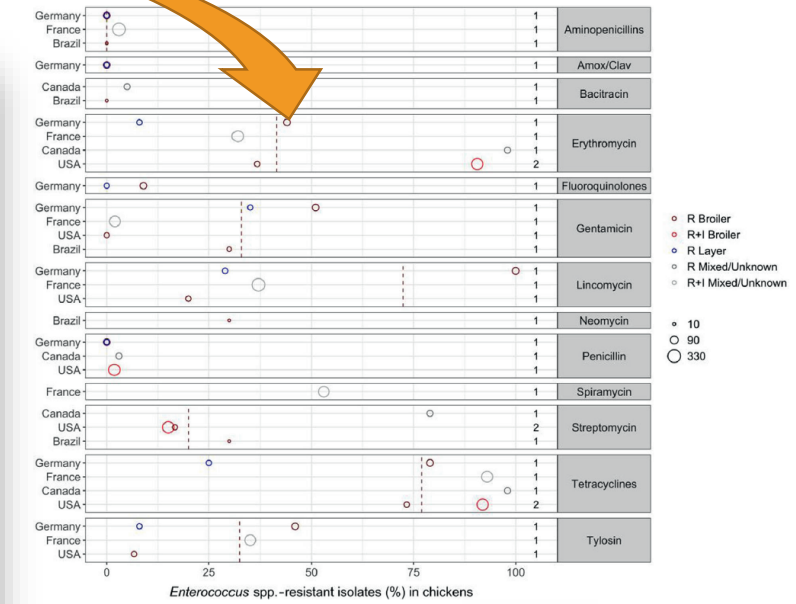
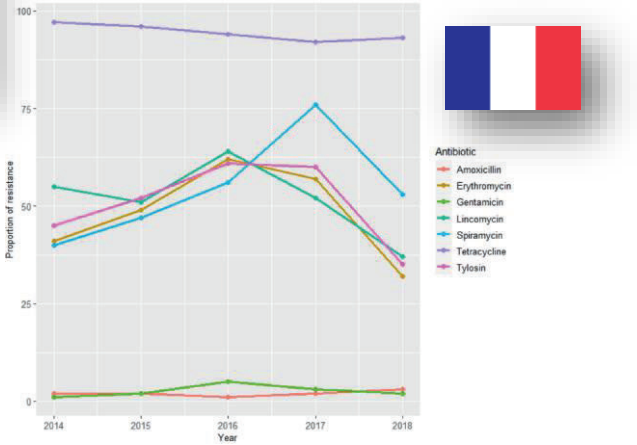
Bacteria species	Number of eligible studies for data extraction (n = 65)[a]
Escherichia coli	46
Enterococcus faecalis or *Enterococcus cecorum*	6
Staphylococcus aureus	5
Riemerella anatipestifer	4
Clostridium perfringens	3
Avibacterium (haemophilus) paragallinarum	2
Bordetella avium	1
Mycoplasma gallisepticum	1
Pasteurella multocida	1
Gallibacterium anatis	1
Mycoplasma synoviae	0
Ornithobacterium rhinotracheale	0
Erysipelothrix rhusiopathiae	0











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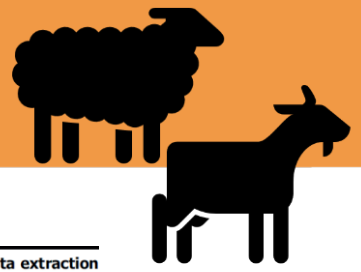
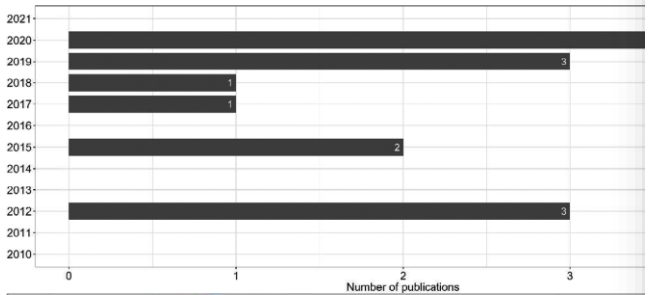
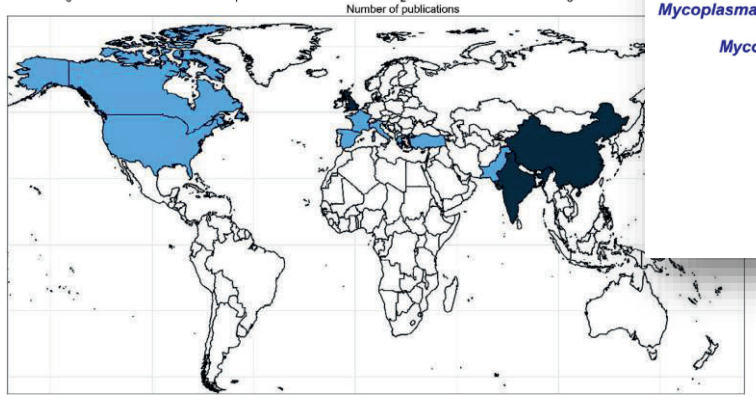
Assessment

