Antimicrobial resistance in bovine respiratory disease (BRD) pathogens

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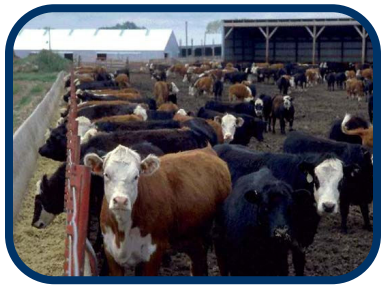
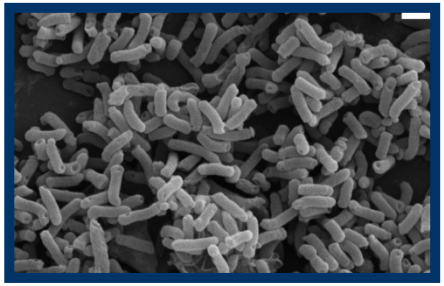
Overview



1. Background on BRD and resistance

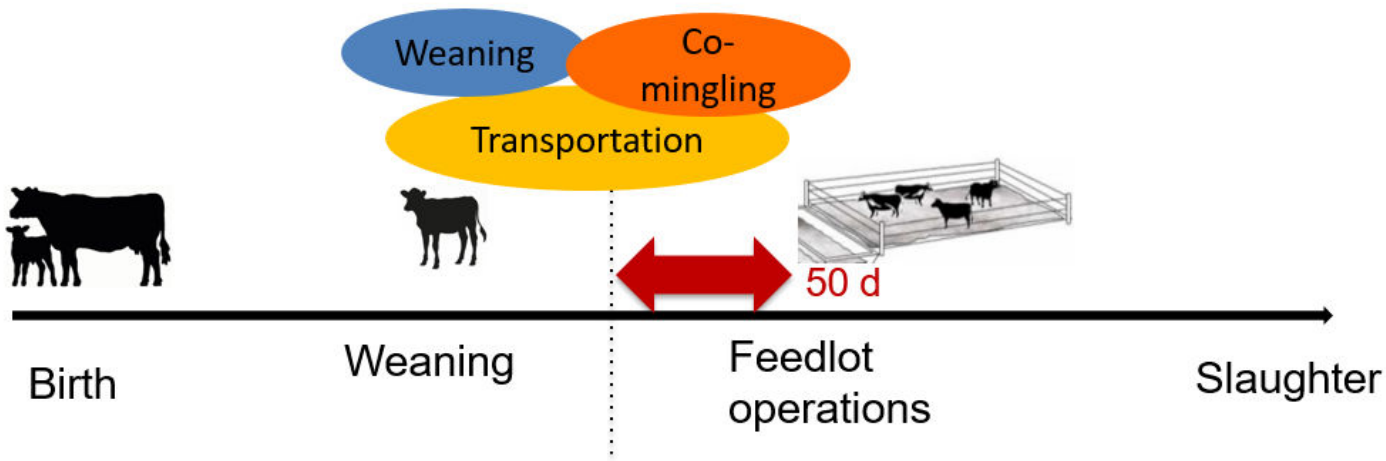


2. Development of resistance in feedlots

3. Mitigating resistance

4. Future research (alternatives to antimicrobials)

The reason for metaphylaxis



- Management practices before and after feedlot arrival can cause stress and bacterial pathogen proliferation and subsequently BRD
- While several factors affect BRD predisposition, antimicrobials are mainly used to mitigate BRD by targeting bacterial pathogens (metaphylaxis = treatment at arrival)

BRD progression

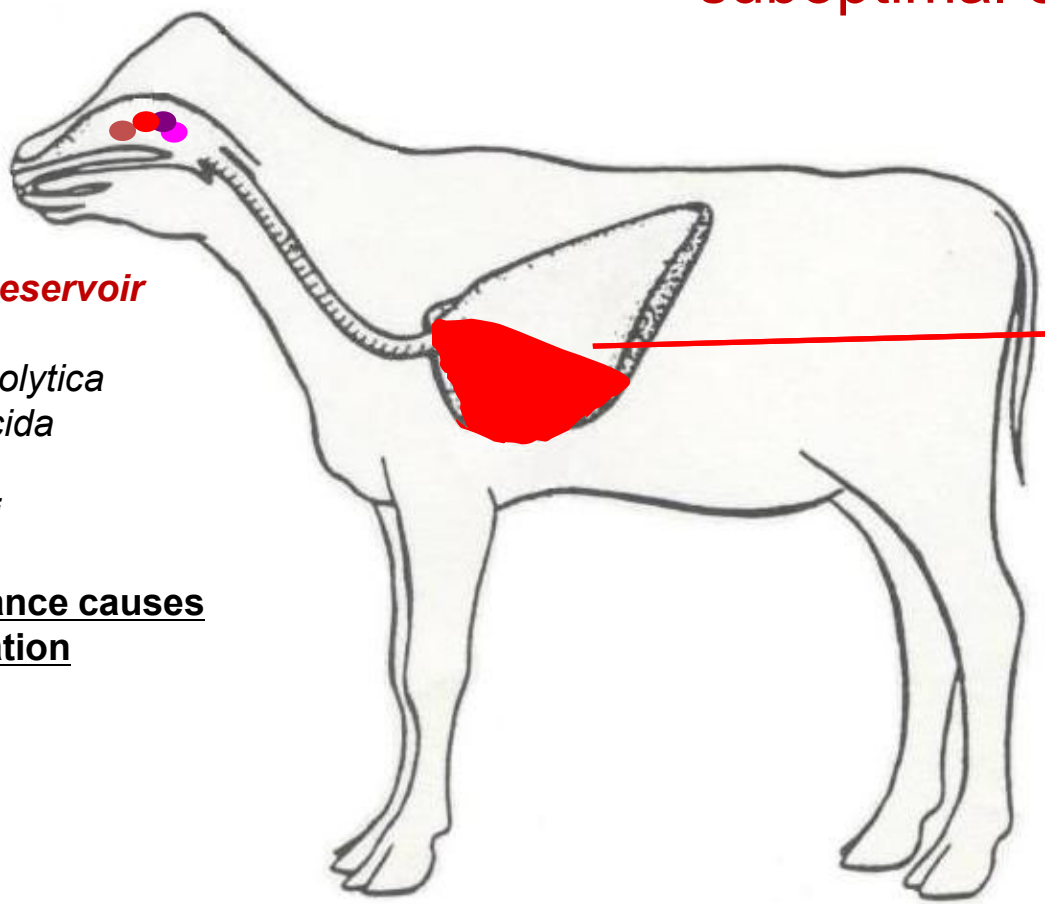
BRD mainly caused by <u>opportunistic</u> pathogens:

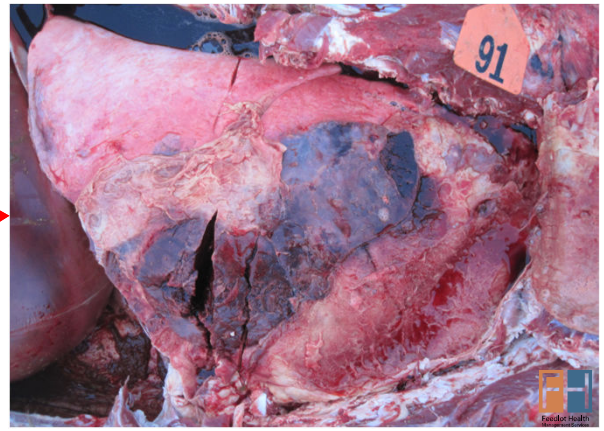
Stress, viral infection and suboptimal environment predispose

URT = Reservoir

M. haemolytica
P. multocida
M. bovis
H. somni

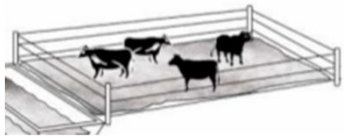
<u>Disturbance causes proliferation</u>



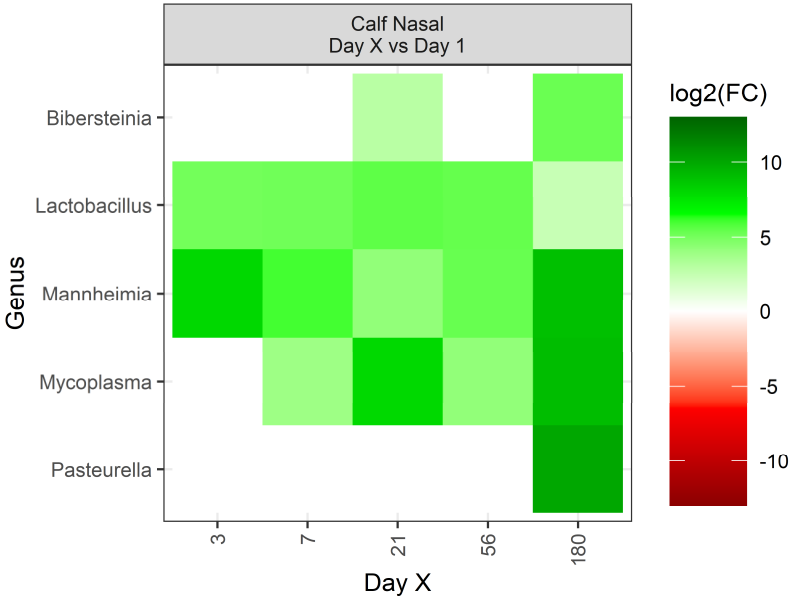


Cranio-ventral distribution of lung lesions

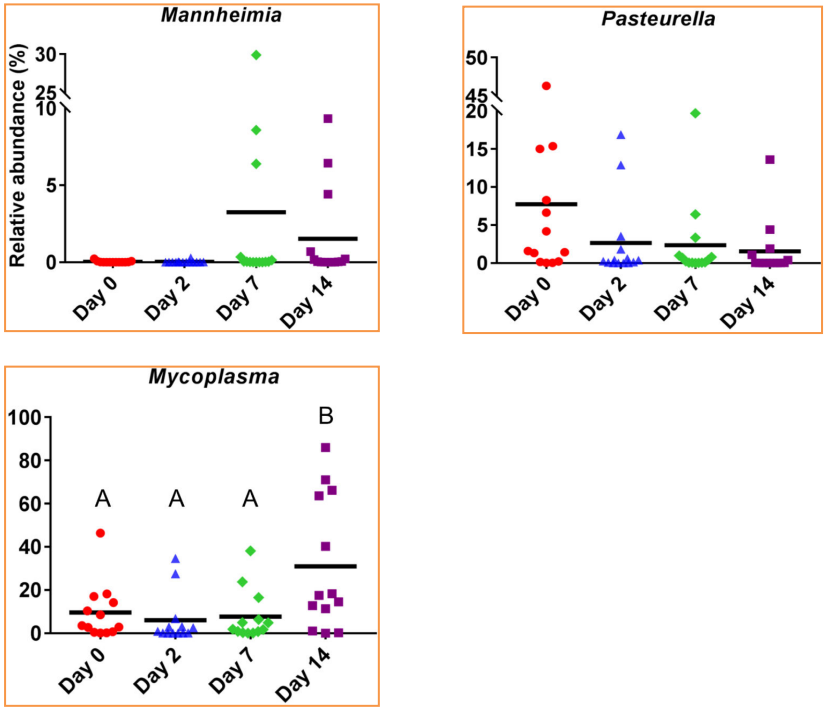
Where do BRD bacteria come from?



