

Antimicrobial use and antimicrobial resistance: animal health and One Health



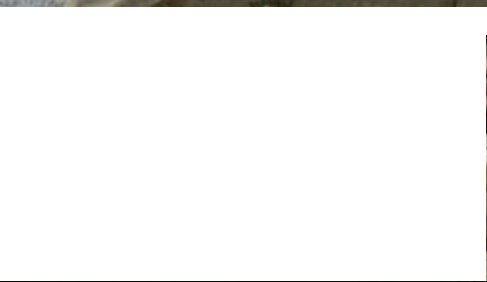
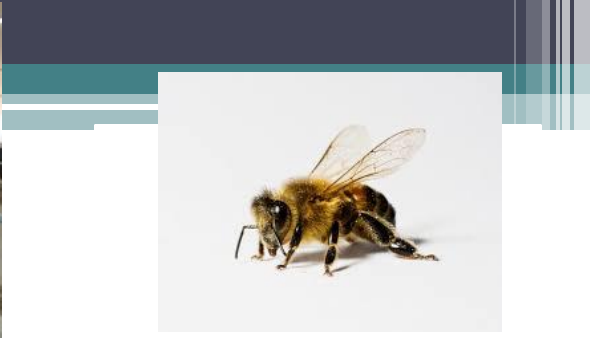
J Scott Weese
DVM DVSc DACVIM FCAHS



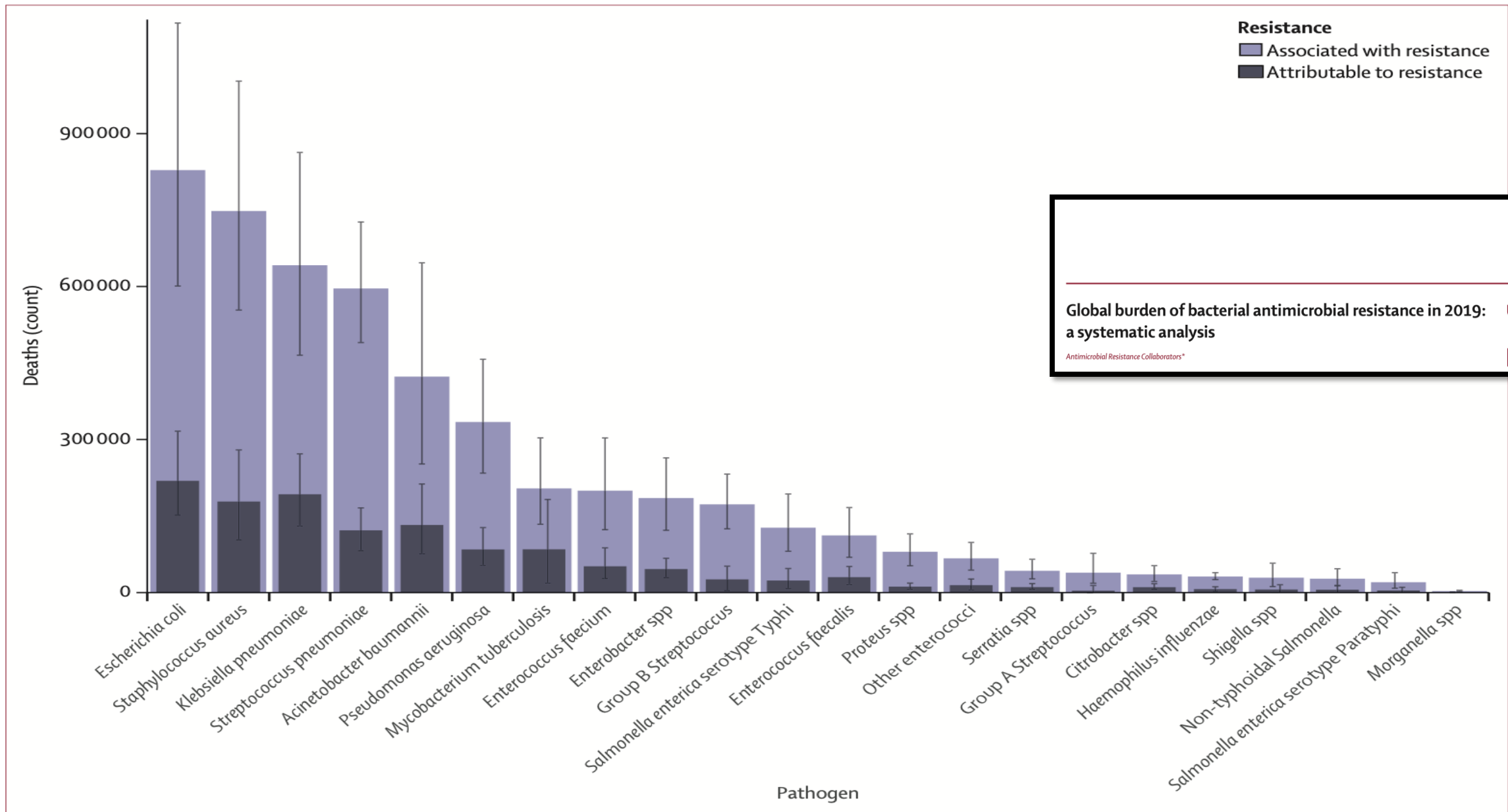
Speaker Disclosure

- Employment: University of Guelph
- Commercial interests: None.
- Patents: None
- Speaking engagements: Merck Animal Health, Vetoquinol, Hills Pet Nutrition, Royal Canin Canada, Zoetis Canada, Canadian Veterinary Medical Association
- Consultancies (5yr): Banfield
- Grants from companies (5yr): None
- Editing/Review: VetMedux

What are the main issues with antimicrobial use in animals?



What percentage of AMR in humans do you think is attributable to AMU in animals?



Articles

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

Antimicrobial Resistance Collaborators*

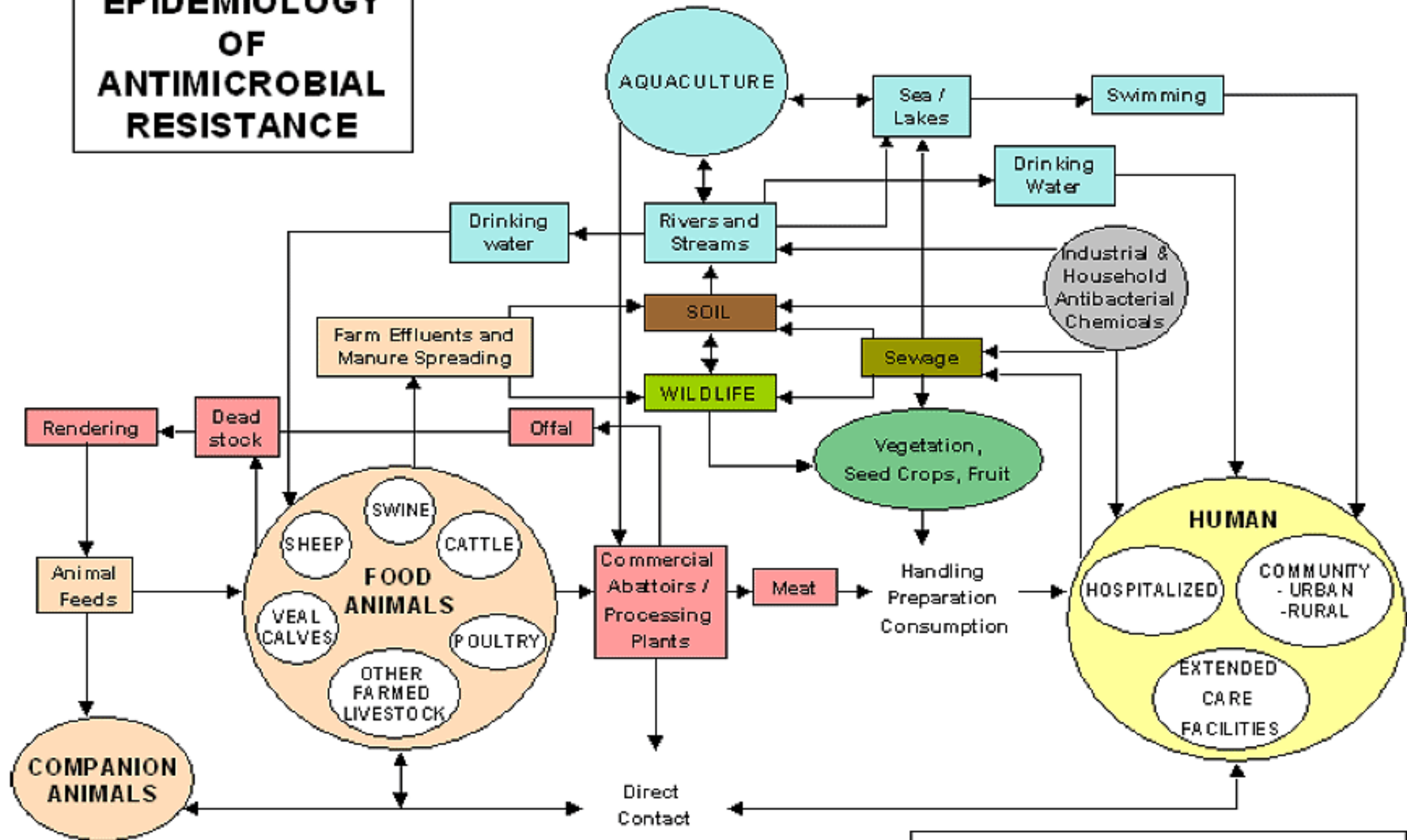
GBD W+G

oa

Figure 4: Global deaths (counts) attributable to and associated with bacterial antimicrobial resistance by pathogen, 2019

Estimates were aggregated across drugs, accounting for the co-occurrence of resistance to multiple drugs. Error bars show 95% uncertainty intervals.

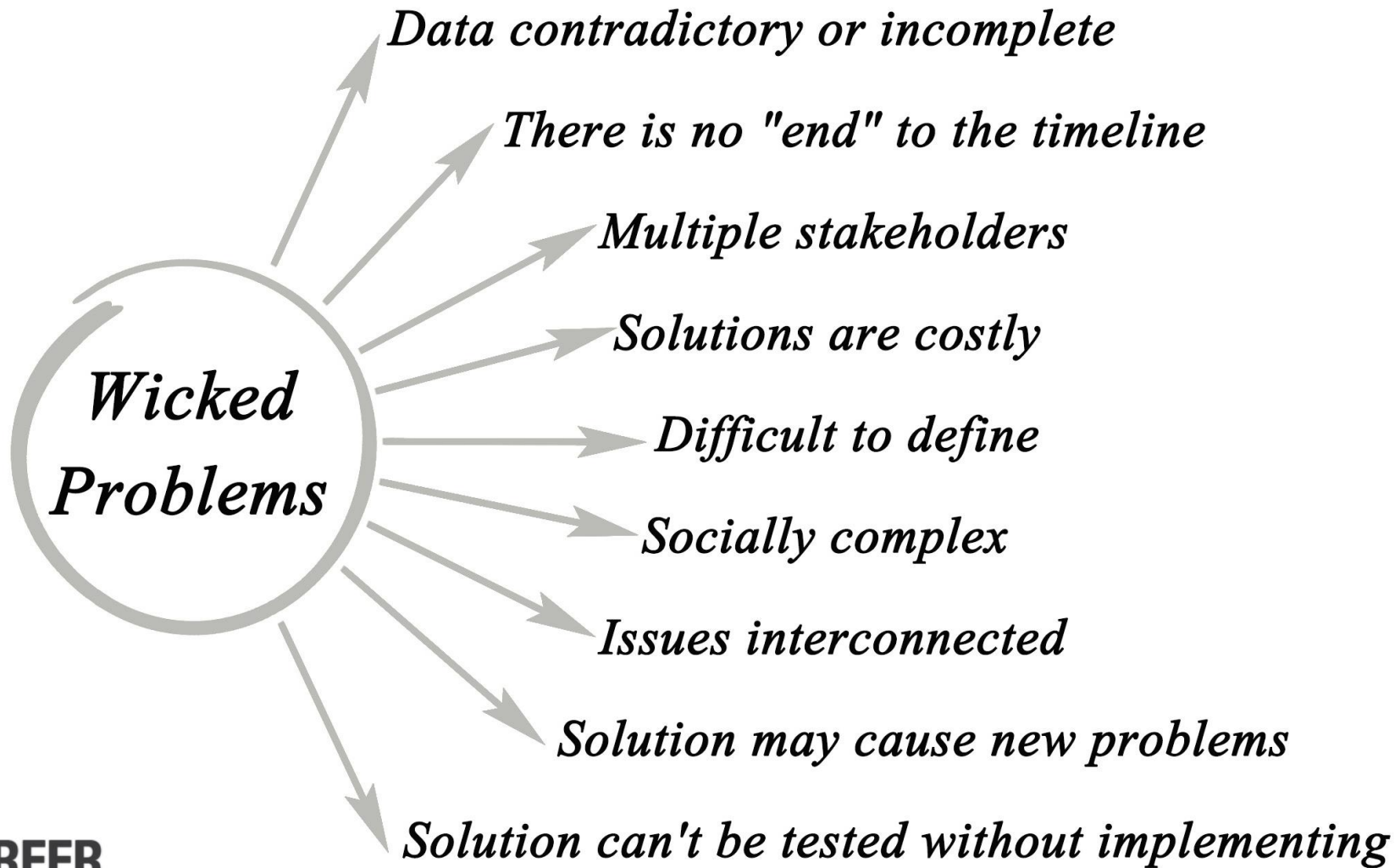
EPIDEMIOLOGY OF ANTIMICROBIAL RESISTANCE



Courtesy of Dr. J Prescott

after Linton AH (1977), modified by Irwin RJ





If an antibiotic could reduce methane production by 50% in cattle, would that be good?

