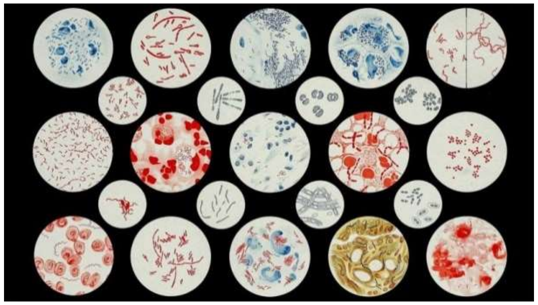
Hans-Peter Kohler

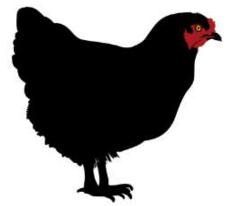
MD, MACP

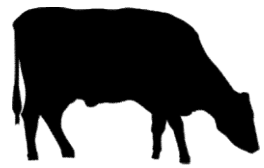
Secretary General, International Society of Internal Medicine

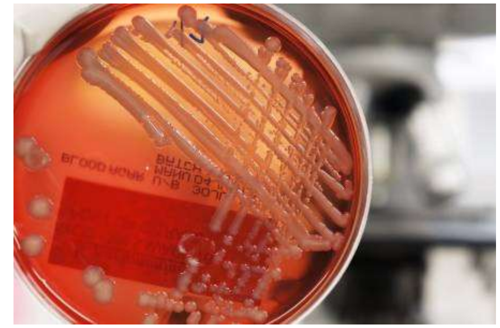
- **Prof. Kohler** was Director and Chief Physician of the Department of Internal Medicine, Tiefenau Hospital, Inselgruppe AG, and Head of "Experimental Haemostasis Group" at the Department of Clinical Research, University of Bern, Switzerland, until he became a full time politician in 2018.
- Previously, he was Head of Internal Medicine at the Department of Trauma and Emergency Medicine at the University Hospital of Bern.
- In 1996, he was awarded a Research Fellowship at the University of Leeds, England, at the Unit of Molecular Vascular Medicine to study the role of blood coagulation factor XIII gene and its relationship to cardio- and cerebrovascular disease and to investigate the interactions between coagulation and fibrinolysis and the insulin resistance syndrome. Prof. Kohler is Secretary General of the International Society of Internal Medicine (ISIM).
- He was involved in a major merging project of public teaching hospitals around Bern, the capital of Switzerland, and in projects concerning the further development of primary health care services. Prof. Kohler published over 100 papers and was involved in several national and international research projects. Research interests are the role of coagulation Factor XIII in vascular disease, genetics of FXIII in regard to haemophilia and thrombosis, and the impact of common genetic variants on cardiovascular risk.
- Dr. Kohler is a Master of the American College of Physicians. He serves as Member of Parliament for the County of Bern with a focus on health politics since many years and was elected as a full-time member of a local government in 2017 managing the department for education and social affairs.

Antimicrobial resistance and food production









Hans Peter Kohler, MD, MACP

Professor of Medicine,

Switzerland

Secretary General,

International Society of Internal Medicine (ISIM)

Aim of the lecture & topics

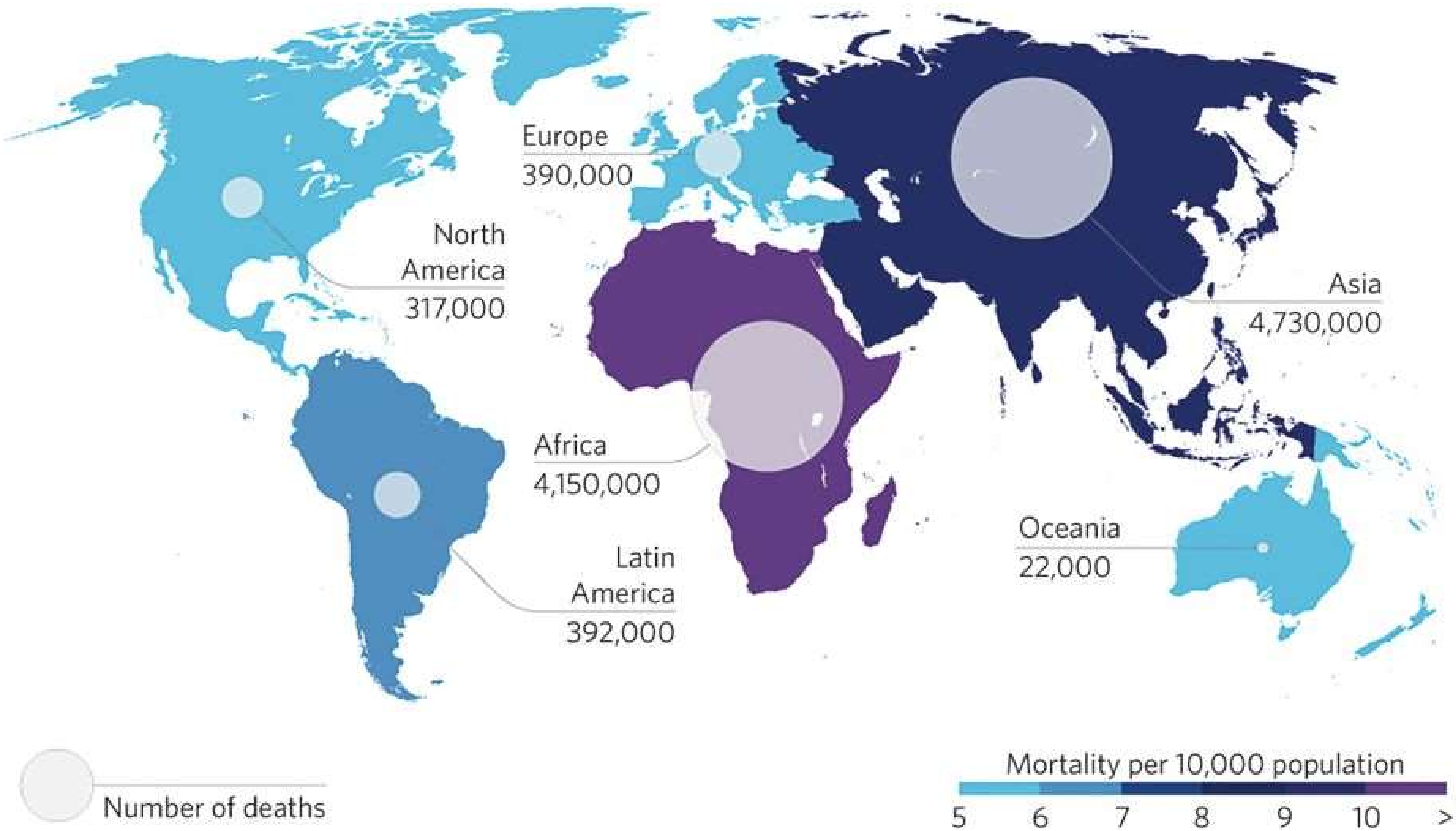
-Introduction to **an unusual medical congress topic**…

-Why does (or should) food production influence our clinical decision making?