Birth Weaning Feedlot operations



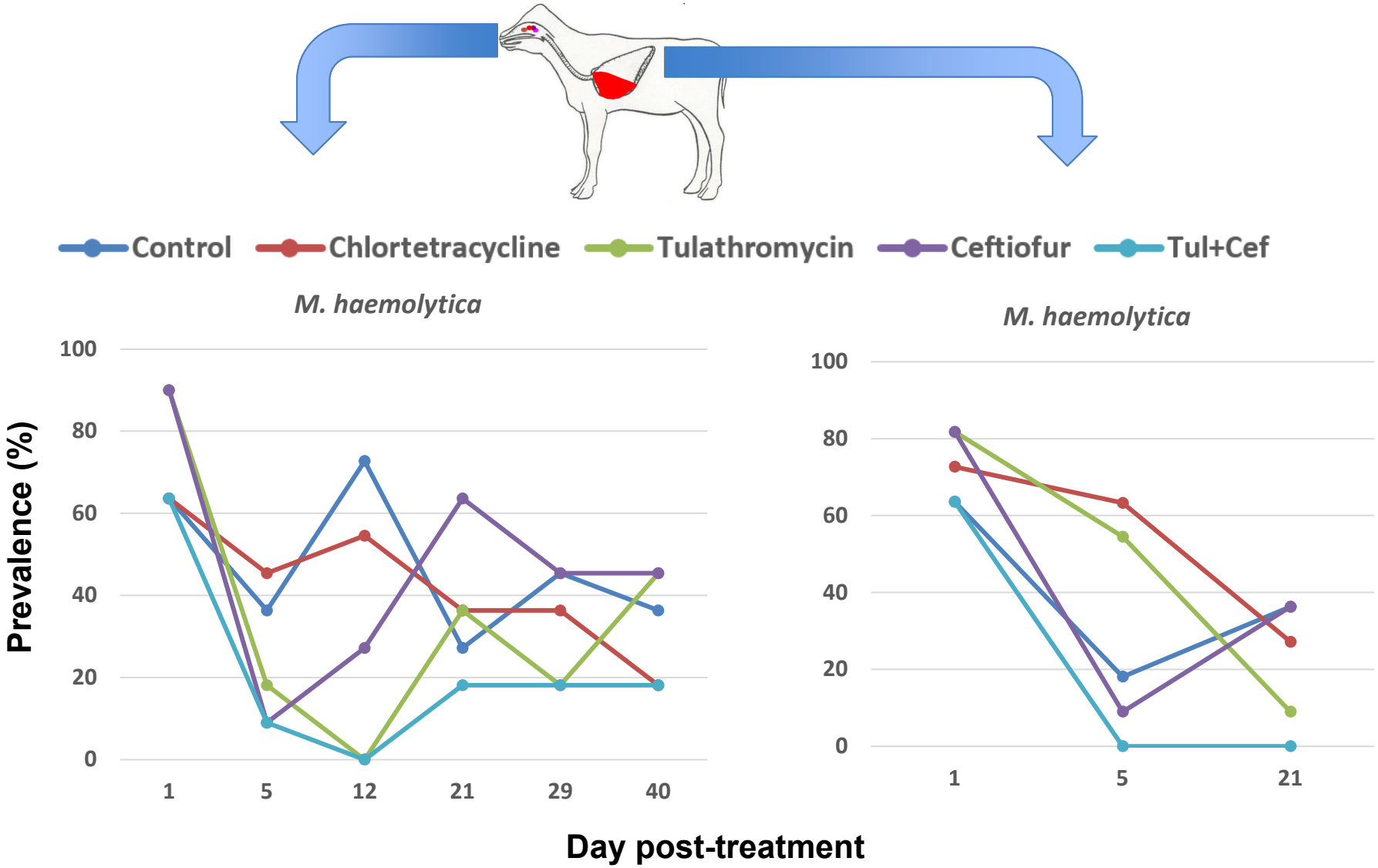
By 180 days of age, *Mannheimia*, *Mycoplasma*, and *Pasteurella* have increased 128-1,024 times the level at birth



BMC 2017. 17:70

Why are antimicrobials effective:

1) treat infections, 2) reduce pathogen colonization



Costs to the agri-food sector if antibiotics are no longer effective, and there are no alternatives to current management practices?

- Livestock producers - loss of profitability
  - Chronic, catastrophic
- To consumers
  - Food prices increase
  - Food security decreases
- Erosion of animal welfare

The importance of antimicrobial efficacy

ECONOMICS OF ANIMAL PRODUCTION

An evaluation of the economic effects of bovine respiratory disease on animal performance, carcass traits, and economic outcomes in feedlot cattle defined using four BRD diagnosis methods

Claudia Blakebrough-Hall,[*,1] Joe P. McMeniman,[†] and Luciano A. González[*,‡]

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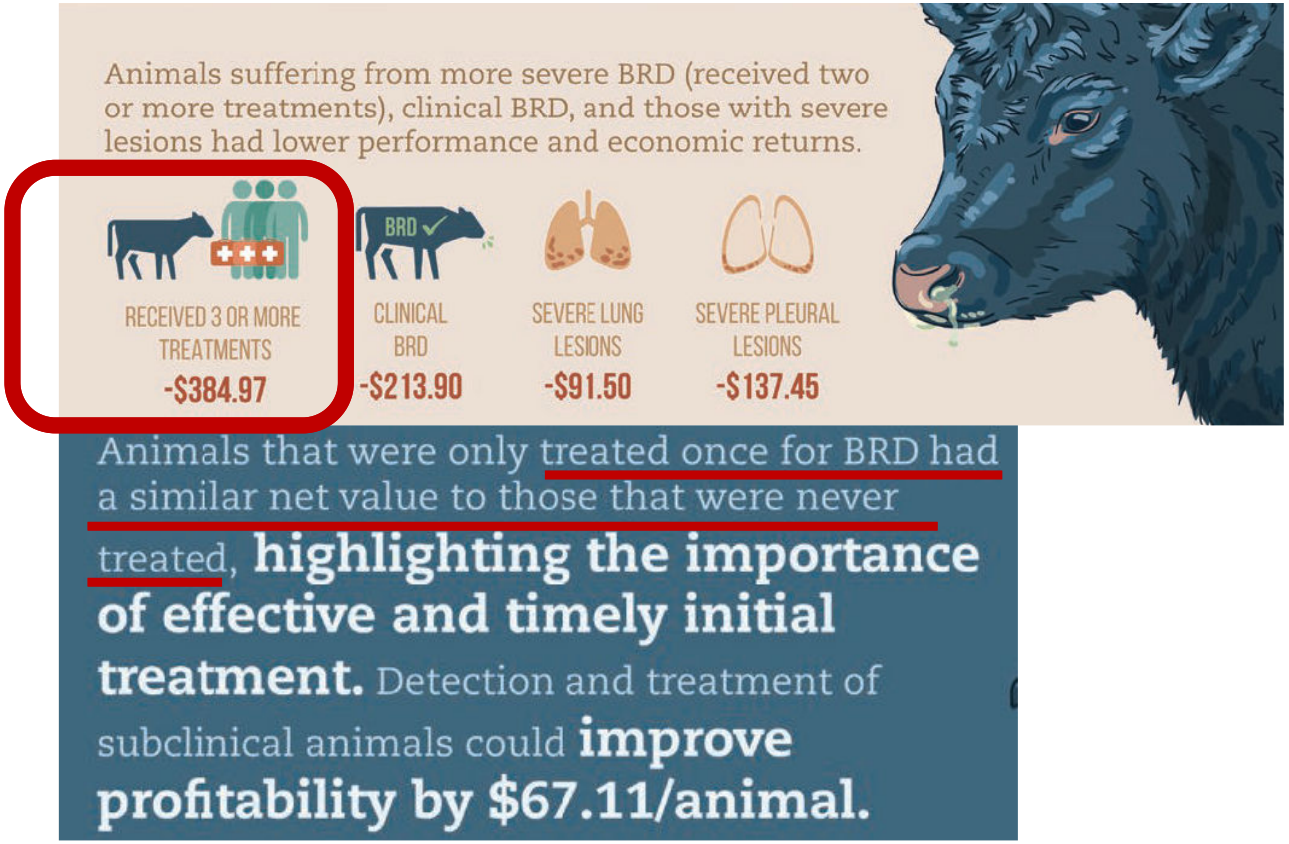
Journal of Animal Science, 2020, 1-11

- Crossbred steers N=898
- Feedlot entry to slaughter analysis

- $1 AUD = $0.98 CDN



The importance of antimicrobial efficacy

- Antimicrobials on arrival (metaphylaxis)
  - Reduce BRD morbidity and mortality
  - *Efficacy varies among antimicrobials*

Table 2
Summary of morbidity and mortality outcomes from published research comparing metaphylactic antimicrobials

Drug Comparison			Morbidity			Mortality		
Drug A	Drug B	Study	Drug A	Drug B	P Value	Drug A	Drug B	P Value
CTC	Tilmicosin	Hellwig et al 1998	47%	44%	≤0.05	NR	NR	NR
Florfenicol	Tulathromycin	Rooney et al 2005	NR	NR	NR	6.97	1.64%	≤0.05
Tilmicosin	Tulathromycin	Nickell et al 2008	68.1%	32.8%	≤0.05	13.5%	3.6%	≤0.05
		Booker et al 2007	14.0%	3.2%	≤0.05	4.9%	2.3%	≤0.05
		Godhino et al 2005	24.9%	14.6%	<0.01	NR	NR	NR
		Kilgore et al 2005	28.7%	13.2%	≤0.01	NR	NR	NR
		Rooney et al 2005	NR	NR	NR	5.0%	2.1%	0.09
		Van Donkersgoed et al 2008	13.0%	3.0%	<0.01	0.2%	0.04%	>0.05
Tilmicosin	Tet-300[a]	Schunict et al 2002	19.6%	22.6%	<0.02	1.4%	1.55%	>0.05
Tilmicosin	Tet-300	Booker et al 2007[b]	14.0%	17.0%	NR	1.88%	2.54%	NR
Tulathromycin	Tet-300	Booker et al 2007	3.42%	17.02%	<0.01	0.30%	2.54	<0.001
Tilmicosin	CCFA-SS[c]	Booker et al 2006	28.84%	27.96%	>0.05	10.93%	8.17	0.003
Tilmicosin	CCFA-SS	Step et al 2007	21.50%	23.50%	>0.05	NR	NR	NR

Vet Clin Food Anim 26 (2010) 285–301
doi:10.1016/j.cvfa.2010.04.006

The importance of antimicrobial efficacy

- Antimicrobials on arrival (metaphylaxis)
  - Improve ADG and feed efficiency
  - *Lower/delayed feed consumption for BRD cases*

Table 3
Summary of feed and gain performance outcomes from published research comparing metaphylactic antimicrobials

Drug Comparison			ADG (lb)			FE (lb)		
Drug A	Drug B	Study	Drug A	Drug B	P Value	Drug A	Drug B	P Value
CTC	Tilmicosion	Hellwig et al 1998	1.5	1.5	>0.05	NR	NR	NR
Florfenicol	Tulathromycin	Rooney et al 2005[a]	3.06	3.18	0.022	NR	NR	NR
Tilmicosin	Tulathromycin	Nickell et al 2008	2.00	2.50	≤0.05	7.10	5.90	≤0.05
		Booker et al 2007	2.58	2.64	≤0.05	6.80	6.94	≤0.05
		Godhino et al 2005	2.62	2.79	<0.01	NR	NR	NR
		Kilgore et al 2005	2.20	3.00	>0.05	NR	NR	NR
		Rooney et al 2005	3.36	3.37	>0.05	NR	NR	NR
		Van Donkersgoed et al 2008	2.87	2.87	>0.05	6.97	7.02	>0.05
Tilmicosin	Tet-300[b]	Schunict et al 2002	2.97	2.97	>0.05	6.45	6.43	>0.05
Tilmicosin	Tet-300	Booker et al 2007[c]	2.58	2.55	NR	6.80	6.92	NR
Tulathromycin	Tet-300	Booker et al 2007	2.64	2.55	<0.01	6.94	6.92	>0.05
Tilmicosin	CCFA-SS[d]	Booker et al 2006	2.71	2.76	>0.05	6.46	6.49	>0.05
Tilmicosin	CCFA-SS	Step et al 2007	2.42	2.45	>0.05	NR	NR	NR

Vet Clin Food Anim 26 (2010) 285–301
doi:10.1016/j.cvfa.2010.04.006

Context and definitions: Intrinsic vs acquired antimicrobial resistance (AMR)

- Some bacteria are inherently resistant to an antibiotic
- Some bacteria are inherently sensitive to the same antibiotic
  - **The AMR problem is when bacteria previously susceptible to an antibiotic become resistant**
- Resistance is ancient and evolved as an integral part of bacterial communities → **mainly as mechanisms to compete**

Antibiotics are Natural

- Antibiotics are natural compounds produced by microorganisms.
- Antibiotic biosynthetic pathways have existed in bacteria for millions of years.