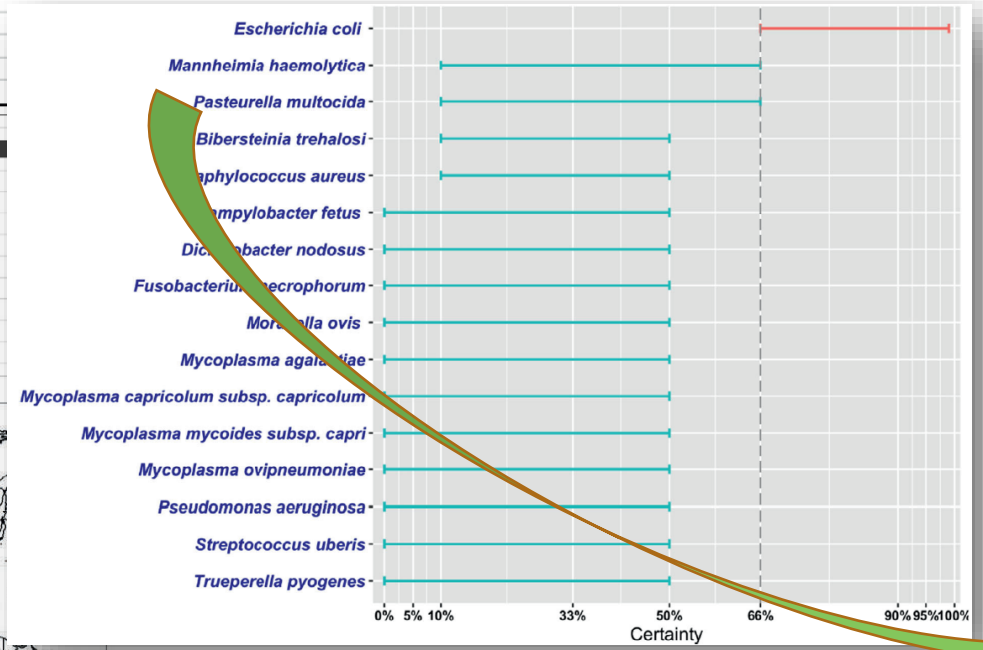


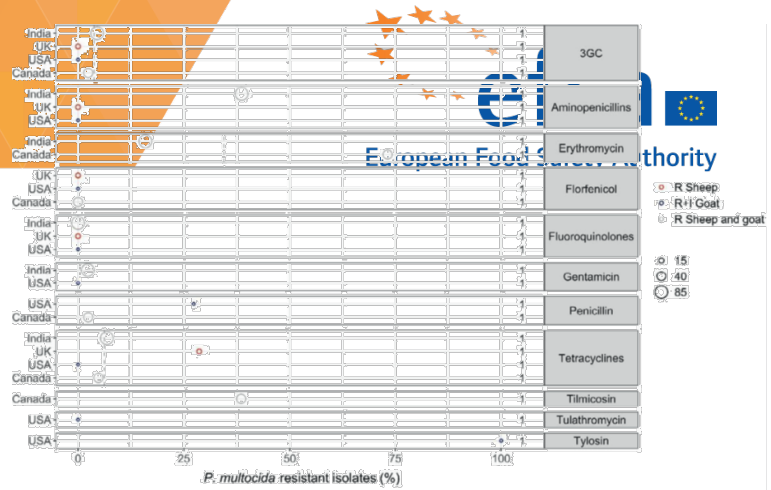
Program		
E. coli		
M. haemo		
P. multo		
B. trehalosi		