-Range of use of antibiotics in food production

-Implications for physicians and patients

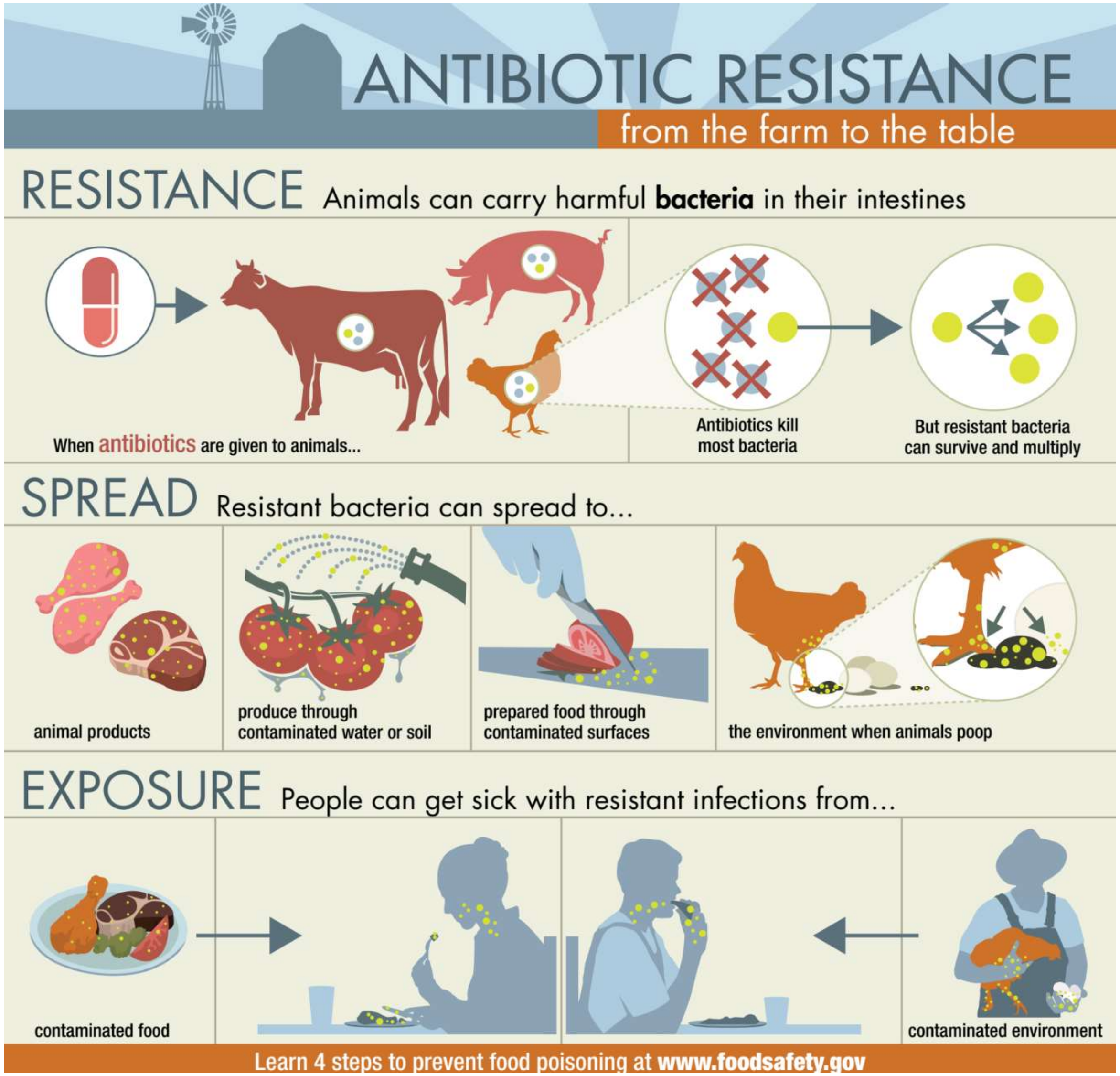
Death toll of antimicrobial resistance by 2050



Nature Microbiology volume 1, Article number: 16187 (2016)

The role of the food industry

From the farm to the table …



www.cdc.gov/foodsafety/from-farm-to-table.html

About 1 in 5
AMR infections
are caused by germs
from **food** and
animals…

Source: Antibiotic Resistant Threats in the US, 2013

Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis

Karen L Tang, Niamh P Caffrey, Diego B Nóbrega, Susan C Cork, Paul E Ronksley, Herman W Barkema, Alicia J Polachek, Heather Ganshorn, Nishan Sharma, James D Kellner, William A Ghali

Message:

Antibiotics used in food-producing animals **are closely related** to those used in human medicine and can select for resistance in these animals.

Cross-species transmission of resistant **bacteria** or resistant **genetic elements** from animals to humans **can and does occur**.

Lancet Planet Health 2017;
1: e316–27

POLICY FORUM

GLOBAL HEALTH

Reducing antimicrobial use in food animals

Consider user fees and regulatory caps on veterinary use

More than 73% of all antimicrobials sold in the world are used in animals!

Van Boeckel et al 2017, Science.

29 SEPTEMBER 2017 • VOL 357 ISSUE 6358 sciencemag.org SCIENCE

Global trends in antimicrobial use in food animals

Thomas P. Van Boeckel[a,1], Charles Brower[b], Marius Gilbert[c,d], Bryan T. Grenfell[a,e,f], Simon A. Levin[a,g,h,1], Timothy P. Robinson[i], Aude Teillant[a,e], and Ramanan Laxminarayan[b,e,j,1]

[a]Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08544; [b]Center for Disease Dynamics, Economics & Policy, Washington, DC 20036; [c]Universite Libre de Bruxelles, B1050 Brussels, Belgium; [d]Fonds National de la Recherche Scientifique, B1000 Brussels, Belgium; [e]Princeton Environmental Institute, Princeton, NJ 08544; [f]Fogarty International Center, National Institutes of Health, Bethesda, MD 20892; [g]Beijer Institute of Ecological Economics, 10405 Stockholm, Sweden; [h]Resources for the Future, Washington, DC 20036; [i]International Livestock Research Institute, 00100 Nairobi, Kenya; and [j]Public Health Foundation of India, New Delhi 110070, India

Contributed by Simon A. Levin, February 18, 2015 (sent for review November 21, 2014; reviewed by Delia Grace and Lance B. Price)

PNAS | **May 5, 2015** | vol. 112 | no. 18 | **5649–5654**

Two main messages:

