Global trends in antimicrobial use and resistance in animals

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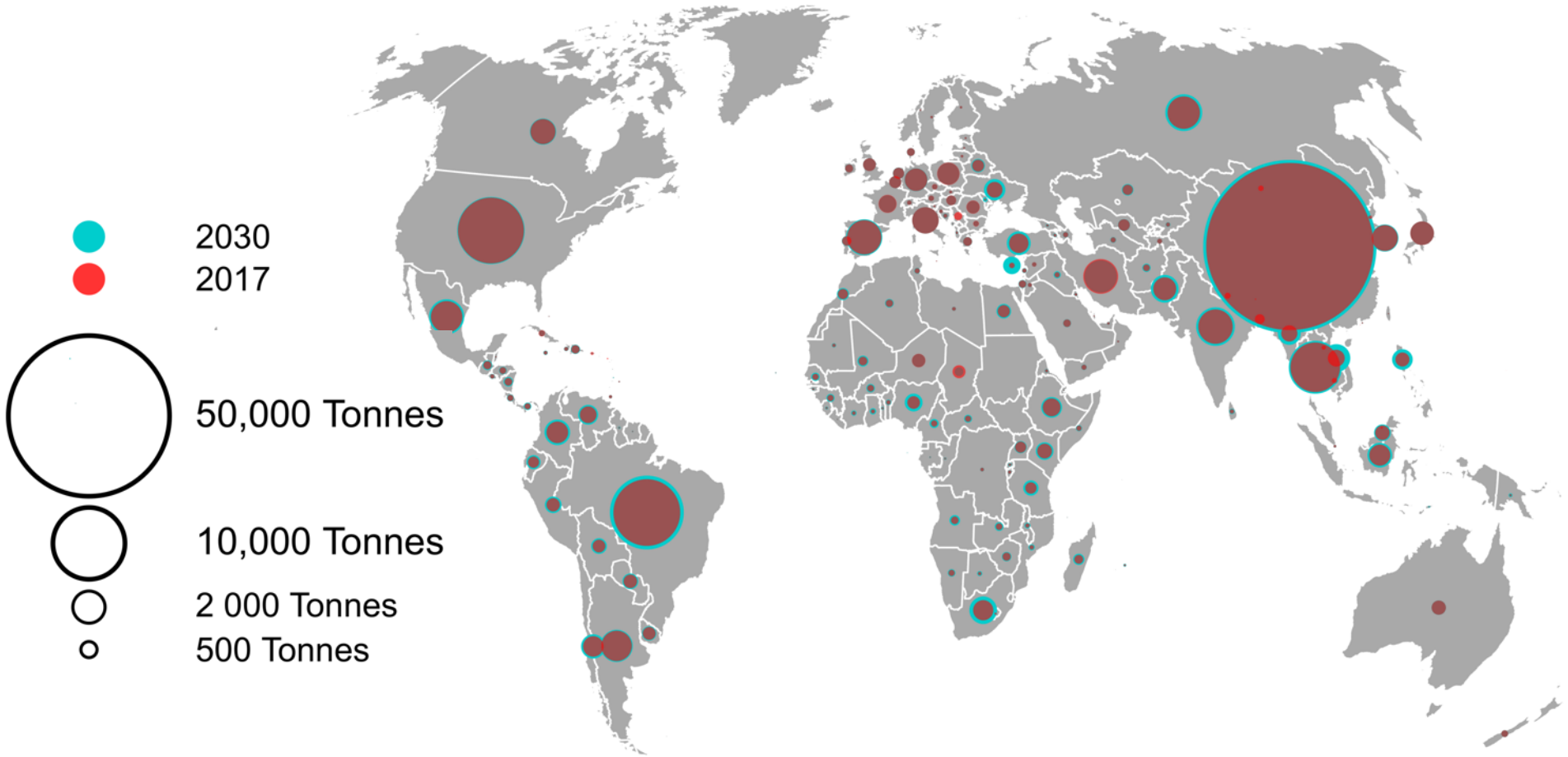
ETH Zurich

Swiss Association for Animal Sciences
01/06/2020

Why AMR in Animals ?

Van Boeckel et al, 2017, *Science*. Reducing antimicrobial use in food animals

Antimicrobial Use in Animals – Global Trends



Version 1, 2010: Van Boeckel et al 2015, PNAS.
Version 2, 2013: Van Boeckel et al 2017, Science.
Version 3, 2017: Tiseo et al 2020, Antibiotics.

Antimicrobial Use in Animals – Switzerland (2017)

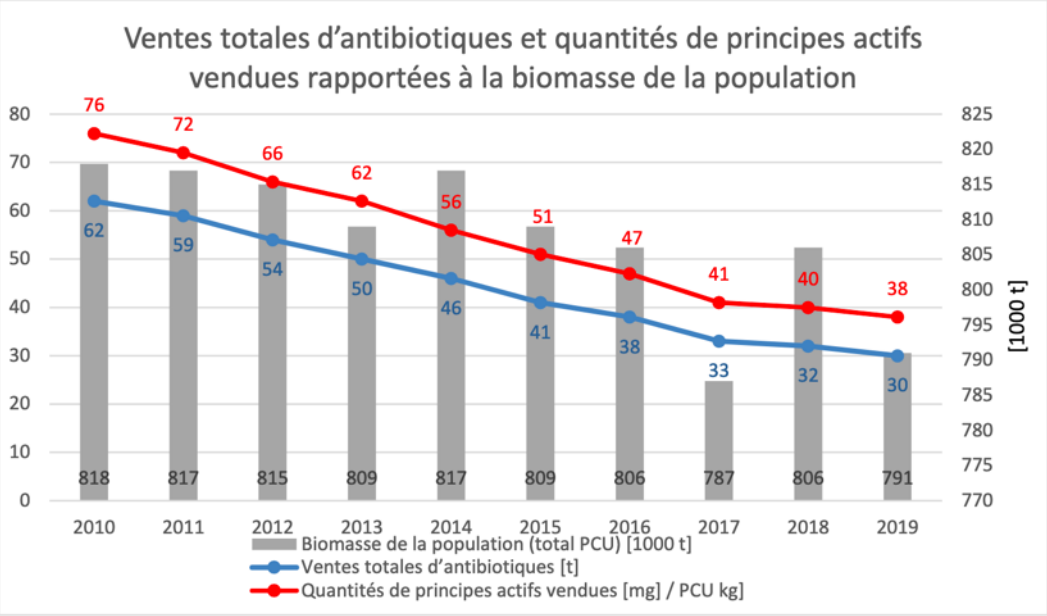
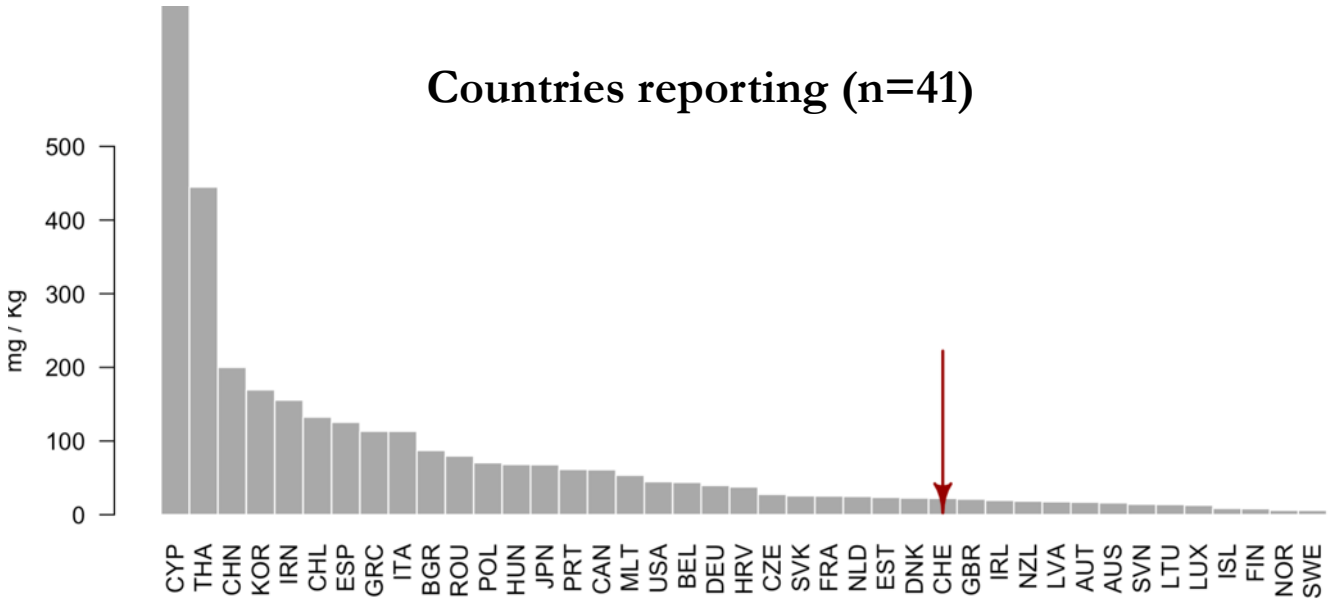
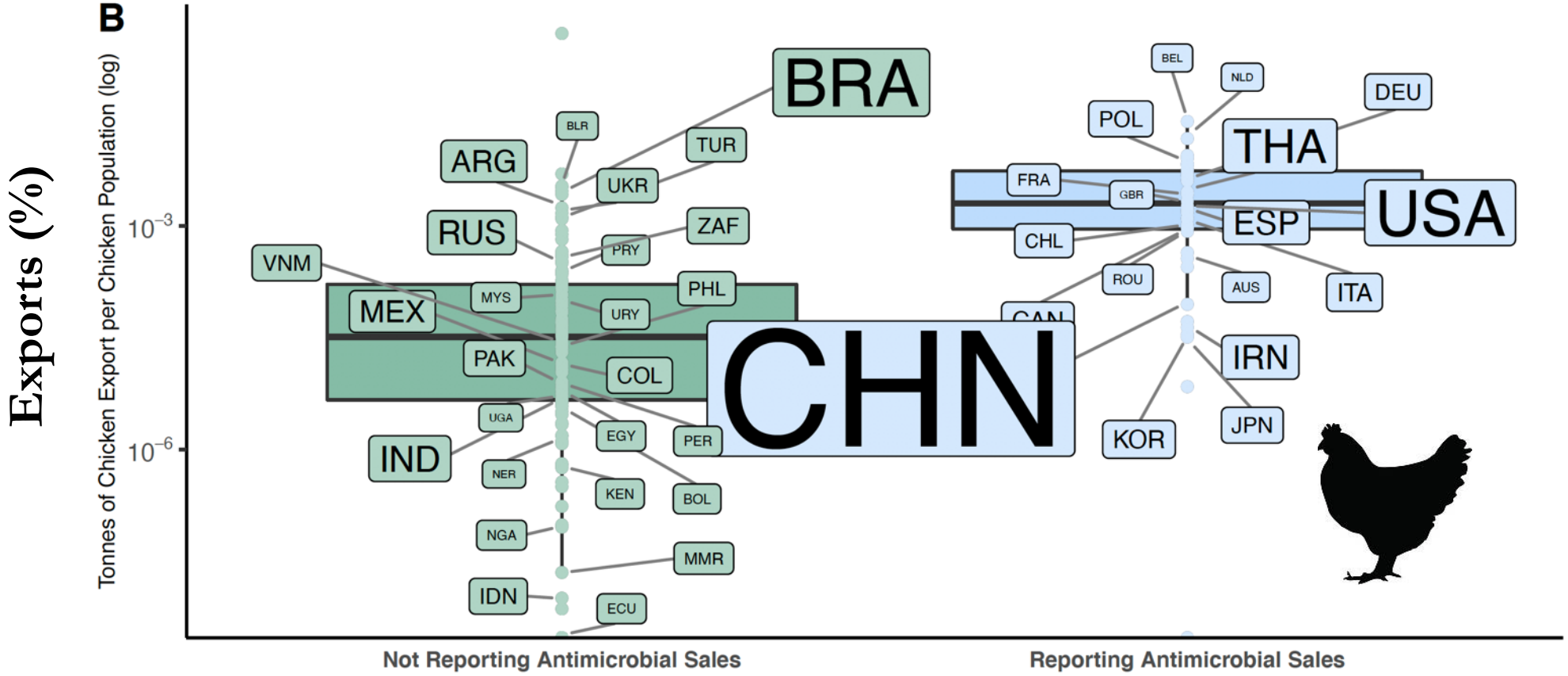


Fig. 1.4 : Ventes totales d'antibiotiques par PCU dans les années 2010 à 2019



Antimicrobial Use in Animals - Meat Exports



Countries that reported antimicorbial sales also **exported a higher proportion of their meat** production (chicken) than countries that did not report antimicrobial sales. A notable **exception** was one of the largest meat exporter the world: **Brazil**.