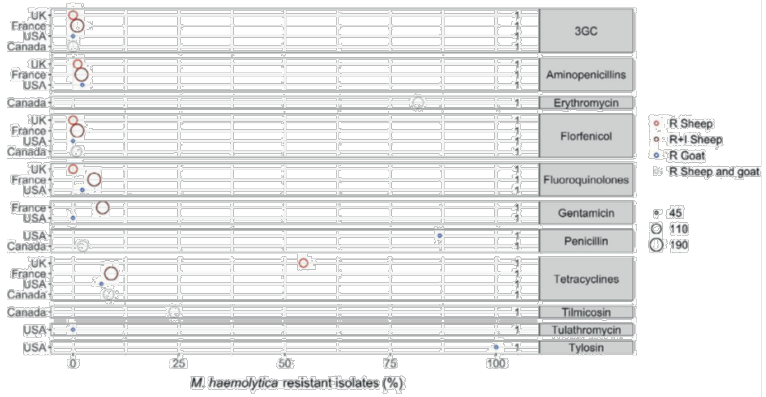
Bacterial species	Number of eligible publications for data extraction (n = 14)[a]
Mannheimia haemolytica	4
Bibersteinia trehalosi	2
Streptococcus uberis	0
Dichelobacter nodosus	0
Moraxella ovis	0
Mycoplasma ovipneumoniae	0
Mycoplasma agalactiae	0
Mycoplasma mycoides subsp. *capri*	0
Mycoplasma capricolum subsp. *capricolum*	0
Fusobacterium necrophorum	0
Trueperella pyogenes	0
Campylobacter fetus	0
Pseudomonas aeruginosa	0