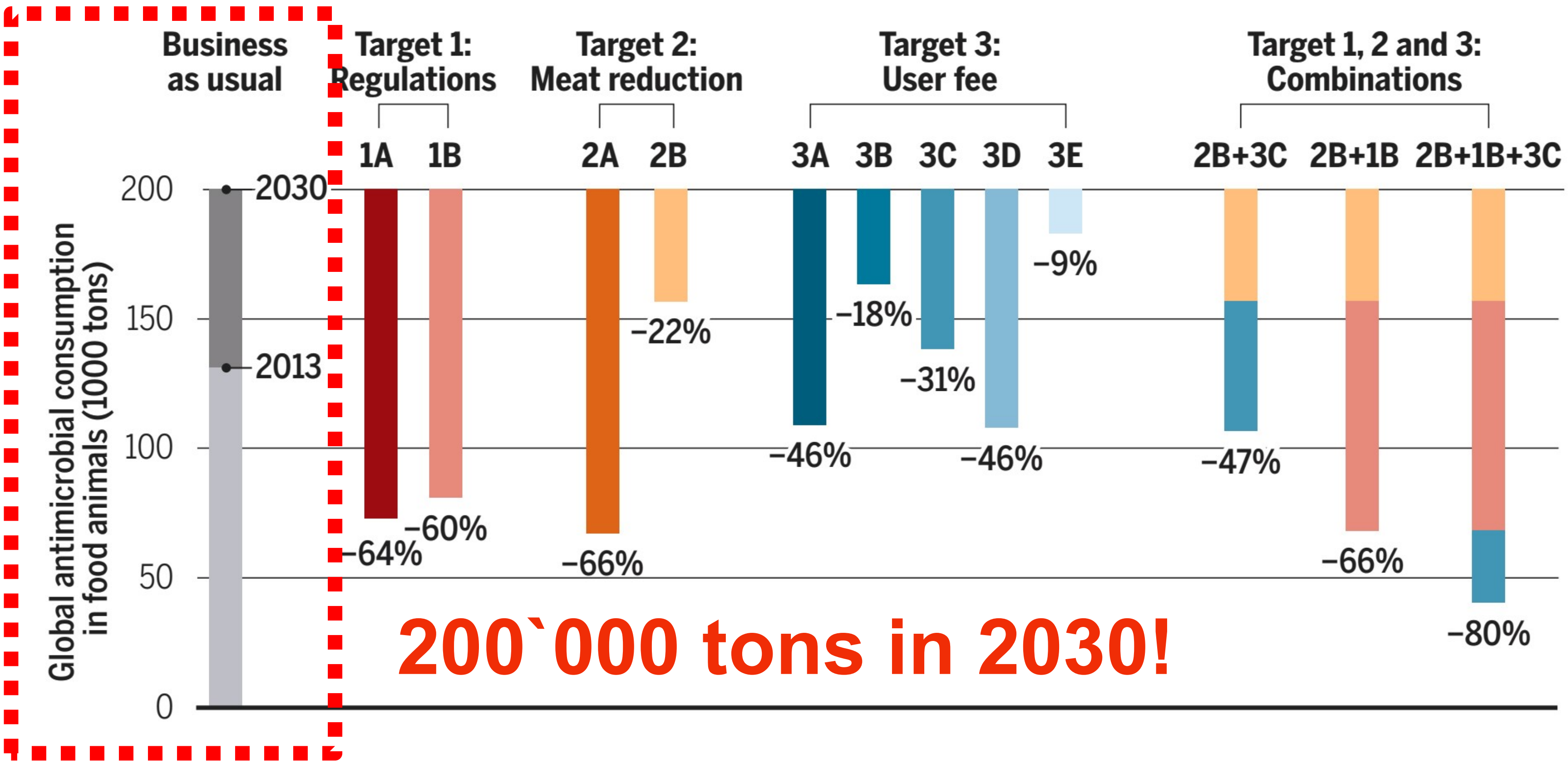
Antimicrobials contribute to the spread of drug-resistant pathogens in **both** livestock and humans, posing a significant public health threat.

Antimicrobial consumption will **rise by 67% by 2030,**
and nearly double in Brazil, Russia, India, China, and South Africa

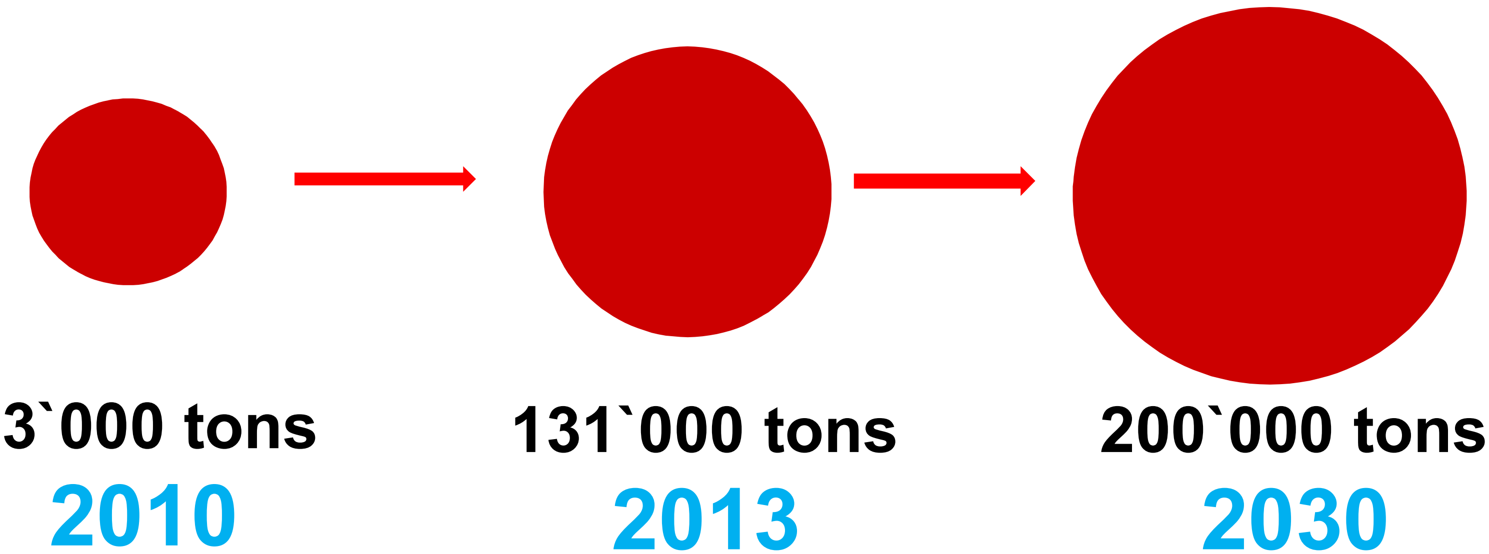
Global consumption in food animals

Antimicrobial consumption in food animals by 2030

Business as usual and intervention policies are shown. Revenue ranges are estimated for different fee rates (TR) and price elasticities of demand (PED). For 3C, 3D, and 3E, PEDs are derived from time series of imports of veterinary antimicrobials in each country (Protocol S4); the global average PED was -0.95. See supplementary materials for discussions of uncertainty in all estimates shown in figures. PCU, population correction unit.



Global consumption of all antimicrobials in food



-Humans and animals use comparable amounts of antimicrobials [118 mg/PCU and 133 mg/kg, respectively(14)]

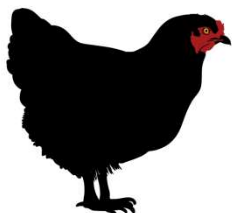
-Since the biomass of animals raised for food exceeds by far the biomass of humans, new resistant mutations are more likely to arise in animals

-Unlike in humans, antimicrobial use in animals is primarily intended for growth promotion and mass prophylaxis

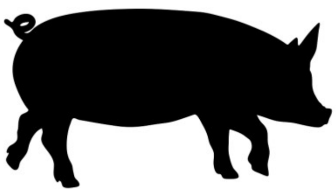
Van Boeckel et al 2017, Science.