Of the antimicrobials distributed or sold* in 2018:



■ were intended for **production animals**



■ were intended for **humans**

■ were intended for **companion animals**



■ were intended for **crops**



*Animal distribution data currently do not account for quantities imported for own use, or as active pharmaceutical ingredients intended for further compounding; hence, these are underestimates of total quantities used.

Of the antimicrobials distributed or sold* in 2018:



78% were
intended for
**production
animals**



21% were
intended
for
humans

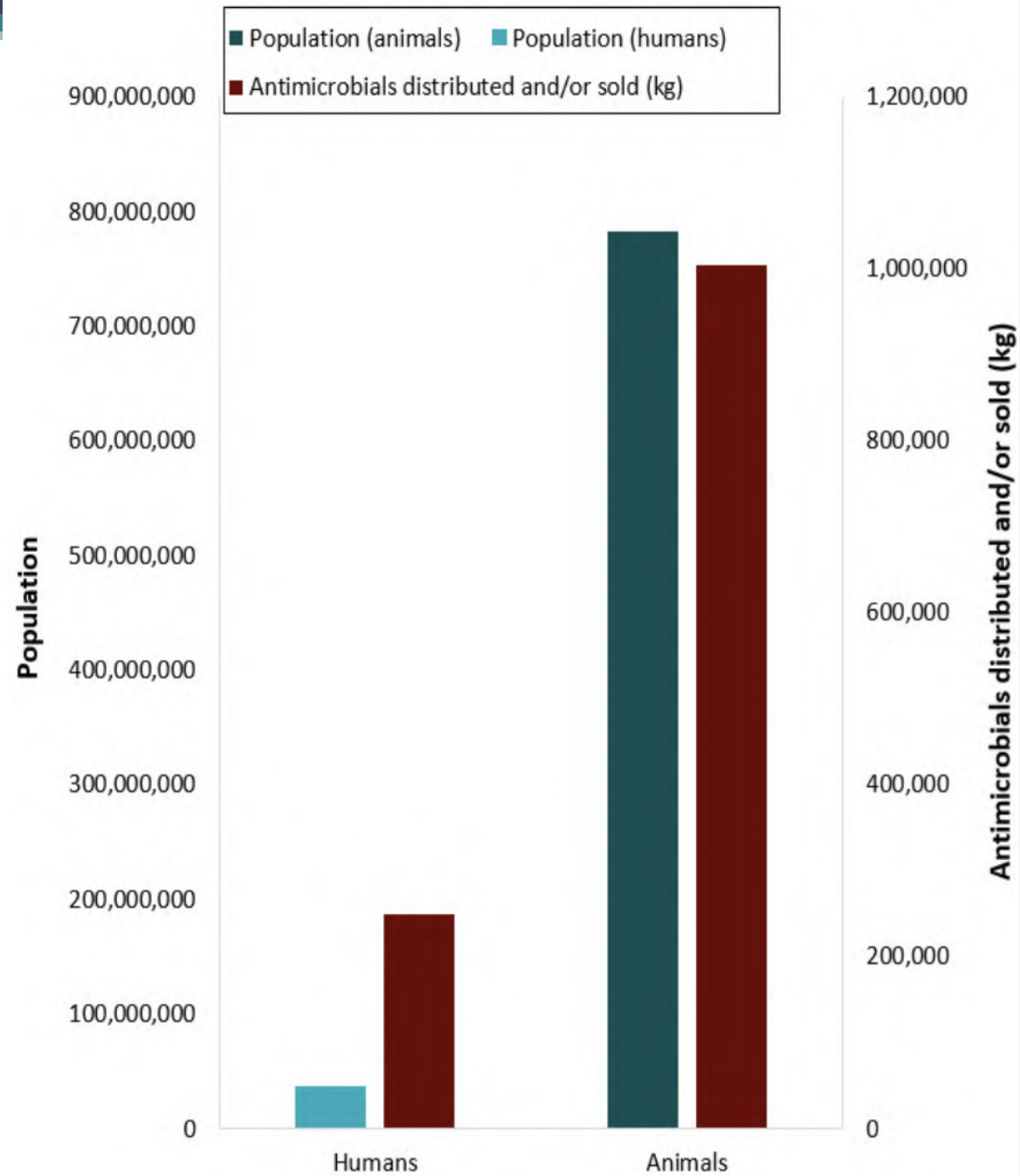
1% were
intended for
**companion
animals**



<1% were
intended
for **crops**



*Animal distribution data currently do not account for quantities imported for own use, or as active pharmaceutical ingredients intended for further compounding; hence, these are underestimates of total quantities used.

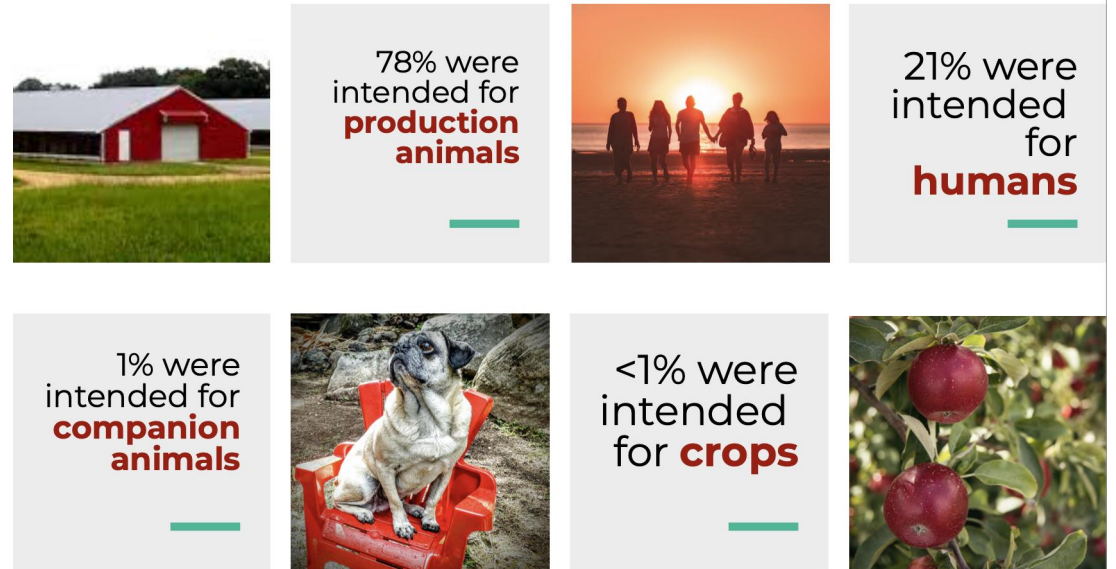


What do the numbers mean?

- All antibiotics aren't alike
- Mass doesn't tell the whole story

Integrated AMU Data

Of the antimicrobials distributed or sold* in 2018:

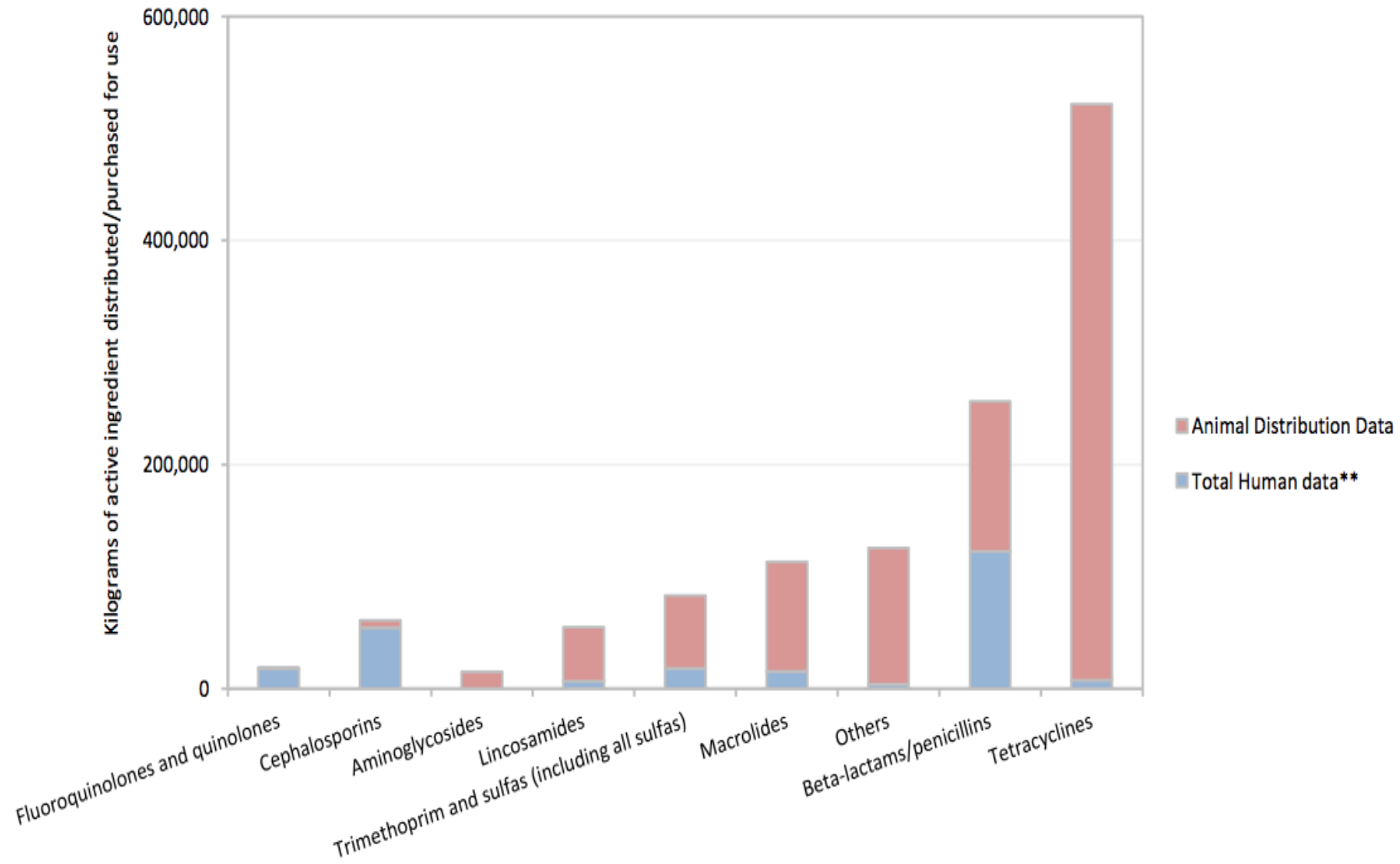


*Animal distribution data currently do not account for quantities imported for own use, or as active pharmaceutical ingredients intended for further compounding; hence, these are underestimates of total quantities used.

Should 'medically important' antibiotics be used in...?