Tiseo et al 2020, Antibiotics.

Antimicrobial Resistance in Animals

(low and middle-income countries)

Why a map of AMR for low- and middle-income countries?

High-Income countries

Systematic Surveillance (NARMS, ESVAC, etc)
Publically available information

↓

Interventions

vs

Low- and Middle-Income Countries

Rapid growth of the livestock sector

Systematic Surveillance
nascent or absent : 1, 2, 5 years..?

↓

Intervention guided by expert opinion.

Problem: the AMR situation in LMICs if not intuitive

Low-Meat consumption
Low access to drugs → **AMR levels are low**

Unregulated Antimicrobial Use
Low Biosecutiry → **AMR levels are high**

What we need :

In the short term, we need an alternative to systematic surveillance for animals in LMICs.

Science

RESEARCH ARTICLE

Global trends in antimicrobial resistance in animals in low- and middle-income countries

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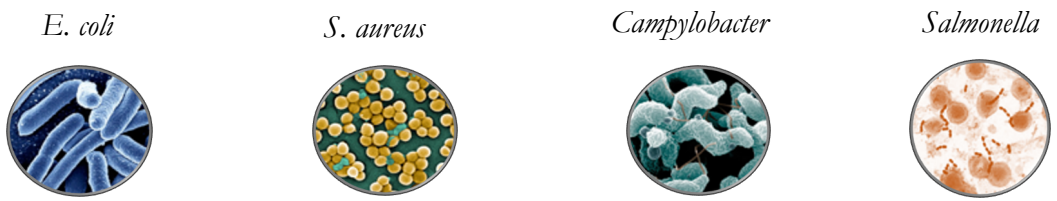
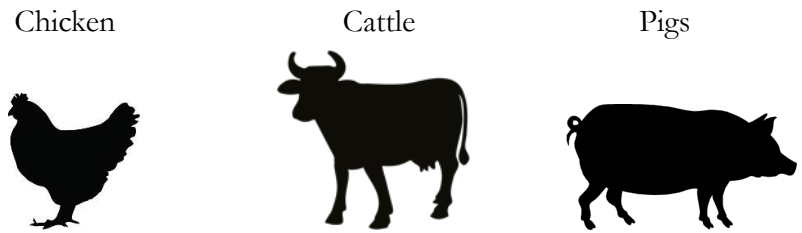
– Hide authors and affiliations

Science 20 Sep 2019:
Vol. 365, Issue 6459, eaaw1944
DOI: 10.1126/science.aaw1944

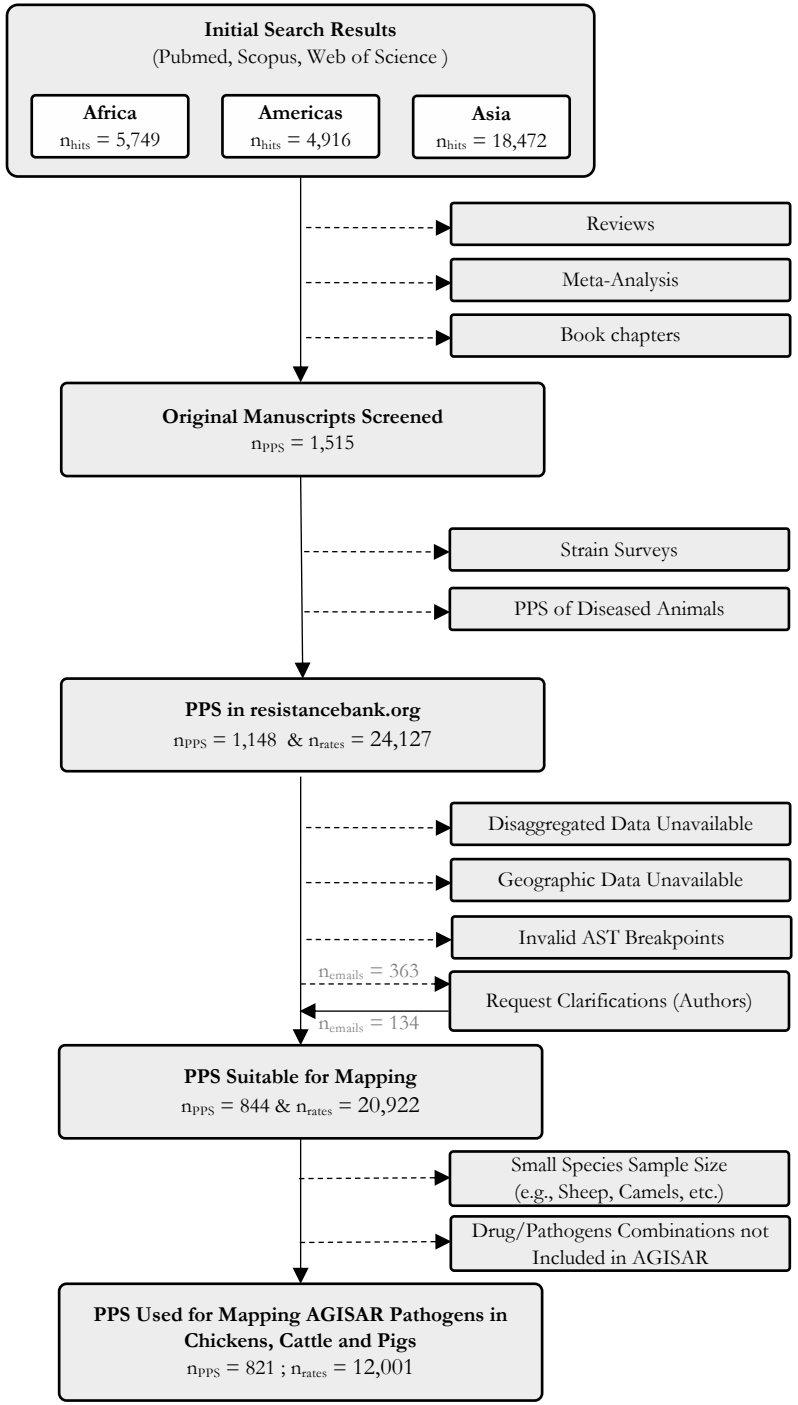
Point **P**revalence **S**urveys of AMR in Animals

Have been conducted for decades by veterinarians and represent a largely untapped source of information to provide geographical perspective of the world's AMR situation in animals.





Drug/Pathogens recommended by AGISAR
WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance



Joao Pires

Reshma Silvester

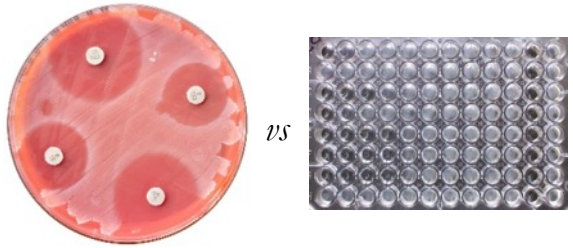
Cheng Zhao

Julia Song

Data Harmonization

1. Methods

Diffusion Microdilution



Method bias?

2. Guidelines

Breakpoints ~ time + CLSI/EUCAST

CLSI

EUCAST EUROPEAN COMMITTEE ON ANTIMICROBIAL SUSCEPTIBILITY TESTING
European Society of Clinical Microbiology and Infectious Diseases

Breakpoint bias?

3. Data Accuracy

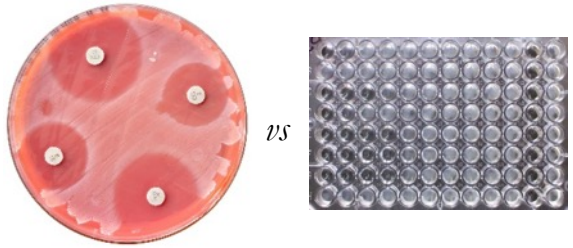
Variations in accuracy of susceptibility testing between labs and countries…

Country bias?

Method Bias?

1. Methods

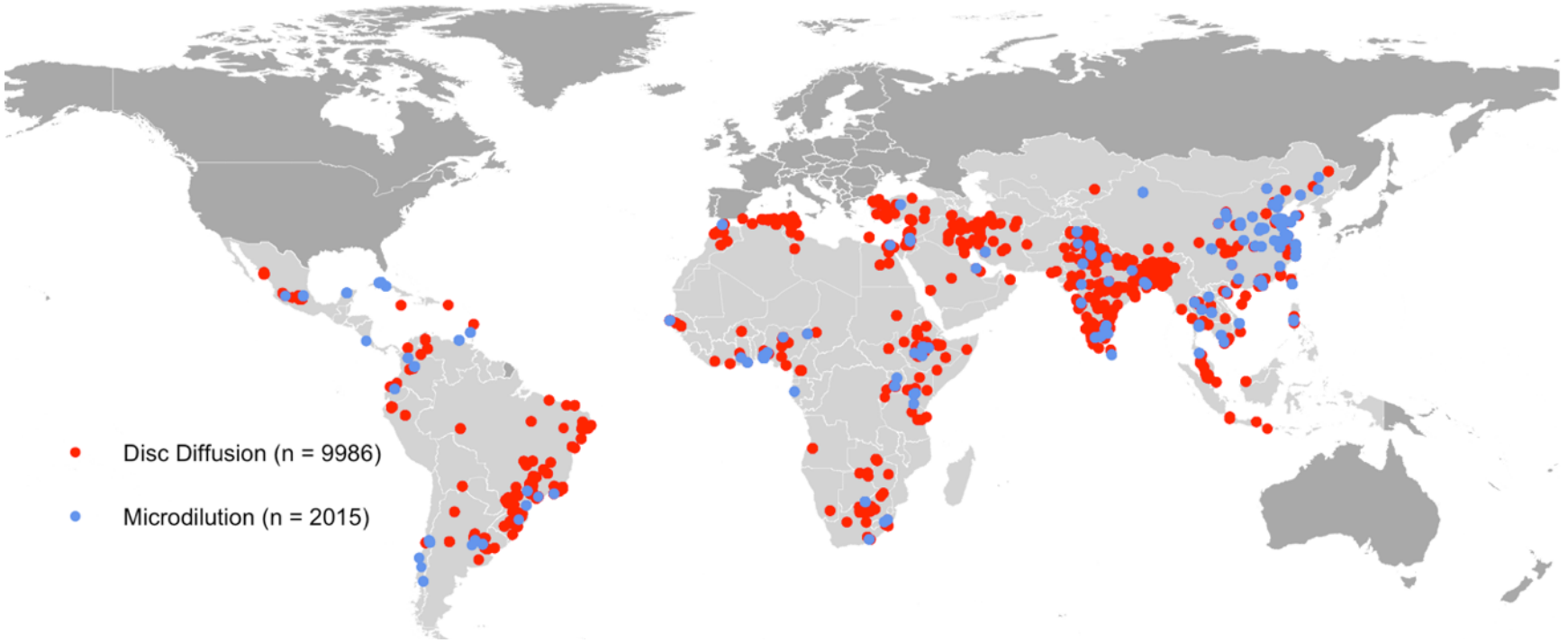
Diffusion Microdilution



vs

➔ No significant difference in resistance by methods for 99.42% of data

Literature: good agreement between methods
Bengtsson et al.; Al-Natour et al.; Jean, S.-S.



