# Panel 1

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## Is a One Health strategy the best approach to seek solutions to antimicrobial resistance?


Canadian Academy of Health Sciences
Académie canadienne des sciences de la santé

# Is a One Health Strategy the Best Approach to Seek Solutions to Antimicrobial Resistance?

PANEL 1 - THOMAS MARRIE AND HERMAN BARKEMA

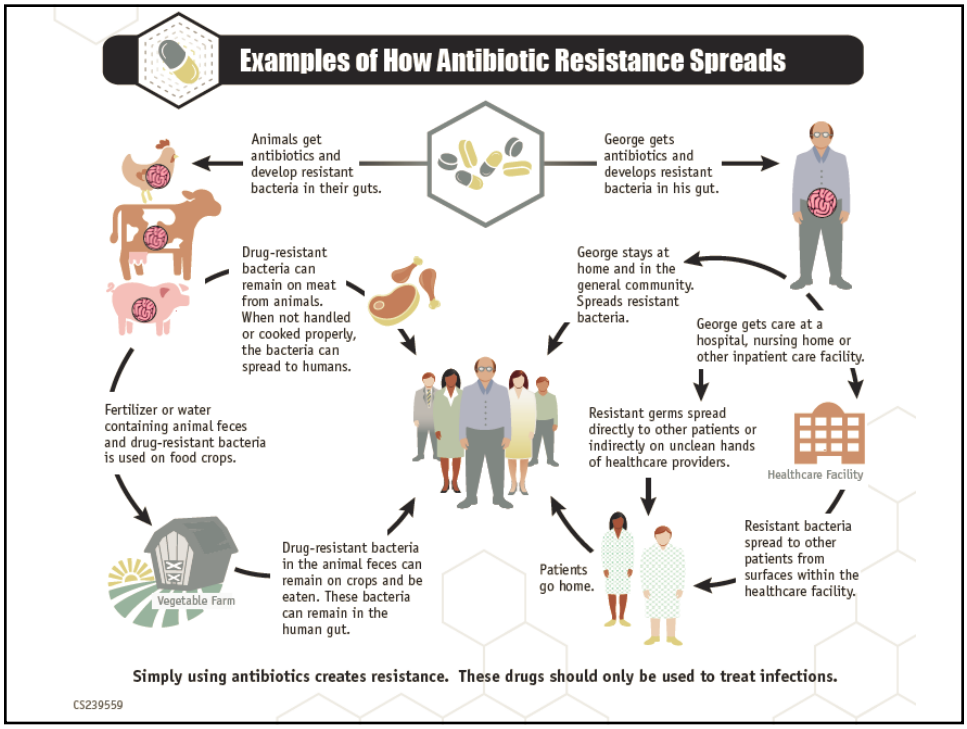
# Outline

1. What is One Health?
2. How does it relate to antimicrobial resistance in humans?
3. Presentation of data to support the concept that One Health is integral to understanding and controlling AMR



# One Health Concept Applied to Antimicrobial Resistance

- Use of antibiotics in animal husbandry and aquaculture with subsequent spread of AROs to humans
- Inappropriate use of antimicrobials in humans also contributing to resistance
- Contamination of environment with fecal waste from 1 and 2 containing ARO's resulting in an ongoing cycle
- Person to person spread – concept of super spreaders
- Modern travel enabling spread of AROs from one corner of the Globe to another
- Not so modern travel – birds with their migration routes leave a fecal trail with AROs




# Economou V, Gousia P. Agriculture

and food animals as a source of antimicrobial resistant bacteria. Inf Drug Resis 2015; 8: 49-61

- 1950 - Stokstrad and Jukes noted that small sub therapeutic doses of penicillin and tetracycline could enhance weight gain in animals. Mech for this still unclear
- 2006 – antimicrobial growth promoters withdrawn in EU. Ionophores continue to be administered
- Metaphylaxis – whole flock is treated even though only a few show clinical symptoms. High dose short duration
- Prophylaxis – antimicrobials in food or drinking water for several weeks.
- Growth promotion