*(Antimicrobial consumption per population correction unit (**PCU**))*

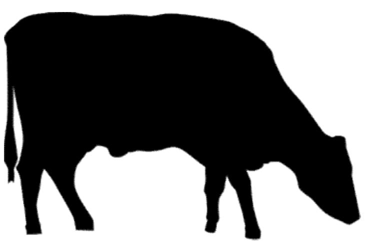
Global average annual consumption of antimicrobials per kilogram of animal produced



148mg to produce 1kg of chicken



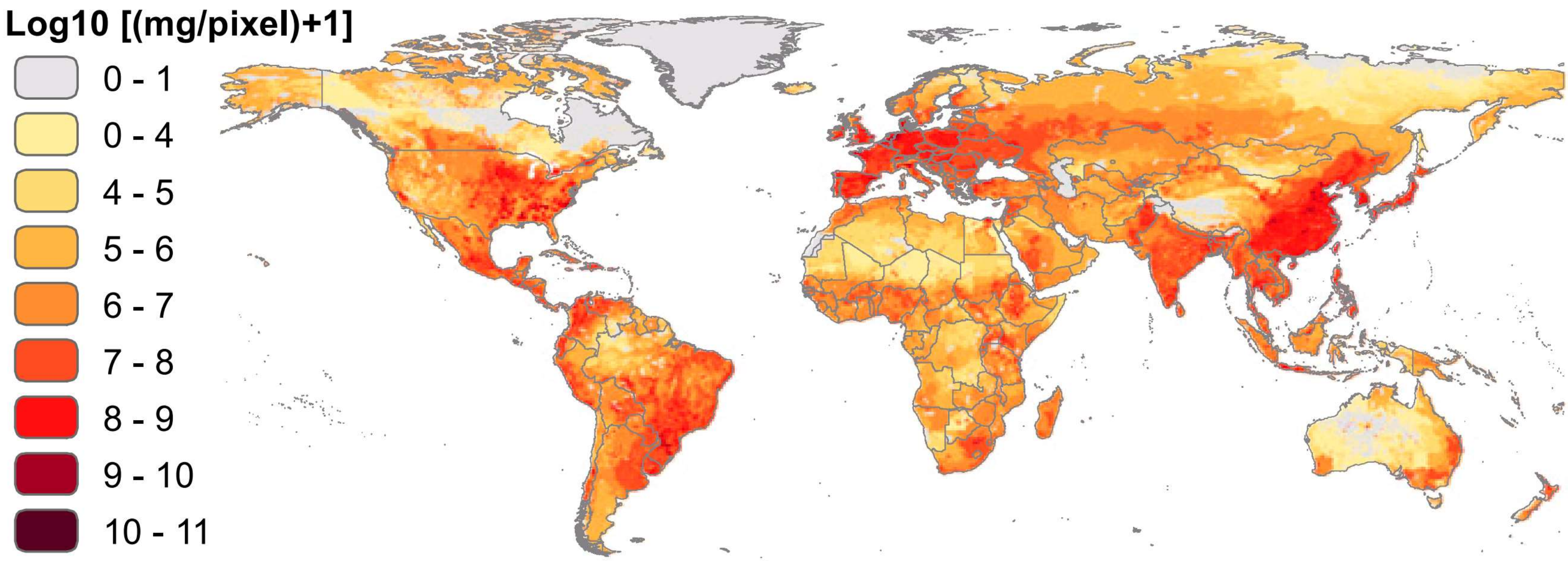
172mg to produce 1kg of pork



45mg to produce 1kg of beef

Thomas P. Van Boeckel et al. PNAS | May 5, 2015 | vol. 112 | no. 18 | 5649–5654

Antimicrobial consumption hotspots



PNAS | May 5, 2015 | vol. 112 | no. 18 | 5649–5654

-Europe!

-Southeast coast of **China**, the Red River delta in Vietnam, the northern suburbs of Bangkok, and the south coast of India

-**South of Brazil**, the suburbs of Mexico City, and midwestern and southern United States

-Nile delta and the city of **Johannesburg** and its surrounding townships

Substances in use in food animals

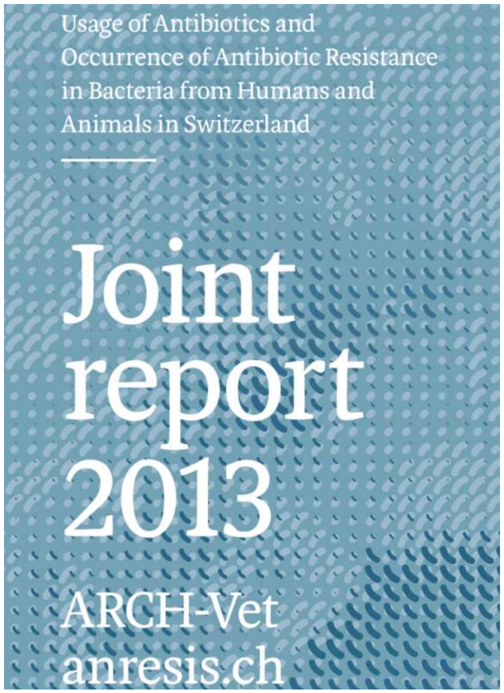
TABLE 2: Substances with prescribed residue limits (MRL) in case of use in food animals

Active substance	Species/Matrix	MRPL	Comments
Amoxicillin	All food producing species (Muscle/Fat/Liver/Kidney/ Milk)	100 µg/kg	For finfish the muscle MRL relates to 'muscle and skin in natural proportions'. MRLs for fat, liver and kidney do not apply to finfish. For porcine and poultry species the fat MRL relates to 'skin and fat in natural proportions'. Not for use in animals from which eggs are produced for human consumption.
Sulfonamides	All food-producing species	100 µg/kg	MRPL determined
Sarafloxacin	Chicken (skin and far/liver	10 µg/kg 100 µg/kg	Working limit determined
Tetracycline	All species/Muscle	100 µg/kg	This MRL refers to the total of the parent drug and its 4 epimers
Oxyetracycline	All species/Muscle	100 µg/kg	This MRL refers to the total of the parent drug and its 4 epimers
Oxolinic acid	All species/Muscle	100 µg/kg	In case of fish, MRL for muscle means muscle and skin in natural proportion
Chlortetracycline	All food-producing species/ muscle	100 µg/kg	In case of fish, MRL for muscle means muscle and skin in natural proportion
Enamectin B1a	Fin fish/muscle	100 µg/kg	In case of fish, MRL for muscle means muscle and skin in natural proportion
Flumequine	Fin fish/muscle	600 µg/kg	In case of fish, MRL for muscle means muscle and skin in natural proportion
Deltamethrin	Fin fish	10 µg/kg	In case of fish, MRL for muscle means muscle and skin in natural proportion
Enrofloxacin (sum of enrofloxacin and ciprofloxacin)	Fin fish/muscle	100 µg/kg	In case of fish, MRL for muscle means muscle and skin in natural proportion

Substances in use

Erythromycin A	Fin fish/muscle	100 µg/kg
Florfenicol (sum of florfenicol and its metabolites measured as florfenicol-amine)	Fin fish/muscle	1000 µg/kg
Paramomycin	Fin fish/muscle	500 µg/kg
Thiamphenicol	Fin fish/muscle	50 µg/kg
Tilmicosin	Fin fish/muscle	50 µg/kg
Trimethroprim	Fin fish/muscle	50 µg/kg
Tylosin A	Fin fish/muscle	100 µg/kg

Occurrence of resistance in Escherichia coli
-Data from Switzerland-



Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Swiss Confederation

Federal Department of Home Affairs FDHA
Federal Food Safety and Veterinary Office FSVO
Animal Health

Federal Office of Public Health FOPH
Communicable Diseases

The report emphasizes the importance of monitoring antimicrobial drug usage and resistance **in both human and veterinary medicine**.

Occurrence of resistance in Escherichia coli from broilers

Table 9. e: Occurrence of resistance in *Escherichia coli* from broilers.

Broilers: *Escherichia coli* (N=189)			**2013**
Antimicrobials	**n**	**%**	**95% CI**
Ampicillin	48	25.4	19.7–32.0
Cefotaxime	1	0.5	0.1–2.9
Ceftazidime	1	0.5	0.1–2.9
Chloramphenicol	2	1.1	0.3–3.8
Ciprofloxacin	67	35.4	29–42.5
Colistin	0	0	0.0–2.0
Florfenicol	0	0	0.0–2.0
Gentamicin	1	0.5	0.1–2.9
Kanamycin	5	2.6	1.1–6.0
Nalidixic acid	65	34.4	28.0–41.1
Streptomycin	29	15.3	10.9–21.2
Sulfamethoxazole	51	27	21.2–33.7
Tetracycline	45	23.8	18.3–30.4
Trimethoprim	27	14.3	10.0–20.0

(N=Total number of tested isolates, n= number of resistant Isolates, %= percentage of resistant isolates, 95% CI: 95% Confidence Interval).