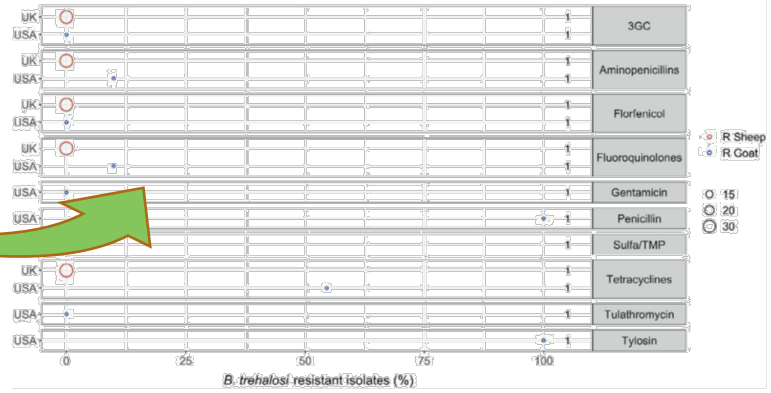












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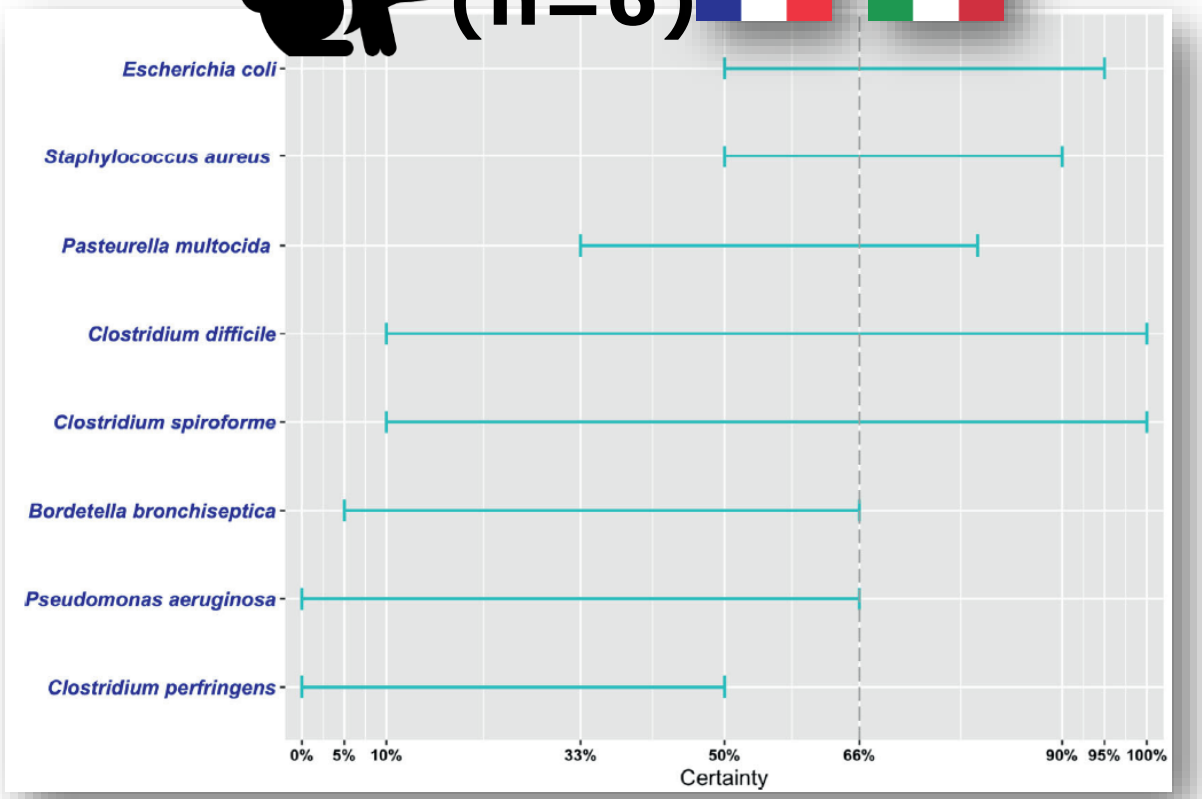
Assessment

(n=6)



