The Role of Vaccination and Disease Diagnosis in Improved Veterinary Antimicrobial Stewardship

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Conflicts of Interest

- Our group developed the ts-11 *Mycoplasma gallisepticum,* the ts-304 *Mycoplasma gallisepticum* and the MS-H *Mycoplasma synoviae* vaccines in collaboration with Bioproperties Pty Ltd, the Protivity *Mycoplasma bovis* vaccine in collaboration with Zoetis Ltd, and the delta gG infectious laryngotracheitis vaccine in collaboration with Bioproperties Pty Ltd.
- Our university and our group received a share of the royalties from these vaccines, and as one of the inventors I receive a share of the royalties from the ts-304, Protivity and delta gG vaccines.

What Is Antimicrobial Stewardship?

- Coordinated set of measures to ensure appropriate use of antimicrobial drugs and minimise their inappropriate use
- Aim is to support and guide therapy when it is needed, while concurrently limiting the selection for antimicrobial resistance
- Well-established in human medicine, but a relatively new discipline in veterinary medicine
- Focused on modifying behaviour by supporting practitioners to make the best decisions about antimicrobial use
- Generally less focused on regulating use and more directed at encouraging optimal use

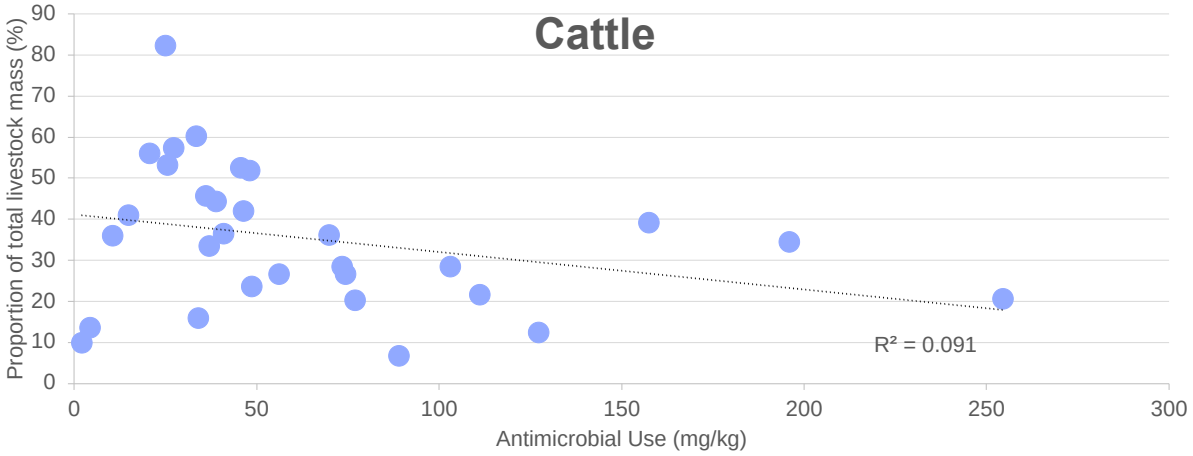
Why Antimicrobial Stewardship?

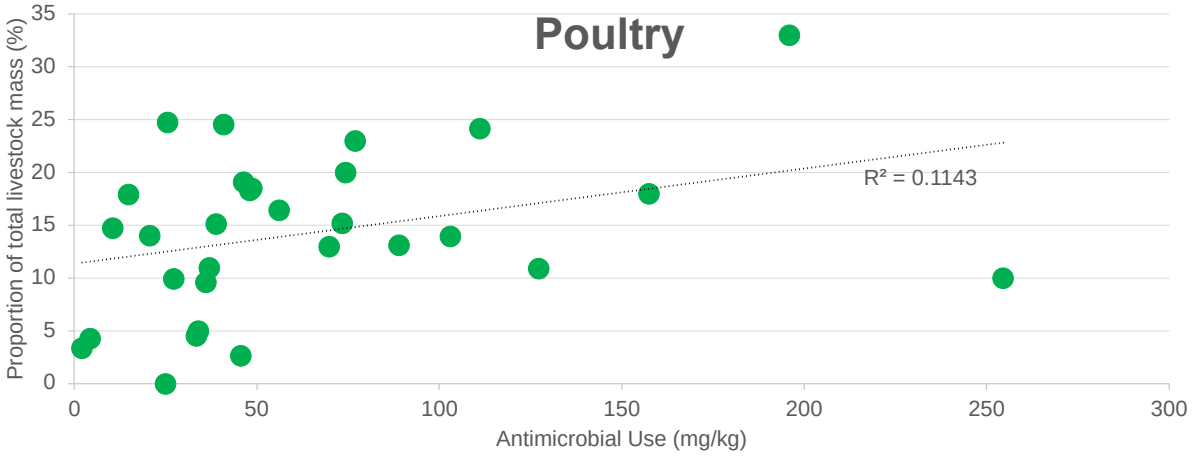
- Antimicrobials remain vital for optimal human and animal health
- Antimicrobial use patterns vary widely, between
  - Veterinarians
  - Species
  - Production systems
  - Countries
- Variation in total amounts used and classes used
- Extent of variation suggests that significant amounts of use has little or no impact on animal health
- This unnecessary use will select for resistance in both “target” and off-target bacterial species with adverse impacts on human and animal health