Breakpoint bias?

2. Guidelines

Breakpoints ~ time + CLSI/EUCAST

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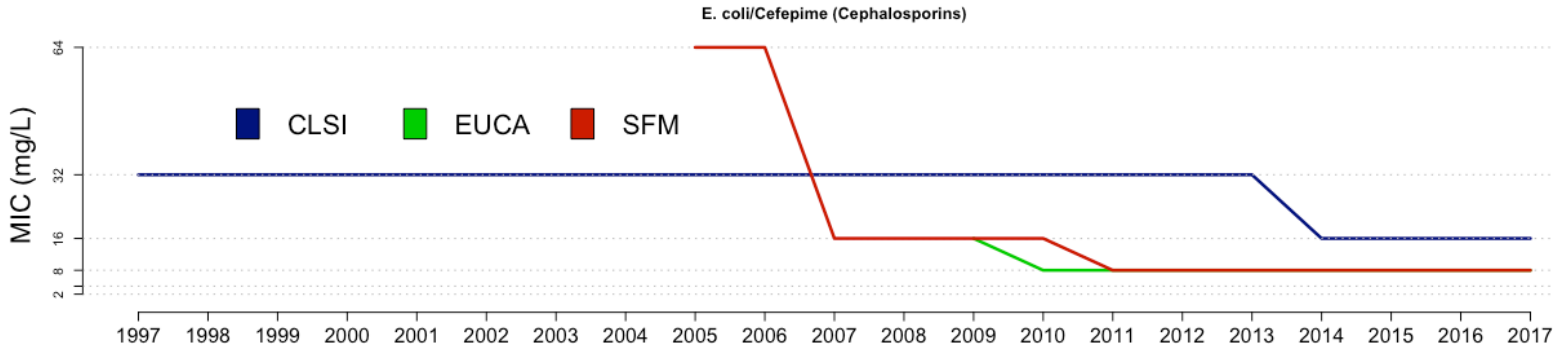
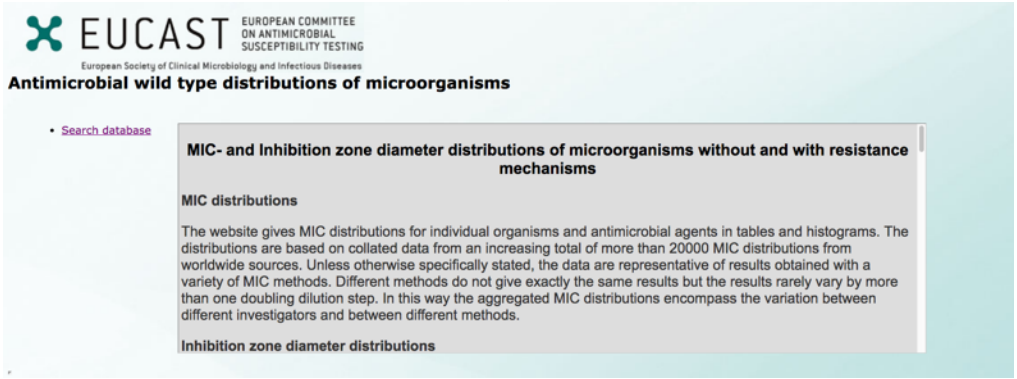


Using MIC/mm distributions



https://mic.eucast.org/Eucast2/

Country bias?

3. Data Accuracy

Variations in accuracy of susceptibility testing between labs and countries…

External Quality Assurance System (EQAS)

DTU Food National Food Institute

DTU

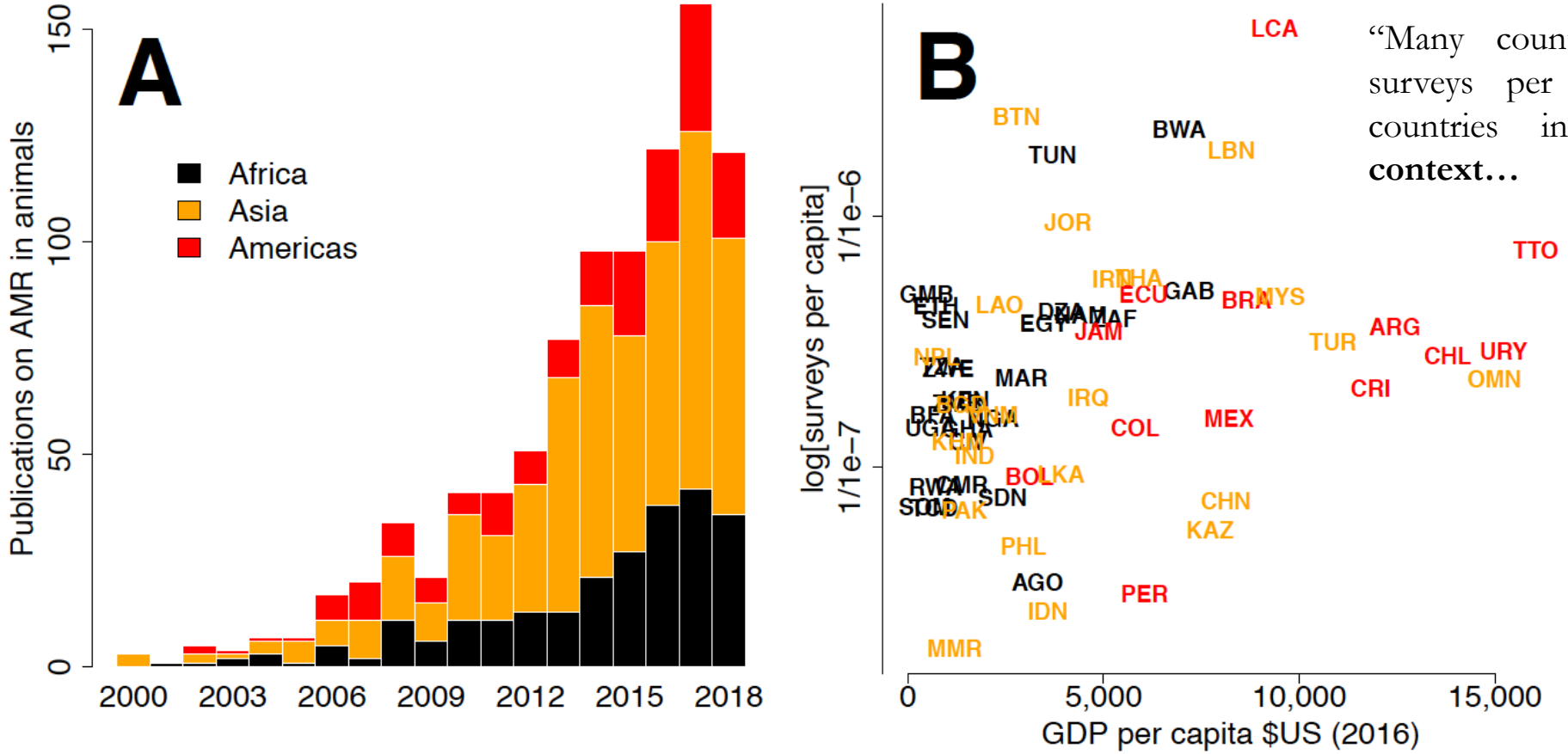
World Health Organization

Participating laboratories receive strains to be identified and go through AST

Results are anonymous and available online

Salmonella
Campylobacter
Shigella (results used as a proxy for *E. coli*)

Number of Surveys *vs* Resources Available

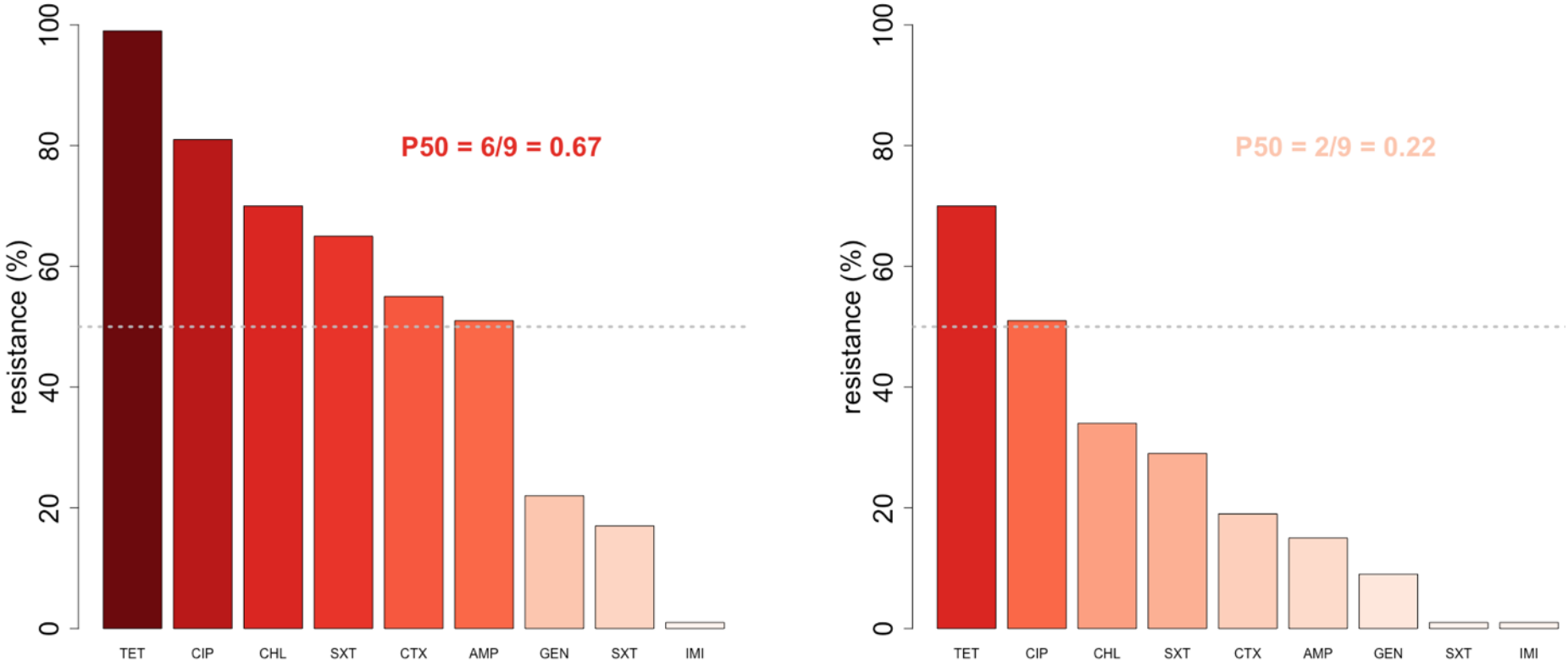


"Many countries in Africa have more surveys per capita than middle-income countries in South America". **Some context…**