Atlantic salmon

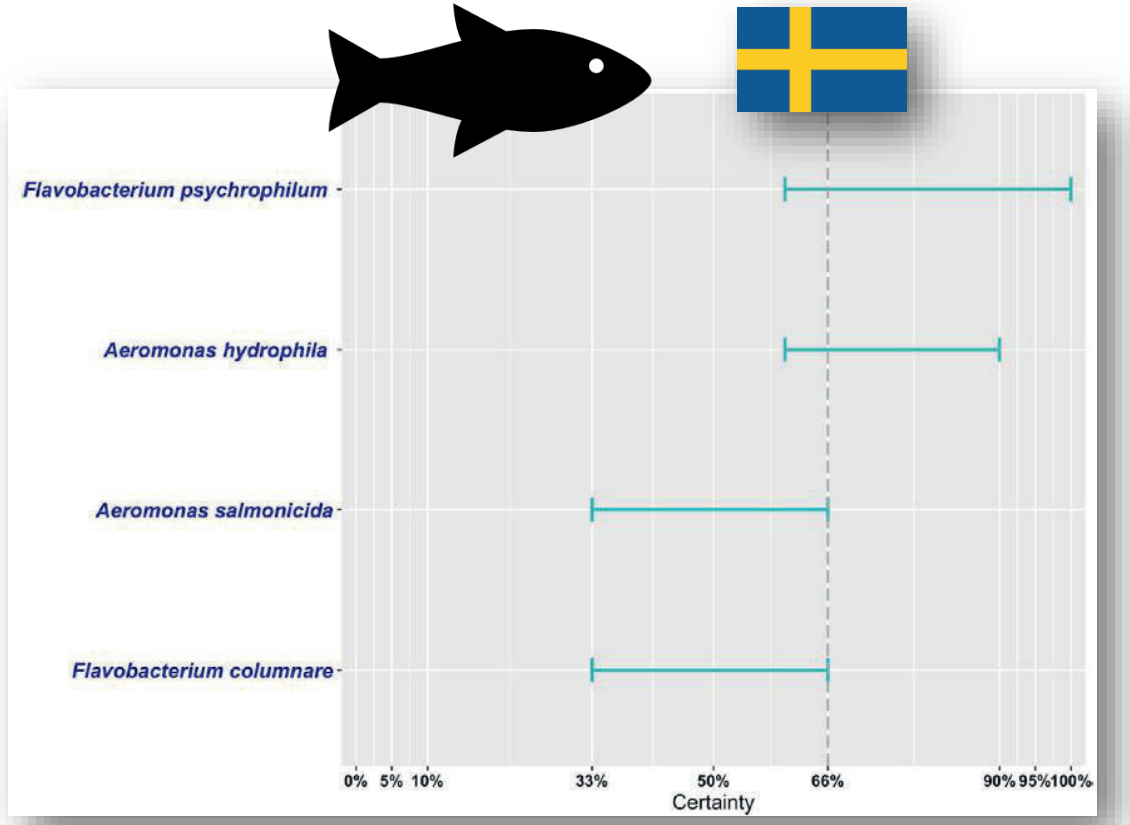
Carp

Rainbow trout

Sea bream

Tilapia

- Ampicillin
- Enrofloxacin
- Florfenicol
- Flumequine
- Oxolinic acid
- Sulfo-trimethoprim
- Oxytetracycline