# Use of Antibiotics in Canada

- Of all the medically important antimicrobials distributed for use in Canada, approx. 82% intended for production animals, 18% for humans, <1% for companion animals, and <1% for crops
- Adjusting for underlying populations and weights there was roughly 1.7 times more antimicrobials distributed for use in animals than humans
- 73% of this in 2014 included antimicrobial classes also used in human medicine

CIPARS 2014 – Annual Report

# What about aquaculture?

- Sulfonamides, penicillins, quinolones, tretracyclines, phenicols widely used
- Quinolones, tetracyclines and phenicols especially widely used in salmon farming
- In some countries effluent from pig farms has contaminated the water of aquaculture farms. This effluent contains residue of antimicrobials fed to pigs

## Gopinath S et al. Role of disease-associated tolerance in infectious superspreaders. PNAS 2014;111:15780

- 1997 Woodhouse 20% of infected hosts (superspreaders) are responsible for 80% of infections
- Demonstrated in cattle herds infected with *E. coli* 0157 H7
- Gopinath et al. used a mouse model of Salmonella to dissect the reasons for superspreaders
- Superspreaders have unique tolerance mechanisms that enable sustained pathogen transmission

## UofC Systematic Review Team

Expertise from Cumming School of Medicine and Faculty of Veterinary Medicine

| | |
|---|---|
| William Ghali (PI) | Karen Tang |
| Susan Cork | Niamh Caffrey |
| Herman Barkema | Diego Nóbrega |
| James Kellner | Alicia Polachek |
| Paul Ronksley | Nishan Sharma |
| Heather Ganshorn | Jill De Grood |

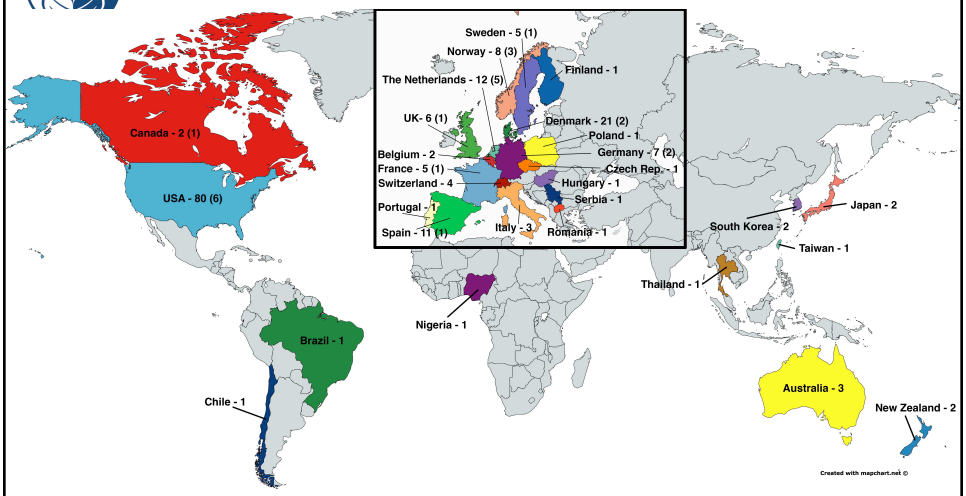
# WHO Research Question 1

Does a **restriction of use of antibiotic agent(s) in food animals** compared to not having that restriction reduce the presence of antibiotic resistant genetic elements and/or **antibiotic resistant bacteria in food animal** populations of any age in any setting?