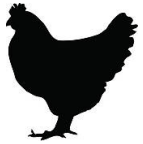
Van Boeckel* & Pires*, *Science* 2019. Global trends in antimicrobial resistance in animals in low- and middle-income countries

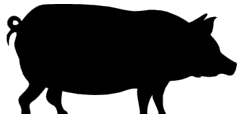
P50: proportion of antimicrobial tested in a survey with resistance higher than 50%

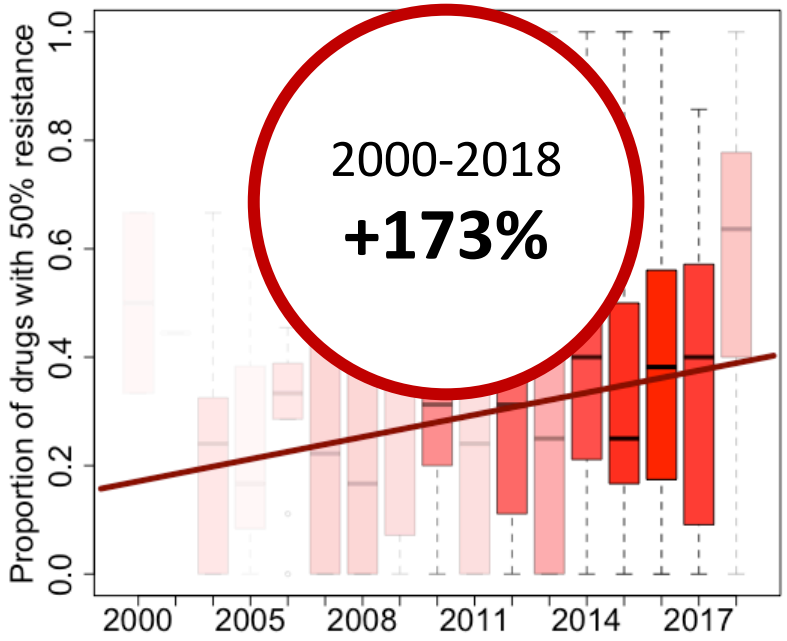
100 samples
Antimicrobial susceptibility testing on 9 drugs

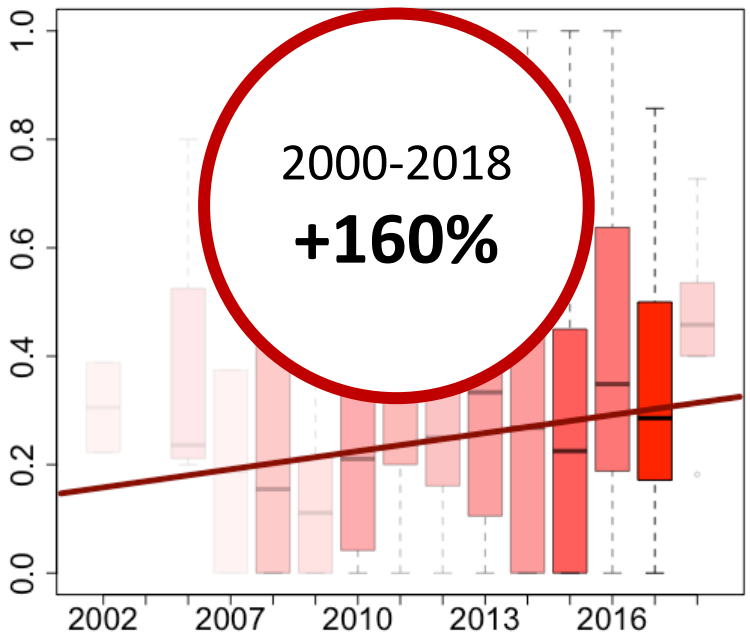


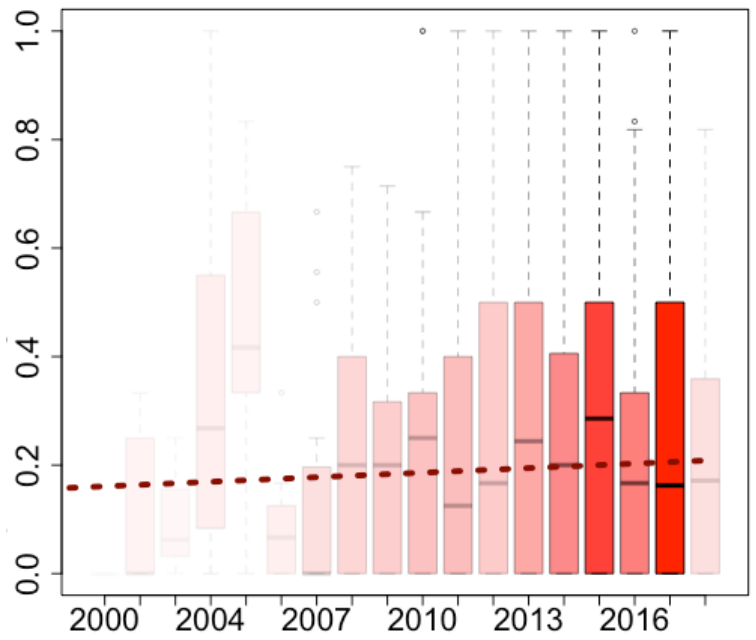
Global Trends (P50)











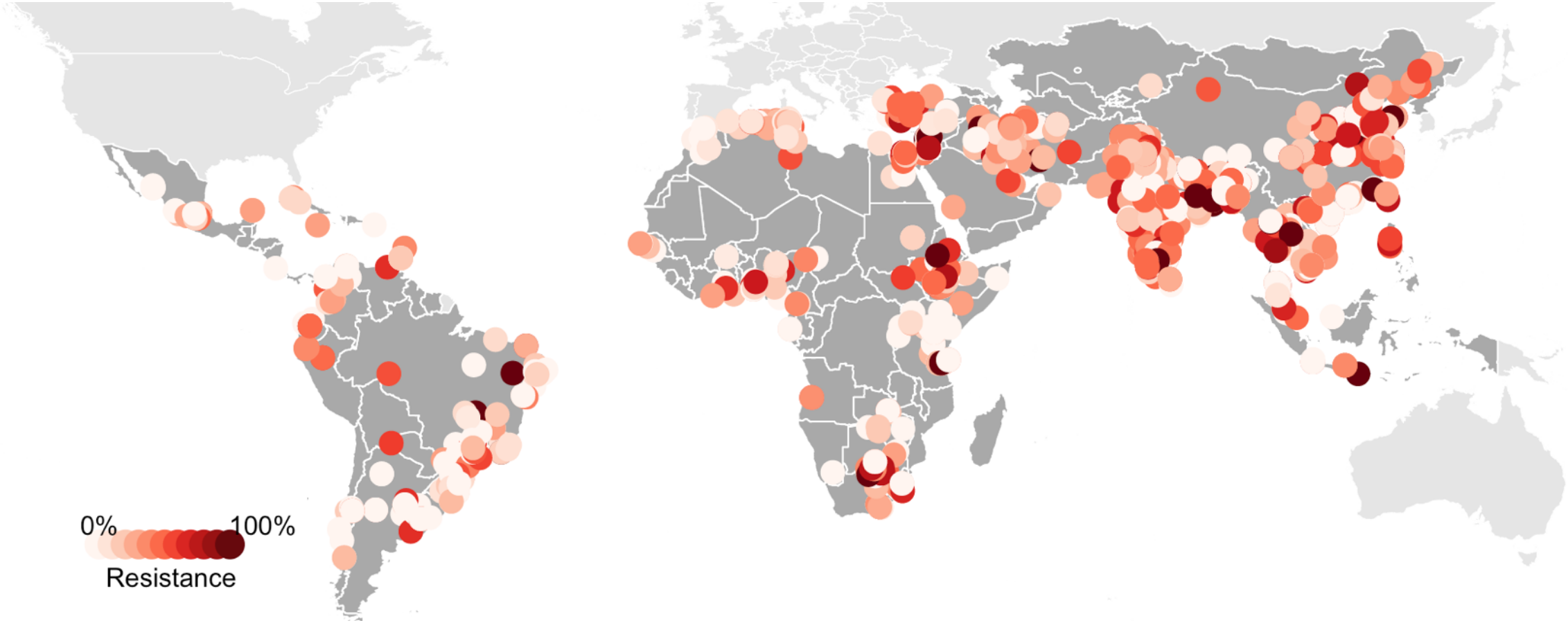
Van Boeckel* & Pires*, *Science* 2019.

Mapping Hotspots of Antimicrobial Resistance in Animals

Surveys
n = 901

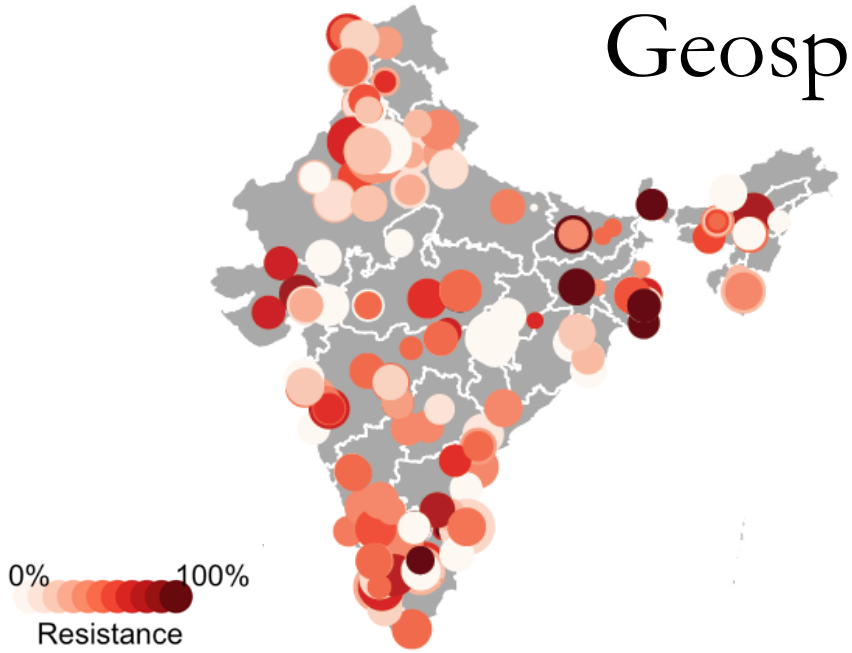
resistance rates
n = 12,933

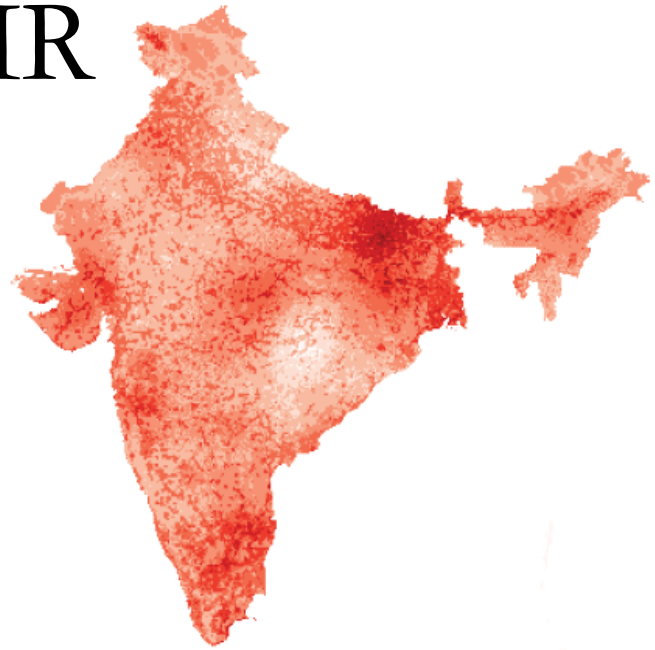
biological samples
n = 285,000



Van Boeckel* & Pires*, *Science* 2019.