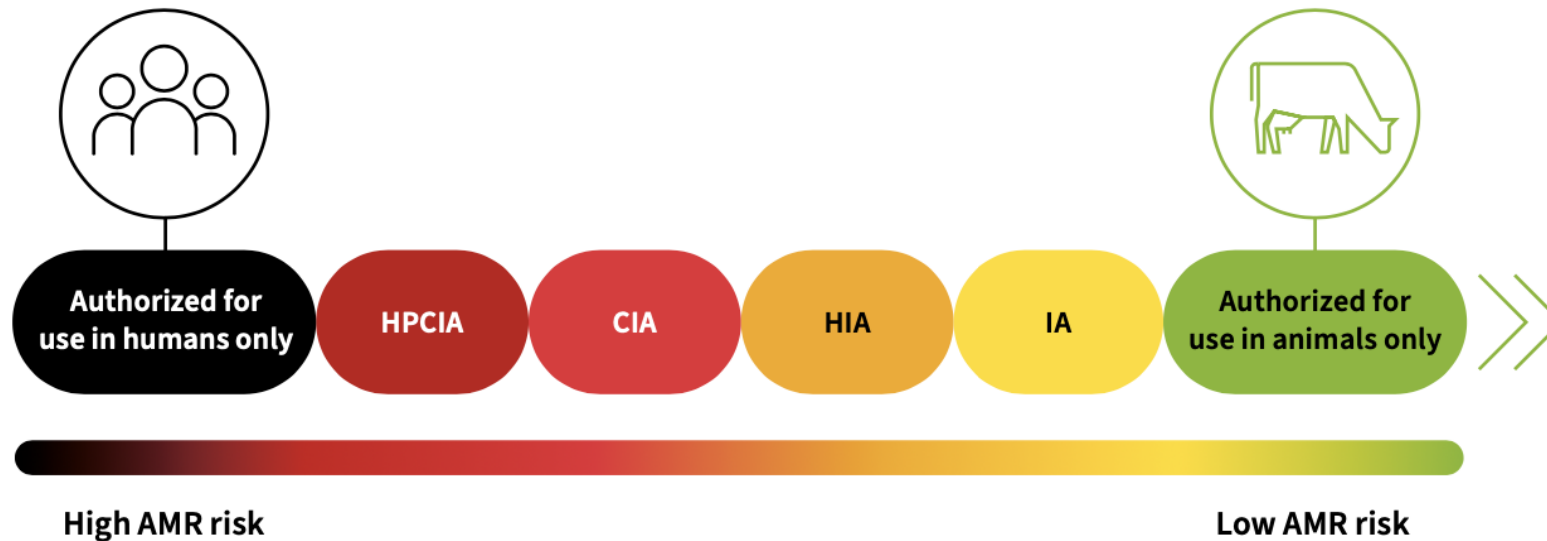
- All animals
- Food animals

Figure 56. Kilograms of medically important antimicrobials distributed and/or sold for use in animals and humans by antimicrobial class, 2016.

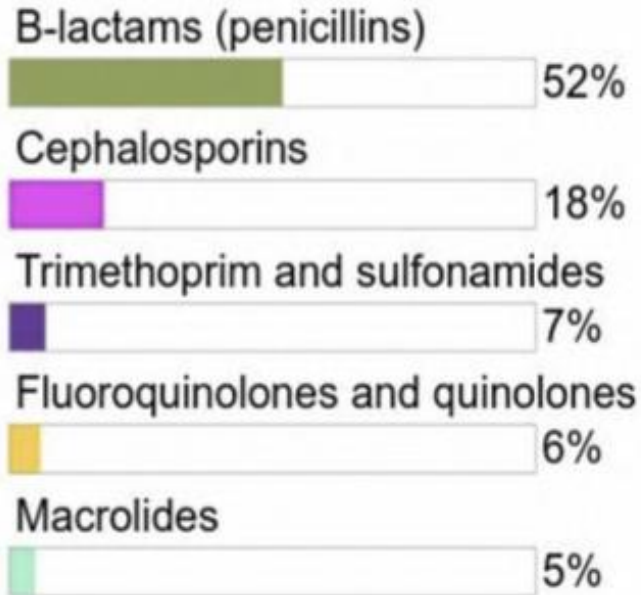


WHO Medically Important Antimicrobials List

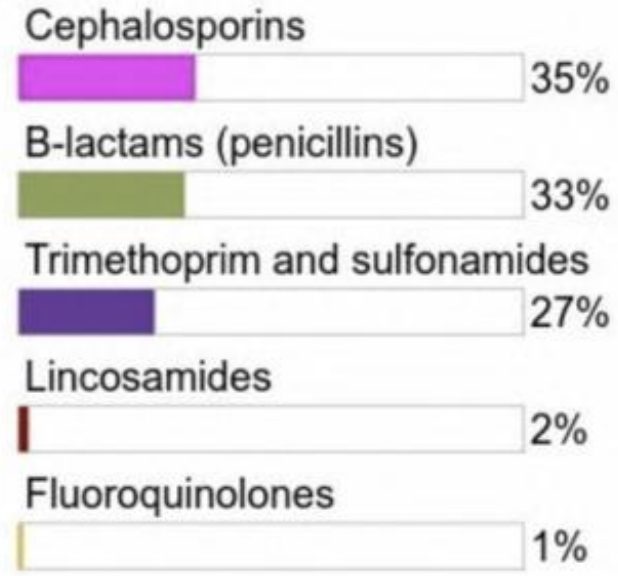
A risk management tool for mitigating antimicrobial resistance due to non-human use



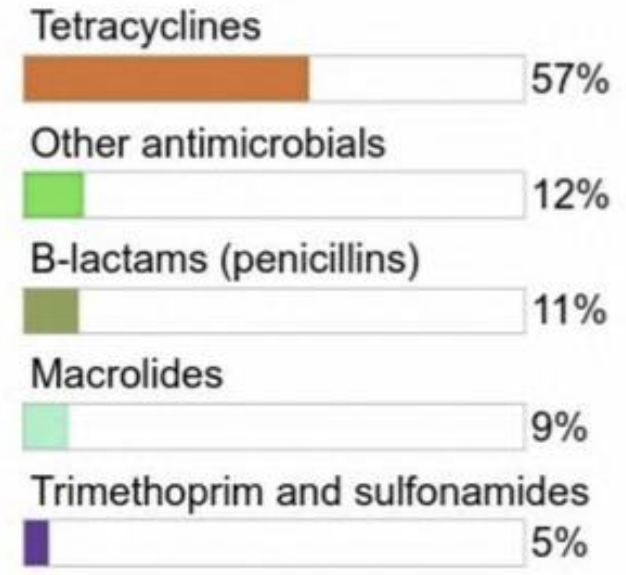
Humans



Companion Animals



Production Animals



What's the most common route of administration?

What's the most common route of administration?

Figure 52: Quantity of antimicrobials (% of total kg) distributed for use in animals, by route of administration, 2014

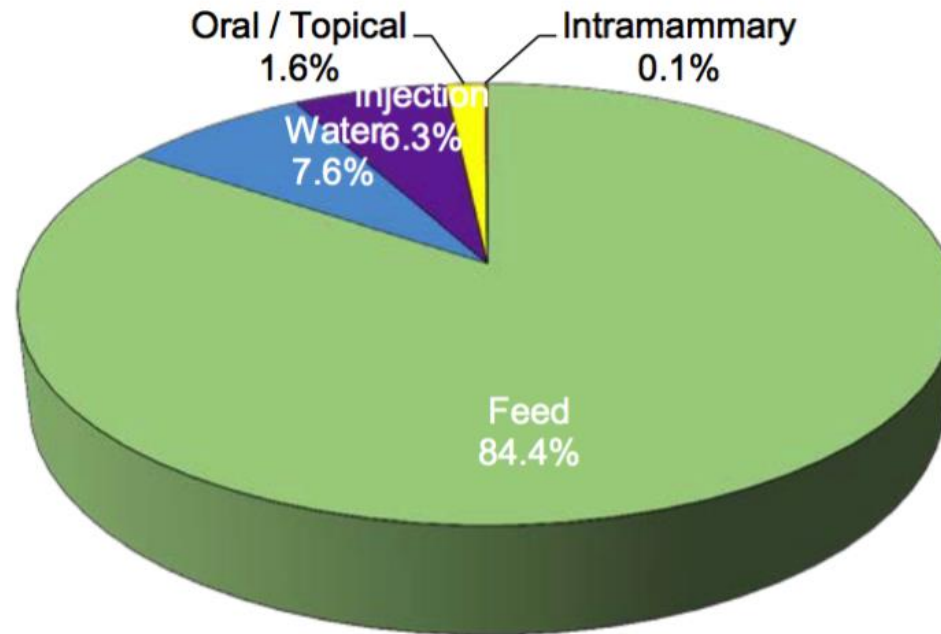
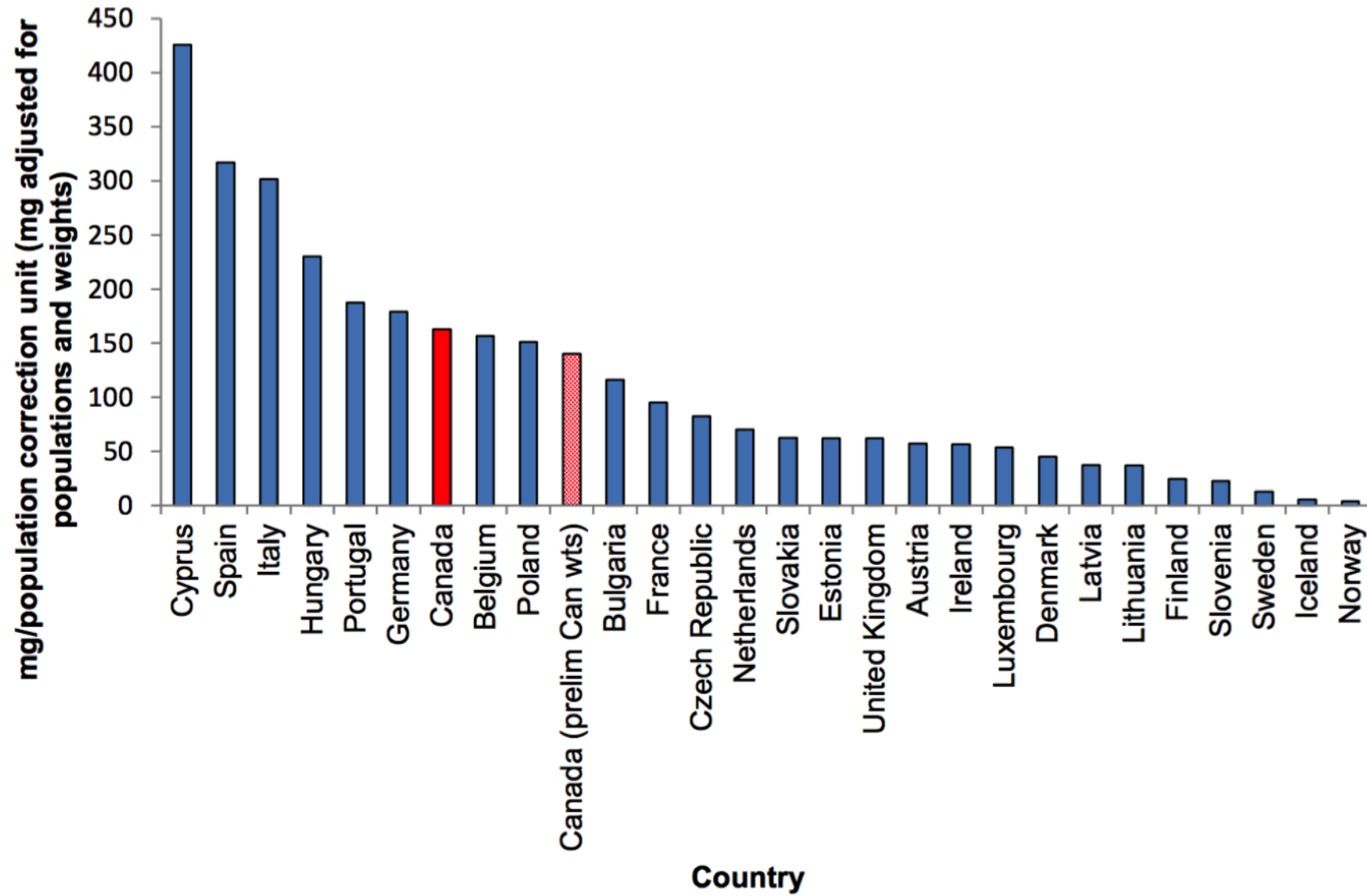


Figure 55: Antimicrobial sales for animals (quantity adjusted by populations and weights) for Canada (2014) and countries participating in the European Surveillance of Veterinary Antimicrobial Consumption Network (2013)



Should antimicrobials be administered to healthy animals to prevent disease?

Type of Use	Definition
Therapy	Administration of an antimicrobial agent to an individual or a group of animals showing clinical signs of an infectious disease.
Prophylaxis	Administration an antimicrobial agent to an individual or a group of animals at risk of acquiring a specific infection or in a specific situation where infectious disease is likely to occur if the antimicrobial agent is not administered.
Metaphylaxis/ disease control	Administration of an antimicrobial agent to a group of animals containing sick animals and healthy animals (presumed to be infected), to minimize or resolve clinical signs and to prevent further spread of the disease.
Growth promotion	Administration of antimicrobial agents to animals only to increase the rate of weight gain or the efficiency of feed utilisation. This typically involves subtherapeutic doses.

Prophylaxis

- Unneeded mass treatment of food animals
- Mass treatment of food animals to compensate for poor management or preventive medicine
- Targeted group treatment to reduce disease and therapeutic AMU
- Targeted individual treatment to prevent high consequence infection (e.g. surgical prophylaxis)

Prophy

- Unneed
- Mass tr
manag
- Targete
- Targete
infectio



The screenshot shows the ILRI website header with navigation links: ABOUT, RESEARCH, WHERE WE WORK, NEWS & EVENTS, and KNOWLEDGE. The article title is "Training livestock vaccinators to tackle East Coast fever in Tanzania", posted on 09 November, 2017 by Brian Kawuma. The article features a photograph of three people in a rural setting. One person is wearing a dark blue shirt and is administering a vaccine to a brown cow. Another person is wearing a purple shirt and glasses, and a third person is wearing a green shirt and a traditional hat. There are other cows in the background.

tic AMU
ce

Should ‘higher tier/big gun....’ antimicrobials be used in animals?