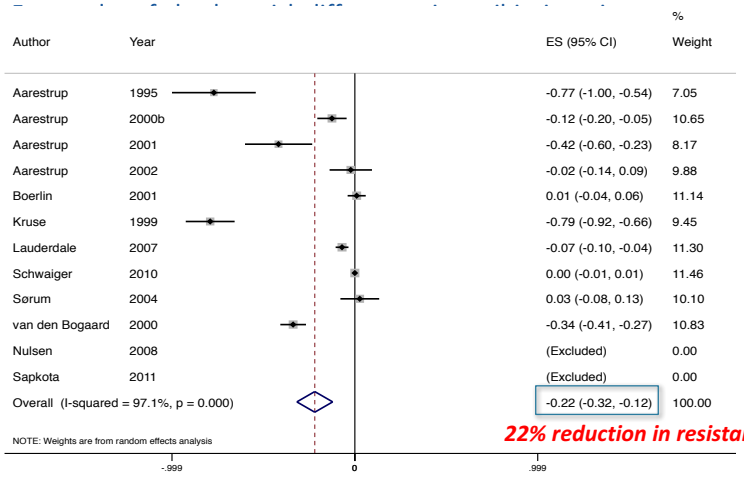
# WHO Research Question 2

Does a **restriction of use of antibiotic agent(s) in food animals** compared to not having that restriction reduce the presence of antibiotic resistant genetic elements and/or **antibiotic resistant bacteria in human populations** of any age in any setting**?**

# Geographic Representation




# Meta-Analysis




***22% reduction in resistance***

# Summary of Meta-Analyses

Pooled between 6-20 studies

- Range RD
  - 0.01 (95% CI -0.19, 0.21) to -0.39 (95% -0.56, -0.23)
- Most pooled risk differences between -0.10 to -0.20

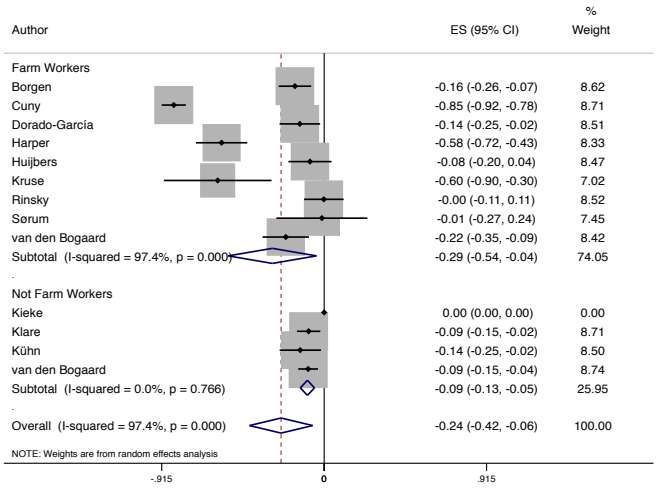
***"The pooled proportion of bacterial isolates resistant to antibiotics was 10-20% lower in intervention groups"***

Similar results with qualitative phenotypic study synthesis (n=68) and genotypic study synthesis (n=46)

# Characteristics human studies

| **Study Characteristic** | | **No. studies (N=21)** |
|---|---|---|
| Intervention | Externally imposed restrictions | 9 |
| | Organic interventions | 2 |
| | Self-reported antibiotic-free | 5 |
| | Voluntary reduction | 5 |
| Bacteria studied | *Campylobacter* spp. | 2 |
| | *Enterococcus* spp. | 8 |
| | Enterobacteriaceae: *E. coli* | 3 |
| | Enterobacteriaceae: *Salmonella* spp. | 1 |
| | *Staphylococcus* spp. | 8 |

# Stratified Meta-Analysis




# Conclusions animal studies

The 175 animal studies (of which 80 were pooled) showed consistent reduction of antibiotic resistance in animals with interventions reducing antibiotic use

Risk reduction varied; generally in the 10-20% range

Findings held:

- Across bacterial groups
- Across sample types
- Across all antibiotic drug classes
- Across all intervention types, whether they were strong versus weak interventions
- Regardless of study quality

# Conclusions human studies

Smaller number of human studies found (N=21)

Of these, 13 were pooled, showing a 24% reduction of antibiotic resistance in humans with interventions reducing antibiotic use in food animals