Geospatial mapping of AMR

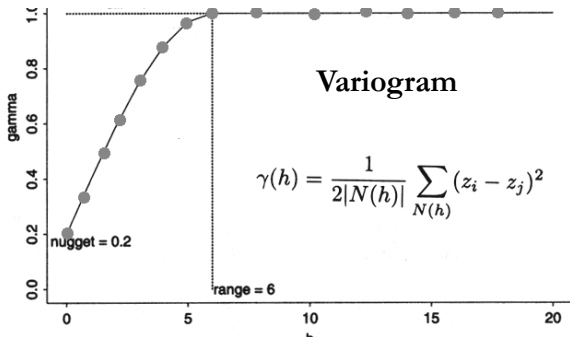




Resistance Here = **Resistance Nearby** + **Covariates (risk factors):** antimicrobial use, animal densities, temperature, travel time to cities, vegetation, etc…

$$P_{50}(x_0, y_0). = \sum_{i=1}^{n} \lambda_i \cdot P_{50}(x_i, y_i) + \sum_{k=1}^{P} \beta_k \cdot Cov_k(x_0, y_0)$$

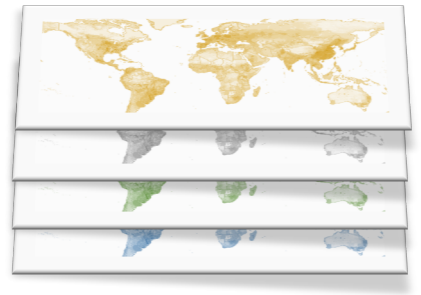
Step 2
Stacking with Universal Kriging



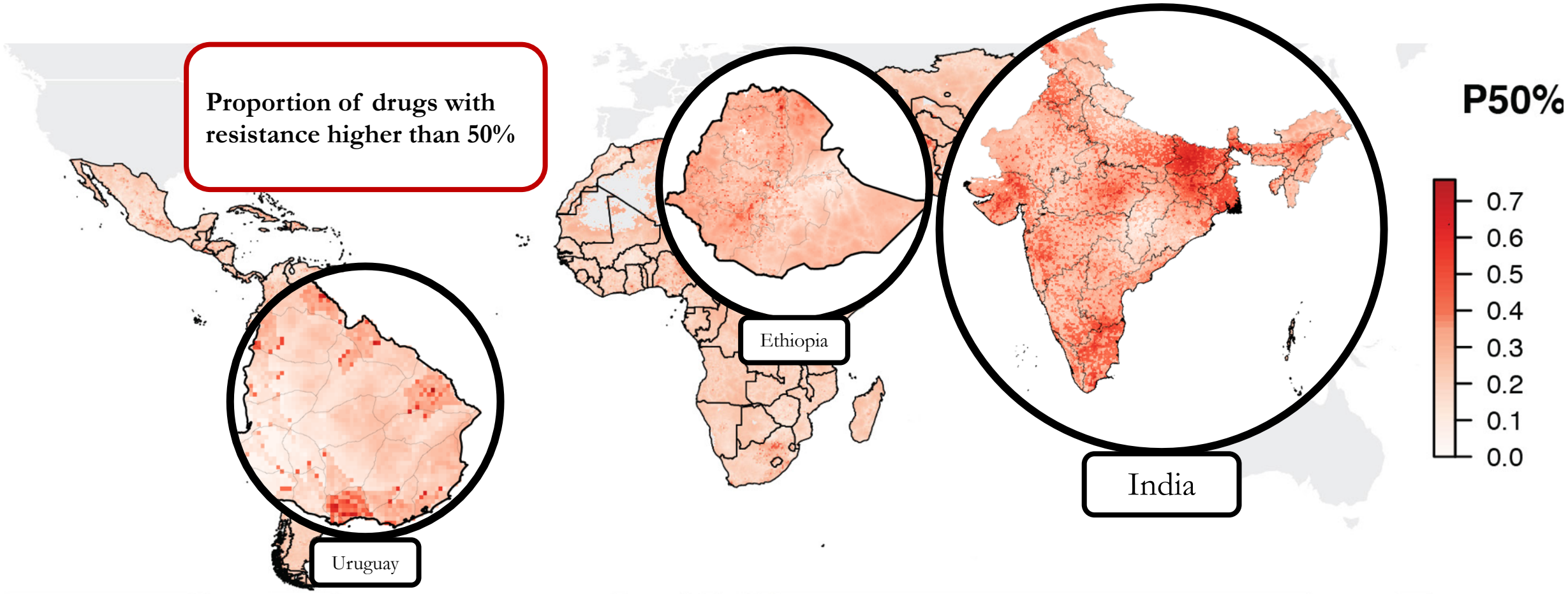
$Cov_1 = P_{Boosted\ Regression\ Trees}$
$Cov_2 = P_{Generalized\ Additive\ Model}$
$Cov_3 = P_{LASSO\ Regression}$

Step 1
trend models

Covariates



Hotspots of Antimicrobial Resistance in Animals



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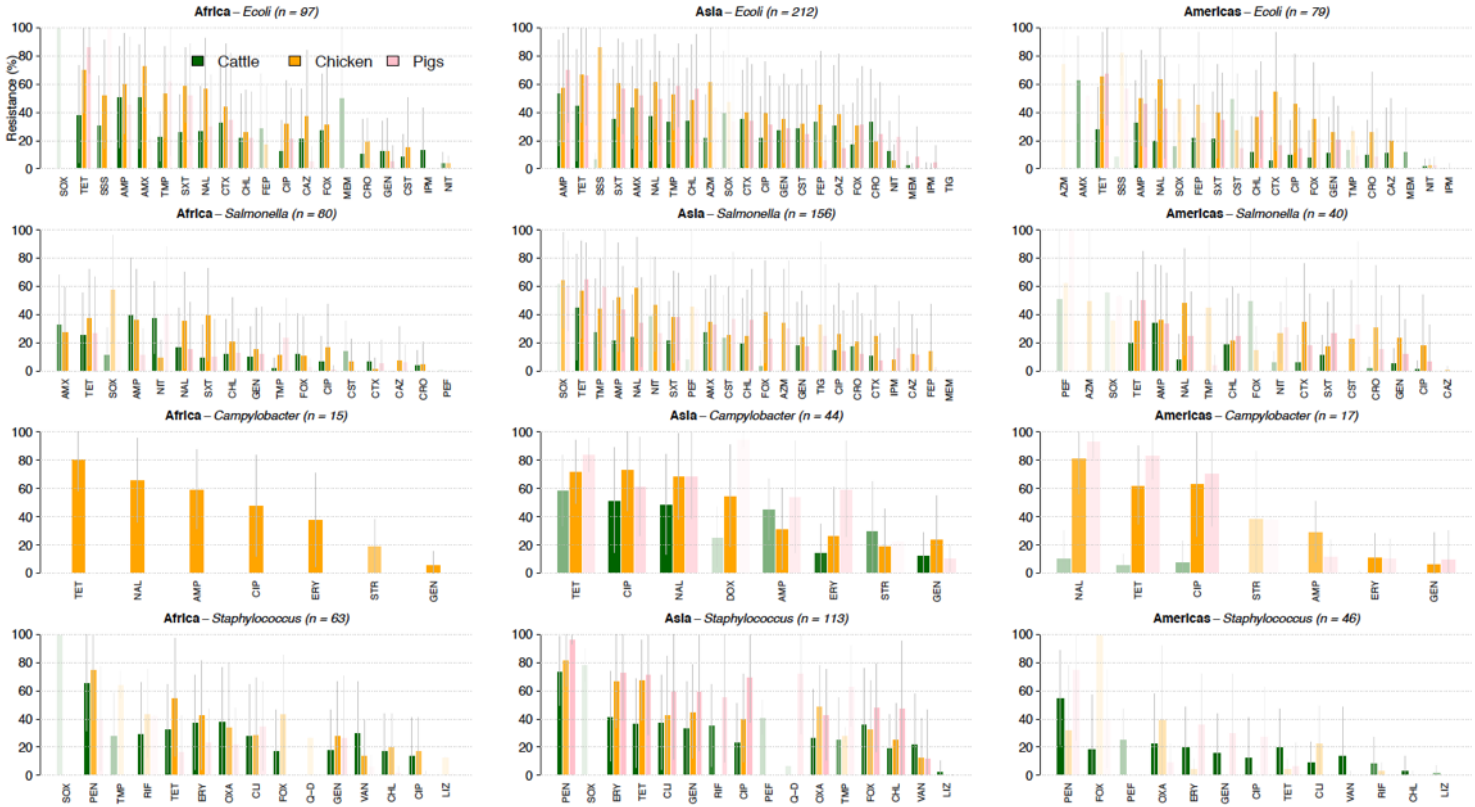
AMR per Drug/Pathogens Combinations



In LMICS, the highest resistance rates are associated with the most commonly used veterinary drugs

Tetracyclines, Sulfonamides, penicillin

In LMICs, medically important antimicrobials

Variations between animals species

Ciprofloxacin & Erythromycin (20-60%)

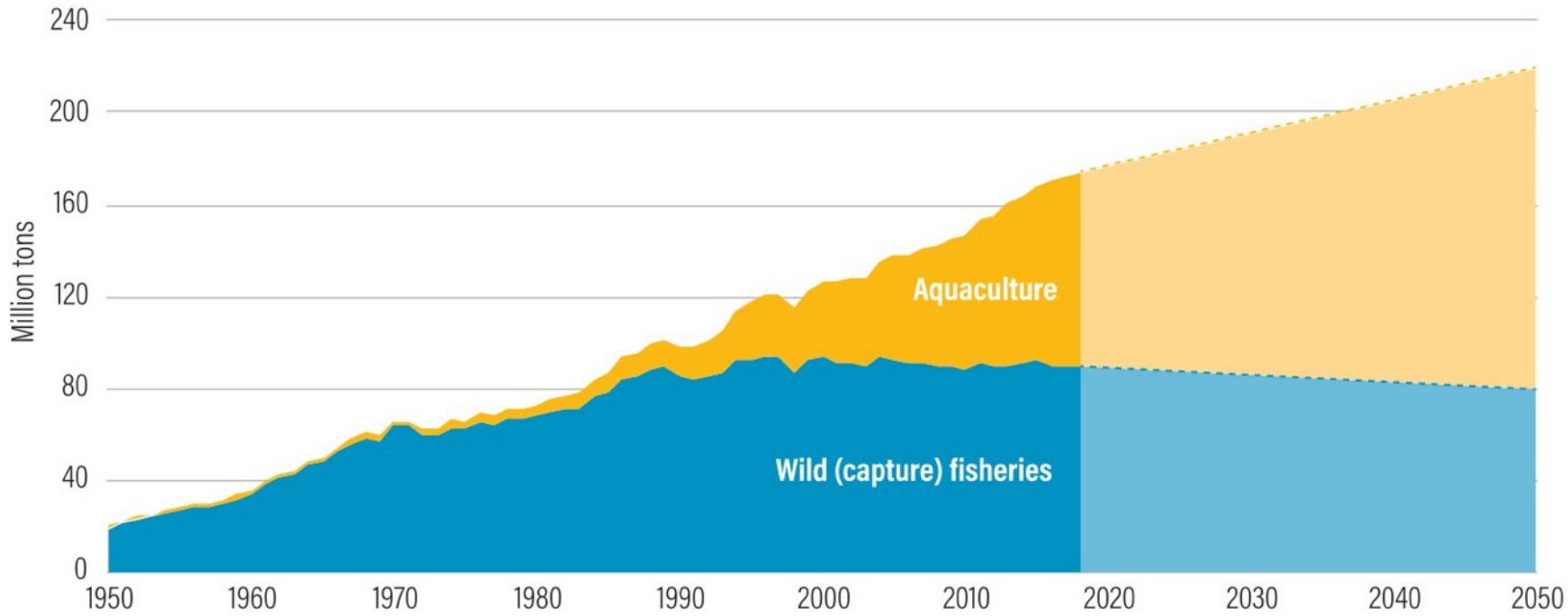
3rd and 4th Gen. Cephalosporins (10-40%)

Gentamicin (5-38%)

Carbapenems (<5%)

	Quinolones	**Gentamicin**
LMICs vs	20-60%.	5-38%
EU vs	60-64%.	2.4-8.9
US.	2.4-4.6%.	2-41%

Aquaculture



Production volumes from cultured fish has overtaken wild fisheries, and is growing faster terrestrial livestock as a source of animals protein.