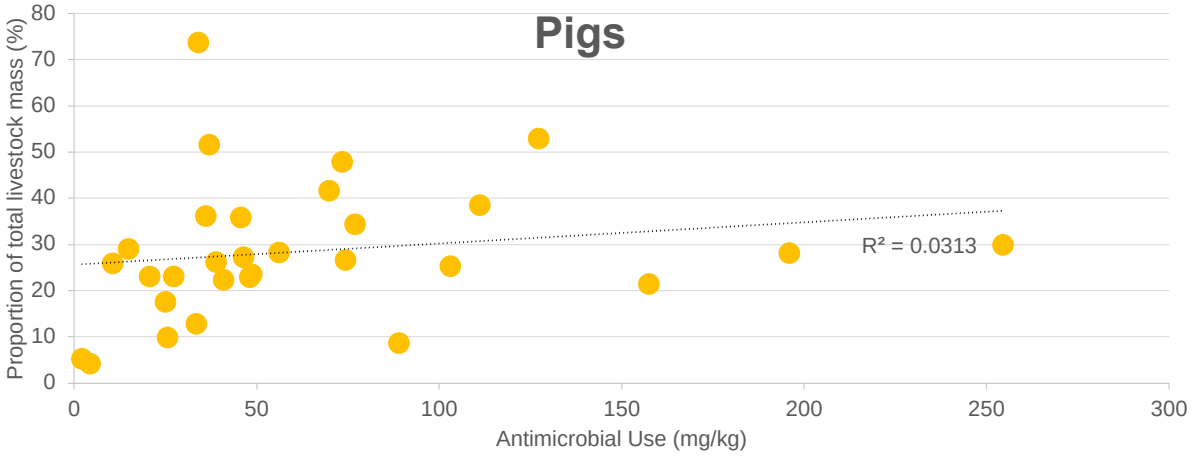
What Are the Underlying Drivers of Antimicrobial Use?

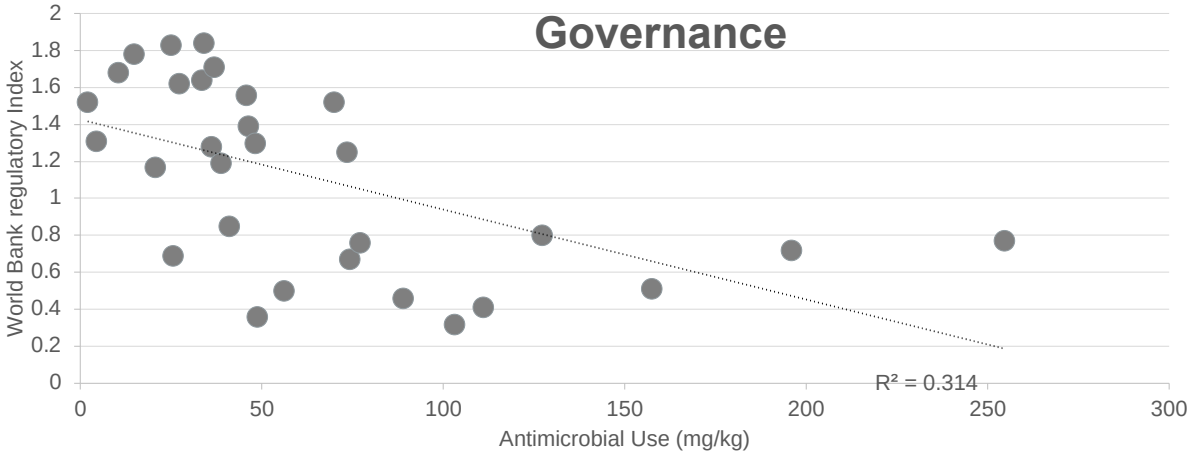
- Use for growth promotion has been progressively banned or severely limited
- Most use in intensively raised livestock is metaphylactic or prophylactic
- Much use is empirical, with limited or no diagnostic investigation to support use, let alone antimicrobial choice
- Apparent response to use drives ongoing use in the absence of diagnostic investigation
- Consequence is that much use is probably inappropriately targeted