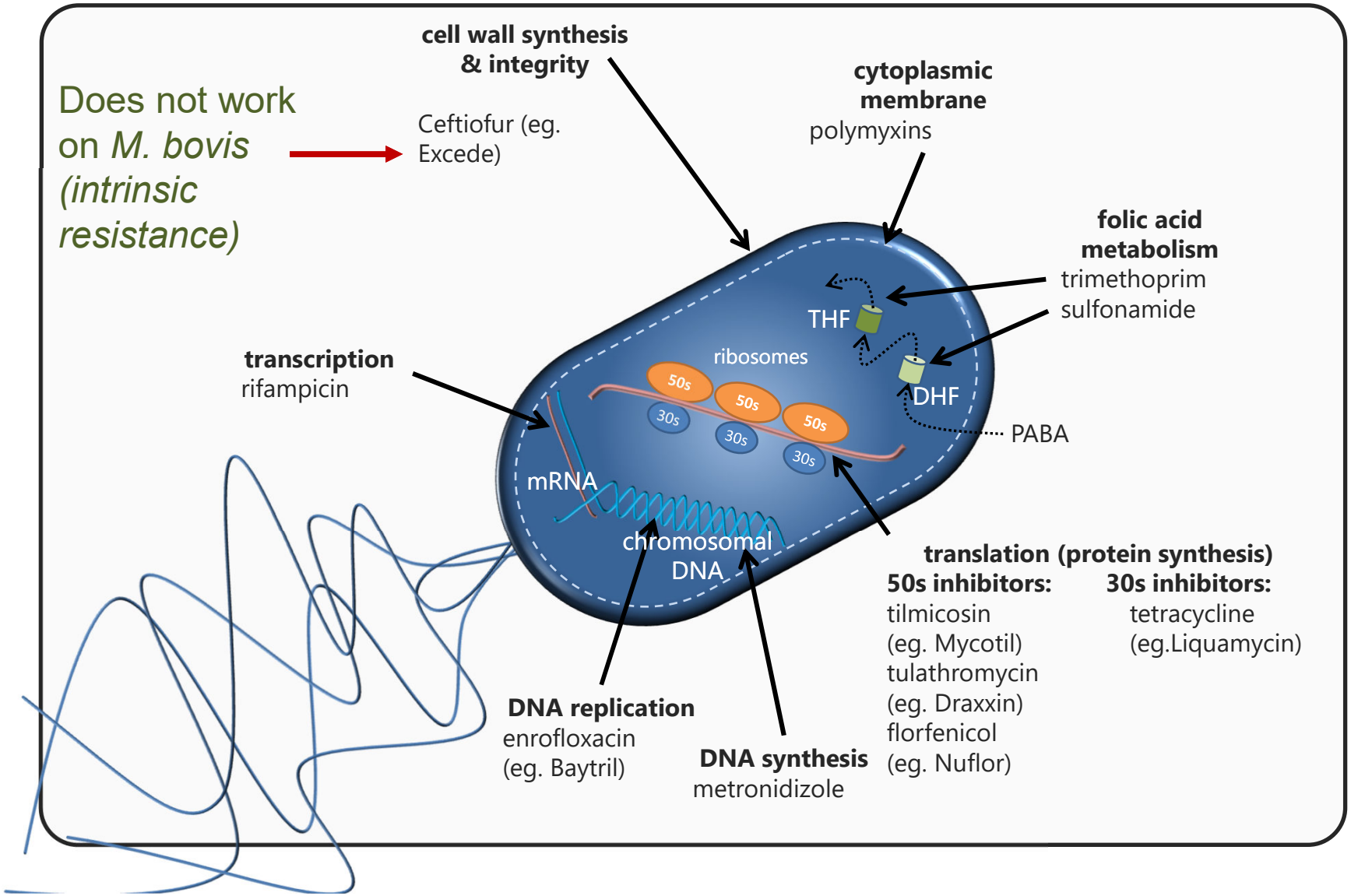
  eg. erythromycin in samples dated to >100 M years

- **In bacteria the roles of antibiotics could be:**
  - To prevent the growth of competitors
  - Inter-microbial signalling molecules
  - Sources of nutrition for bacteria

Typically bacteria producing the antibiotics encode resistance mechanisms

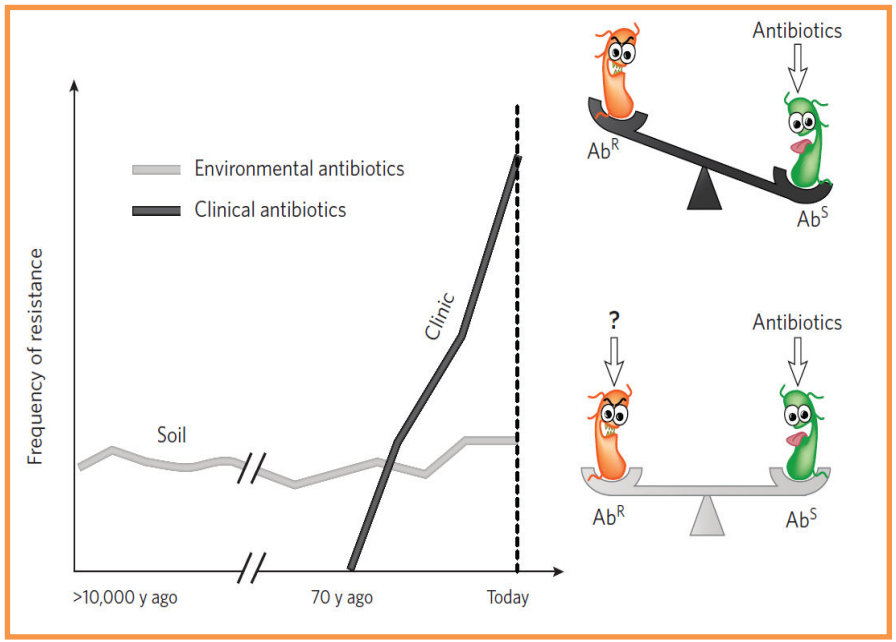
Antibiotic	Producer organism
Penicillin	*Penicillium chrysogenum*
Cephalosporin	*Cephalosporium acremonium*
Griseofulvin	*Penicillium griseofulvum*
Bacitracin	*Bacillus subtilis*
Polymyxin B	*Bacillus polymyxa*
Amphotericin B	*Streptomyces nodosus*
Erythromycin	*Streptomyces erythreus*
Neomycin	*Streptomyces fradiae*
Streptomycin	*Streptomyces griseus*
Rifamycin	*Streptomyces mediterranei*
Daptomycin	*Streptomyces roseosporus.*
Spectinomycin	*Streptomyces spectabilis.*
Tetracycline	*Streptomyces rimosus*
Vancomycin	*Streptomyces orientalis*
Chloramphenicol	*Streptomyces venezuelae*
Gentamicin	*Micromonospora purpurea*

Antimicrobial classes and resistance genes – differentiated by cellular targets

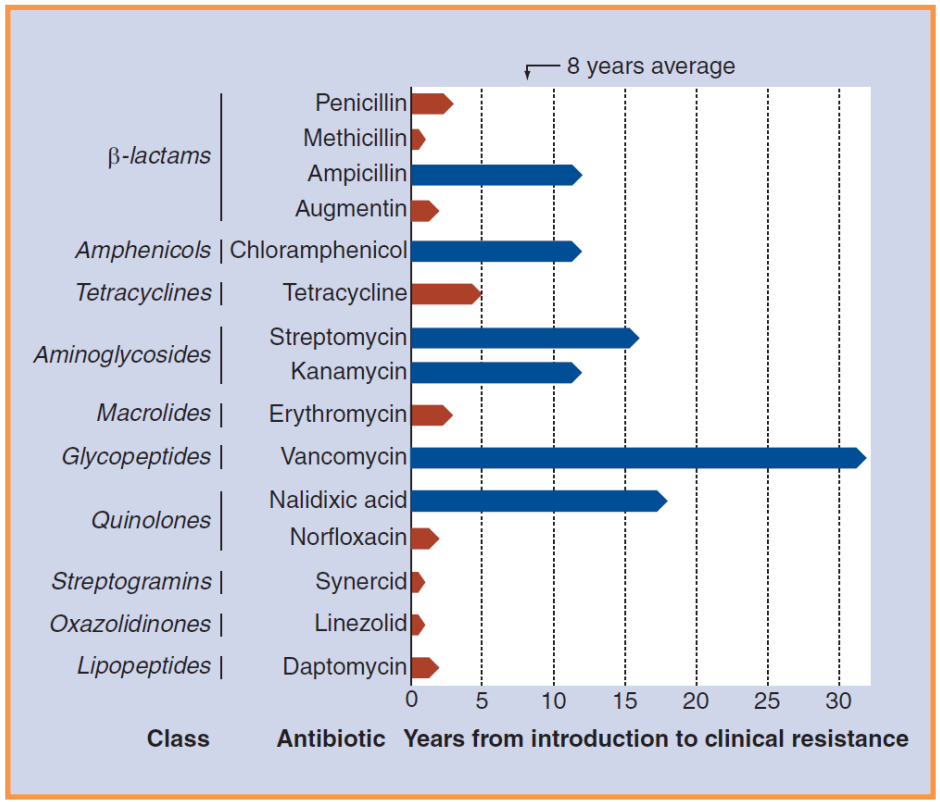


Antimicrobial use (AMU) increases resistance → but the time for resistance is antibiotic-dependent

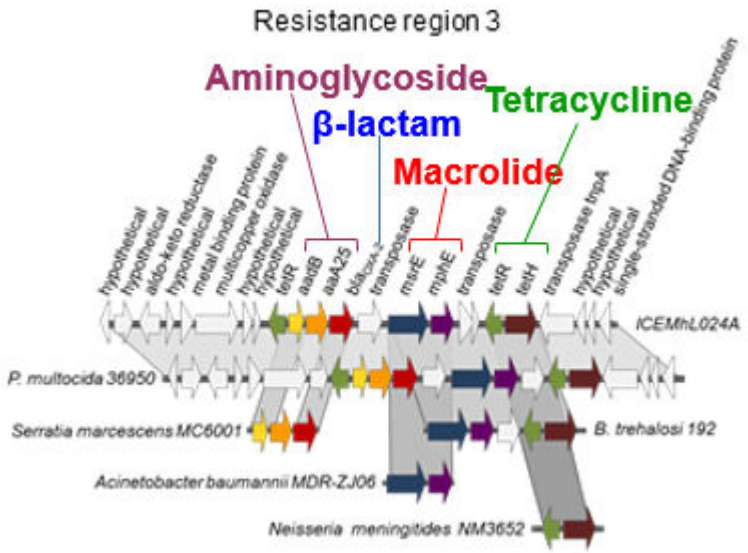
Chait et al., 2012

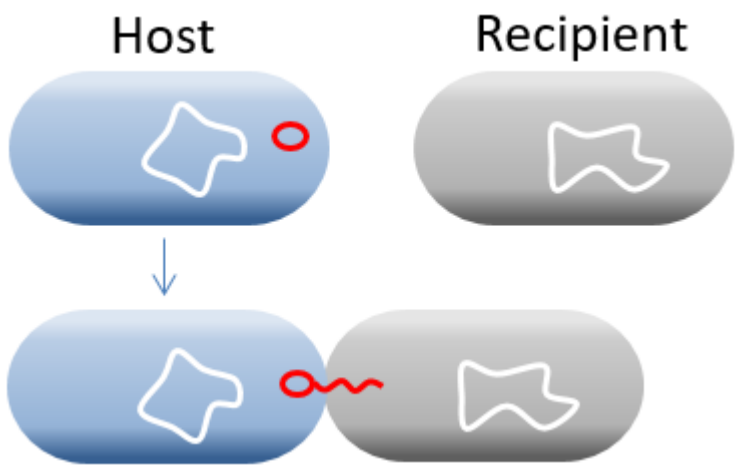


Schmieder and Edwards, 2012



BRD pathogens have developed ways to circumvent antimicrobials (acquiring resistance genes)





The worst case scenario → resistance to all available antimicrobials and transferable between bacteria

PLoS ONE 2016, 11(2): e0149520

Study 1. Antimicrobial resistance in *P. multocida* and *M. bovis* isolated from Alberta feedlot cattle that were sampled 8 years apart

- In 2008-2009, we performed a surveillance study on *M. haemolytica* and showed resistance was low (N= ~3000 isolates)
  - Less than 4% to oxytetracycline and 0.5% to tulathromycin
- The isolates were collected 1-2 years after approval of tulathromycin (Vet. Microbiol., 2011. 149:390; Front. Microbiol., 2013, 4:297)