ESBL / pAmpC-producing Escherichia coli in food producing animals

Table 9. h: Occurrence of resistance in ESBL/AmpC producing *Escherichia coli* from broilers.

Broilers: ESBL/pAmpC – producing *Escherichia coli* (N=47)			**2013**
Antimicrobials	**n**	**%**	**95% CI**
Ampicillin	47	100	92.4–100
Cefotaxime	47	100	92.4–100
Cefotaxime/Clavulanic acid	2	4.3	1.2–14.2
Ceftazidime	44	93.6	82.5–98.7
Ceftazidime/Clavulanic acid	6	12.8	6–25.2
Cefazolin	47	100	92.4–100
Cefepime	16	34	22.2–48.3
Cefoxitin	7	14.9	7.4–27.7
Cefpodoxime	47	100	92.4–100
Ceftriaxone	47	100	92.4–100
Cefalotin	47	100	92.4–100
Chloramphenicol	1	2.1	0.4–11.1
Ciprofloxacin	19	40.4	27.6–54.7
Colistin	0	0	0–7.6
Florfenicol	0	0	0–7.6
Gentamicin	3	6.4	2.2–17.2
Imipenem	0	0	0–7.6
Kanamycin	3	6.4	2.2–17.2
Meropenem	0	0	0–7.6
Nalidixic acid	18	38.3	25.8–52.6
Piperacillin/Tazobactam	0	0	0–7.6
Streptomycin	16	34	22.2–48.3
Sulfamethoxazole	36	76.6	62.8–86.4
Tetracycline	23	48.9	35.3–62.8
Trimethoprim	33	70.2	56–81.3

If passed on to humans there may be significant consequences for human medicine.

-extended-spectrum beta-lactamase (**ESBL**)
-plasmid-mediated AmpC beta-lactamase (**pAmpC**) genes

Occurrence of resistance in MRSA in livestock

Table 9. k: Occurrence of resistance in MRSA from pigs.

Pigs: Methicillin-resistant *Staphylococcus aureus* (N=73)			2013
Antimicrobials	**n**	**%**	**95%CI**
Cefoxitin	73	100.0	95–100
Chloramphenicol	0	0.0	0–5
Ciprofloxacin	4	5.5	2.2–13.3
Clindamycin	63	86.3	76.6–92.4
Erythromycin	60	82.2	71.9–89.3
Fusidic acid	2	2.7	0.8–9.5
Gentamicin	6	8.2	3.8–16.8
Kanamycin	6	8.2	3.8–16.8
Linezolid	0	0.0	0–5
Mupirocin	2	2.7	0.8–9.5
Penicillin	73	100.0	95–100
Quinupristin/Dalfopristin	63	86.3	76.6–92.4
Rifampin	1	1.4	0.2–7.4
Streptomycin	46	63	51.5–73.2
Sulfamethoxazole	2	2.7	0.8–9.5
Tetracycline	73	100	95–100
Tiamulin	63	86.3	76.6–92.4
Trimethoprim	69	94.5	86.7–97.8
Vancomycin	0	0	0–5

In countries with a high prevalence of MRSA in livestock, persons at particular risk (e.g. veterinarians, pig farmers, veal producers) should be tested for MRSA **before entering hospitals** and decolonised if found positive

RESEARCH ARTICLE SUMMARY

ONE HEALTH

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

Thomas P. Van Boeckel*†, João Pires†, Reshma Silvester, Cheng Zhao, Julia Song, Nicola G. Criscuolo, Marius Gilbert, Sebastian Bonhoeffer‡, Ramanan Laxminarayan‡

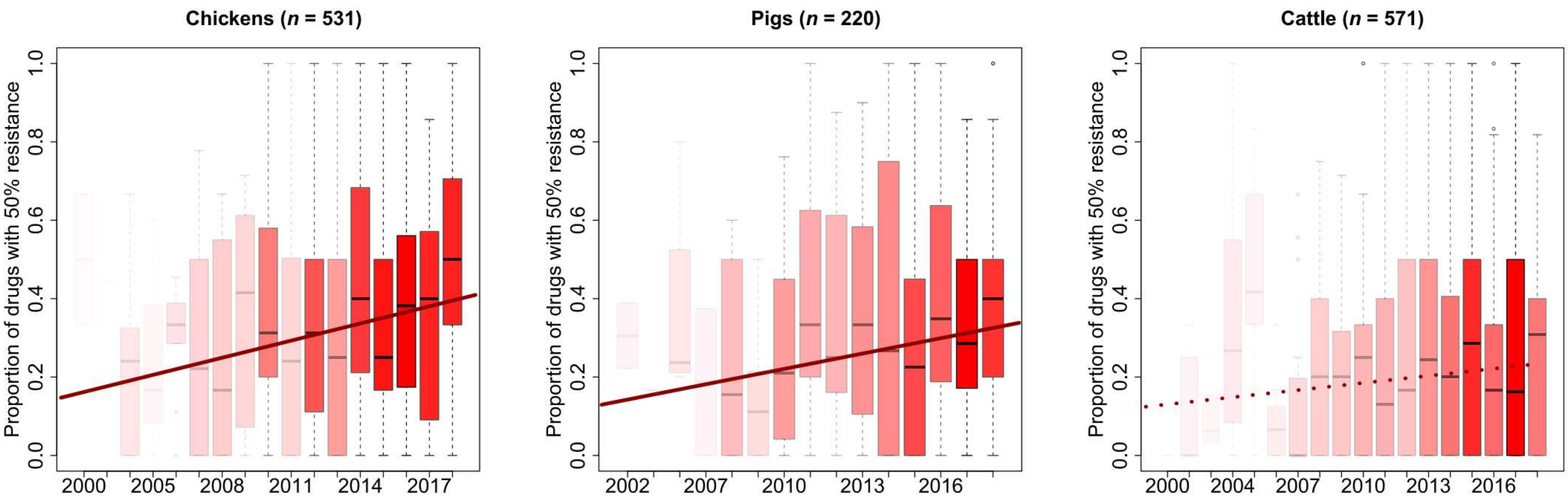
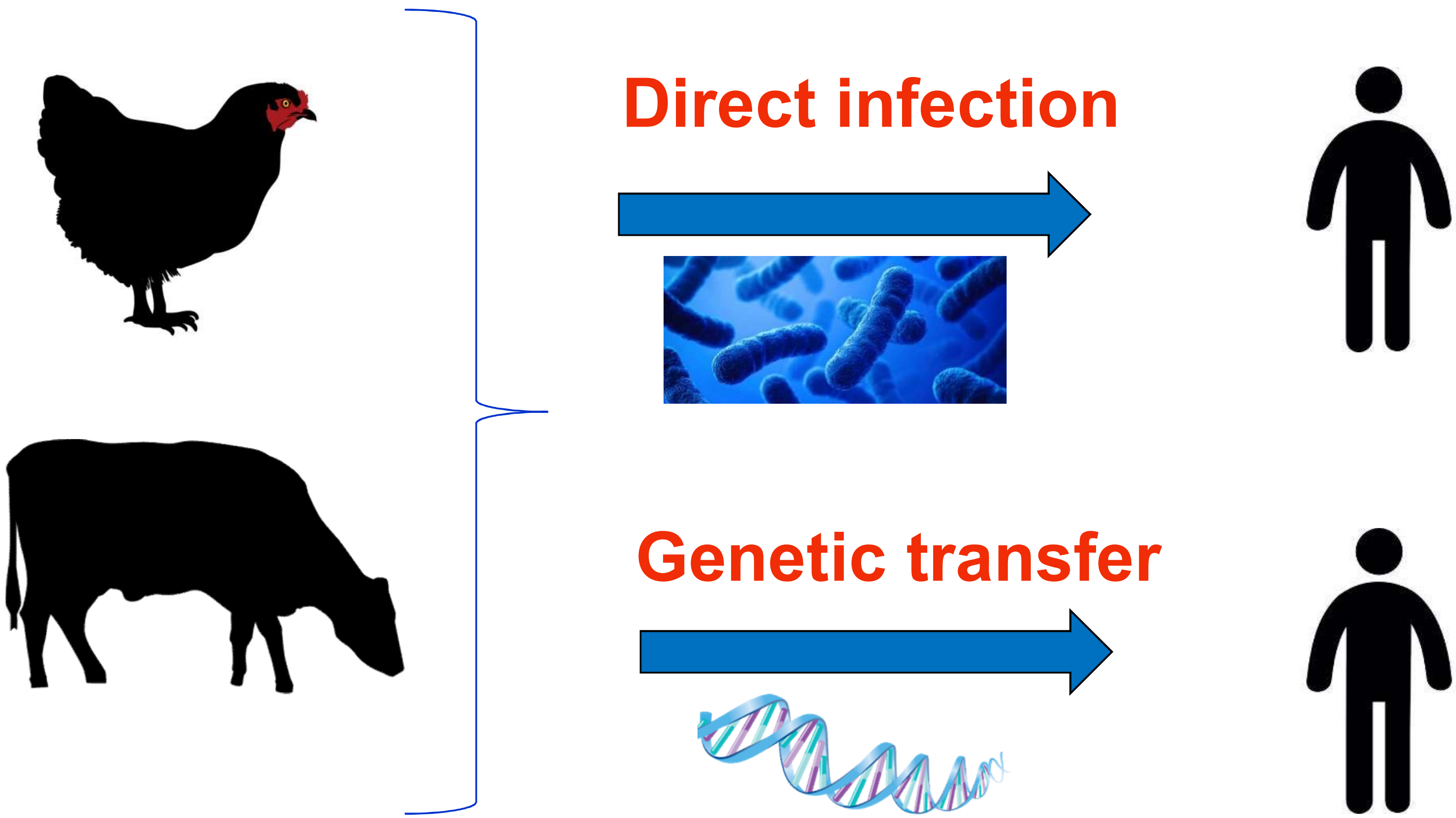