Result	Staphylococcus pseudintermedius
Level	1+
Amoxicillin/Clavulanate	R
Ampicillin	R
Cefovecin	R
Cefoxitin	R
Cephalothin	R
Clindamycin	R
Enrofloxacin	R
Gentamicin	R
Marbofloxacin	R
Orbifloxacin	R
Tetracycline	R
Trimethoprim/Sulfa	R



Result	Staphylococcus pseudintermedius
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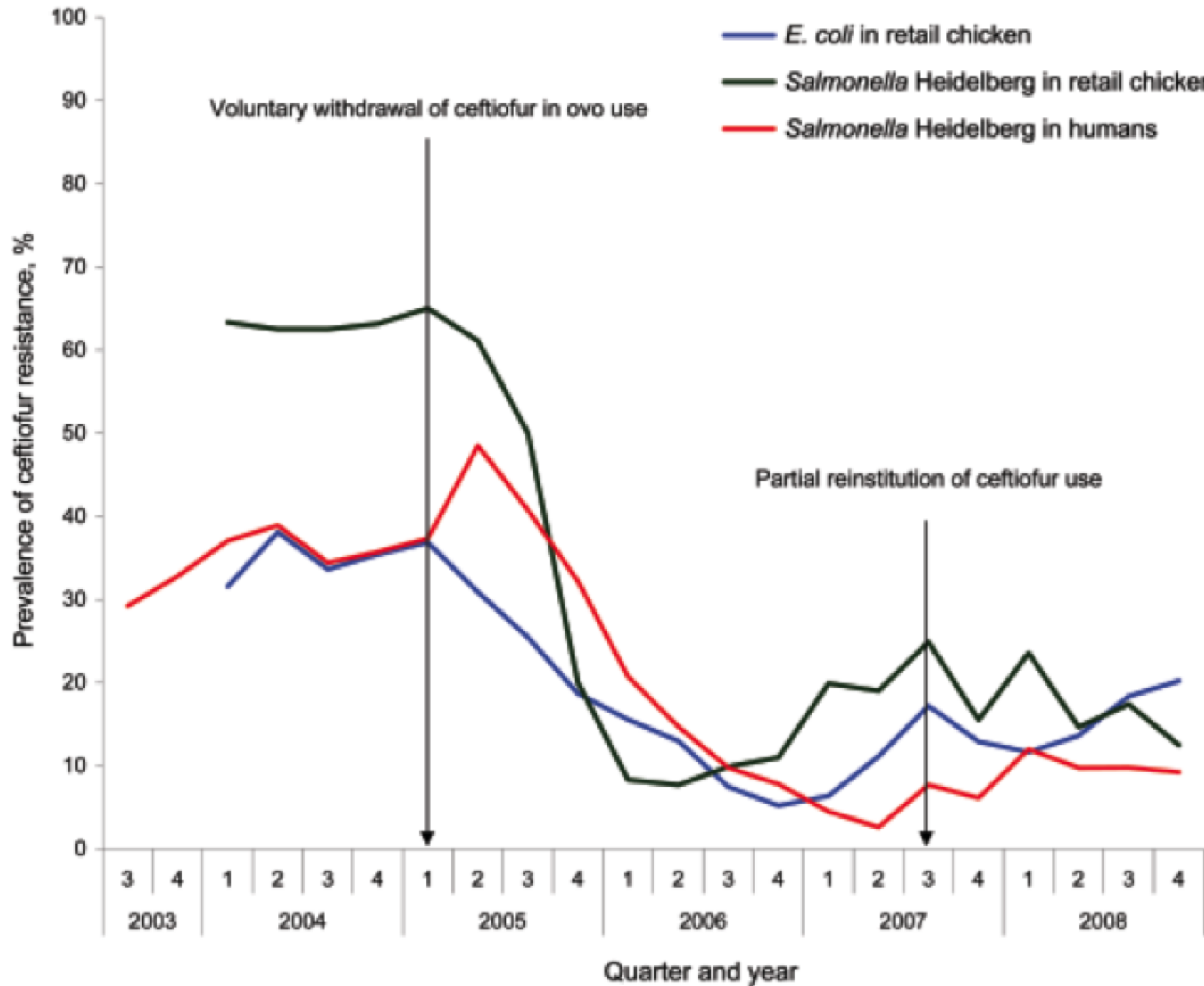
- Should we..
 - Treat, even if a higher tier drug is needed
 - Try a lower tier drug it's resistant to to 'try something'
 - Let Mother Nature take her course
 - Euthanize

Does restriction of antimicrobials in animals have an impact on resistance?

- Yes..but....
 - Some conflicting data
 - Between bacteria
 - Between drugs
 - Between studies
 - Focused on single bug/drug combinations

Ceftiofur Resistance in *Salmonella enterica* Serovar Heidelberg from Chicken Meat and Humans, Canada

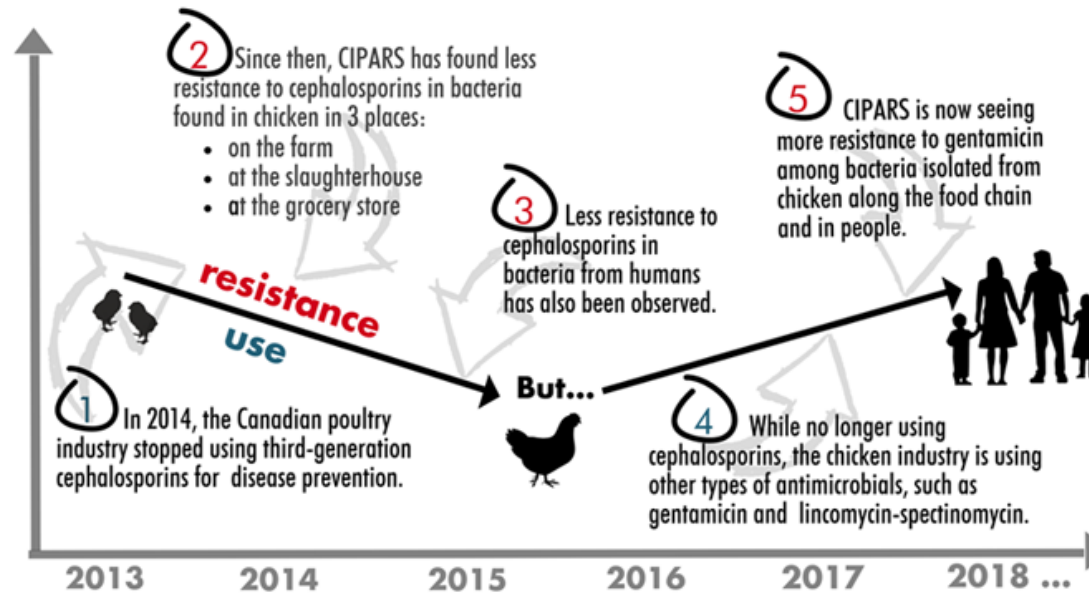
Lucie Dutil, Rebecca Irwin, Rita Finley, Lai King Ng, Brent Avery, Patrick Boerlin, Anne-Marie Bourgault, Linda Cole, Danielle Daignault, Andrea Desruisseau, Walter Demczuk, Linda Hoang, Greg B. Horsman, Johanne Ismail, Frances Jamieson, Anne Maki, Ana Pacagnella, and Dylan R. Pillai



The complex battle against antimicrobial resistance

Highlights of one important story that CIPARS is following

The Canadian poultry industry is fighting back against antimicrobial resistance



The poultry industry has committed to removing the preventive use of other types of antimicrobials like gentamicin that are important to human medicine by the end of 2018.

CIPARS expects to see less resistance to gentamicin among monitored bacteria with changing AMU practices in the poultry industry.

What are third-generation cephalosporins?

Third-generation cephalosporins, such as ceftiofur and ceftriaxone, are a group of antimicrobials that are important for treating infections in people and animals. Ceftriaxone is used in people and ceftiofur is used in animals. To know more about it please consult the 2016 CIPARS Annual Report.

ISBN: 978-0-660-28310-4 Catalogue number: HP40-230/2018E-PDF Publication number: 180546



Antibiotic use selects for resistance...

So...

Antibiotic-free farms should have less resistance



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Contents lists available at ScienceDirect

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic



Zinc resistance of *Staphylococcus aureus* of animal origin is strongly associated with methicillin resistance

Lina M. Cavaco^{1,*}, Henrik Hasman¹, Frank M. Aarestrup¹

Research Group for Antimicrobial Resistance and Molecular Epidemiology, National Food Institute, Technical University of Denmark, Copenhagen, Denmark

Zoonoses and Public Health

ORIGINAL ARTICLE

Zinc Oxide Therapy Increases Prevalence and Persistence of Methicillin-Resistant *Staphylococcus aureus* in Pigs: A Randomized Controlled Trial

M. J. Slifierz¹, R. Friendship² and J. S. Weese¹

Short communication

Effects of tetracycline and zinc on selection of methicillin-resistant *Staphylococcus aureus* (MRSA) sequence type 398 in pigs

Arshnee Moodley^{a,*}, Søren Saxmose Nielsen^b, Luca Guardabassi^a

^a Department of Veterinary Disease Biology, Faculty of Life Sciences, University of Copenhagen, Frederiksberg C, 1870, Denmark

^b Department of Large Animal Sciences, Faculty of Life Sciences, University of Copenhagen, Frederiksberg C, 1870, Denmark

- What can a single person, sector, government, nation or international organization do to control AMR?

UNGA 2024...

Inicio » Events » **United Nations General Assembly: High-Level Meeting on AMR**

Global Events, High-level advocacy

United Nations General Assembly: High-Level Meeting on AMR

 From 26/09/2024 to 26/09/2024

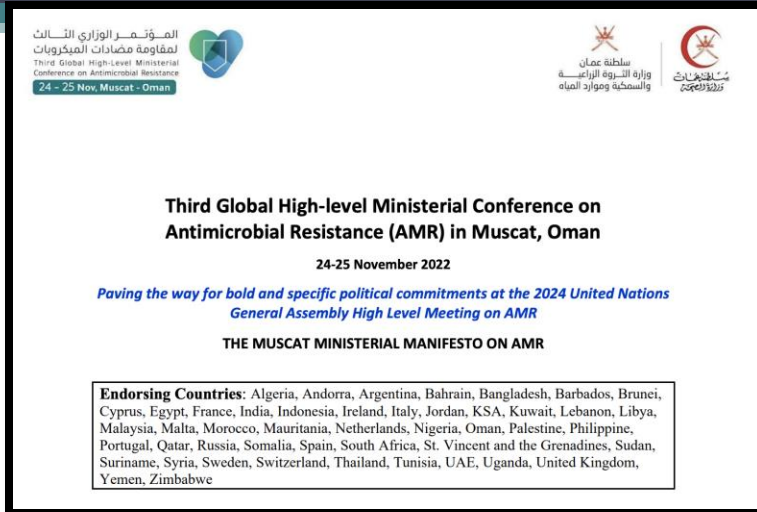
 9:00am - 6:00pm (GMT)

 New York, United States of America

Priority areas/themes

- Equity
- One Health: strengthening human and animal health systems with substantive consideration of the environment
- Reflecting the needs of LMICs and countries that bear the burden of AMR (and potentially control measures)
- Prevention, prevention, prevention

Targets



ANNEX to MUSCAT MINISTERIAL MANIFESTO ON AMR

Explanation and rationale behind the targets included in the Muscat Manifesto

Target 1: Reduce the total amount of antimicrobials used in the agri-food system at least by 30-50%¹ by 2030 from the current level;

Target 2: Zero use of medically important antimicrobials for human medicine in animals for non-veterinary medical purposes or in crop production and agri-food systems for non-phytosanitary purposes;

Target 3: Ensure that ACCESS group antibiotics are at least $\geq 60\%$ of overall antibiotic consumption in humans by 2030

Do we need antimicrobial use targets in animals?

We could drop antibiotic use (kgs) by >50% with one move....

Out with the old...