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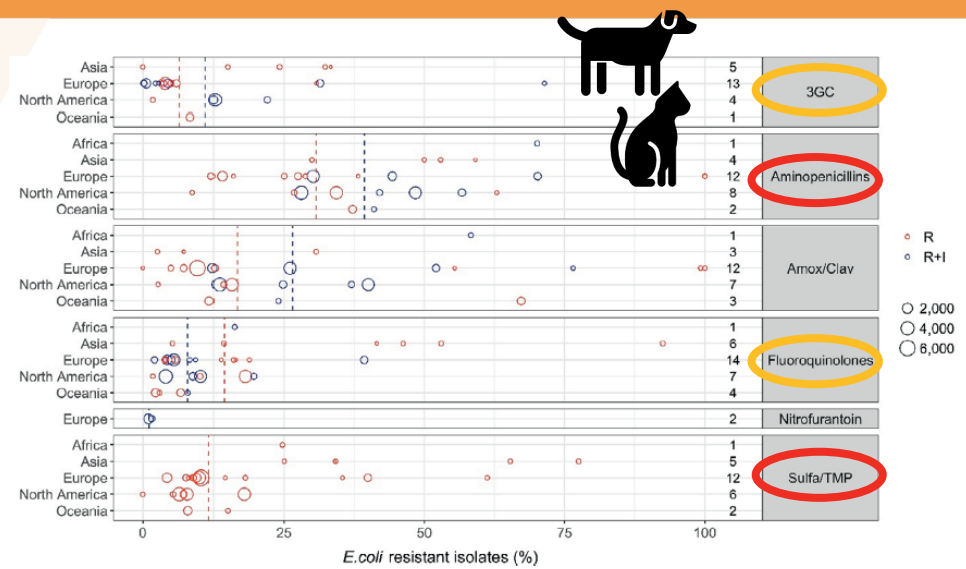
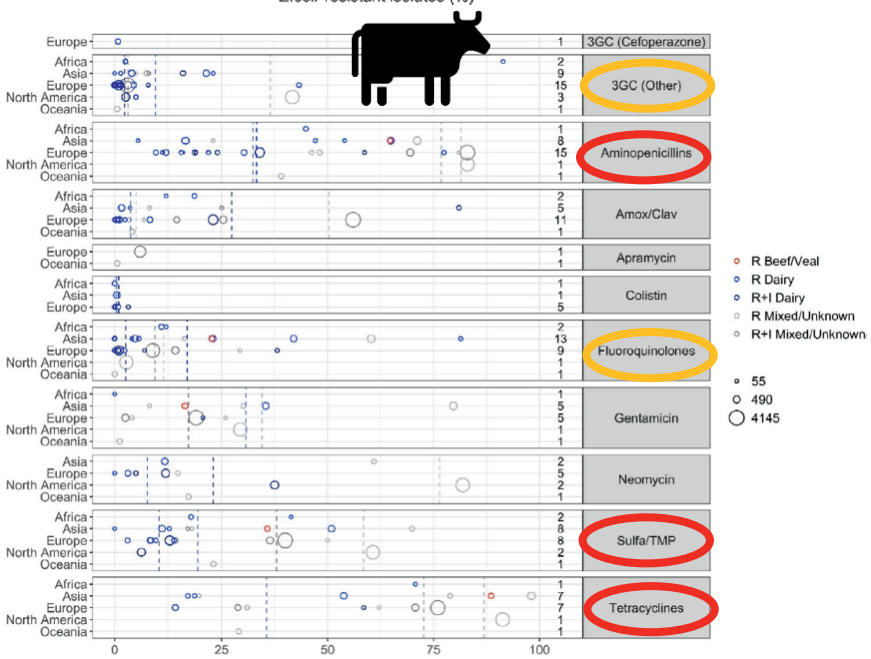
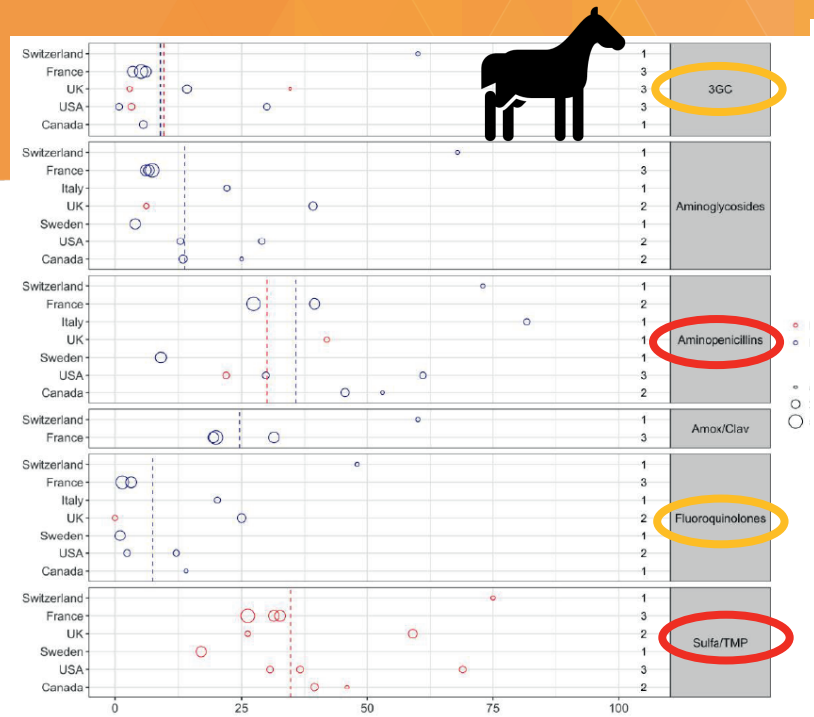
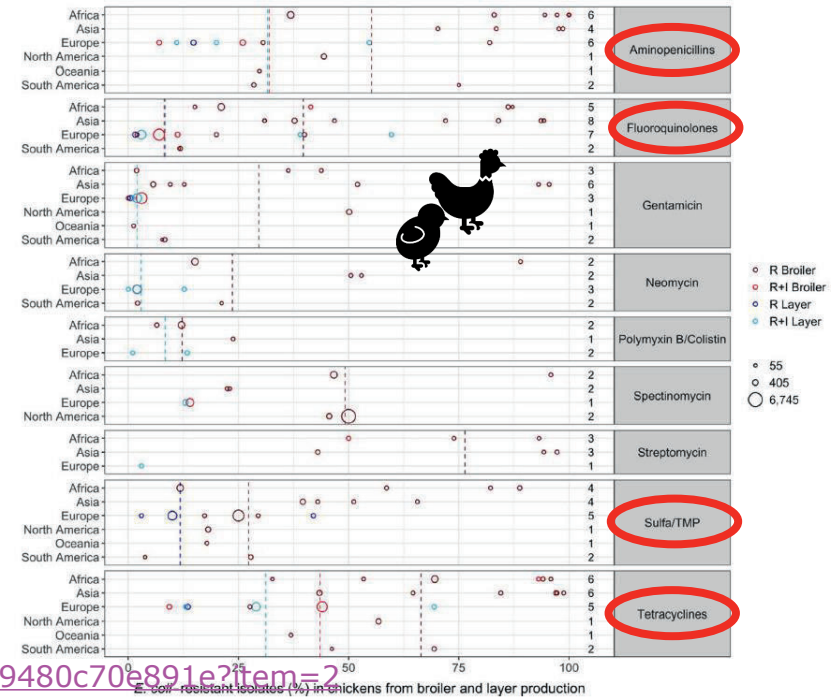
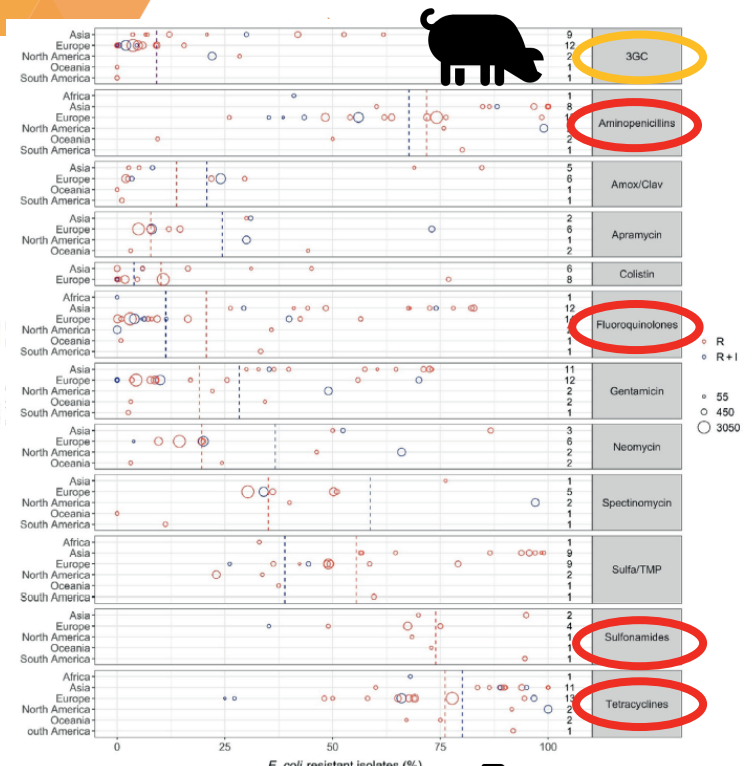
E. coli: its own thing