Fig. 2. Increase in antimicrobial resistance in LMICs. Proportion of antimicrobial compounds with resistance higher than 50% (P50) is shown. Solid lines indicate statistically significant (5% level) increases of P50 over time; shading indicates the number of surveys per year relative to total number of surveys per species.

*Low- and middle-income countries (**LMICs**)*

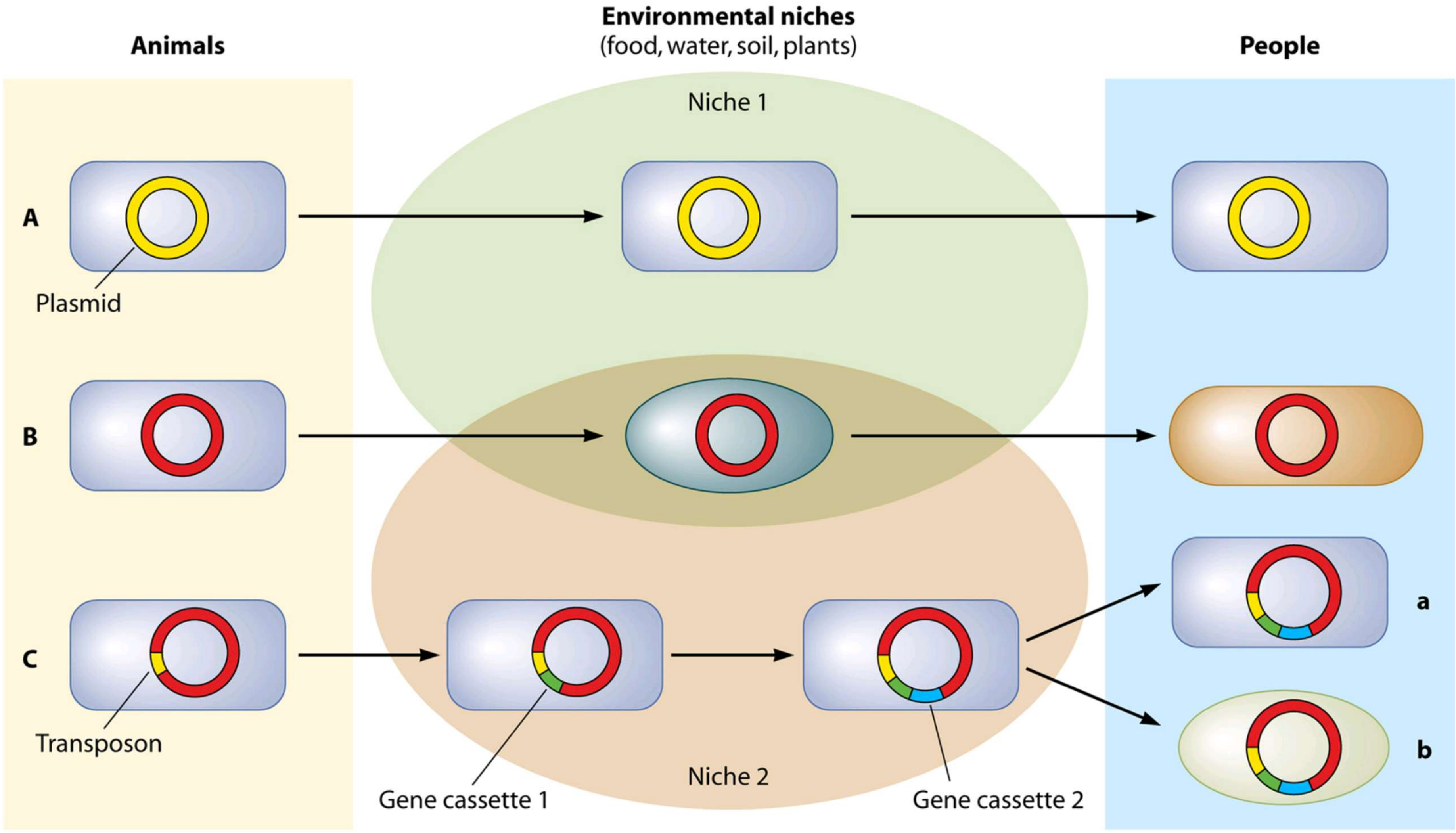
Van Boeckel *et al.*, *Science* **365**, 1266 (2019) 20 September 2019

Share of human AMR attributable to animals



Genetic transport that occurs as bacteria migrate from animal to human environments

CLINICAL MICROBIOLOGY REVIEWS, Oct. 2011, p. 718–733



(B) The genetic structure passes through one or more different hosts, ending in a new host (humans)
(C) The host and its plasmid-borne genes pass through the environment, picking up gene cassettes en route

The consumer decides....

Intensive production

-Diseases
-Cheap production
-Antibiotics

Freeland/Extensive

-Less diseases
-Expensive production
-Less or no AB

cheap

Intensive

Extensive

expensive

Who thinks of antibiotic resistance ???