Why Does Antimicrobial Use Vary Between Countries







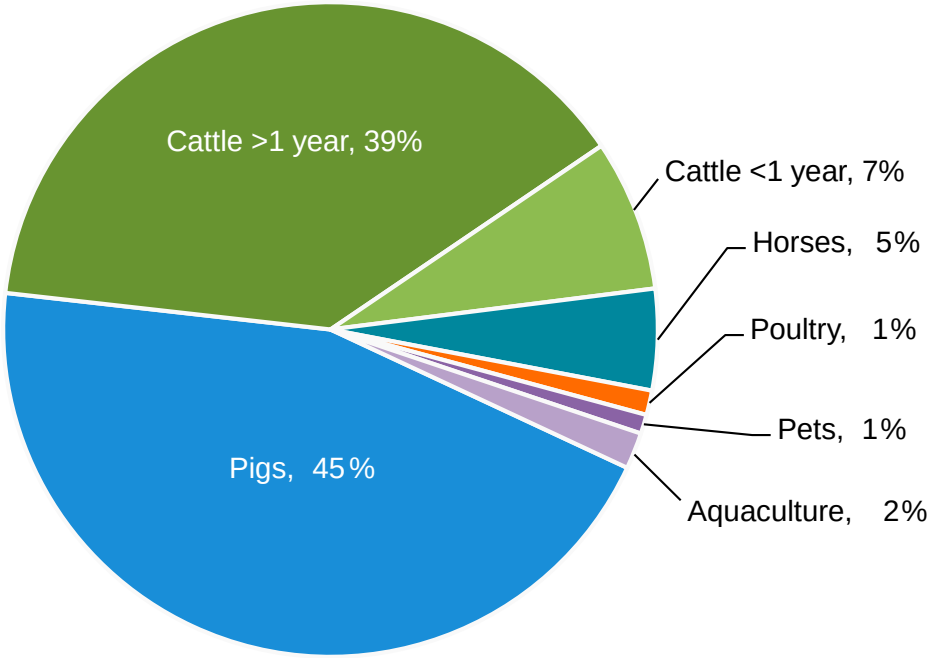


From the 13th ESVAC Report (2022) and https://databank.worldbank.org/source/worldwide-governance-indicators

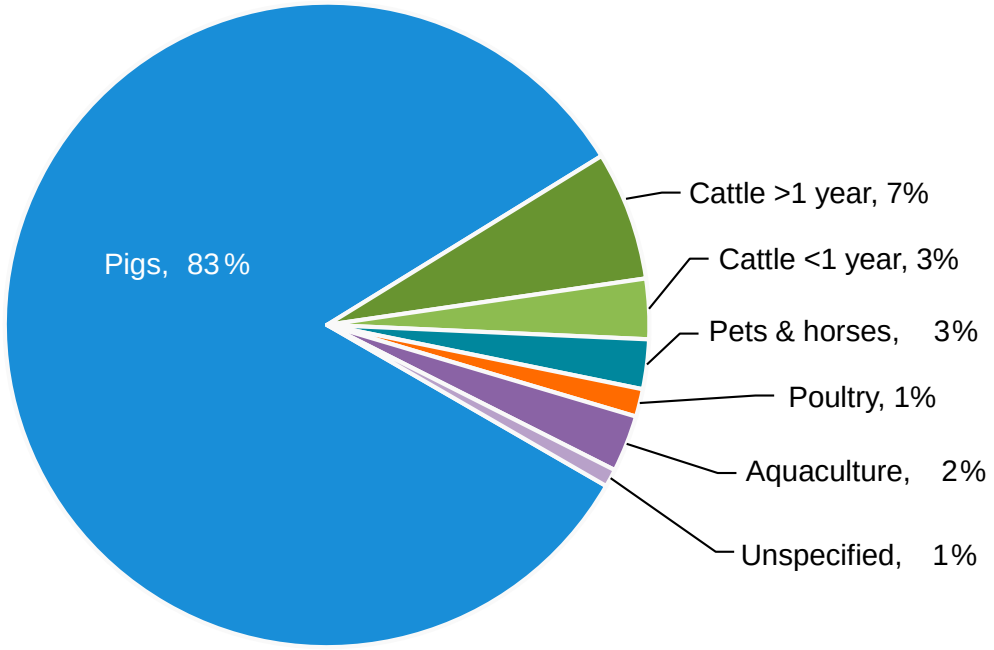
What Drives Variation in Use Between Countries?