- Procaine penicillin
 - 20 mg/kg q12h
- Amoxicillin-clavulanic acid
 - 12.5-25 mg/kg q8-12h
- Amoxicillin
 - 11-22 mg/kg q8h
- Oxytetracycline
 - 6.6-11 mg/kg q24h

In with the new

- Enrofloxacin (HPCIA)
 - 5 mg/kg q24g
- Ceftiofur (HPCIA)
 - 1 mg/kg q24h
- Tulathromycin (HPCIA)
 - 2.5 mg/kg once
- Cefovecin (HPCIA)
 - 8.8 mg/kg once

Bacterial cystitis in dogs

- 1000 dogs treated for cystitis
- Pre-intervention
 - 22 kg of antibiotic; amoxicillin 22 mg/kg PO q12h
- Post-intervention #1
 - 2.5 kg of antibiotic marbofloxacin 5 mg/kg PO q24h
- Post-intervention #2
 - 0.9 kg of antibiotics: cefovecin 8.8 mg/kg SC once

My (ever evolving) thoughts on targets

- We need them
 - But are not **yet** well equipped to set them or monitor them
- Non-evidence-based targets might be ignored, impractical or inadequately aspirational (or drive poor decisions)
- Targets may be political red lines

- Kgs is a poor (close to useless) metric
 - Crude, can be manipulated, not linked to actual risk
- We need actionable, understandable, appropriateness of use targets
- Targets need to be at national and sector level
 - International targets are for show, +/- motivation

Targets

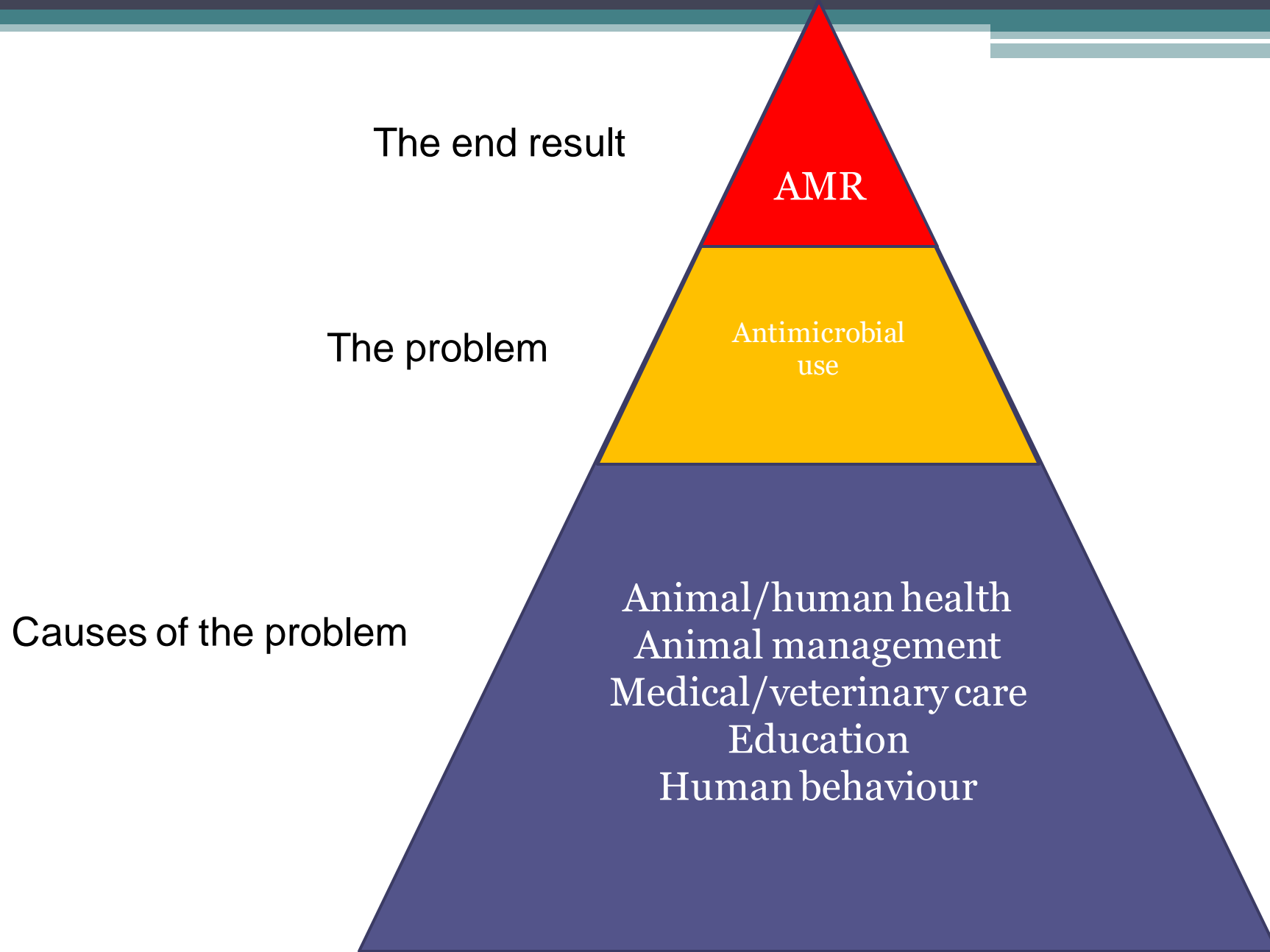
- no use of medically important antimicrobials for growth promotion in any country by 2030
- no use of highest-priority critically important antimicrobials (HPCIA) for group prophylaxis in animals
- 100% of AMU is done under the guidance of a veterinary professional
- species and life-stage specific targets (e.g. prophylaxis of less than 40% of groups of post-weaning piglets, prophylactic treatment of less than 20% of dry cows)
- percentage of AMU that is consistent with national or international AMU guidelines

- access to at least one first line antimicrobial for common diseases in all countries
- access of all animal producers to a veterinarian or trained allied animal health professional
- free availability of guidelines that are relevant for the species, region and language of veterinarians and other prescribers
- access to preventive health tools such as vaccination

Should we have animal-only antimicrobials?



What is the actual problem??



Veterinary/animal sector innovation needs

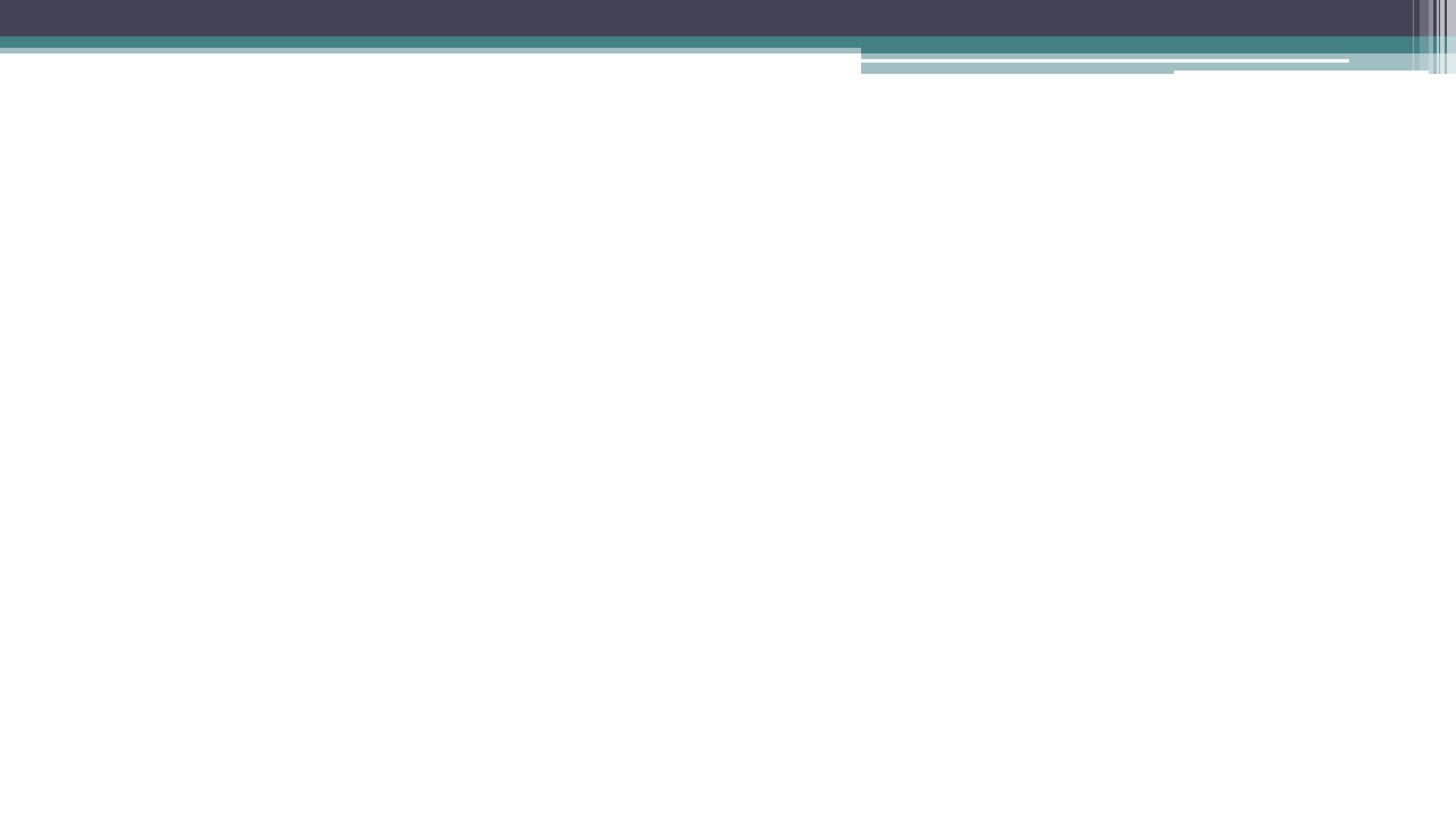
- Vaccines and preventives
 - Better animal management innovations
 - Readily accessible, high quality treatment guidelines
 - Rapid, patient side/field diagnostic testing
 - Better empowerment and education of women in LMICs
-
- Innovation to improve prevention, diagnosis and implementation, not new antimicrobials

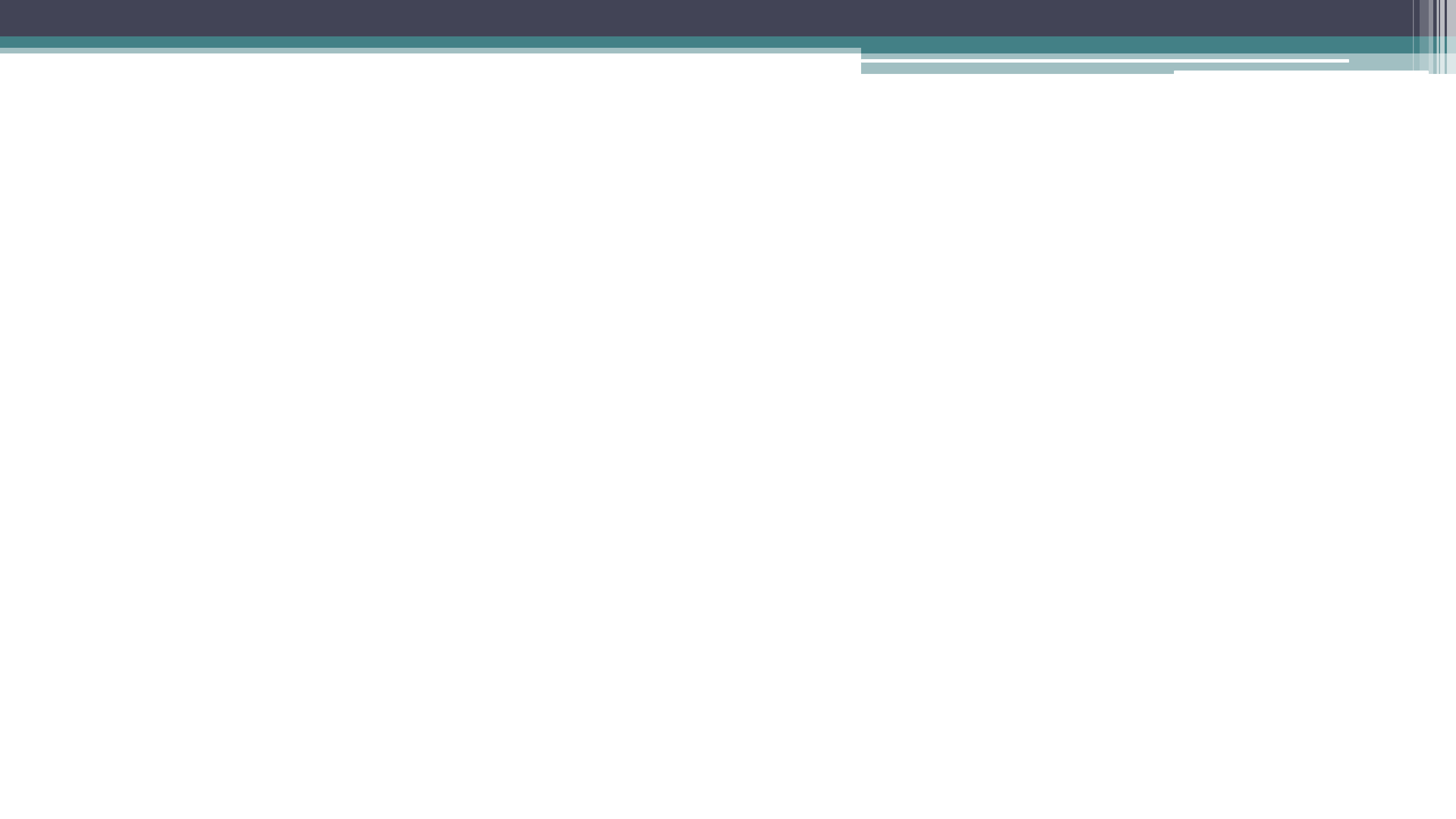
What would have the biggest impact on antimicrobial use in humans and animals?