Aquaculture

Substances used in aquaculture

TABLE 2: Substances with prescribed residue limits (MRL) in case of use in food animals			
Active substance	**Species/Matrix**	**MRPL**	**Comments**
Amoxicillin	All food producing species (Muscle/Fat/Liver/Kidney/ Milk)	100 µg/kg	For finfish the muscle MRL relates to 'muscle and skin in natural proportions'. MRLs for fat, liver and kidney do not apply to finfish. For porcine and poultry species the fat MRL relates to 'skin and fat in natural proportions'. Not for use in animals from which eggs are produced for human consumption.
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Enrofloxacin (sum of enrofloxacin and ciprofloxacin)	Fin fish/muscle	100 µg/kg	In case of fish, MRL for muscle means muscle and skin in natural proportion



Aquaculture

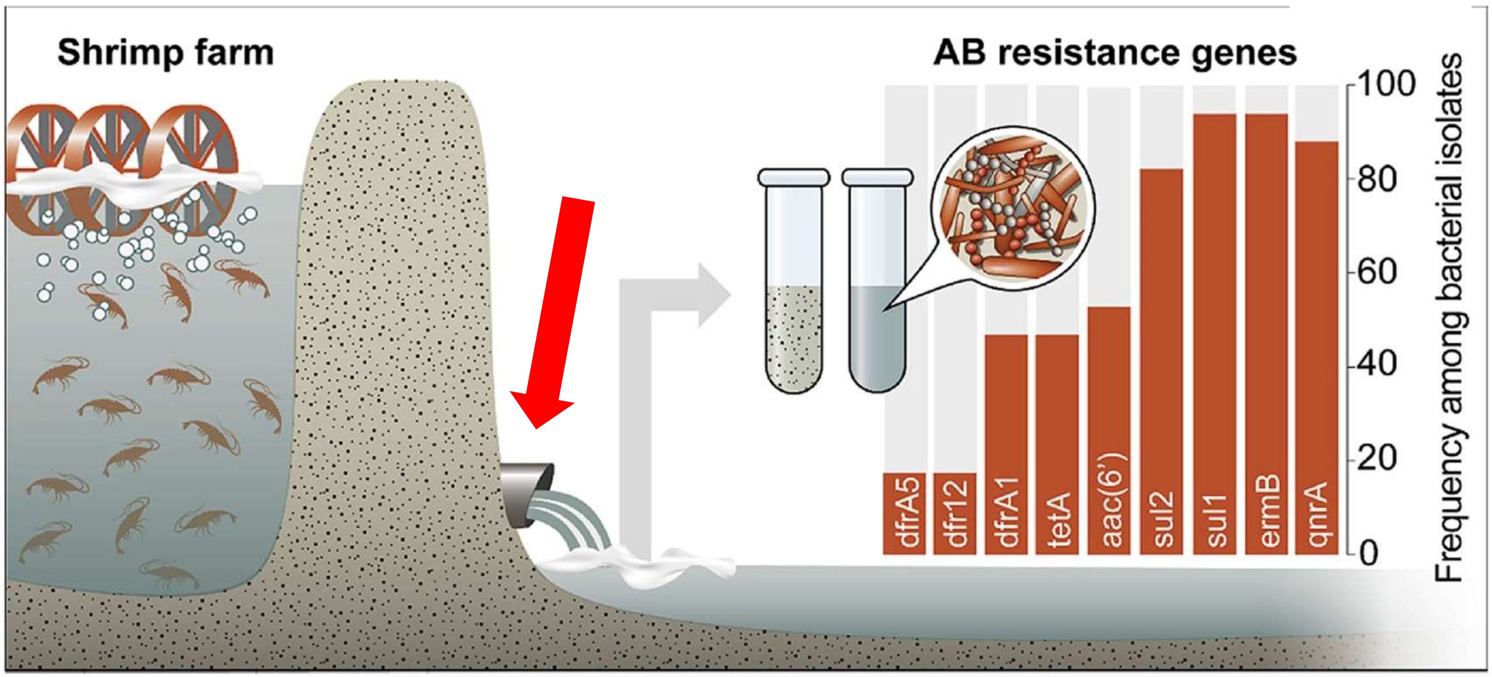
Antibiotics in Aquaculture –
Use, Abuse and Alternatives

Jaime Romero[1], Carmen Gloria Feijoó[2] and Paola Navarrete[1]
[1]Universidad de Chile, Biotechnology Laboratory,
Institute for Nutrition and Food Technology (INTA)
[2]Universidad Andrés Bello, Laboratory of Developmental Biology, Santiago
Chile

Antimicrobial-resistant bacteria in aquaculture present a risk to public health. The appearance of acquired resistance in fish pathogens means that such resistant bacteria **can act as a reservoir of resistance genes** from which genes can be further disseminated and may ultimately **end up in human pathogens**.

https://www.researchgate.net/publication/259575990

Analysis of antibiotic multi-resistant bacteria and resistance genes in the effluent of an intensive shrimp farm (Long An, Vietnam)