→ **How has resistance in BRD pathogens changed since this study?**

Design: *M. bovis* and *P. multocida*

Cohort 1

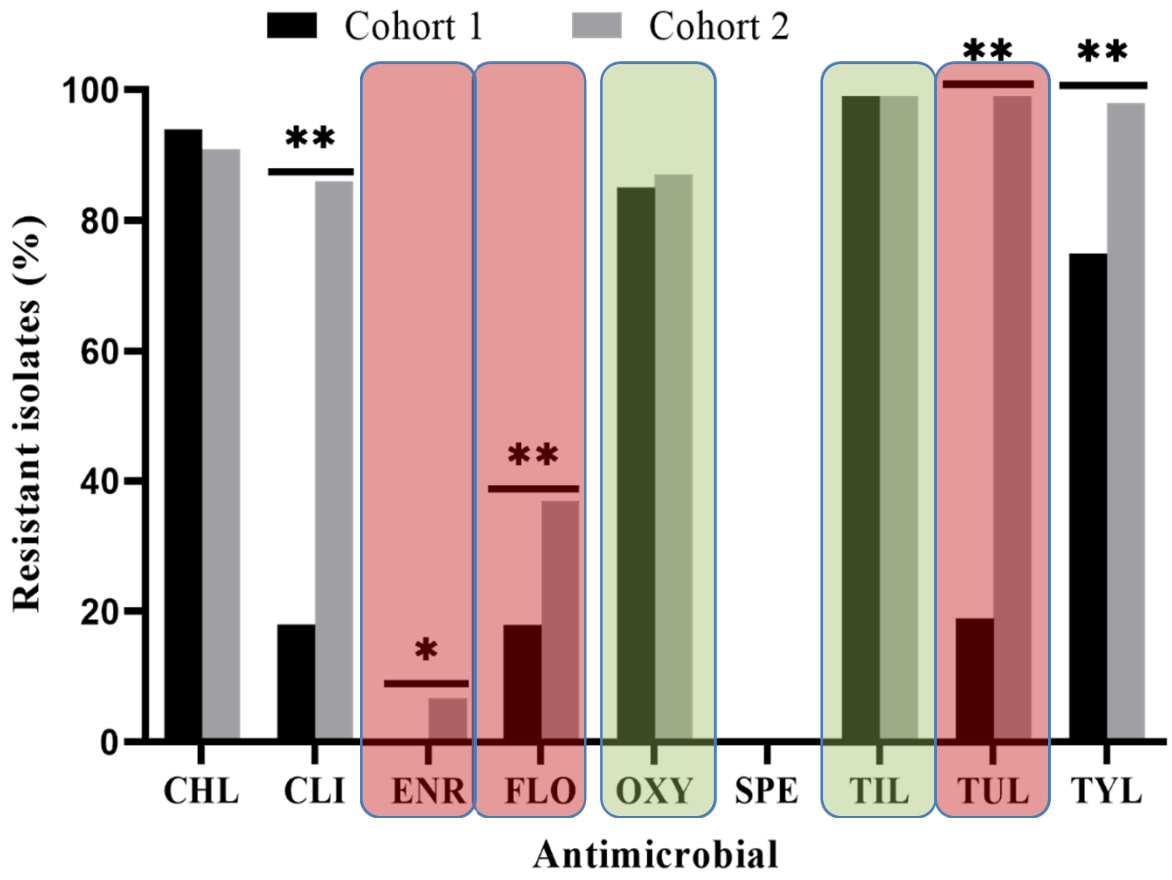
- Surveillance study in **2008-2009** (Vet. Microbiol., 149:390)
- Nasopharyngeal (NP) swab samples were collected from cattle animals at ≥60 days on feed
- 1,500 calves were sampled, and from these, 311 selected for study enrolment
- Cattle were either administered tulathromycin or oxytetracycline at feedlot entry.

Cohort 2

- A case-controlled study in **2015-2016** (Vet. Microbiol., 208:118
- NP swabs were collected from a total of 208 BRD cases and 104 healthy controls.
- Cattle were administered tulathromycin at feedlot arrival, and two pulses of chlortetracycline during the first 21 days of feeding.

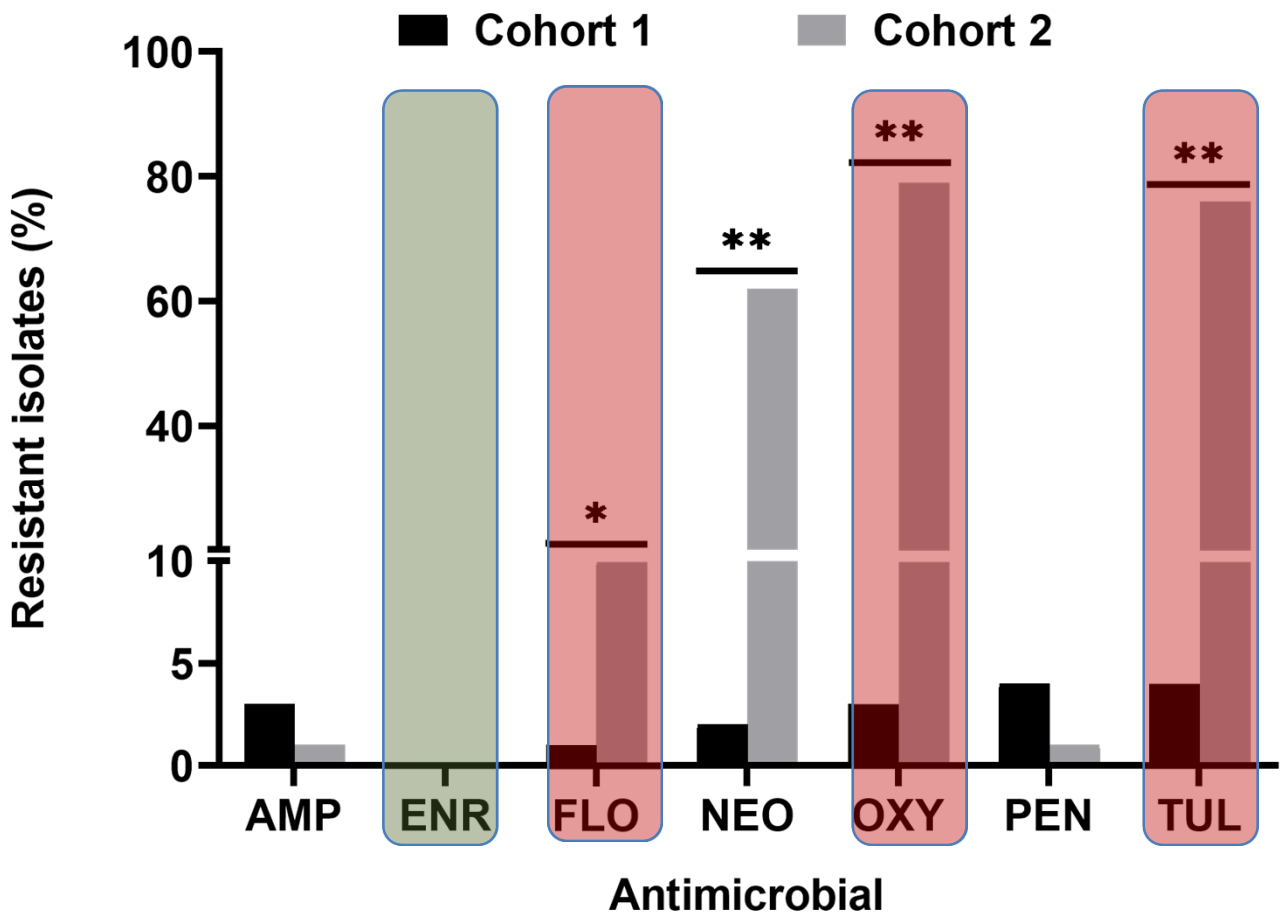
***M. bovis* and *P. multocida* were isolated and tested for antimicrobial resistance**

Results: *M. bovis*



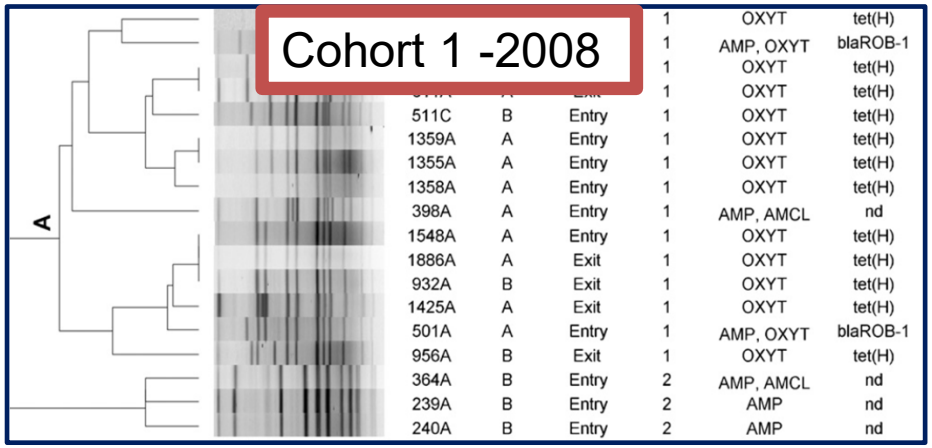
Chlortetracycline (CHL), clindamycin (CLI), enrofloxacin (ENR), florfenicol (FLO), oxytetracycline (OXY), spectinomycin (SPE), tilmicosin (TIL), tulathromycin (TUL), tylosin (TYL). * indicates P < 0.05 and* *indicates P<0.005.

Results: *P. multocida*

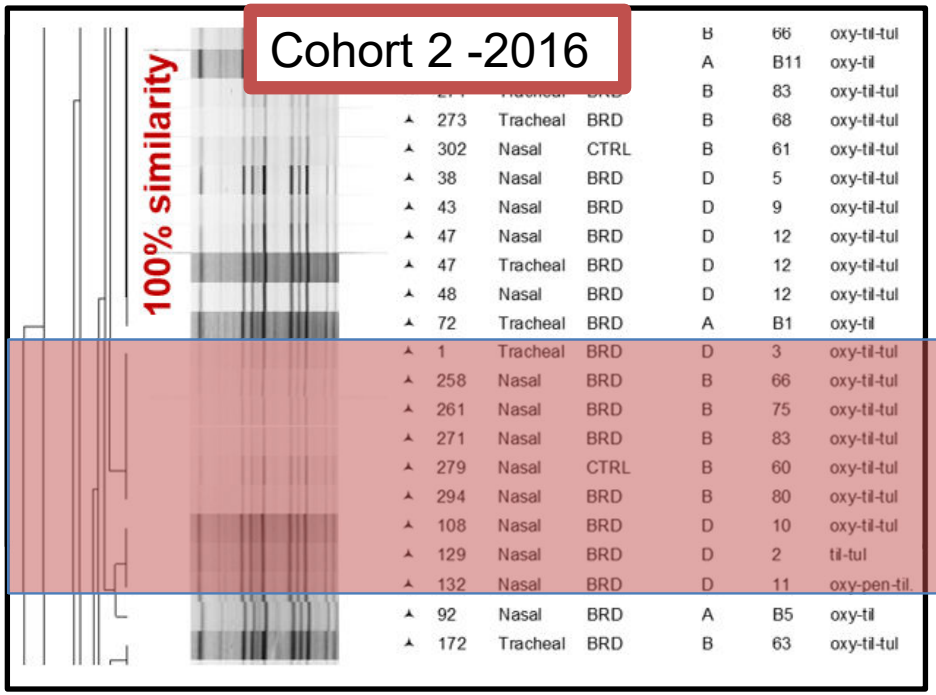


Don’t use the same antimicrobials for metaphylaxis and treatment

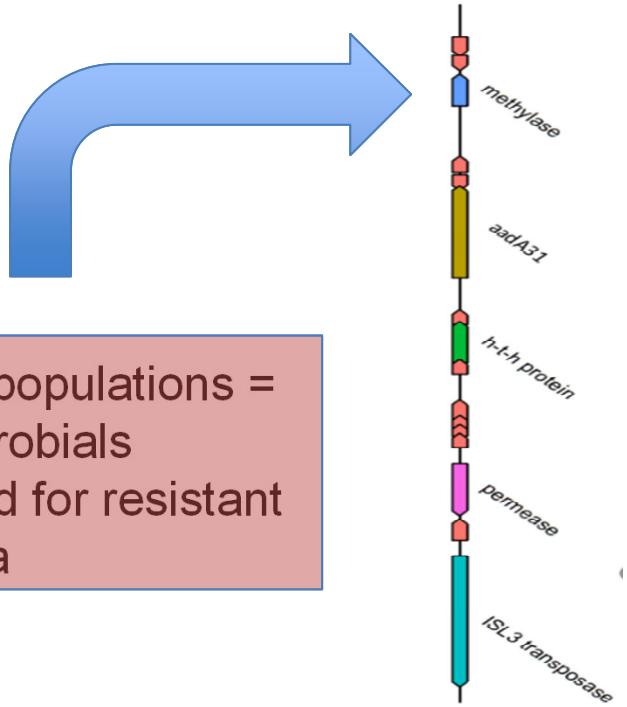
Results: *P. multocida diversity changed*



- **Genotyped by pulsed-field gel electrophoresis (PFGE)**
- **Genetic relatedness of resistant isolates was diverse**
- **Limited clonal spread**



Clonal populations = antimicrobials selected for resistant bacteria



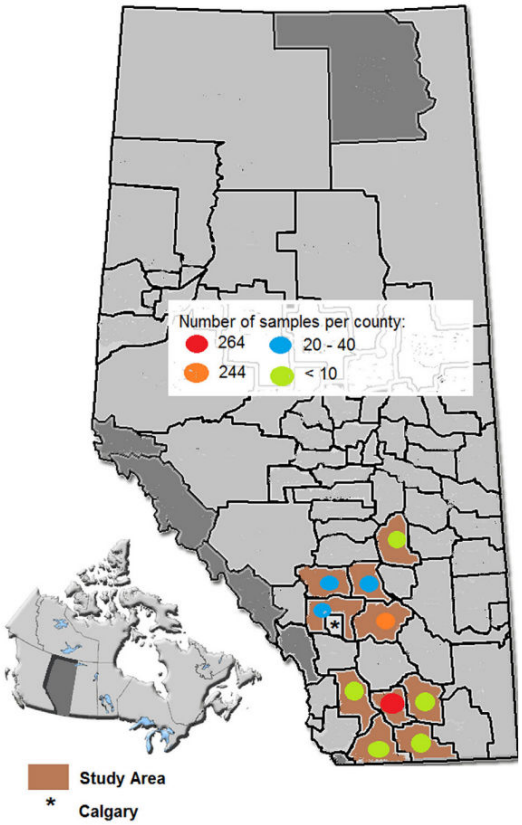
Results: overall

- Between 2008 to 2012, tetracyclines and macrolides were the most widely used antimicrobials in Canadian feedlots (Braut et al., 2019).
- Tulathromycin accounting for 88% of individual macrolide use.
  - In Canada, tulathromycin was marketed for BRD treatment and prevention in 2007.
  - The use of tulathromycin in feedlots likely led to the development of widespread resistance in *P. multocida* and *M. bovis* within **8 years** of its availability.