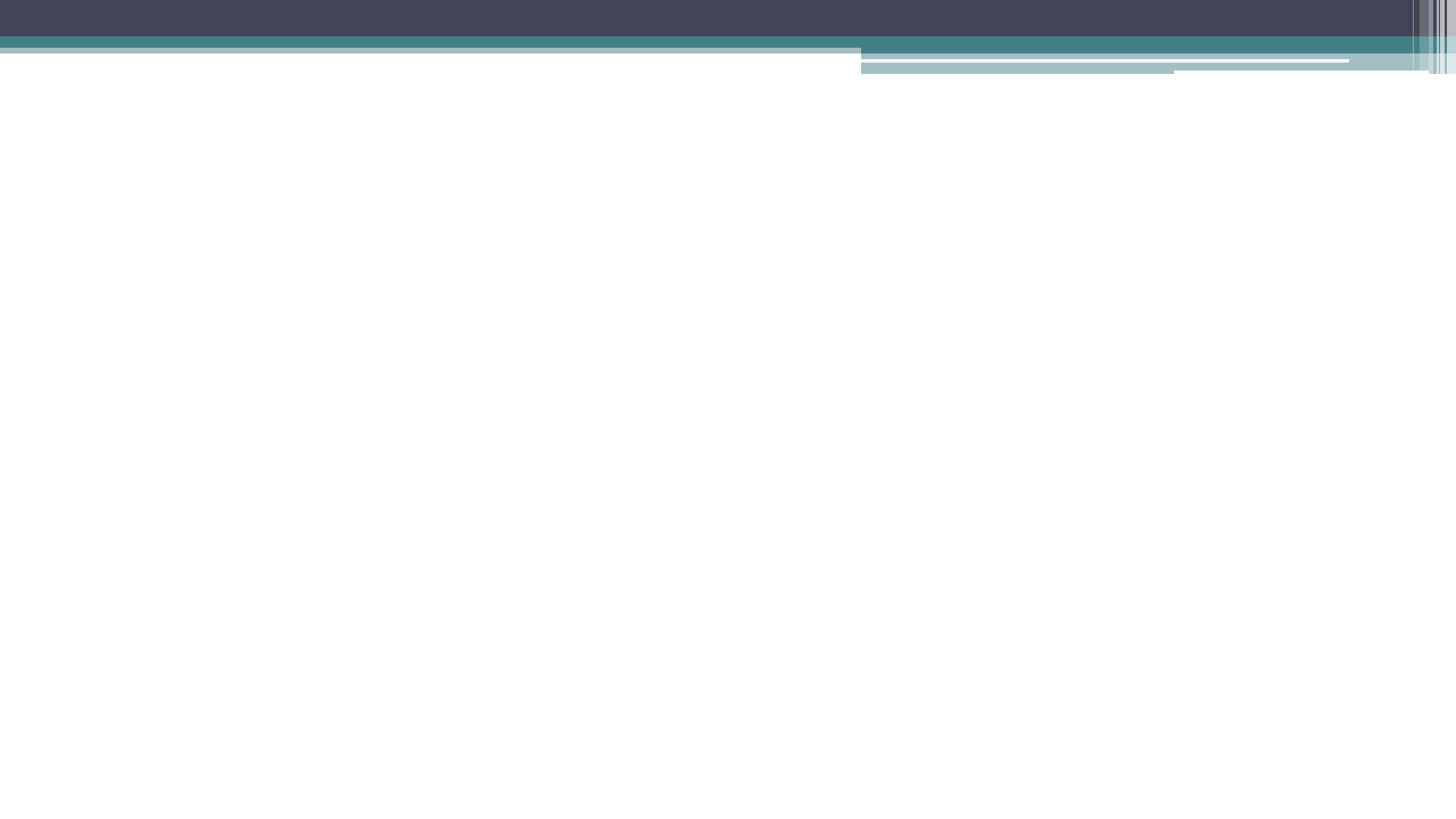
What would have the biggest impact on antimicrobial use in humans and animals?

- Improved human and animal health systems
 - Better IPAC
 - Improved WASH
 - Better and equitable access to preventive medicine
 - Better access to healthcare
 - Improve health to reduce the need for antibiotics

- jsweese@uoguelph.ca
- **Twitter: weese_scott**
- <http://www.wormsandgermsblog.com>







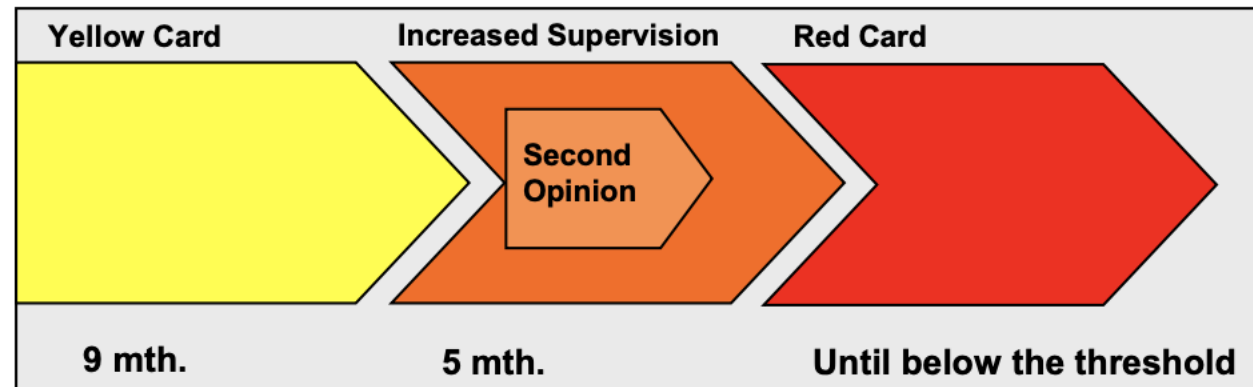
- Suboptimal animal management, resistance to change, defensive medicine and risk aversion (while ignoring AMR risk) underpin the ‘problem of AMR’ in animals
- These are what we need to address



**Ministry of Environment
and Food of Denmark**
Danish Veterinary and
Food Administration

Special provisions for the reduction of the consumption of antibiotics in pig holdings (the yellow card initiative)

The Yellow Card



Figur 1. The Yellow Card Initiative in short

Tabel 1. Development in thresholds for pigs.

Thresholds for pigs (in ADD per 100 animals per day*)	Piglets, sows, gilts and boars	Weaner pigs up to 30 kg	Finishers
Herd average Nationwide (2009)	2,6	14	4
Thresholds September 2010 – May 2013	5,2	28	8
Thresholds June 2013- October 2014	5	25	7
Thresholds November 2014 – March 2017	4,3	22,9	5,9
Thresholds April 2017* - December 2017	4,1	21,8	5,6
Thresholds Januar 2018 →	3,8	20,2	5,2

Close to a Decade of Decrease in Antimicrobial Usage in Danish Pig Production—Evaluating the Effect of the Yellow Card Scheme

Ana Carolina Lopes Antunes* and Vibeke Frøkjær Jensen

Division for Diagnostics & Scientific Advice—Epidemiology, Center for Diagnostics, National Veterinary Institute, Technical University of Denmark, Lyngby, Denmark

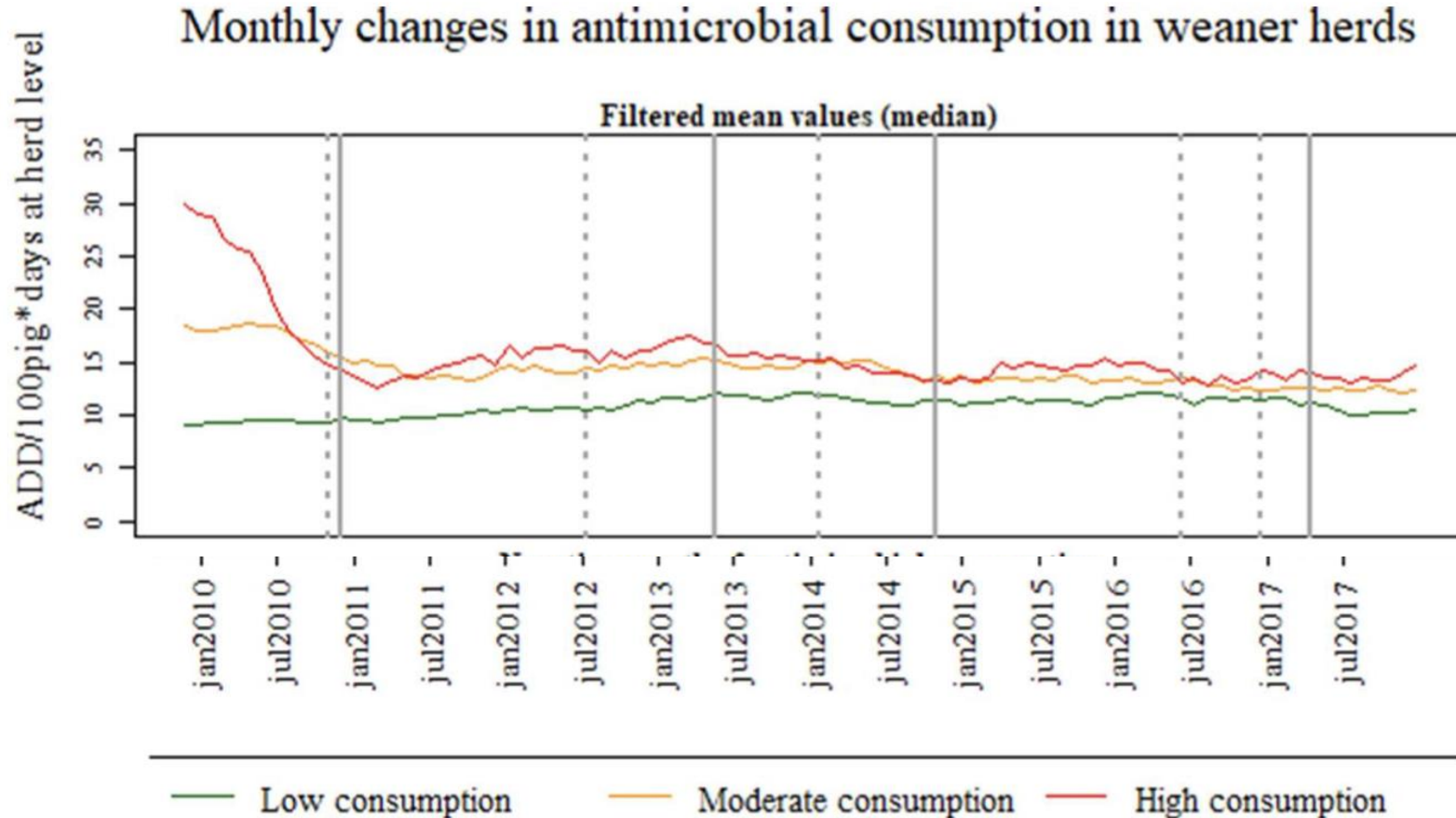


TABLE 1 | Changes in the Yellow Card scheme legislation in Denmark since its implementation.

The publication date of new legislation	The period when Yellow Cards were issued based on the new thresholds ^b	Piglets, sows, and gilts ^a	Weaners up to 30 kg ^a	Slaughter pigs and gilts ^a
2 Dec 2010	Aug 2011–May 2013	5.2	28	8
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20 Dec 2016	Jan 2018–	3.8	20.2	5.2

^aThresholds for antimicrobial consumption measured in ADD/(100 pigs*days) at the herd level.

^bAfter the announcement of new legislation, Yellow Cards were issued according to the new thresholds from 9 months after the legislation date, i.e., based on antimicrobial usage forwards from date of the legislation.

- It's not only 'antibiotics' that drive antibiotic resistance
- "It makes sense" isn't evidence.



- What is the net impact of a stopping prophylactic lower tier drug use in food animals if...
 - Disease rates increase
 - More important drug classes are used for treatment
- Is it ethical to use antibiotics as a 'crutch' to enable suboptimal practices?
 - What about in LMICs?