- Much speculation that overuse is driven by poor governance, and thus a focus on increased regulation of animal health
- Governance is a factor, but is probably an enabler, not a driver
- A focus on regulation will not provide solutions to the underlying drivers of use
- Drivers of use are most likely to be ongoing, incompletely resolved problems with disease control
- A focus on better addressing animal health issues is likely to result in voluntary reductions in antimicrobial use

Antimicrobial Use in Pigs in Denmark



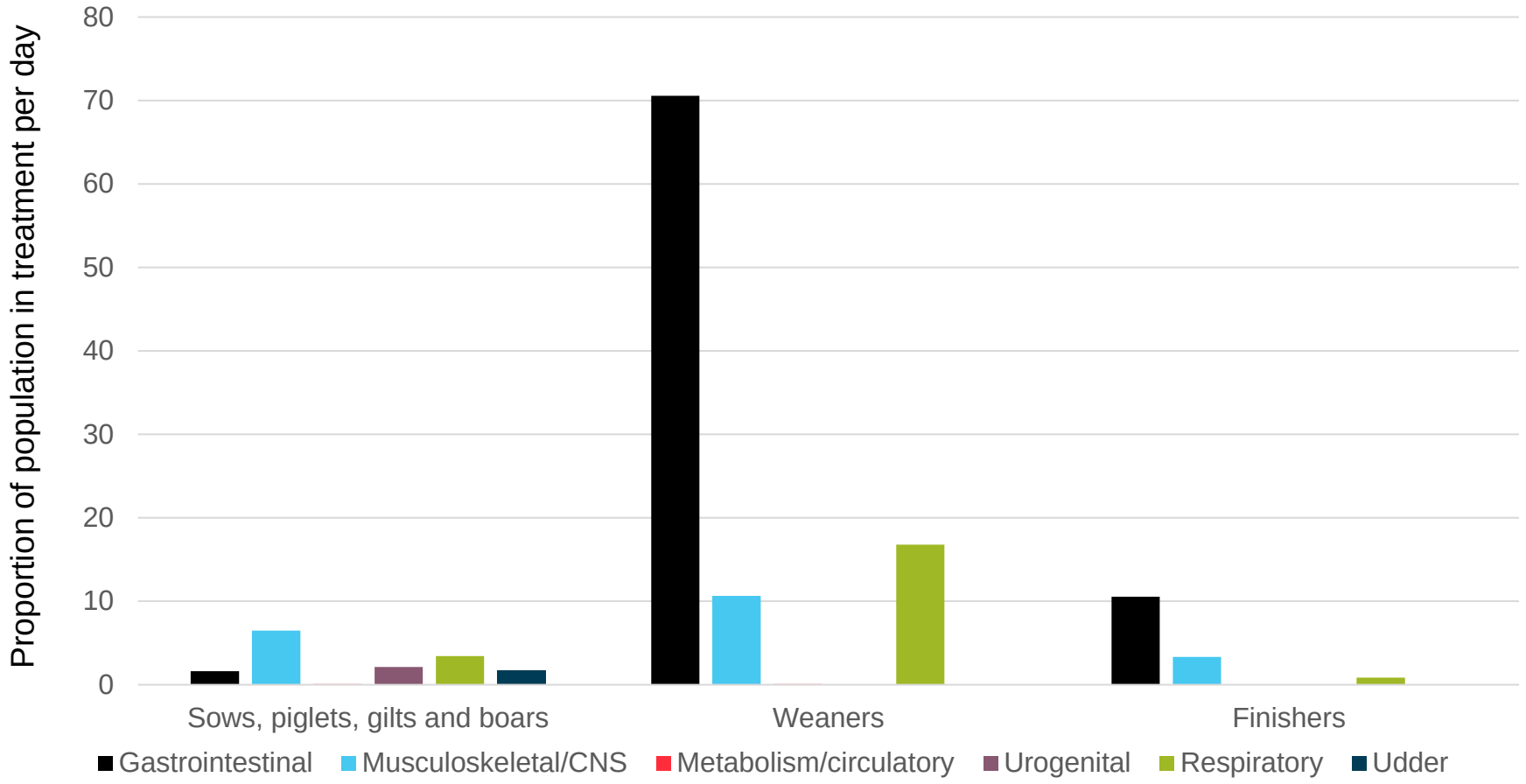
Live biomass of each animal species



Active antimicrobial compound used in each species

From: DANMAP 2022 – Antimicrobial Consumption in Animals

Indications for Antimicrobial Use in Pigs



From: DANMAP 2022 – Antimicrobial Consumption in Animals

Addressing the Drivers for Use in Pigs

- Better control of bacterial disease in pigs likely to have a significant impact on AMU in developed countries
- Gastrointestinal disease in weaners and finishers, respiratory disease in weaners and arthritis probably the major drivers of use
- Suggests a need for better control of post-weaning colibacillosis, swine dysentery, proliferative enteritis, respiratory and systemic mycoplasmoses, and other bacterial arthritides (*Streptococcus suis*, *Erysipelothrix rhusiopathiae, Glaesserella parasuis*)
- Greater use in weaners and finishers indicates that vaccination is a viable solution

Enablers and Barriers of Focus on Vaccination

- Effective vaccination controls losses and reduces drive for AM use
- Minimal ongoing maintenance, so better compliance
- Efficacy not immediately apparent, requiring diagnostic reassurance
- Vaccination (and improved biosecurity) are sunk costs for farmers
- AM treatment appears more cost-effective and benefits are more obvious