Other publications:

Antimicrobial Susceptibility of Bacteria That Cause Bovine Respiratory Disease Complex in Alberta, Canada

R. Michele Anholt[1], Cassidy Klima[2], Nick Allan[3], Heather Matheson-Bird[3], Crystal Schatz[4], Praseeda Ajitkumar[5], Simon JG Otto[6,7], Delores Peters[6], Karin Schmid[8], Merle Olson[9], Tim McAllister[2] and Brenda Ralston[6]*



- Sampled 7 veterinary practices (BRD morbidity/mortality)
- Of all *M. heamolytica, P. multocida, H. somni, M. bovis* isolated (n=745):
  - 90% resistance to at least one macrolide
  - 47% were multidrug resistant to 4-5 antimicrobials
- *P. multocida*
  - 30% resistant to tulathromycin
  - 56% resistant to oxytetracycline
- *M. bovis*
  - 92% resistant to tulathromycin
  - 80% resistant to oxytetracycline

→ When does resistance occur throughout production?

Front. Vet. Sci. 4:207.
doi: 10.3389/fvets.2017.00207

Study 2. Genetic relatedness and antimicrobial resistance in respiratory bacteria from beef calves sampled from spring processing to 40 days after feedlot entry

Vet. Microbiol. 2020, 240:108478

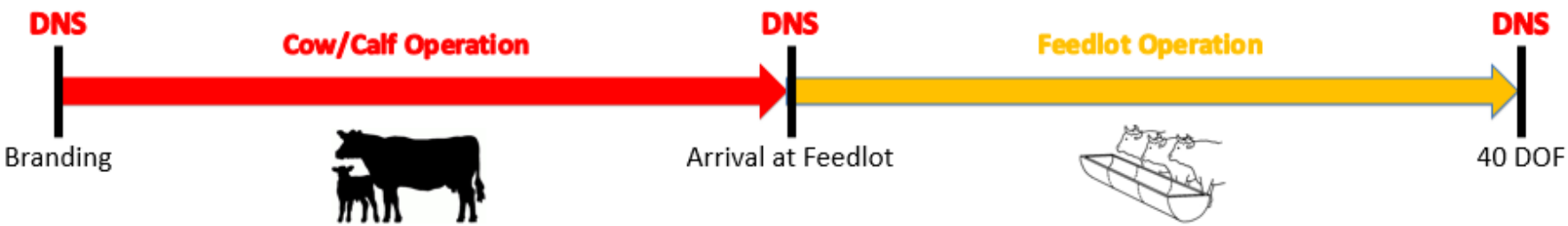
- Several studies have shown resistance to multiple classes of antimicrobials in BRD bacteria isolated at single feedlot time points

  → When is resistance most likely to occur throughout production (farm or feedlot)?

Design:

- Total of 120 steer calves enrolled at **3 farms** (40 calves/farm) in southern Alberta

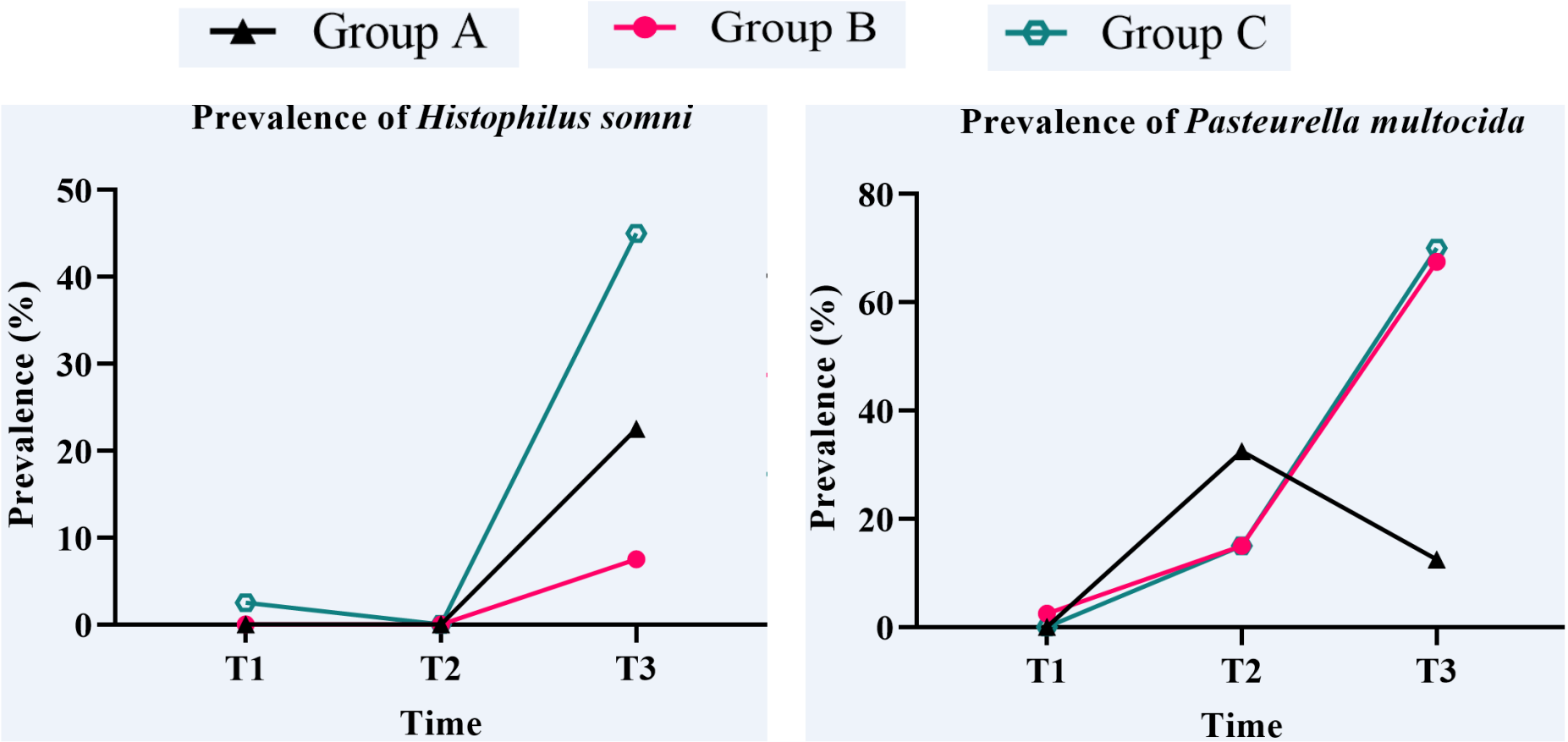
- Candidate farms selected for:
  - Sufficient inventory
  - Producers could retain ownership of calves through to study completion



Design:

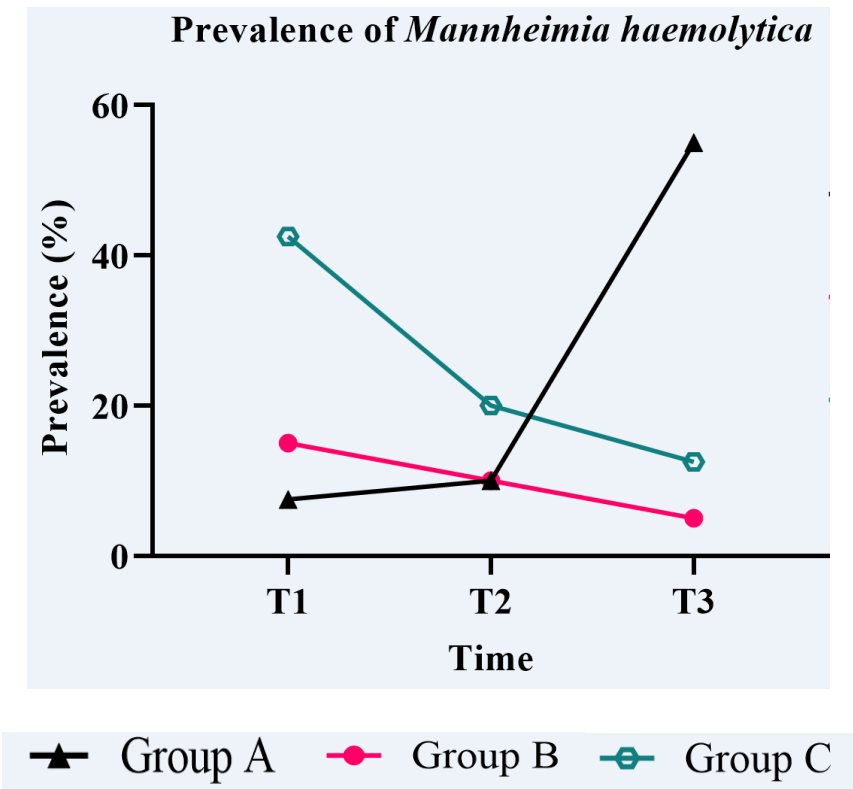
Treatment	Commercial name	Target[a]	Time of treatment[b]					
			Calf-ranch			Feedlot		
			Group A	Group B	Group C	Group A	Group B	Group C
Vaccines	One Shot[c]	Bacterin toxoid for *Mannheimia haemolytica type A1*	X					
	Bovi-Shield Gold One Shot[d]	BRSV, BVD types 1 and 2, IBR, PI3, *Mannheimia haemolytica*		X	X	X	X	X
	Somubac[d]	*Histophilus somni*			X			
	Ultrabac7/Somubac[d]	Clostridial disease and *Histophilus somni*	X			X		X
	Vision 8 Somnus with Spur[e]	Clostridial disease and *Histophilus somni*		X			X	
Antimicrobials	Micotil[f]	Tilmicosin antimicrobial						X
	Zactran[g]	Gamithromycin antimicrobial				X		
	Aureomycin 220[d]	Chlortetracycline (in-feed)			X[h]	X[i]		X[j]

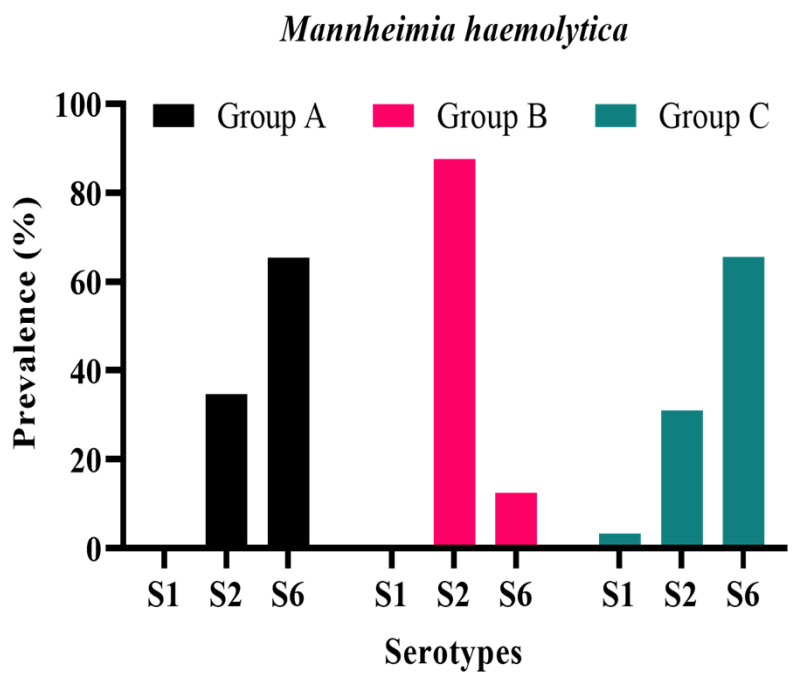
Results: NP prevalence of *P. multocida* and *H. somni*