Diarrheic Calf Treatment Algorithm

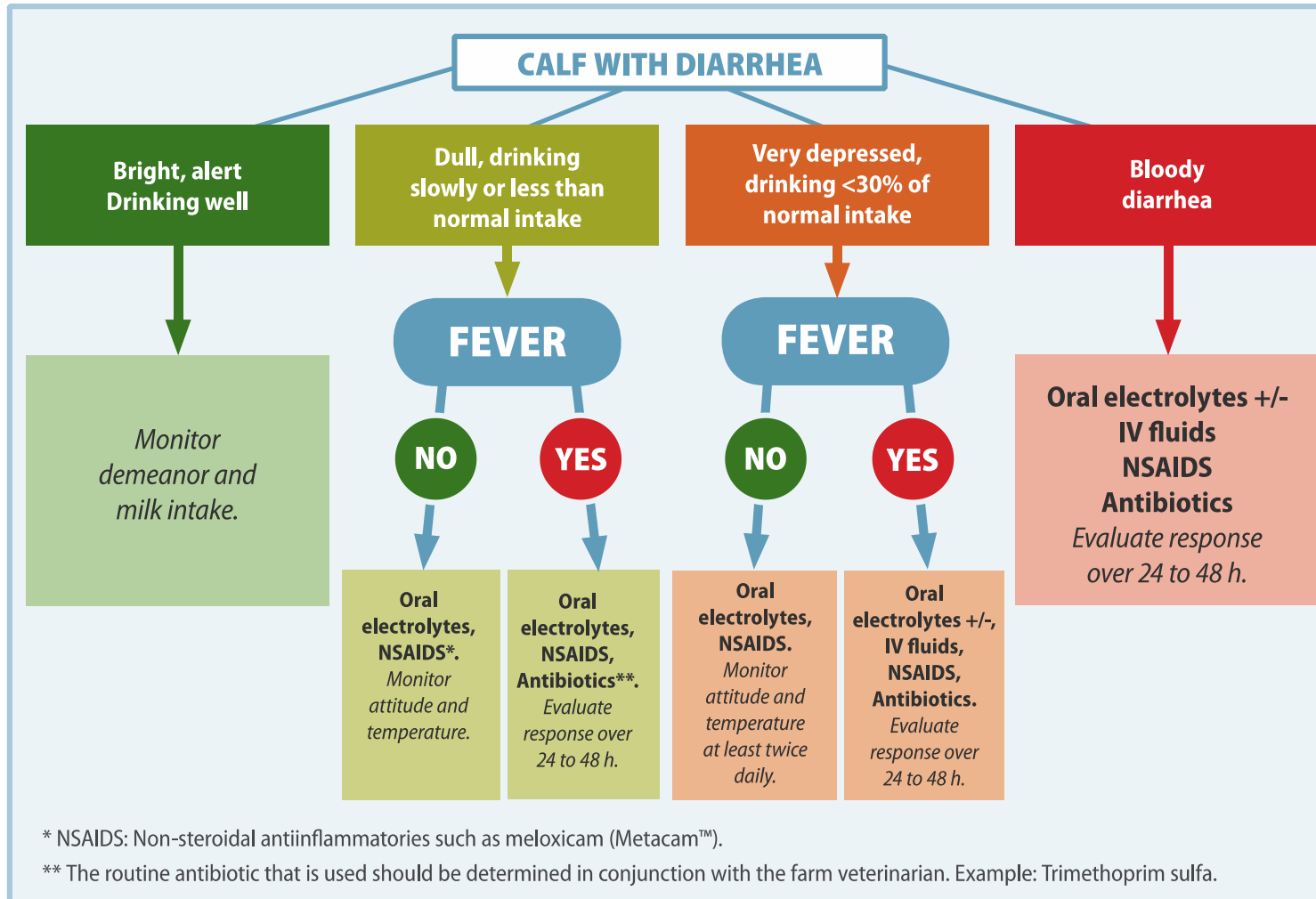
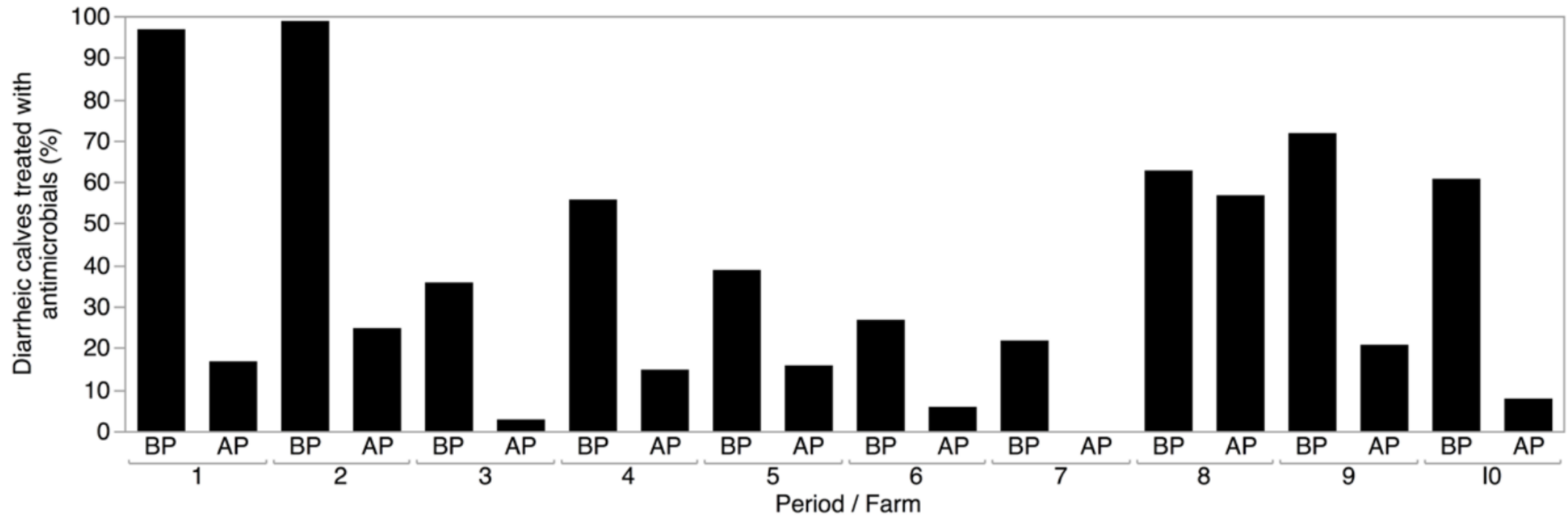


Figure 5.2: Antimicrobial treatment rates in 10 dairy farms before (BP) and after (AP) implementation of an algorithm for treatment of diarrheic calves.



Barriers

- Education of users and vets
- Confidence in not recommending/administering antimicrobials
- Farm culture

- Defensive medicine

- Bad outcomes are very evident (and ascribed to no AMU), good ones are not evident

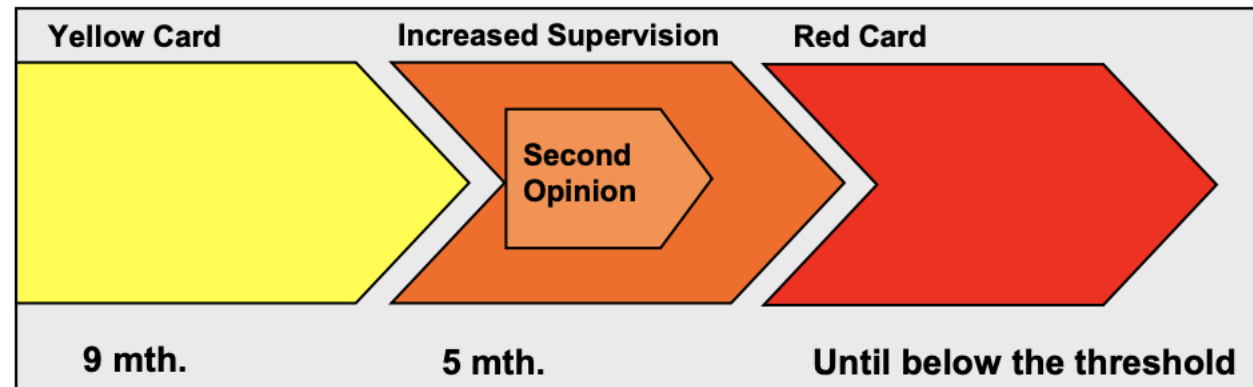




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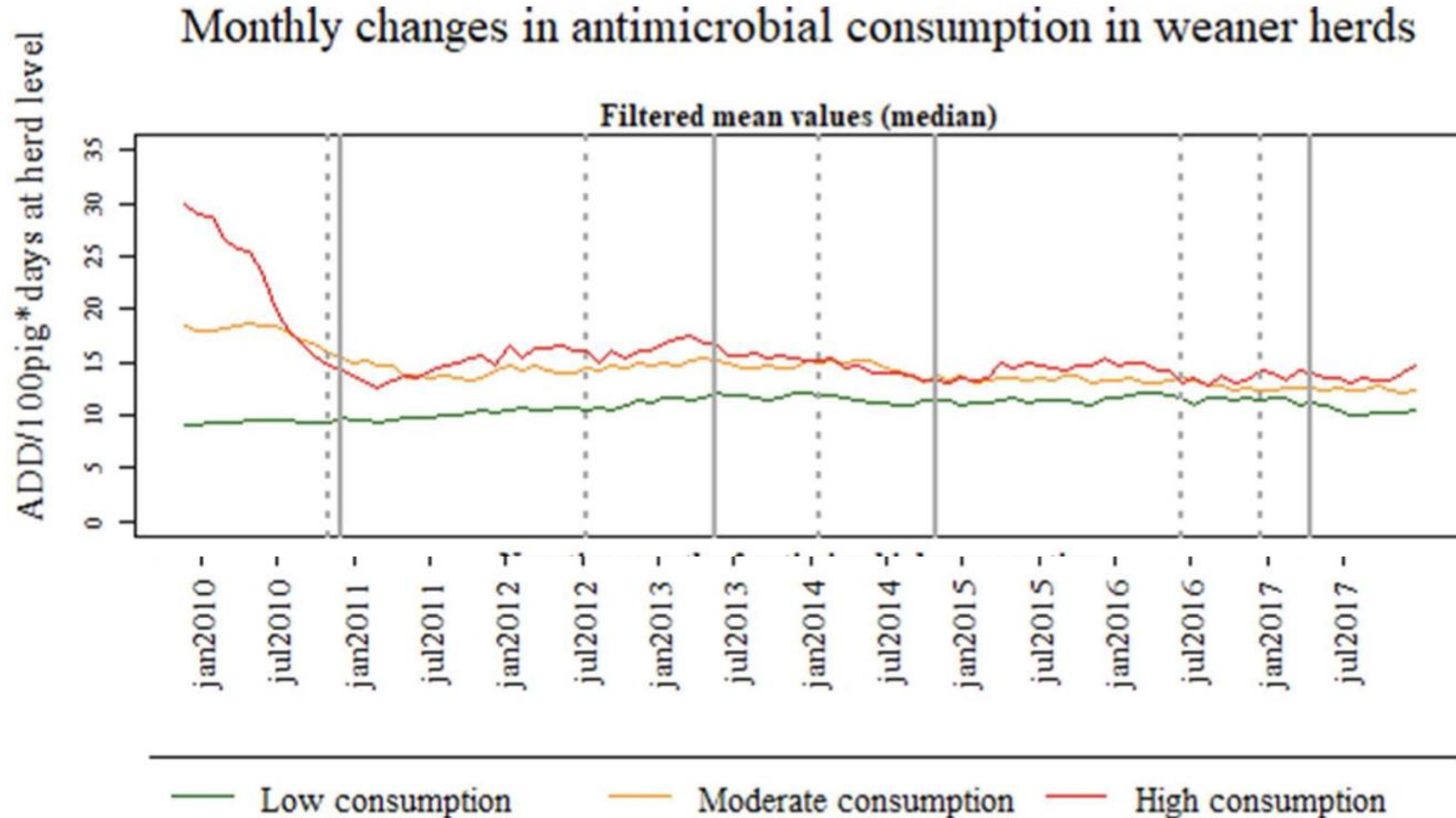


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Barriers??