Mechanisms indirect

Effect stronger in farm workers

Findings held:

- Across strong versus weak interventions
- Regardless of whether interventions were well-described
- When meeting abstracts were removed
- When ecological studies were removed

However, quality of these studies was not great

# Why would a One Health Approach be beneficial?

Surveillance

- Many resistant bacteria have multiple hosts and increased prevalence can be transmitted from many species
- Same standards for sampling, testing and reporting from different sources, nationally and internationally
- Important for trust in food sources to monitor these as well

Research

- Comparative biology of AMR in different species
- Find alternatives for antimicrobials (collaboration with pharma)
- The prescribers and users are humans. How to motivate MDs, DVMs, and farmers to reduce prescription of antibiotics?

Control measures

- Alignment of control measures in different species and monitoring the effect in different species
- Joint training of MDs and DVMs (education and CE; social science)
- infection prevention and control + availability of MDs and DVMs

# Why would a One Health Approach be beneficial?

To avoid a non-productive blame game

Working together limits adversarial responses, motivates both sides, and stimulates accepting responsibility and taking necessary actions

Be an example for less developed countries where AMR increases at an alarming speed, livestock farming and human presence are intertwined, consumption of food from animal origin increases every year, and animal production without growth promotion is still very difficult

One Health is more than human and animal health. Not a lot is known about the role of the environment in the development of the global resistome

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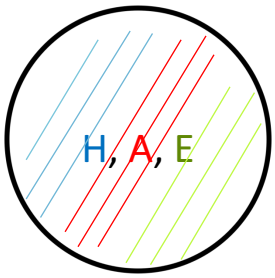
PANEL 1

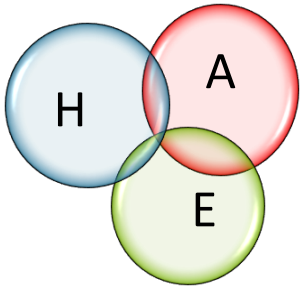
LINDSAY NICOLLE

## Restraining Resistance

ONE HEALTH




REALITY




Human, Animal, Environment

## One (Human) Health

What proportion of antimicrobial resistance in humans is attributable to antimicrobial resistance in animals?

Do interventions to limit antimicrobial resistance in animals limit resistance in humans?

## WHO Priority Pathogens List for R & D of New Antibiotics (Feb,2017)

| | | |
|---|---|---|
| Priority 1: | Critical | *A. baumanii*, CP resistant<br>*P. aeruginosa*, CP resistant<br>Enterobacteriaceae, CP; ESBL (±) |
| Priority 2: | High | *E. faecalis*, VR<br>MRSA, VR & Intermediate<br>*H. pylori*, clarithromycin R<br>Campylobacter spp FQ res<br>Salmonella FQ res (±)<br>*N. gonorrhea*, ceph res, FQ res |
| Priority 3: | Medium | *S. pneumoniae* Pen non-sus<br>*H. influenzae*, amp res<br>Shigella spp, FQ res (±) |
| Tuberculosis – "other dedicated programs" | | |

Conclusion: Animal origin for human ARO is exceptional, not the norm.

## CDC: Antibiotic Resistant Solutions Initiative

- $264 million, 2016

Anticipated outcomes: Reduction Rate

| | |
|---|---|
| *C. difficile infection* | 58% |
| Healthcare CRE | 60% |
| HC MDR Pseudomonas | 35% |
| Bloodstream MRSA | 50% |
| MDR Salmonella | 25% |
| Invasive pneumococcal disease | 25% |
| MDR tuberculosis | 15% |
| MDR gonorrhea | 2% |

## Managing Antimicrobial Resistance: Human

- surveillance
- limit transmission (infection control)
  - acute care
  - long term care
  - community (±)
- decrease antimicrobial use (stewardship)
  - acute care
  - long term care
  - community
- innovation

## OneHealth: an Artificial Construct

Interferes with discussion and program development:

-inefficient

-misdirects resources/duplicates efforts

For limited areas of relevant overlap:

- commit
- communicate
- collaborate

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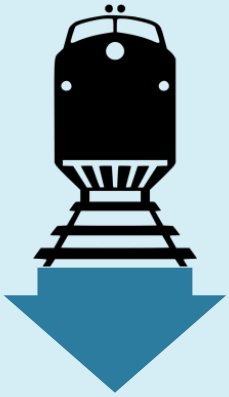
# Is a One Health Strategy the Best Approach to Seek Solutions to Antimicrobial Resistance?