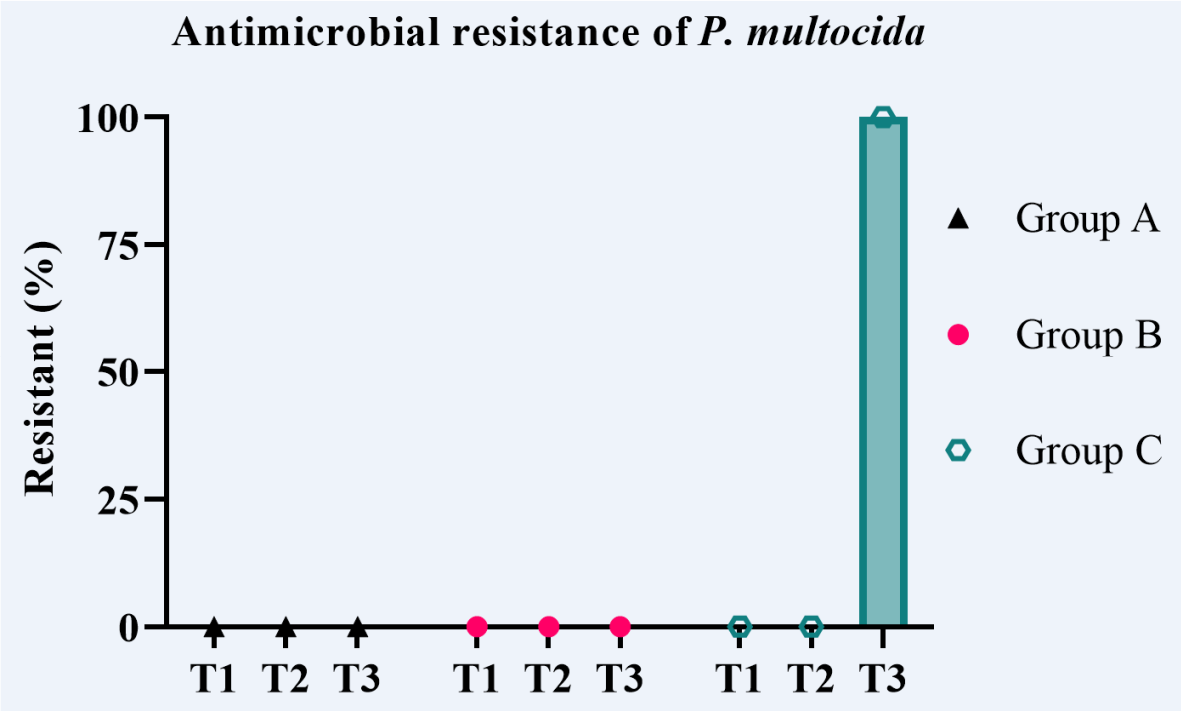
T1 = on-farm branding
T2 = feedlot arrival
T3 = 40 days after feedlot arrival

Results: NP prevalence of *M. haemolytica*





Results: Prevalence of resistant *P. multocida* – oxytetracycline and neomycin



T1 = on-farm branding
T2 = feedlot arrival
T3 = 40 days after feedlot arrival

Isolates (N=28) from Group C (100%) were resistant to oxy + neo

All were clones = pathogen transfer

Farms were not a source of resistant BRD pathogens

Resistance increased in feedlots but at varying rates (likely due to AMU)

Study 3. Comparison of pathogenic bacteria in the upper and lower respiratory tracts of cattle either directly transported to a feedlot or co-mingled at auction markets prior to feedlot placement

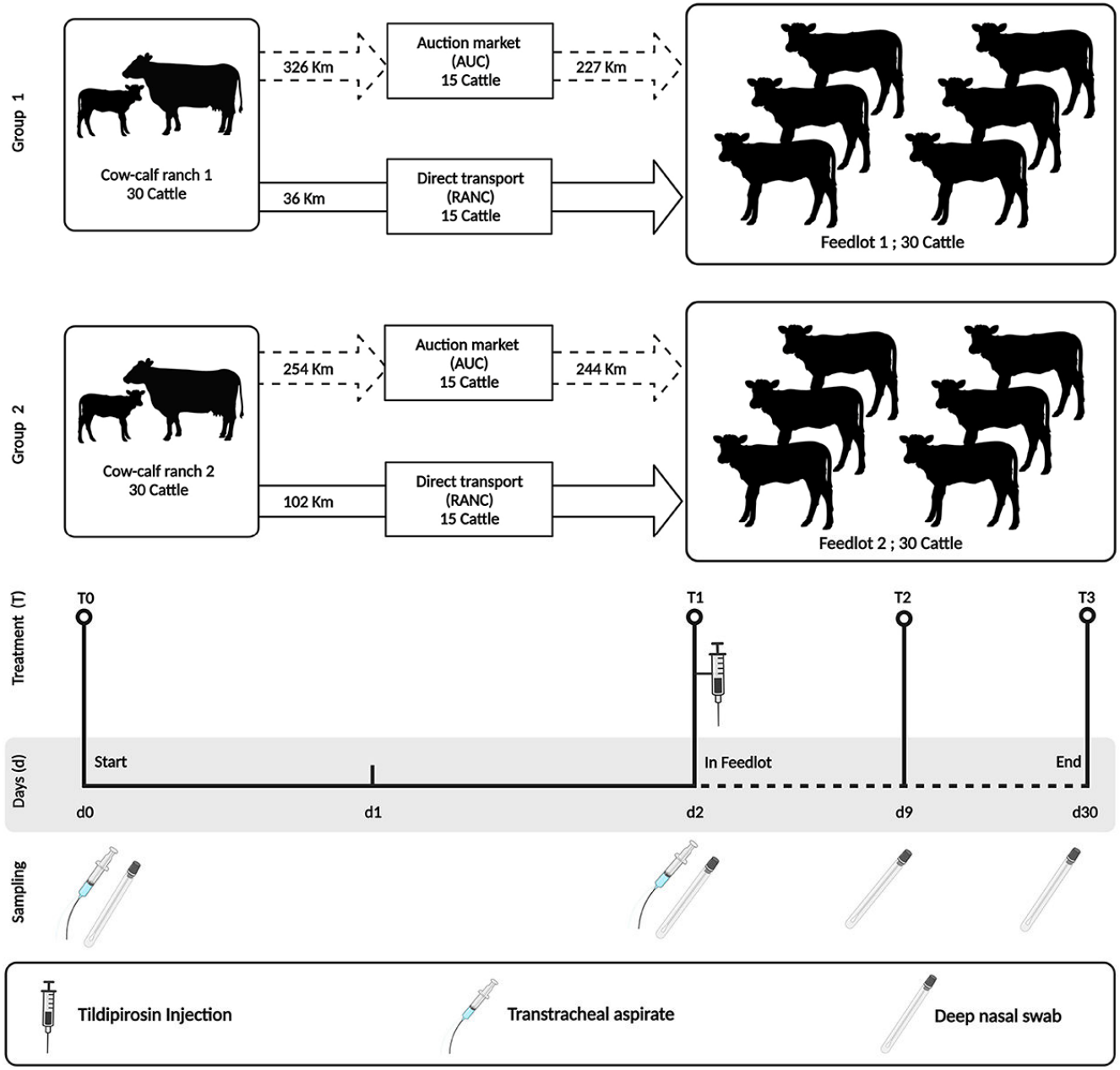
Front. Vet. Sci. 9:1026470.

- It has been suggested that sourcing cattle directly from ranches reduces exposure to BRD-related bacteria (North Am Food Anim Pract. (2010) 26:57–71)

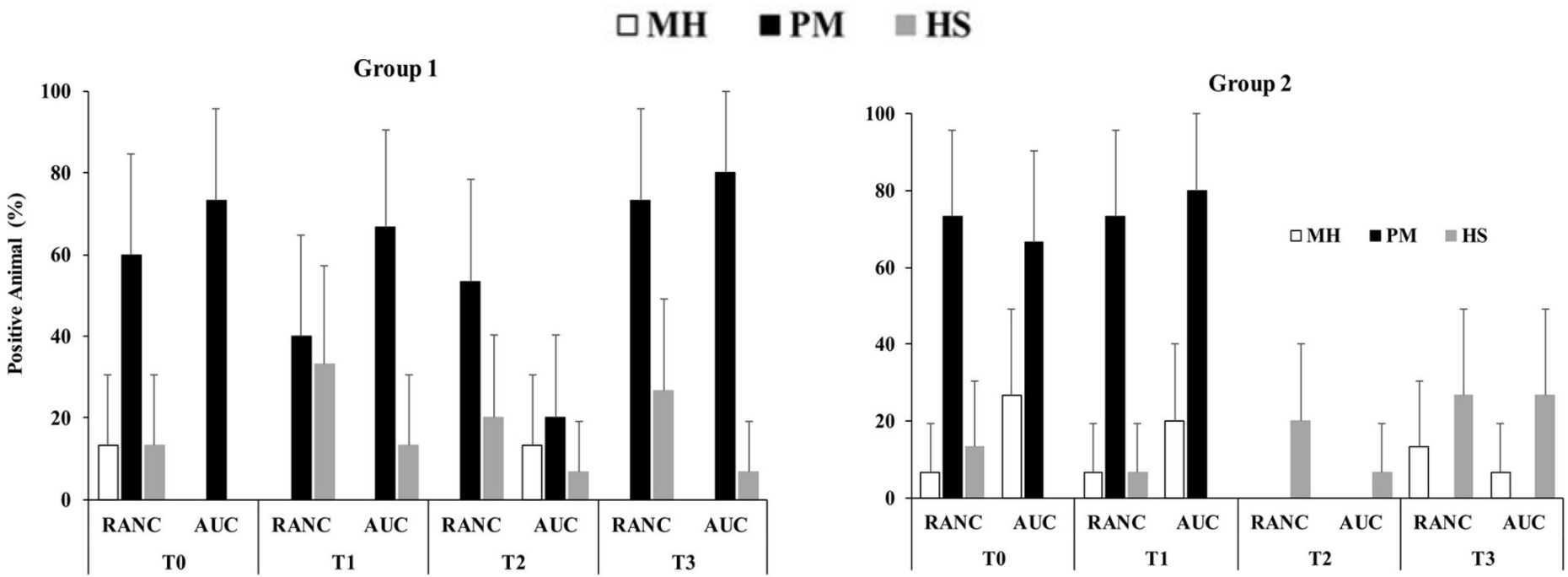
→ Are auction markets a potential source of BRD pathogens or resistance?

Design:

No AMU before transportation



Results: NP prevalence of *M. haemoltyica* (MH), *P. multocida* (PM), and *H. somni* (HS)



T0 = before transport
T1 = at feedlot arrival
T2 = 7 days after feedlot arrival
T3 = 28 days after feedlot arrival

Results: isolation of resistant pathogens

Group 1

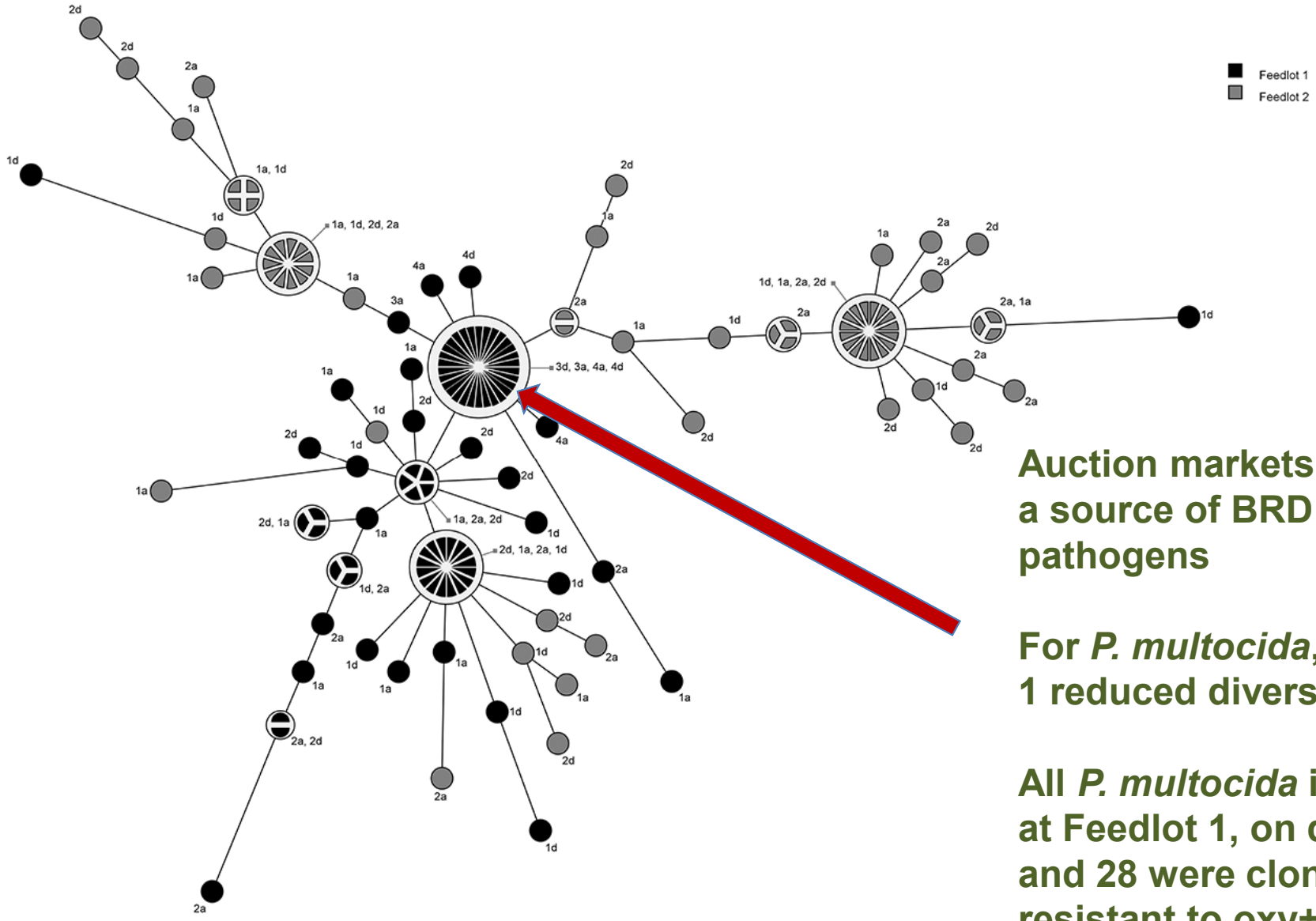
	Auction Market				Ranch Direct				Resistance
	T0	T1	T2	T3	T0	T1	T2	T3	
H. somni				1				3	oxy
M. haemolytica				1				1	oxy/til/tul
P. multocida			3	12			8	11	oxy/til/tul