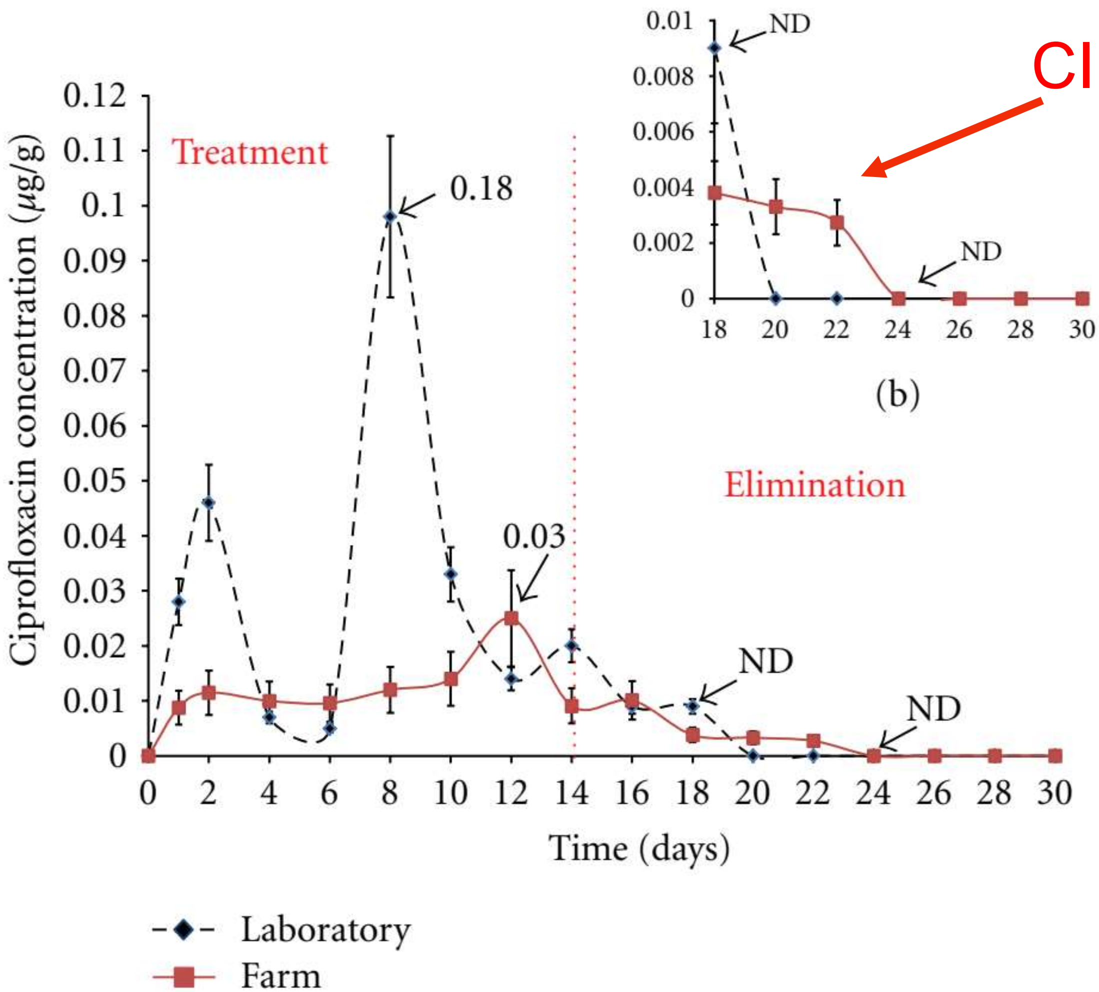


Bacterial strains, e.g. **Klebsiella pneumoniae** and Aeromonas hydrophila, showing multi-resistance traits were isolated.

Journal of Environmental Management, Volume 214, 15 May 2018, Pages 149-156

Research Article

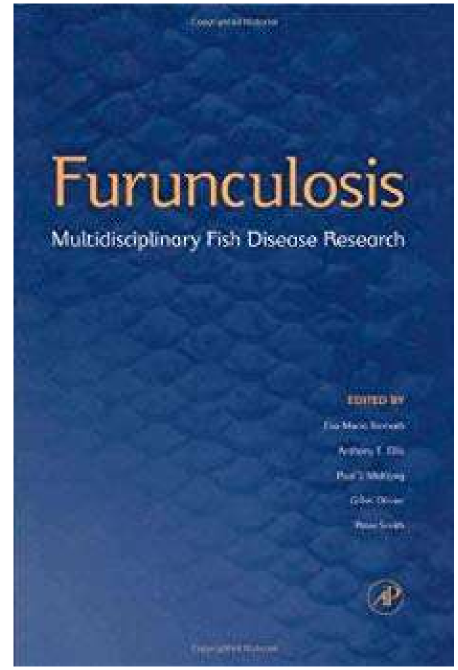
Accumulation and Elimination of Enrofloxacin and Ciprofloxacin in Tissues of Shrimp *Litopenaeus vannamei* under Laboratory and Farm Conditions



CIPRO elimination time

ISRN Pharmaceutics
Volume 2012, Article ID 374212, 7 pages
doi:10.5402/2012/374212

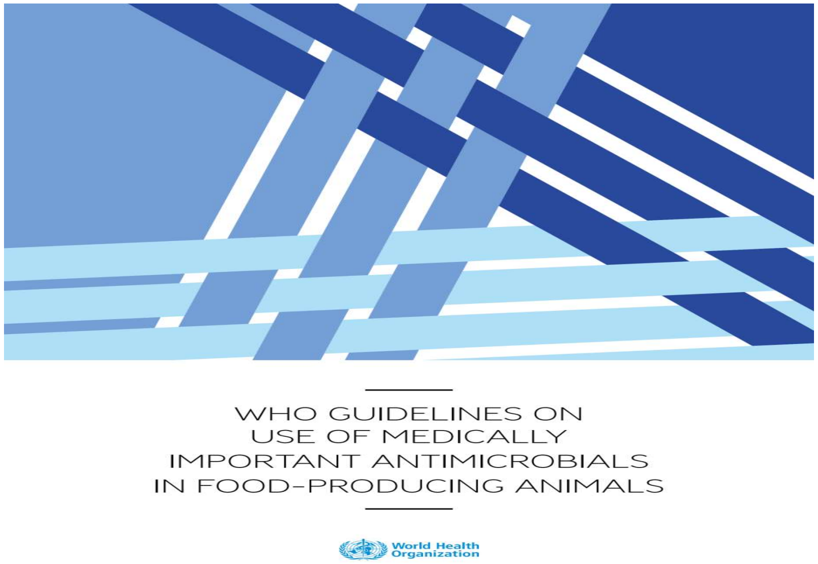
Vaccination or antibiotics

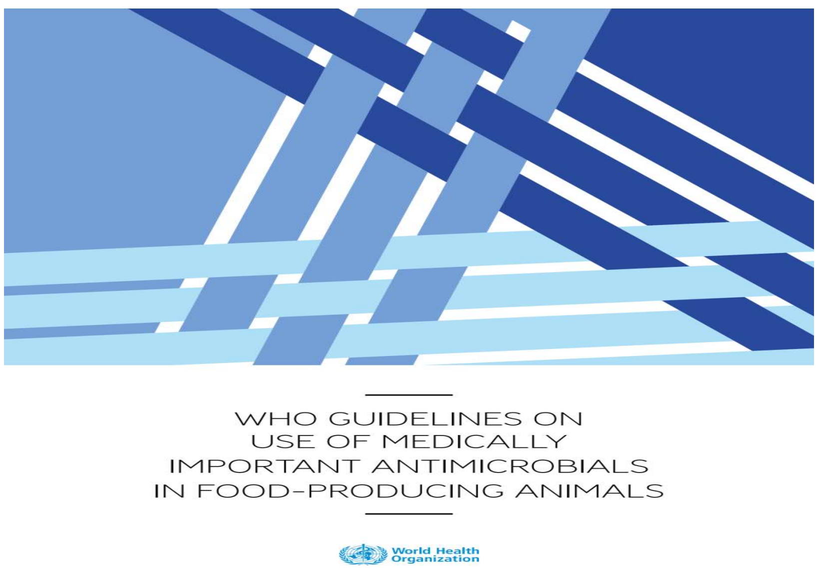


Vaccinating salmon: How Norway avoids antibiotics in fish farming

Problem: furunculosis

WHO guideline on use of medically important AB in food-producing animals





WHO recommendations

No AB for *growth promotion* !

Recommendation 2: Growth promotion use

We recommend complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion.

No AB for *prevention* !

Recommendation 3: Prevention use (in the absence of disease)

We recommend complete restriction of use of all classes of medically important antimicrobials in food-producing animals for prevention of infectious diseases that have not yet been clinically diagnosed.

WHO recommendations

No AB that are currently not used!

Best practice statement 2
Medically important antimicrobials that are not currently used in food production should not be used in the future in food production including in food-producing animals or plants.*

No critically important AB for human medicine

Recommendation 4b
We suggest that antimicrobials classified as highest priority critically important for human medicine should not be used for treatment of food-producing animals with a clinically diagnosed infectious disease.

An unexpected surprise…

Australian seagulls carry antibiotic-resistant superbugs

- **10 July 2019**

Seagulls all over Australia are carrying superbugs resistant to antibiotics, scientists say.

They found more than 20% of silver gulls nationwide carrying bacteria such as E. coli, which can cause urinary tract and blood infections and sepsis.

The research has raised fears that the antibiotic-resistant bacteria- similar to superbugs which have hit hospitals - could infect humans and other animals.

The birds are believed to have contracted the bugs from scavenging in rubbish and sewage.

Take home messages

-**Antibiotic stewardship** for physicians **and food producers !**

-Physicians should be aware of AMR in food production !

-Avoid excessive prescription in your daily clinical work !

-Monitoring of antimicrobial drug usage and resistance is mandatory in **both human and veterinary medicine**.

-**Education of food producers !**

-Global AB consumption in food animals must be reduced!
*(Politics, **tougher regulations**, international programs, **WHO**)*

Thank you !