- Antimicrobial drugs less dependent on a cold chain
- Need strong veterinary support and strong evidence of financial benefit for vaccination

Low- and Middle-Income Countries

- Much greater AM use overall, especially in poultry (500 mg/kg in Nepal; 460 mg/kg in Pakistan, 190 mg/kg in Sri Lanka)
- Limited animal health workforce and lack of access to and use of diagnostic support
- Laboratory investigation often only sought after several rounds of unsuccessful, farmer-initiated antimicrobial treatment trials
- Much more limited access to effective vaccines
- Pack sizes of vaccines a problem for small scale farmers and uptake potentially reduced by substandard products and misdiagnoses
- Density of small holdings with limited infrastructure limits efficacy of biosecurity

Antimicrobial Use for Undiagnosed Disease

- Treatment in the face of mortalities – lack of diagnosis often leads to use for vaccine preventable viral disease
- Treatment of secondary infections – incomplete diagnosis with a focus on cultivable bacteria leads to escalated treatment of secondary *E.coli* infections rather than addressing primary problem
- Danger of AMR surveillance data being used to guide treatment of colibacillosis
- Use of unsuitable mycoplasma vaccines in meat chicken flocks could be driving use

What Is Needed in Low- and Middle-Income Countries?

- Greater resourcing of animal health infrastructure and personnel
- In-field access to rapid diagnostic testing for bacterial and viral diseases - many effective vaccines either not available or rarely used, in part because of the lack of diagnostic information supporting their value
- Greater emphasis on farm biosecurity, particularly on sources of stock - in some countries many smaller poultry farmers are quite new to the industry

What Is Needed in Low- and Middle-Income Countries?