Group 2

	Auction Market				Ranch Direct				
	T0	T1	T2	T3	T0	T1	T2	T3	
H. somni		1			1				ceft/pen

T0 = before transport
T1 = at feedlot arrival
T2 = 7 days after feedlot arrival
T3 = 28 days after feedlot arrival

Results: genetic relatedness of *P. multocida*



Auction markets were not a source of BRD pathogens

For *P. multocida*, Feedlot 1 reduced diversity

All *P. multocida* isolated at Feedlot 1, on days 7 and 28 were clones and resistant to oxy+til+tul

Other publications:

Prevalence and Risk Factors Associated With Antimicrobial Resistance in Bacteria Related to Bovine Respiratory Disease—A Broad Cross-Sectional Study of Beef Cattle at Entry Into Canadian Feedlots

Sara Andrés-Lasheras[1], Reuben Ha[1], Rahat Zaheer[1], Catrione Lee[1], Calvin W. Booker[2], Craig Dorin[3], Joyce Van Donkersgoed[4], Rob Deardon[5,6], Sheryl Gow[7,8], Sherry J. Hannon[2], Steve Hendrick[9], Michele Anholt[5,10] and Tim A. McAllister[1]

Front. Vet. Sci. 8:692646.
doi: 10.3389/fvets.2021.692646

AMR will develop whenever antimicrobials are used extensively.

- resistance can increase in feedlots
- resistant bacteria can be introduced into the feedlot through purchased cattle
- lots of variation between feedlots

Study 4. Prevalence of BRD pathogens in feedlot water bowls

- We have shown in several studies that bacterial clones are transferred between cattle.

  → **Could water bowls be a source of resistant BRD pathogens?**

Design:

- 16 pens sampled for water
- prior to cattle placement (D0), and 7, 14, 21, and 28 d after cattle placement.

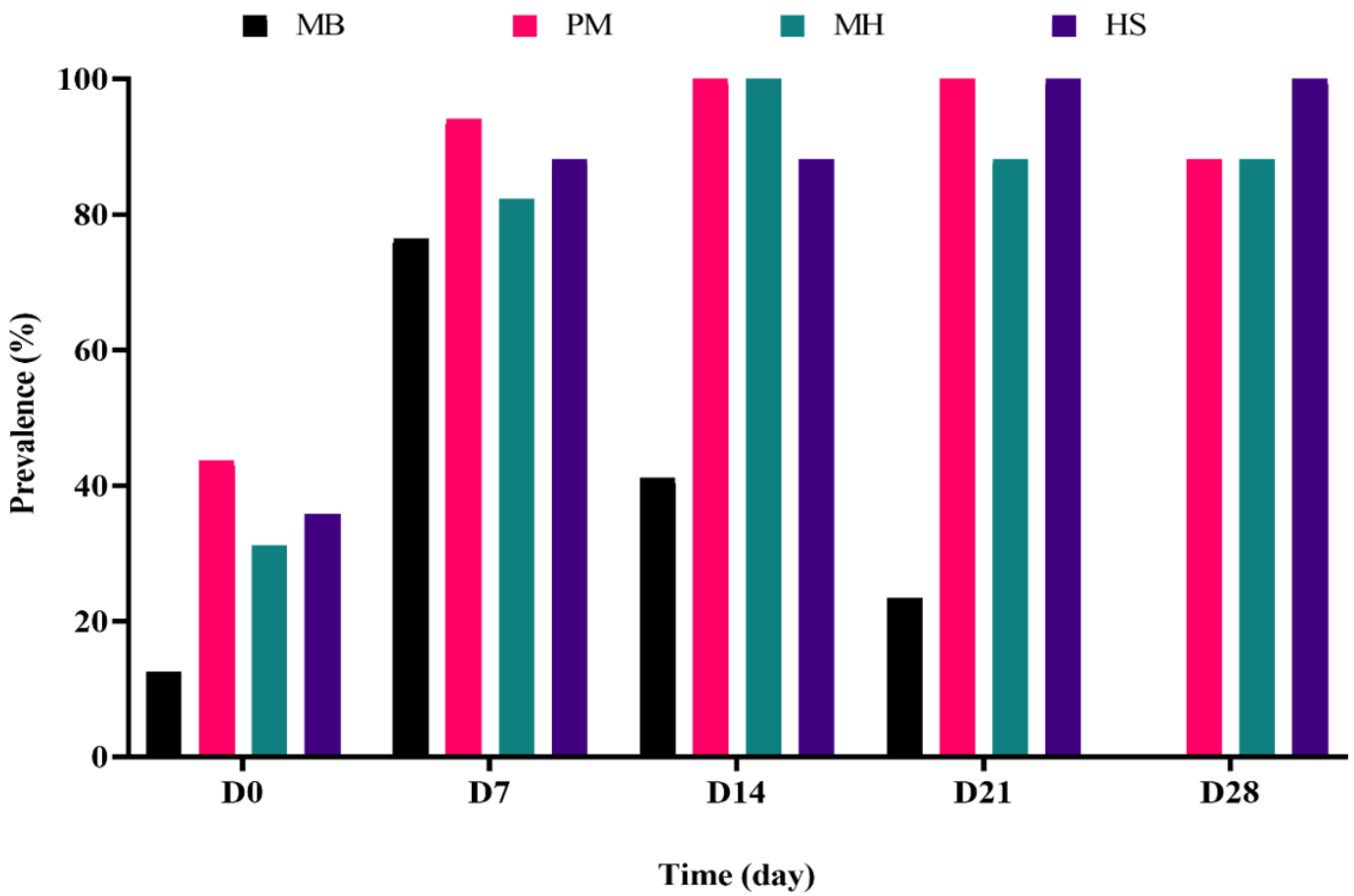
1 L filtered

MH, PM, HS, MB isolation

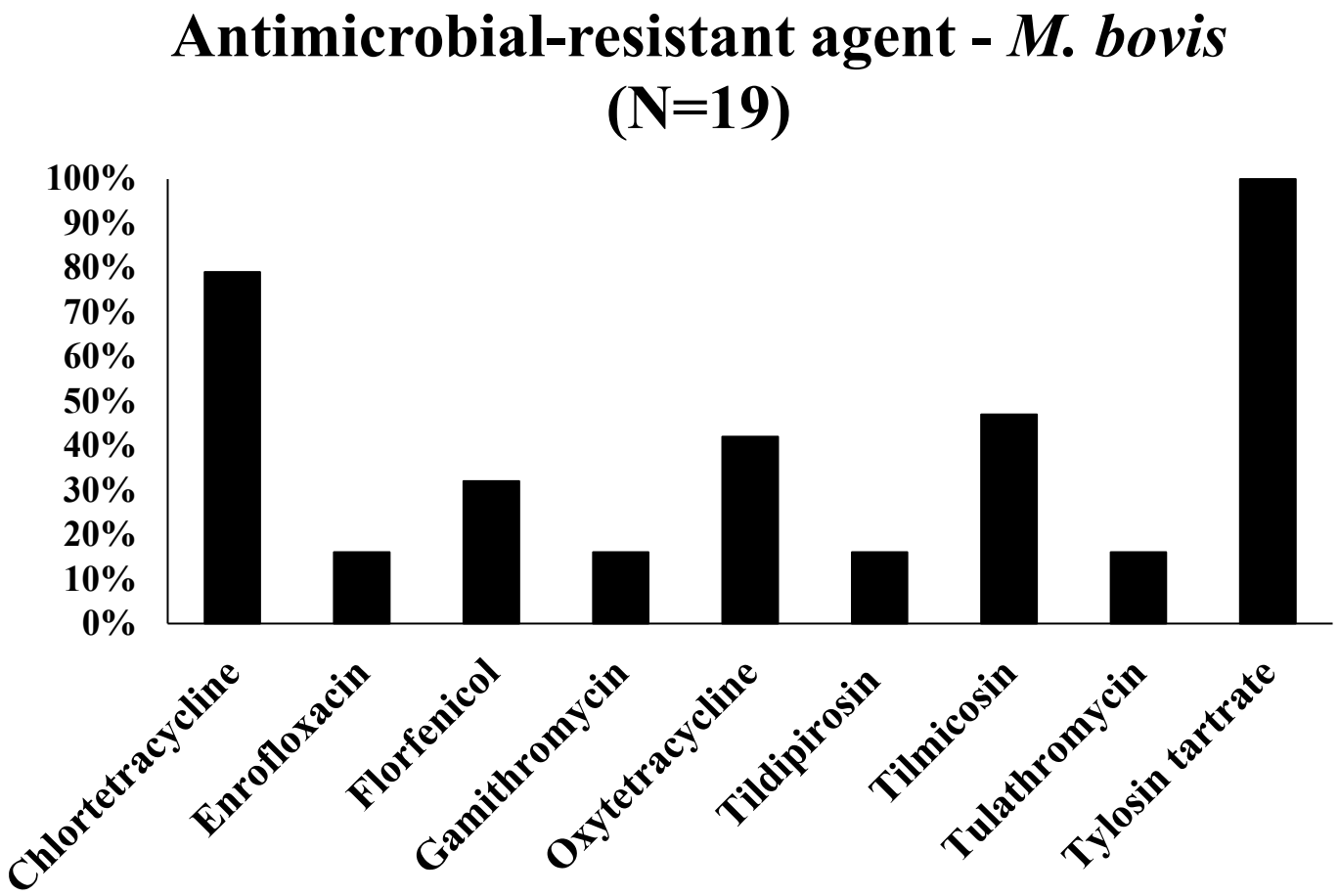
DNA extracted for PCR-based prevalence

Tested for susceptibility

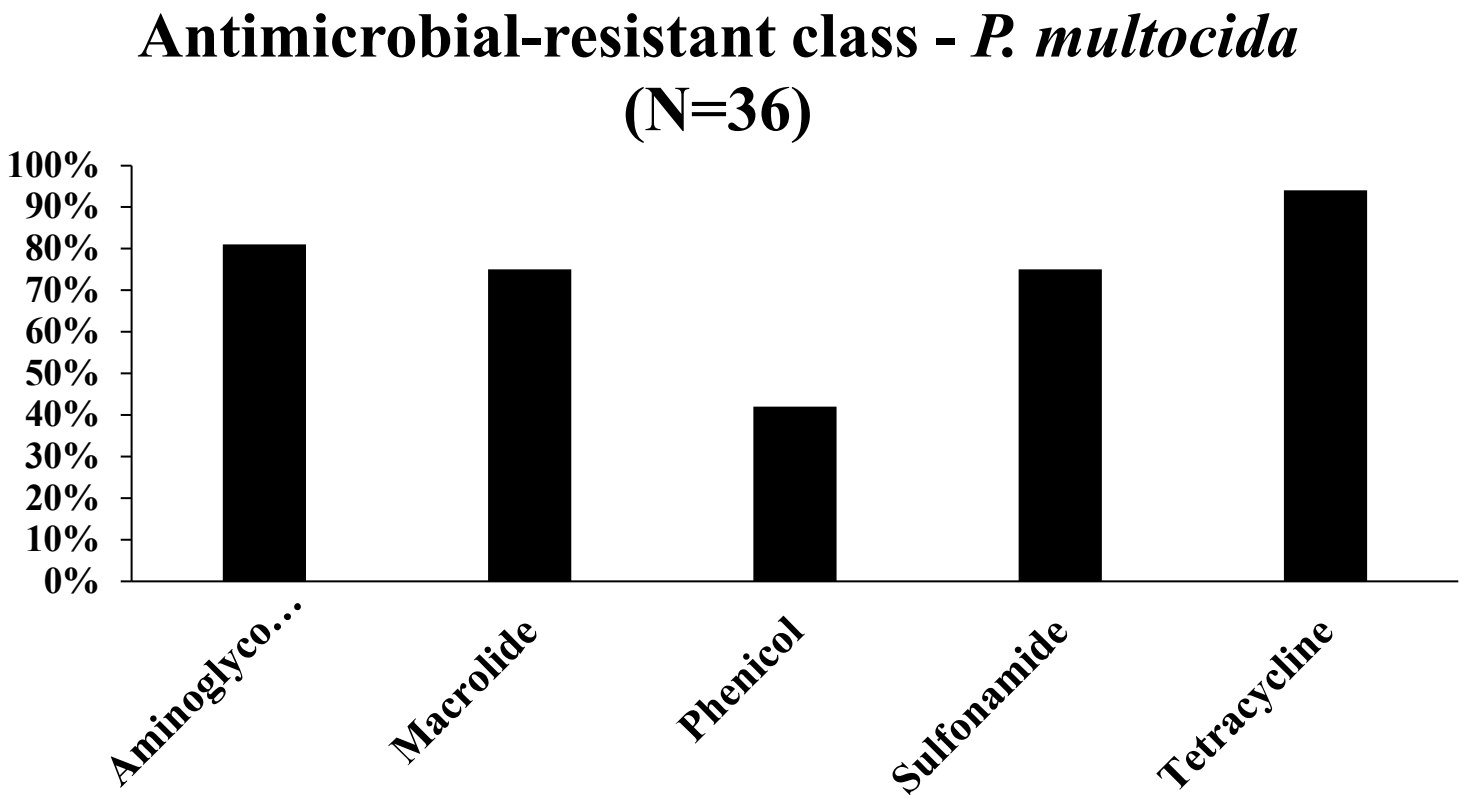
Results: PCR-based prevalence (N=17 pens)