Source: FAO

Aquaculture

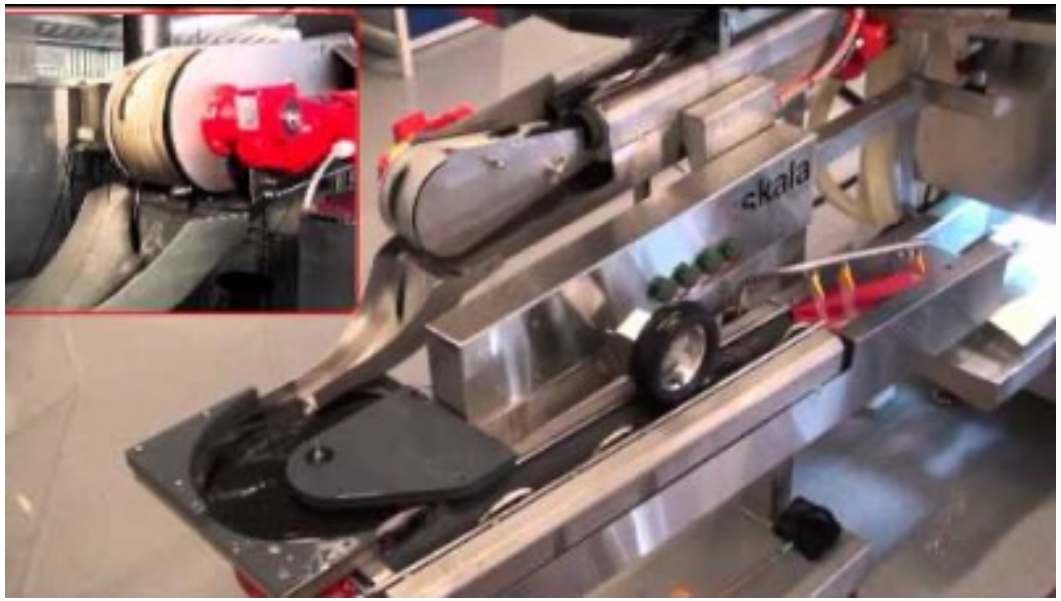
World Health Organization

Vaccinating salmon: How Norway avoids antibiotics in fish farming

October 2015

Norway has cut antibiotic use in salmon—one of the principal foods consumed in the country and a major export—to virtually zero. This has led to a flourishing industry and a reduction in the risk of antibiotic resistance in humans.

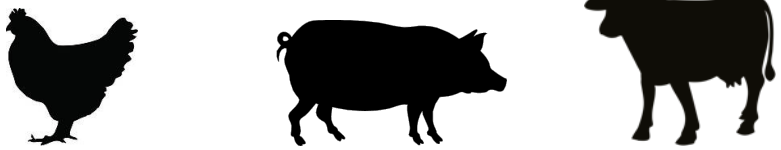
Aeromonas salmonicida
furunculosis



Terrestrial Animals vs Aquaculture

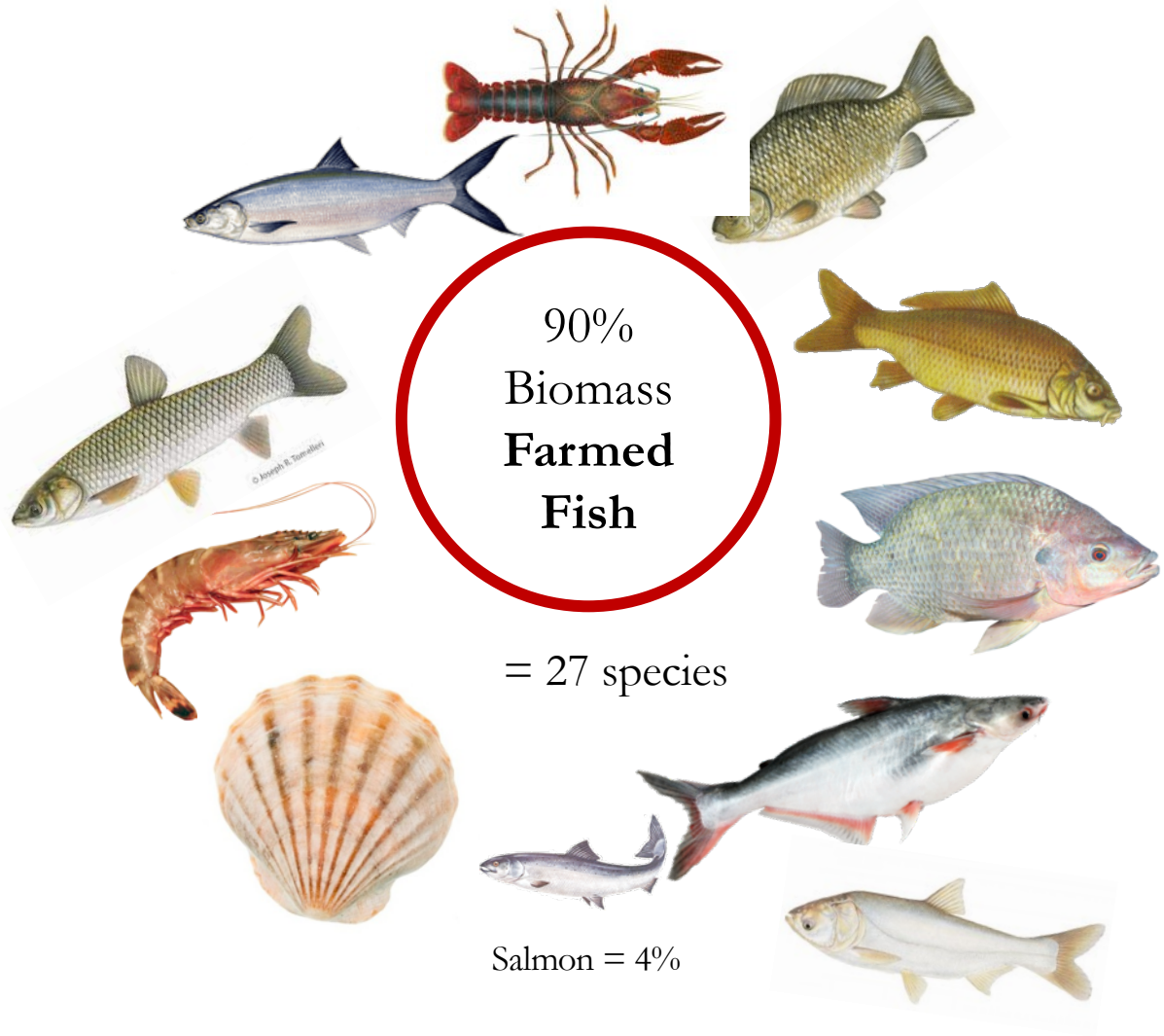
90%
Biomass
Livestock

= 3 species



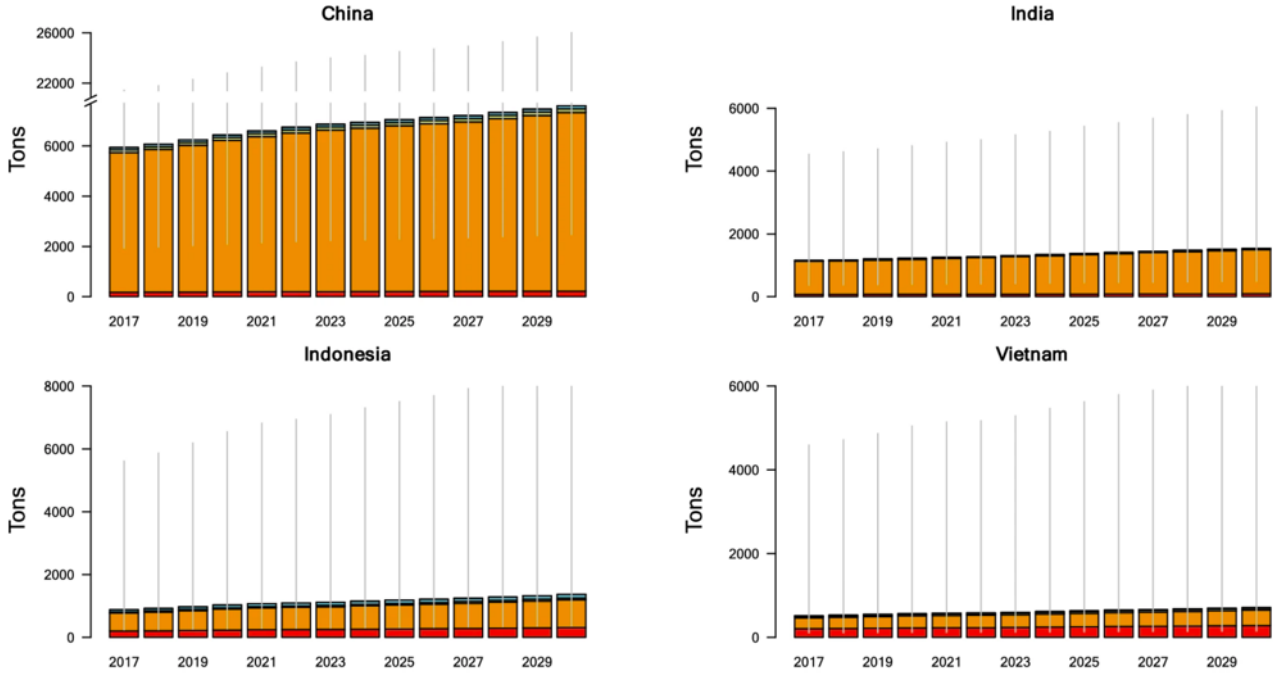
90%
Biomass
Farmed
Fish

= 27 species



Salmon = 4%

Aquaculture – Antimicrobial Use



Dan Schar
(USAID Bangkok)

146 Surveys

2 surveys

Catfish
Pooled
Salmon
Shrimp
Tilapia
Trout

Most commonly farmed fish in the world (China)

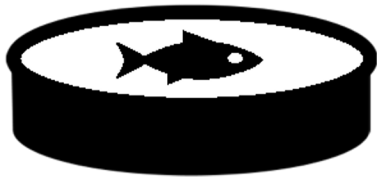
Grass Carp
Ctenopharyngodon idella

Silver Carp
Hypophthalmichthys molitrix

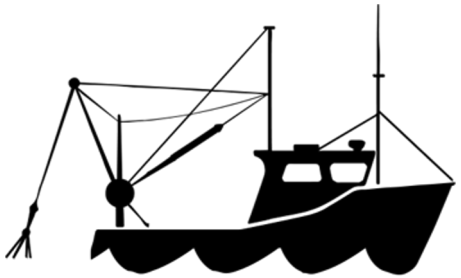
"We know that we know very little"