## PANEL 1

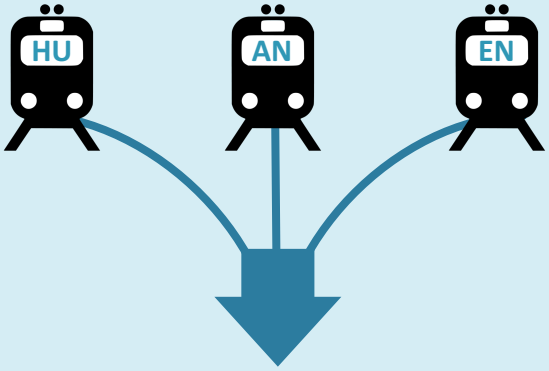
By Carlton Gyles

## To AMR Reduction Central Station

**One Health Route**



**Fast Track for AMR Reduction**




PANEL 1 Carlton Gyles

# The Argument

- **One health -** complex concept, still evolving
- : *"Human or livestock or wildlife health can't be **discussed** in isolation anymore. There is just one health."*
- **Ecosystem health – the environmental piece**
- AMR reduction strategies should not be encumbered with the growing pains of the One Health movement



# One Health – still evolving

- A movement to forge **co-equal partnerships**
- **All inclusive collaborations** between physicians, osteopathic physicians, veterinarians, dentists, nurses and other scientific, health and environmentally related disciplines
- American Medical Association, American Veterinary Medical Association, American Academy of Pediatrics, American Nurses Association, American Association of Public Health Physicians, American Society of Tropical Medicine and Hygiene, CDC, USDA, U.S. National Environmental Health Association (NEHA)

# One Health Involves Numerous Groups

- Human medical practitioners
- Animal medical practitioners
- Dentists
- Public health personnel
- Microbiologists
- Pharmacologists
- Infection control personnel
- Nurses
- Research scientists
- Government agencies
- Ecologists



# AMR Reduction Involves Numerous Organizations

- Health Canada
- Public Health Agency of Canada
- Canadian Institutes of Health Research
- Canadian Food Inspection Agency
- Agriculture and Agri-Food Canada
- National Research Council
- Industry Canada
- Canadian Veterinary Medical Association
- Canadian Animal Health Institute
- Provinces and Territories*

# One Health and AMR

- **One Health > Zoonotic diseases**
- *"A One Health approach is important because 6 out of every 10 infectious diseases in humans are spread from animals."* – CDC
- AMR in animals is a **minor contributor** to the AMR problem in humans **> Already addressed**
- The existing approach involving **compartmentalization with periodic discussion > Working well**
- **Repeal and replace > Will not work as well**

PANEL 1 Carlton Gyles

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# Is a One Health Strategy the Best Approach to Seek Solutions to Antimicrobial Resistance?

ROUND 2

PRESENTER NAME

## Other than bird characteristics what do these two species have in common?



## Wang J et al. The role of wildlife (wild birds) in the global transmission of antibiotic resistance genes. Zoological Res 2017; 38: 55-80

- At least 80 species of wild life ( mostly birds) have been found to be carriers of ESBL producing Enterobacteriacea.
- Franklin's gulls
- Black Headed gull
- Yellow Legged gulls
- Herring gulls
- Birds of Prey
- Canada goose
- Rooks
- Cattle Egret etc

## Drs. Nicole and Gyles – its OK – some people say there is no change in our climate ……..