- Greater access to appropriate vaccines, particularly for intensively farmed livestock, with supporting data on financial benefits
- Better incentives for private veterinarians to engage in vaccination programs
- More responsible marketing of animal health products

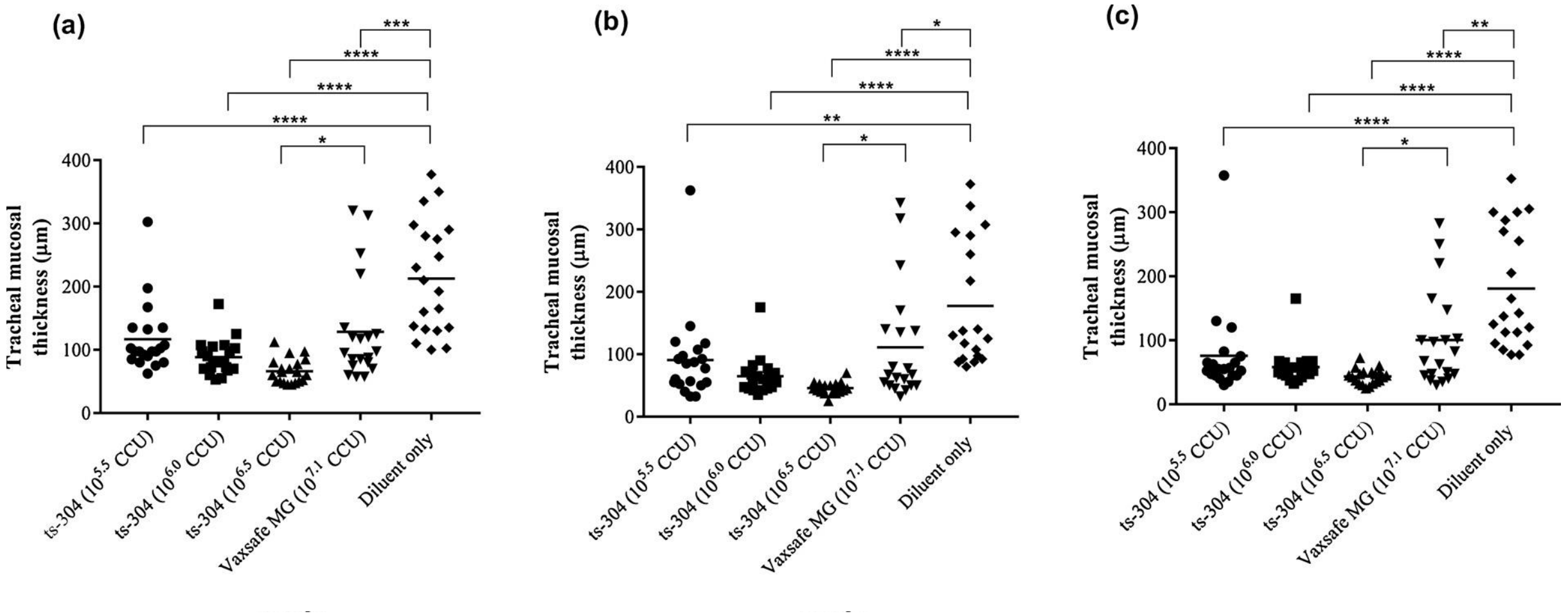
Mycoplasmoses – an Important Driver of Antimicrobial Use in Poultry

- Mycoplasmas often overlooked as underlying cause of chronic disease problems
- Ongoing challenges in eradication in Australia led to development of attenuated vaccines in the 1980s
- Use of these vaccines has eliminated mycoplasmas as a disease problem in our broiler and layer industries and reduced tylosin use in poultry by 90%
- More use of such vaccines across Asia will reduce use of AMs to control mycoplasmas and to treat and prevent *E. coli* infections and other undiagnosed health problems