- Political will
 - Countering lobbies
 - Public interest in AMR
- Industry buy-in
- Adequate data collection
- Regulatory mechanisms (F/P/T barriers)
- Support to improve AMU
- Funding

Map View

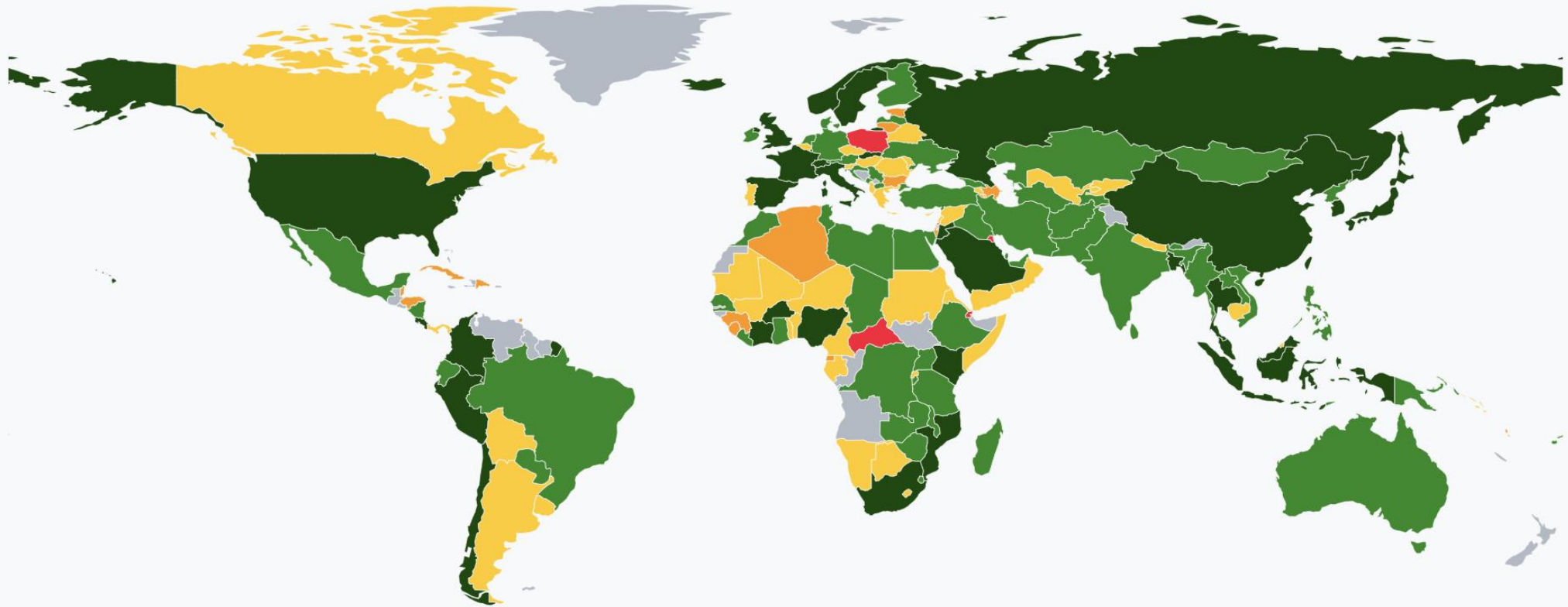
Visualization View






Table View

Response Overview

Download Responses

Print



-  A - No national AMR action plan.
-  B - National AMR action plan under development.
-  C - National AMR action plan developed.
-  D - National AMR action plan being implemented.
-  E - National AMR action plan being implemented and actively monitored through a monitoring and evaluation framework.



Global Leaders Group on Antimicrobial Resistance

The establishment of a Global Leaders Group on Antimicrobial Resistance was recommended by the Interagency Coordination Group (IACG) on Antimicrobial Resistance. The Global Leaders Group includes members from Member States, civil society and the private sector.

About

The Interagency Coordination Group (IACG) on Antimicrobial Resistance concluded its mandate by submitting its [report](#) to the UN Secretary-General (UNSG) in April 2019. The UNSG reiterated his commitment to antimicrobial resistance in a [report](#) that underlined the importance of implementing the recommendations. Furthermore, he requested the Tripartite Organizations (FAO, OIE and WHO) in close consultation with his office to propose the terms of reference and mechanisms for establishment of the One Health Global Leaders Group on antimicrobial resistance (Global Leaders Group) as a key global governance structure.

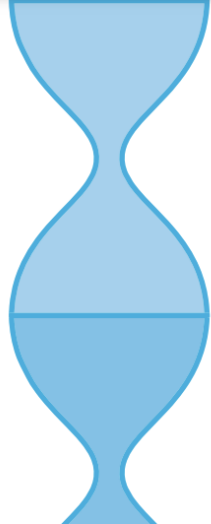
The Tripartite Joint Secretariat on Antimicrobial Resistance developed draft Terms of Reference for the Global Leaders Group based on



GLOBAL LEADERS GROUP ON ANTIMICROBIAL RESISTANCE

Antimicrobial Use in Food Systems

*Statement of the Global Leaders Group on Antimicrobial Resistance
August 2021*



1. Infection prevention and control

- **All countries** should prioritize infection prevention and control, including water, sanitation and hygiene, biosecurity and vaccination programmes as interventions to prevent and mitigate infectious disease risk and AMR across all sectors; and
- **International technical, financing and research and development organizations and partners** should support countries to improve access to and use of existing and new affordable diagnostic testing, disease prediction tools, vaccines, safe and efficacious non-antimicrobial alternatives and appropriate nutrition for infection prevention, control and treatment in terrestrial and aquatic animals, and where applicable for plants.

2. Reducing antimicrobial use

All countries should:

- Recognize the importance of antimicrobials for animal health and welfare and plant production in their national policies and regulatory frameworks and eliminate the use of antimicrobials to compensate for inadequate infection prevention and control, management and other modifiable deficiencies in management of animal and plant health;
- Markedly reduce the overall use of antimicrobials, particularly the Highest Priority Critically Important Antimicrobials for terrestrial and aquatic animals and plants;
- End the use of medically important antimicrobials for growth promotion, starting immediately with the Highest Priority Critically Important Antimicrobials, then continuing to other categories; and
- Limit antimicrobial prophylaxis and metaphylaxis in animals and plants to well-defined situations, with a goal of markedly reducing use and ensuring that all use is performed with regulatory oversight and under the direction of an authorized prescriber.

3. Oversight and governance

All countries should:

- Ensure effective governance and professional oversight of the sales and use of antimicrobials and stewardship of antimicrobials in all sectors, including the development and implementation of evidence-based guidelines for treatment, control and prevention; and
- Eliminate or markedly reduce over-the-counter sales of antimicrobials that are important for medical or veterinary purposes and implement stringent rules to strengthen and increase professional oversight for terrestrial and aquatic animal and plant use.

International technical, financing and research and development organizations and partners should:

- Establish mechanisms to improve and broaden appropriate access to good quality antimicrobials worldwide; and
- Encourage and support the development and improvement of comparable national and international surveillance systems to enable countries to establish antimicrobial use and resistance baselines and set progressive, ambitious, science-based and nationally relevant targets for responsible and sustainable antimicrobial use across all sectors.

Information notes



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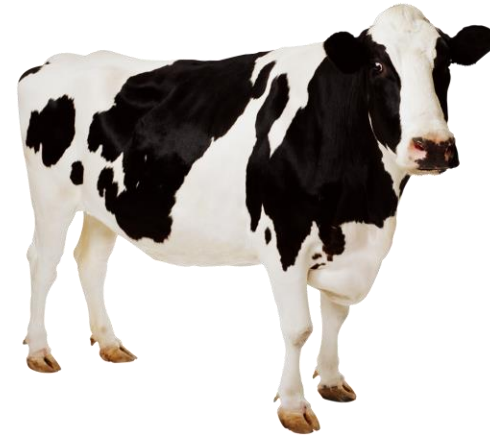


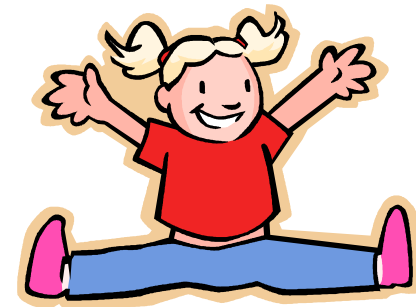
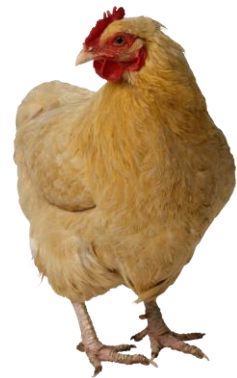
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Antibiotic use in 'animals'





Therapeutic



Prophylactic



Metaphylactic



Growth promotion

Therapeutic



Prophylactic





Variable
(often short)
lifespan

Withdrawal
times



Limited
human
contact



Environmental
contamination

Economic
value

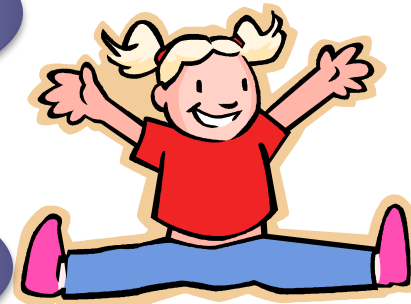
Longer lifespan:
cumulative
exposure

Close contact
with humans

Abundant
extra-label
use

Wide range of
drug classes

Human-
animal bond



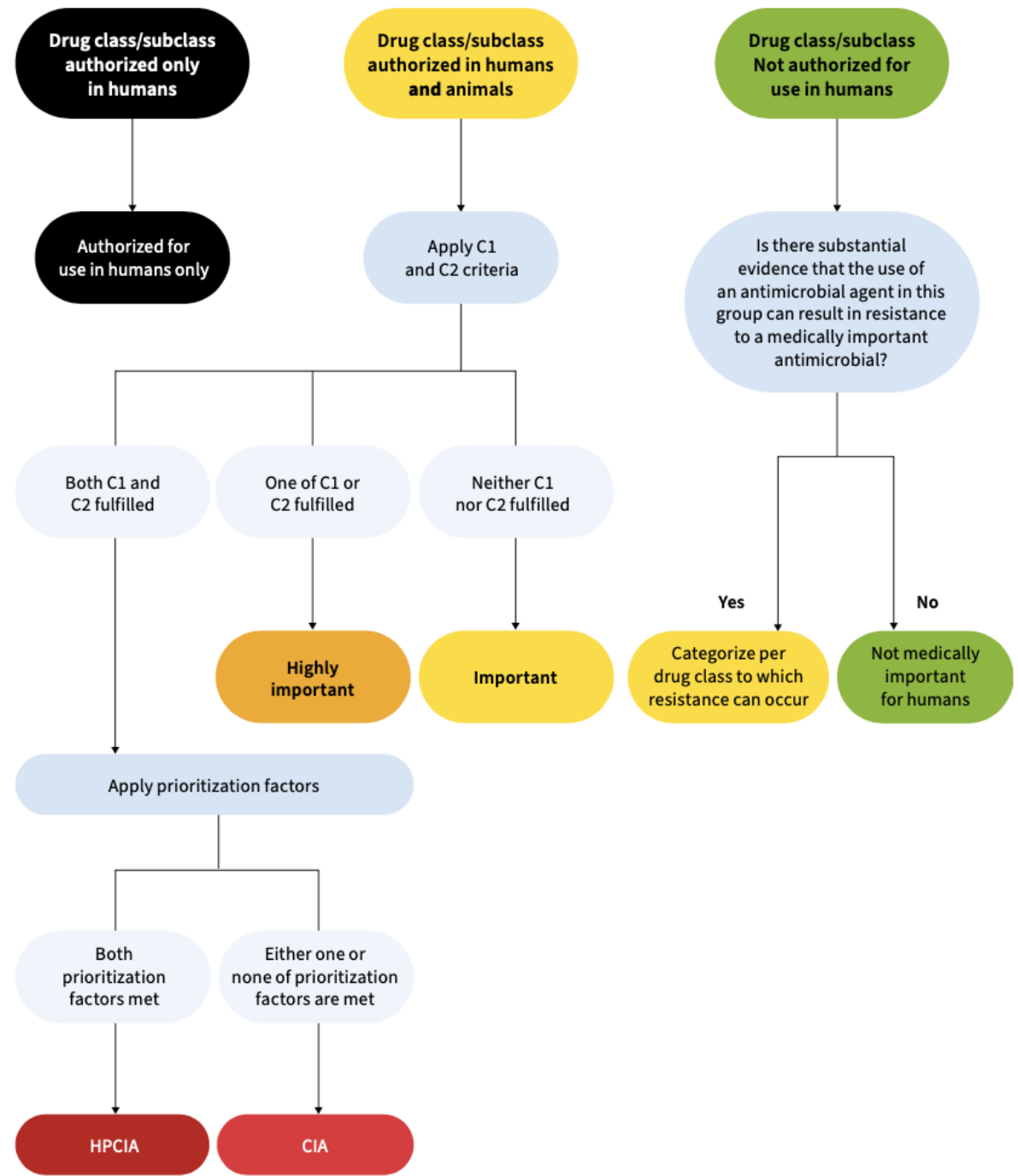
- Is antimicrobial stewardship in animals targeting
 - Human health?
 - Animal health?
 - Human/animal/environmental health?

I could implement an intervention today to reduce antimicrobial use in dogs with urinary tract infections by 80–90%.

Great, right?

Easier analogy

- Dropping your yearly alcohol consumption from 50L of light beer to 30 L of vodka isn't a good thing
 - But it's a decrease



Barriers??

- Political will
 - Countering lobbies
 - Public interest in AMR
- Industry buy-in
- Adequate data collection
- Regulatory mechanisms (F/P/T barriers)
- Support to improve AMU
- Funding