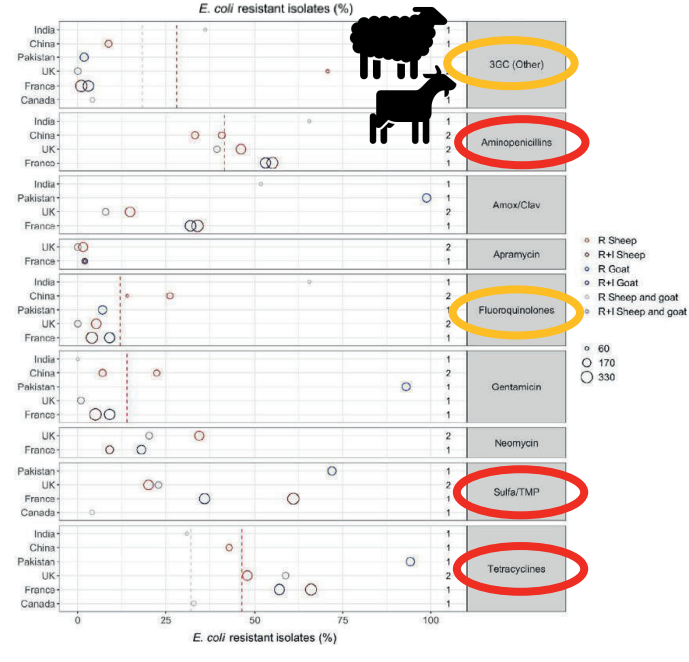












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- Most problems applicable to all animal species (to a different degree)
  - lack of standardized methodology/breakpoints/definitions (especially in certain cases)
  - Heterogeneity in the (sometimes very scarce) information available (infected vs. subclinical vs. clinically affected animals, treatments…)
  - National monitoring programs can be of great use (but need to be harmonized)
  - Absence of evidence (of AMR in a given pathogen) is certainly not evidence of absence in certain cases (e.g., *Mycoplasma*, *Brachyspira*)
  - Treatment failure may not be related with microbiological AMR (e.g., *E. cecorum* in poultry) and microbiological AMR may not necessarily lead to treatment failure (e.g. *P. aeruginosa* in dogs)

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Working Group composition

WG experts:

- ALVAREZ Julio – chair
- BICOUT Dominique
- DEWULF Jeroen
- DREWE Julian
- HILBERT Friederike
- GUARDABASSI Luca
- MADER Rodolphe
- ROMALDE Jesus
- SMITH Peter

EFSA staff:

- BALDINELLI Francesca
- OSVALDI Verena

Hearing experts:

- Inputs for specific hosts/ pathogens

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