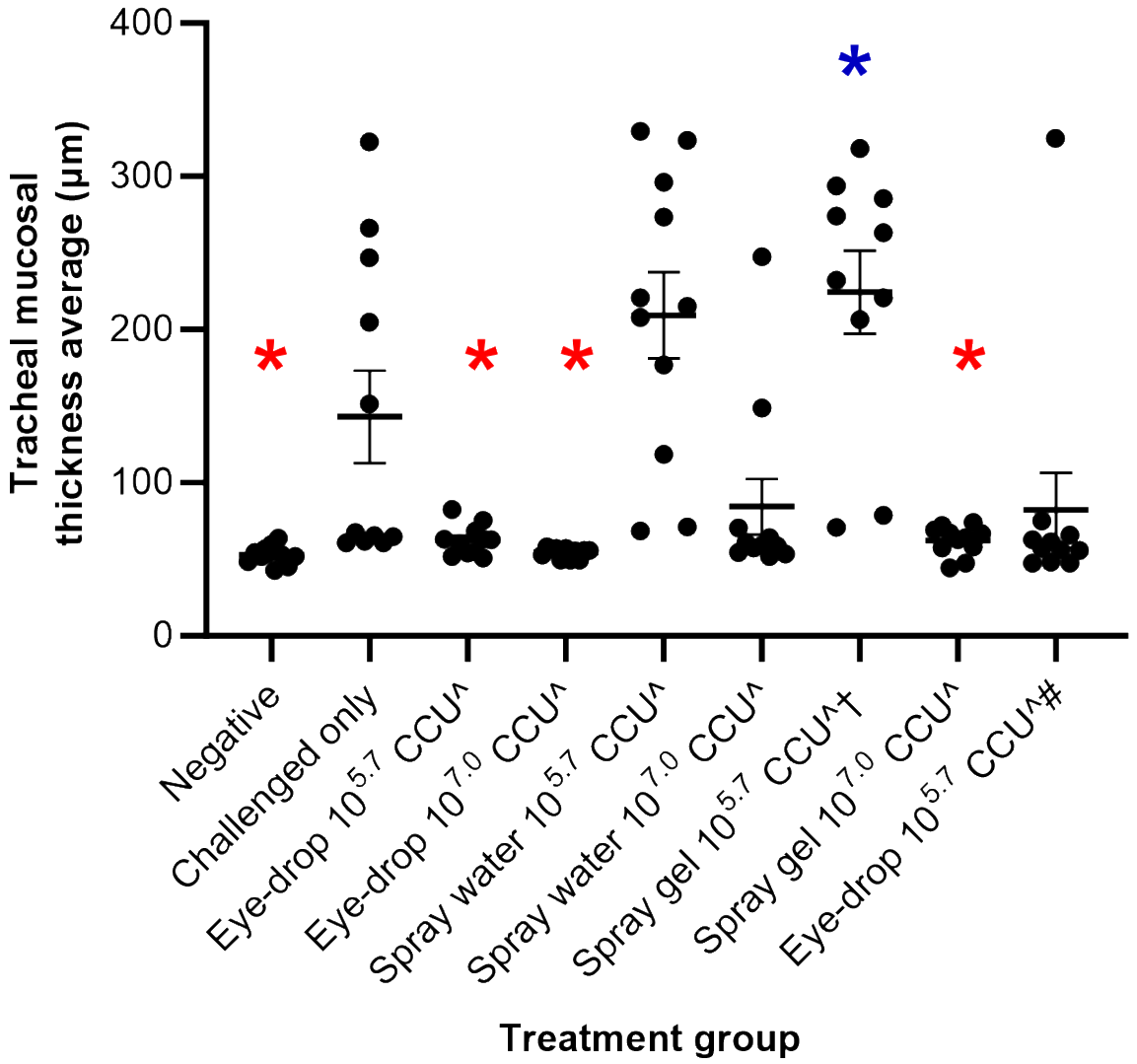
Enhancing Use of Current Mycoplasma Vaccines

- Derived a more adherent clone (ts-304) from the commercial ts-11 *M. gallisepticum* vaccine (Vaxsafe MG)
- New ts-304 vaccine has at least 40-fold greater potency than current ts-11 vaccine
- Suggested it had potential for use in situations previously found to be problematic
- Use in turkeys, day old birds, in face of antimicrobial use
- Improve control through stock acquisition pathways – more universal vaccination of breeders and of long-lived meat birds

Tracheal Mucosal Thickness in Chickens After Infection



Day old vaccination of chickens with ts-304



What Could this Mean in the Field?

- Mycoplasma vaccines can have wider application
- Use in breeder flocks will reduce AM use in broilers
- Delivery in the hatchery will increase use across Asia
- Efficacy even after antimicrobial use may ease switch from reliance on therapy
- Control of endemic respiratory viral pathogens will also be needed
- A focus on extending understanding and application of existing vaccines could have considerable value in reducing AM use in poultry

Major Antimicrobial Stewardship Measures in Livestock

- Focus best placed on addressing the drivers of use, rather than restricting use
- Biosecurity needed to prevent introduction onto farms
- Disease control programs that limit transmission on-farm
- Accessible guidelines for symptomatic treatment
- More accessible diagnosis of outbreaks of disease and mortality
- Effective vaccination programs, addressing common viral and bacterial pathogens
- Probably a need to improve focus on developing vaccines that reduce transmission, not just severity of disease

Our Current Team – Thank You