Schar et al 2020, Scientific Reports

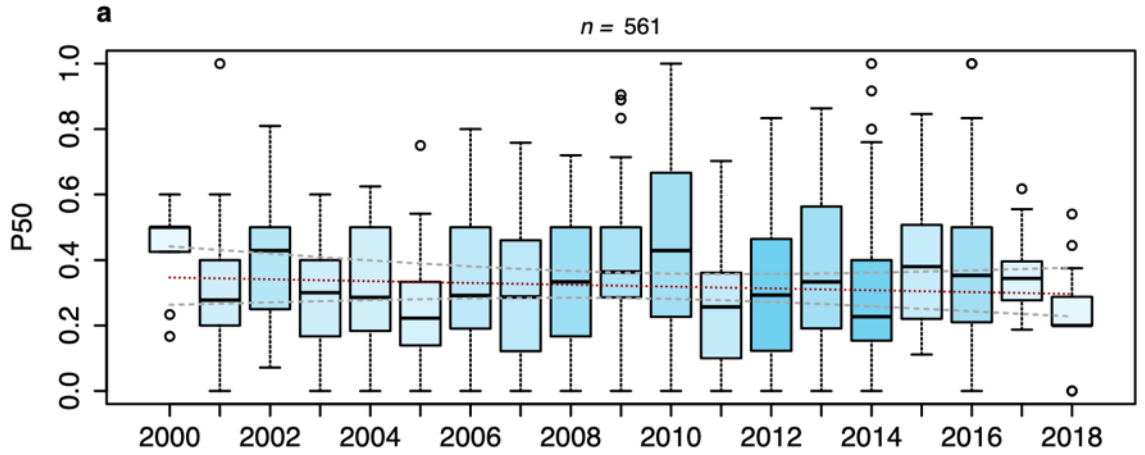
Aquaculture – Antimicrobial Resistance in Asia

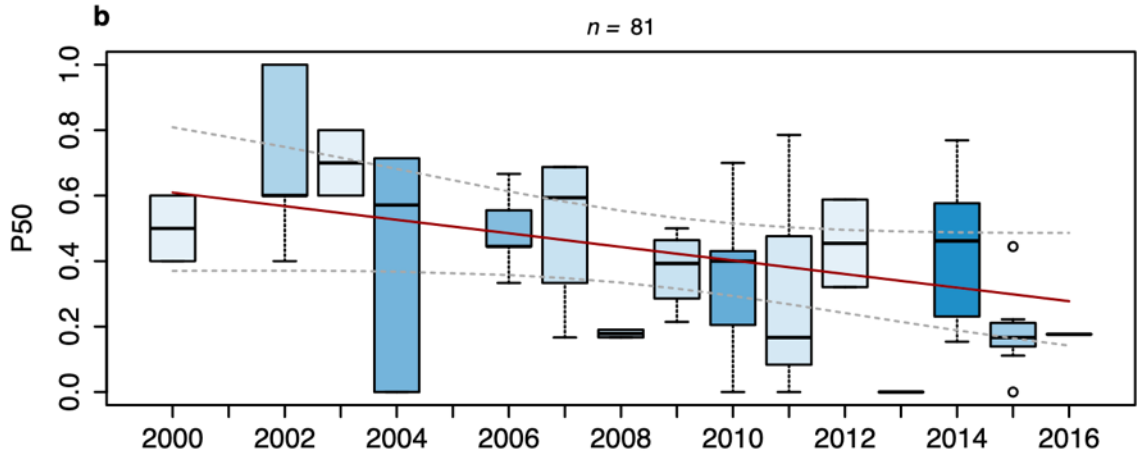


Cultured



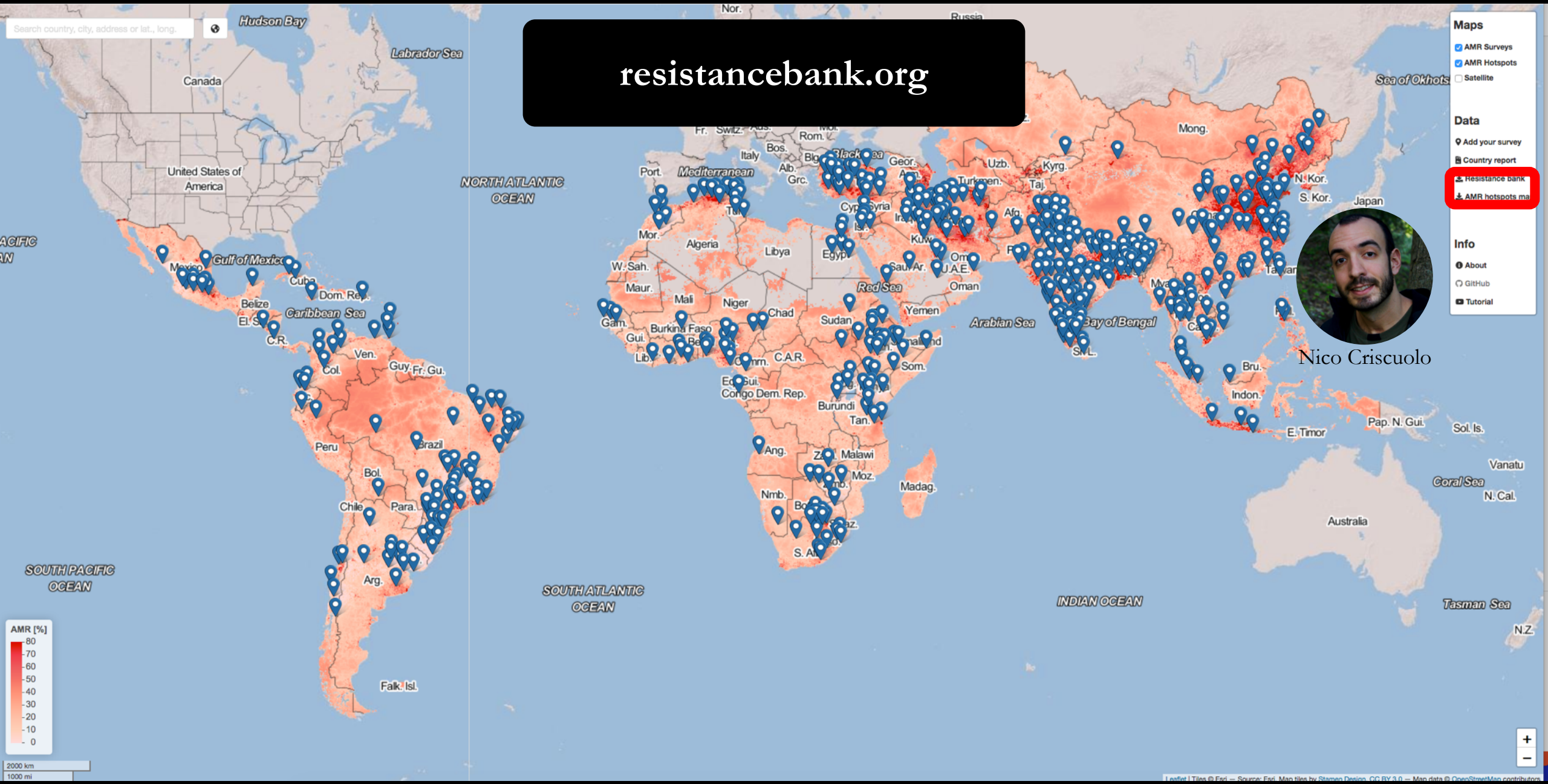
Captured



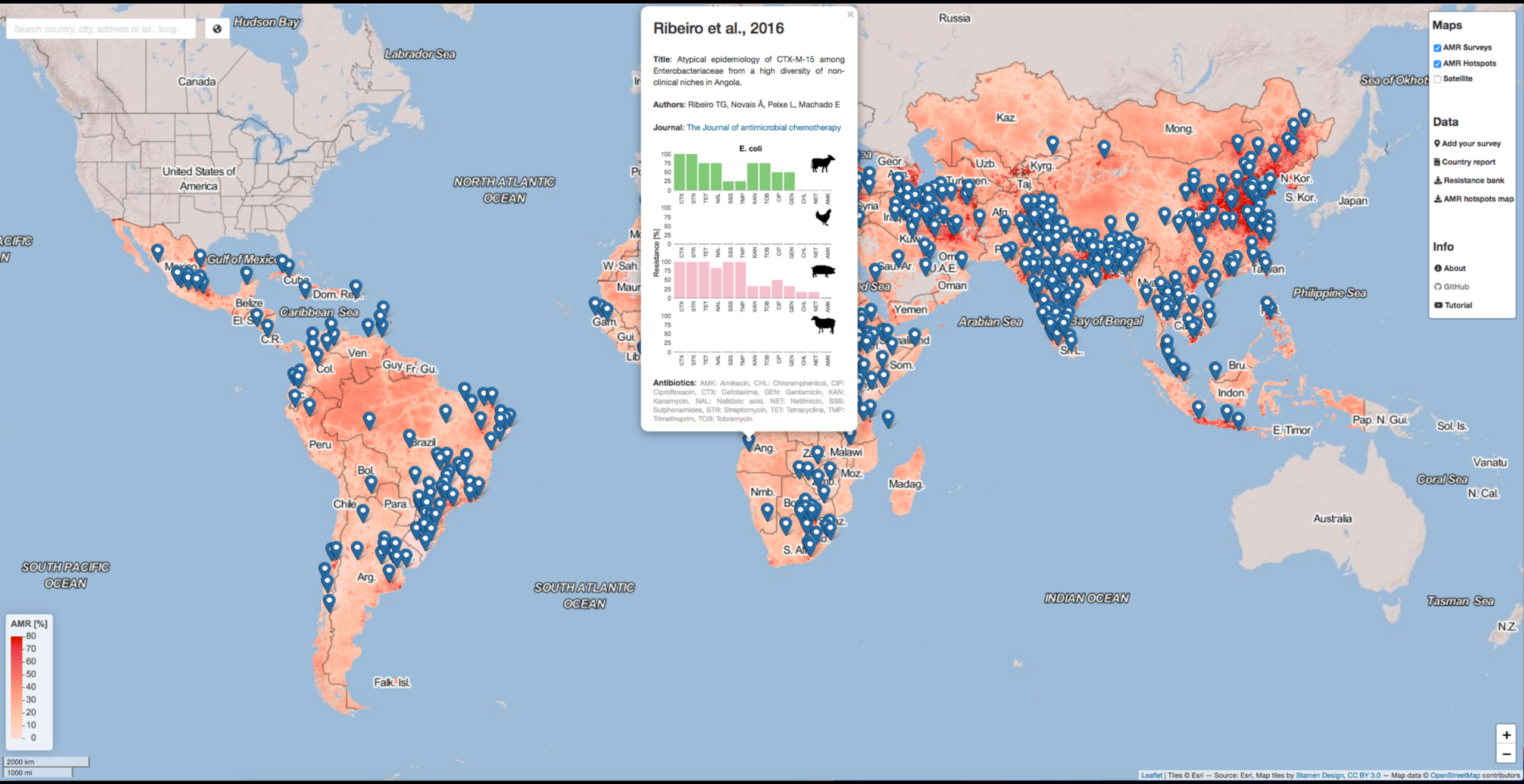


Schar et al, Submitted

resistancebank.org



Nico Criscuolo


Search country, city, address or lat., long.
Hudson Bay
Labrador Sea
Canada
United States of America
NORTH ATLANTIC OCEAN
Gulf of Mexico
Mexico
Cuba
Dom. Rep.
Belize
El S.
C.R.
Caribbean Sea
Ven.
Col.
Guy.
Fr. Gu.
Peru
Brazil
Bol.
Chile
Para.
Arg.
Falk. Isl.
SOUTH PACIFIC OCEAN
SOUTH ATLANTIC OCEAN
W. Sah.
Gam.
Gui.
Ang.
Nmb.
S. Af.
Malawi
Moz.
Madag.
INDIAN OCEAN
Russia
Kaz.
Mong.
Uzb.
Kyrg.
Taj.
Turkmen.
Geor.
Afg.
Kuw.
Saud. Ar.
U.A.E.
Oman
Yemen
Arabian Sea
Bay of Bengal
Sri L.
Som.
N. Kor.
S. Kor.
Japan
Taiwan
Philippine Sea
Indon.
Bru.
E. Timor
Pap. N. Gui.
Sol. Is.
Vanatu
Coral Sea
N. Cal.
Australia
Tasman Sea
N.Z.
Sea of Okhot
Ribeiro et al., 2016
Title: Atypical epidemiology of CTX-M-15 among Enterobacteriaceae from a high diversity of non-clinical niches in Angola.
Authors: Ribeiro TG, Novais Â, Peixe L, Machado E
Journal: The Journal of antimicrobial chemotherapy
E. coli
Resistance [%]
CTX STR TET NAL SSS TMP KAN TOB CIP GEN CHL NET AMK
Antibiotics: AMK: Amikacin, CHL: Chloramphenicol, CIP: Ciprofloxacin, CTX: Cefotaxime, GEN: Gentamicin, KAN: Kanamycin, NAL: Nalidixic acid, NET: Netilmicin, SSS: Sulphonamides, STR: Streptomycin, TET: Tetracycline, TMP: Trimethoprim, TOB: Tobramycin
Maps
AMR Surveys
AMR Hotspots
Satellite
Data
Add your survey
Country report
Resistance bank
AMR hotspots map
Info
About
GitHub
Tutorial
AMR [%]
80 70 60 50 40 30 20 10 0
2000 km
1000 mi
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Search country, city, address or lat., long.

Hudson Bay
Labrador Sea
Canada
United States of America
NORTH ATLANTIC OCEAN
Gulf of Mexico
Mexico
Cuba
Dom. Rep.
Belize
El S.
Caribbean Sea
C.R.
Ven.
Guy.
Fr. Gu.
Col.
Ec.
Peru
Brazil
Bol.
Chile
Para.
Arg.
SOUTH PACIFIC OCEAN
Falk. Isl.
Sol. Is.
Vanatu
N. Cal.
Tasman Sea
N.Z.

AMR [%]
80
70
60
50
40
30
20
10
0

2000 km
1000 mi

Select country

India (IND)

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Antimicrobial resistance in animals in India

resistancebank.org

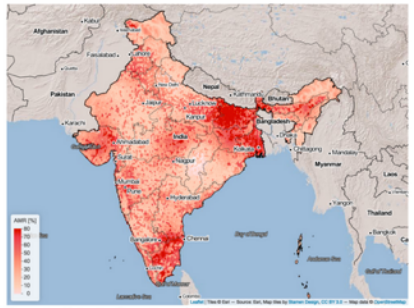

Figure 1. Hotspots. Percentage of antimicrobial drugs with resistance higher than 50%, Van Boeckel & Pires, Global Trends in Antimicrobial Resistance in Animals in Low- and Middle-Income Countries, Science 365, (2019).

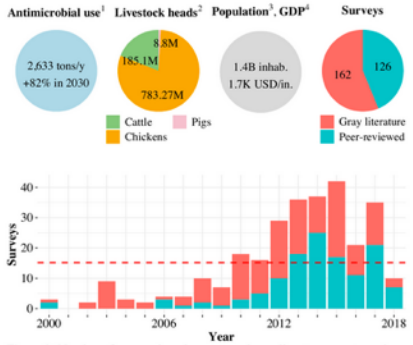

Figure 2. Number of peer-reviewed surveys and gray literature reports, and average number of point prevalence surveys per year (red line).

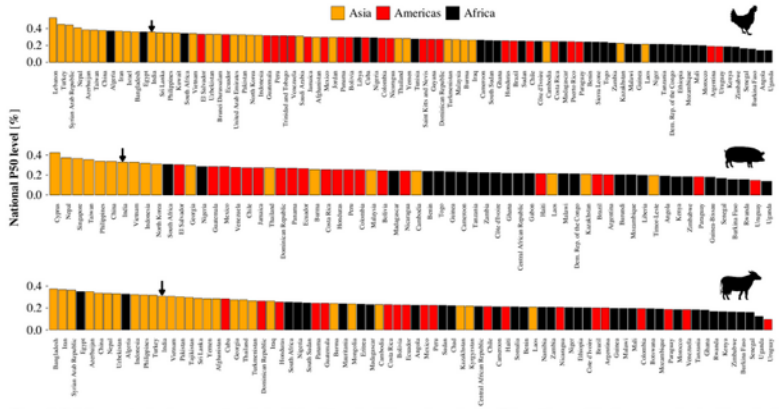

Figure 3. Relative country-level exposure to antimicrobial resistance in chickens, pigs and cattle. This metric quantifies the exposure levels of the animal populations. The analysis was restricted to countries with at least 10 million chicken, 250,000 pigs, and 500,000 cattle heads.

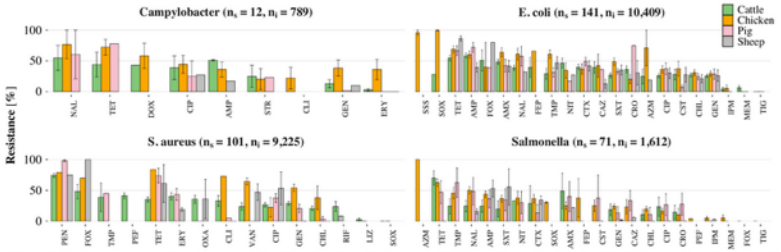

Figure 4. Resistance rates, number of surveys (n_s) and total number of isolates tested (n_i) by pathogen listed by the AGISAR consortium. See protocol S1 in Van Boeckel & Pires, Science 365, (2019).

[1]Data updated to 2013. Source: Van Boeckel et al., Reducing antimicrobial use in food animals, Science 357, 1350 - 1352 (2017).
[2]Data updated to 2017. Source: FAOSTAT.
[3]Data updated to 2018. Source: World Development Indicators.
[4]Data updated to 2016. Source: World Bank Group.

Disclaimer

The information in this country-report result from the aggregation, and extrapolation of data from surveys conducted by independent scientists. It does not reflect the official positions of a country's veterinary authorities on its antimicrobial resistance levels in animals. The detailed methodology and data source for this country-report are presented in Van Boeckel & Pires, 2019.

Maps

- AMR Surveys
- AMR Hotspots
- Satellite

Data

- Add your survey
- Country report
- Resistance bank
- AMR hotspots map

Info

- About
- GitHub
- Tutorial

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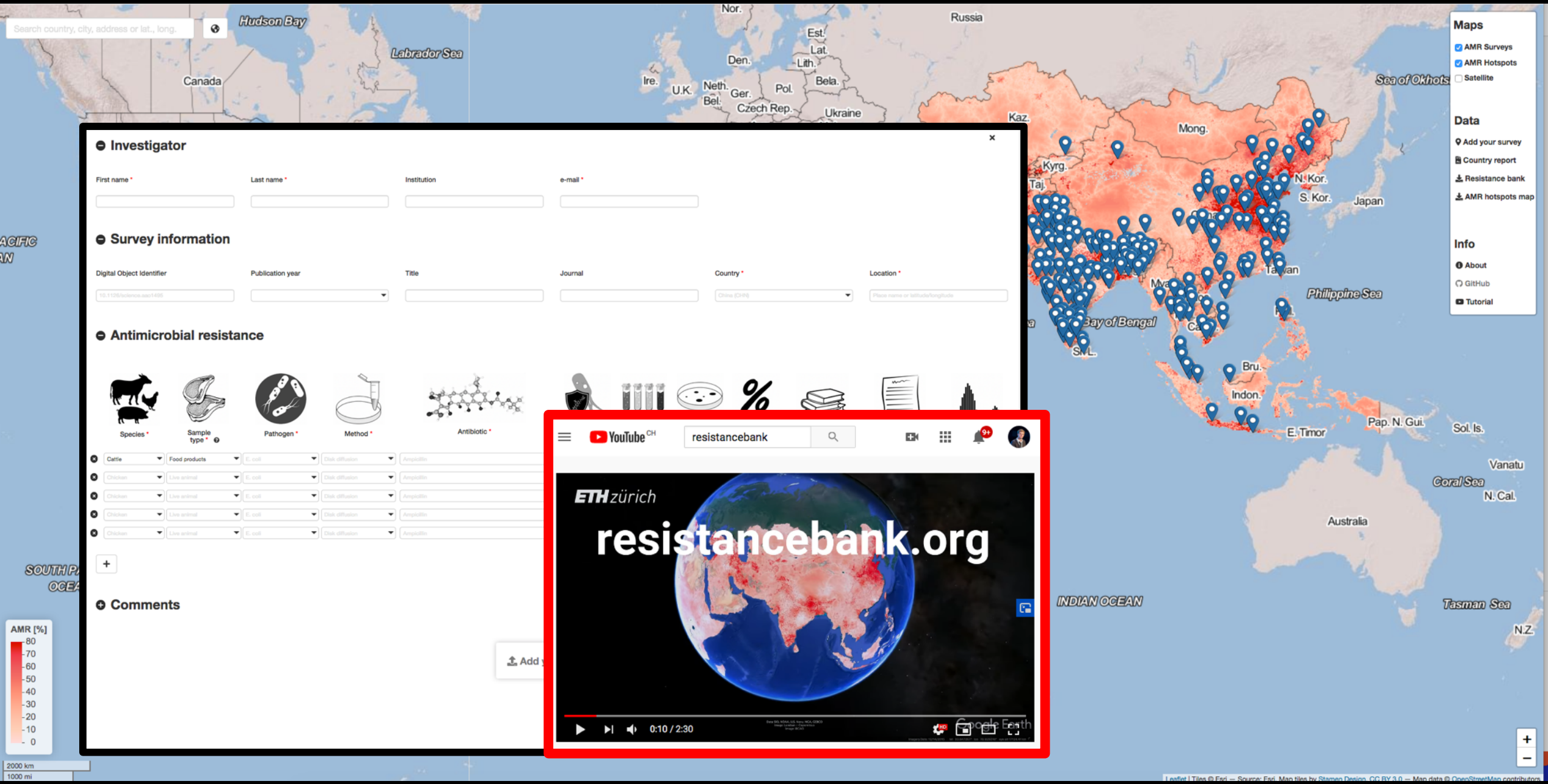
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Nor.
Russia
Est.
Lat.
Lith.
Den.
Ire.
U.K.
Neth.
Bel.
Ger.
Pol.
Bela.
Czech Rep.
Ukraine
Kaz.
Mong.
Kyrg.
Taj.
N. Kor.
S. Kor.
Japan
Sea of Okhots
Taiwan
Philippine Sea
Bay of Bengal
Sri L.
Bru.
Indon.
E. Timor
Pap. N. Gui.
Sol. Is.
Vanatu
Coral Sea
N. Cal.
Australia
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Last name *
Institution
e-mail *
Survey information
Digital Object Identifier
Publication year
Title
Journal
Country *
Location *
Antimicrobial resistance
Species *
Sample type *
Pathogen *
Method *
Antibiotic *
Cattle
Food products
Chicken
Live animal
E. coli
Disk diffusion
Ampicillin
Comments
Add
AMR [%]
80
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2000 km
1000 mi
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resistancebank
ETH zürich
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Thank You