Results: isolated bacteria (low recovery)



Results: isolated bacteria (low recovery)



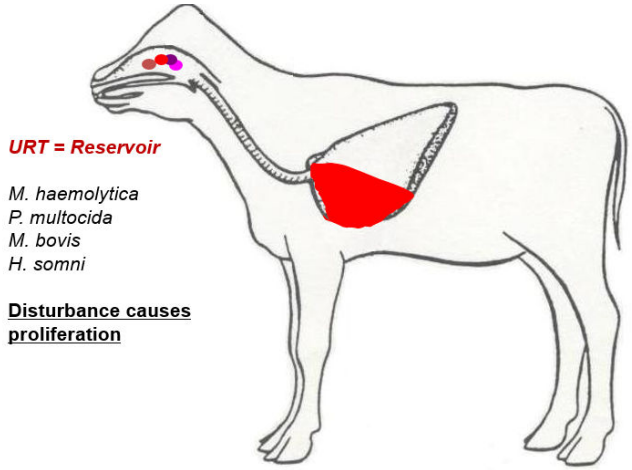
- Water may be a source of resistant BRD pathogens in pens
- Having two water sources was associated with lower respiratory disease risk compared to only one water source (Rojas et al., Vet. Sci. 2022, 9, 646)

How do we reduce resistance?

→ Reduce antimicrobial use by lowering BRD rates…

Achieved through reducing colonization and proliferation of BRD pathogens by:

1) Enhanced host immunity (vaccination)
2) Reduced host stress (preconditioning)



Vaccination – viruses

- Meta-analysis of viruses
  - (modified live) BoHV-1, BVDV (1 and 2), BRSV, Pi3

Systematic review and meta-analysis of the effectiveness of commercially available vaccines against bovine herpesvirus, bovine viral diarrhea virus, bovine respiratory syncytial virus, and parainfluenza type 3 virus for mitigation of bovine respiratory disease complex in cattle

Miles E. Theurer, DVM; Robert L. Larson, DVM, PhD; Brad J. White, DVM, MS

JAVMA, Vol 246, No. 1, January 1, 2015

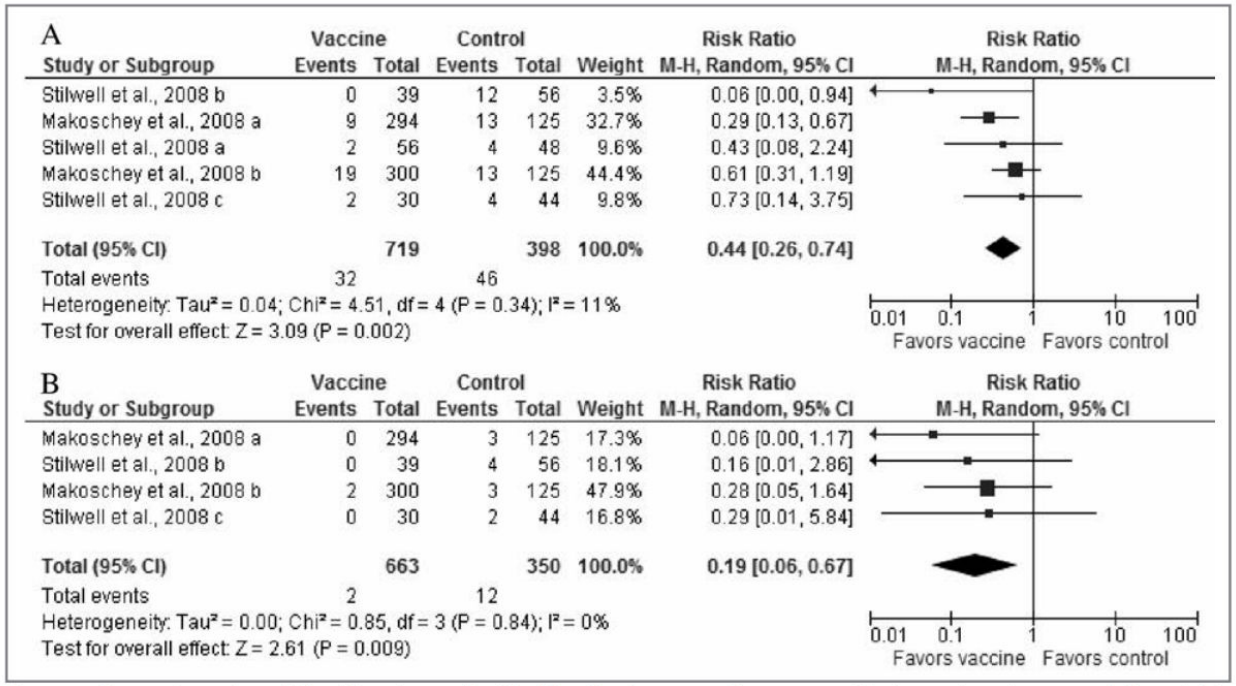


Figure 1—Forest plots of morbidity (A) and mortality (B) risk ratios from natural exposure trials that evaluated commercially available vaccines against BHV-1, BVDV, BRSV, and PI3 for protection against BRDC in beef calves. Plots were generated in a meta-analysis of data from individual trials within studies reported in the published literature. Events represent the total number of calves identified as having morbidity (A) or death (B) associated with BRDC. Weight represents the stratum weight calculated as the inverse of the estimate variance. The control group comprised nonvaccinated calves. M–H = Mantel-Haenszel risk ratio. Lowercase letters (a, b, c) indicate different trials (ie, subgroups) within the same study.

Lots of variation between studies

Overall, vaccination reduced the risk of BRD morbidity and mortality

Vaccination - bacteria

- Meta-analysis of bacteria
  - *M. haemolytica, P. multocida*

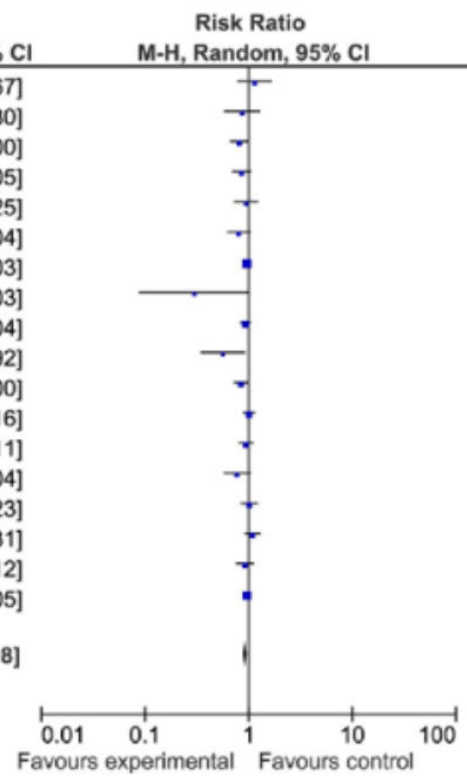
Evidence-Based Effectiveness of Vaccination Against *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni* in Feedlot Cattle for Mitigating the Incidence and Effect of Bovine Respiratory Disease Complex

R.L. Larson, DVM, PhD[a,*], D.L. Step, DVM[b]

Vet Clin Food Anim 28 (2012) 97–106

Study or Subgroup	Vaccinated Events	Vaccinated Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Amstutz a 1981	38	108	33	107	1.4%	1.14 [0.78, 1.67]
Bateman 1988	29	90	32	86	1.3%	0.87 [0.58, 1.30]
Bechtol 1996	100	295	124	296	4.3%	0.81 [0.66, 1.00]
Bechtol 1996	78	161	91	160	4.3%	0.85 [0.69, 1.05]
Frank 2002	37	60	39	60	2.7%	0.95 [0.72, 1.25]
Ives 1999	60	162	75	162	2.9%	0.80 [0.62, 1.04]
Jim 1988	444	781	766	1291	17.2%	0.96 [0.89, 1.03]
Loan 1989	3	50	10	50	0.1%	0.30 [0.09, 1.03]
MacGregor 2003	447	1652	480	1652	11.6%	0.93 [0.83, 1.04]
Malcolm-Callis 1994	16	60	28	59	0.9%	0.56 [0.34, 0.92]
McLean a 1990	89	147	109	152	6.4%	0.84 [0.72, 1.00]
McLean b 1990	116	160	109	152	8.4%	1.01 [0.88, 1.16]
Purdy 1986	34	41	52	59	6.2%	0.94 [0.80, 1.11]
Smith 1986	55	218	73	223	2.3%	0.77 [0.57, 1.04]
Thorlakson a 1990	122	284	122	289	5.1%	1.02 [0.84, 1.23]
Thorlakson b 1990	134	291	122	289	5.4%	1.09 [0.91, 1.31]
Thorlakson c 1990	107	276	122	289	4.6%	0.92 [0.75, 1.12]
Thorlakson d 1990	259	363	274	368	14.8%	0.96 [0.88, 1.05]
Total (95% CI)		**5199**		**5744**	**100.0%**	**0.93 [0.89, 0.98]**
Total events	2168		2661			

Heterogeneity: Tau² = 0.00; Chi² = 21.23, df = 17 (P = 0.22); I² = 20%
Test for overall effect: Z = 2.97 (P = 0.003)



Vaccination reduced the risk of BRD morbidity

Mortality was not impacted

Fig. 1. Forest plot of RR for 18 trials comparing cumulative morbidity incidence of feedlot cattle vaccinated against *M haemolytica* (15 trials) or *M haemolytica* + *P multocida* (3 trials) compared to controls.

Preconditioning programs – can reduce BRD rates

- Goal: spread stressful events over a period of time so calves do not experience all within a few days
- Common components of preconditioning (Wilson et al., 2017)
  - Weaning prior to sale (from days to weeks, e.g. 45 days)
  - Dehorning and castration with adequate time allowed for healing prior to sale
  - Training of calves to eat from a bunk and drink from a watering station
  - Vaccination for respiratory viruses, bacteria and clostridial diseases

Preconditioning parameters tested

Reference	Pre-conditioning	Feedlot Effect
Daniels et al., 2000	Castration before **vs.** after arrival	↑ ADG, ↓ mortality
Boyles et al., 2007	Pasture weaned **vs.** abrupt weaned	↓ BRD morbidity, = ADG after 1 and 4 wks
Step et al., 2008	45 day wean + vaccinated **vs.** abrupt wean	↑ DMI, ↓ BRD morbidity
Perrett et al., 2018	Dams vaccinated pre-breeding **vs.** unknown Dam history	In high-risk cattle: ↓ BRD morbidity and mortality

Example: Health performance of feeder calves sold at conventional auctions versus special auctions of vaccinated or conditioned calves in Ontario (Macartney et al., 2003)

1) Conventional calves

n = 6018

2) Vaccinated calves

n = 5651

Vaccination = IBR, Pi3, BVDV, BRSV, *H. somni, M. haemolytica*
Boost at least 2 weeks prior to auction and 2 to 4 weeks after the initial dose

+

Dehorned and castrated at least 2 months prior to auction

3) Preconditioned calves

n = 644

Vaccination = IBR, Pi3, BVDV, BRSV, *H. somni, M. haemolytica*
Boost at least 2 weeks prior to auction and 2 to 4 weeks after the initial dose

+

Dehorned and castrated at least 2 months prior to auction

+

Weaned at least 4 weeks prior to auction

Macartney et al., 2003

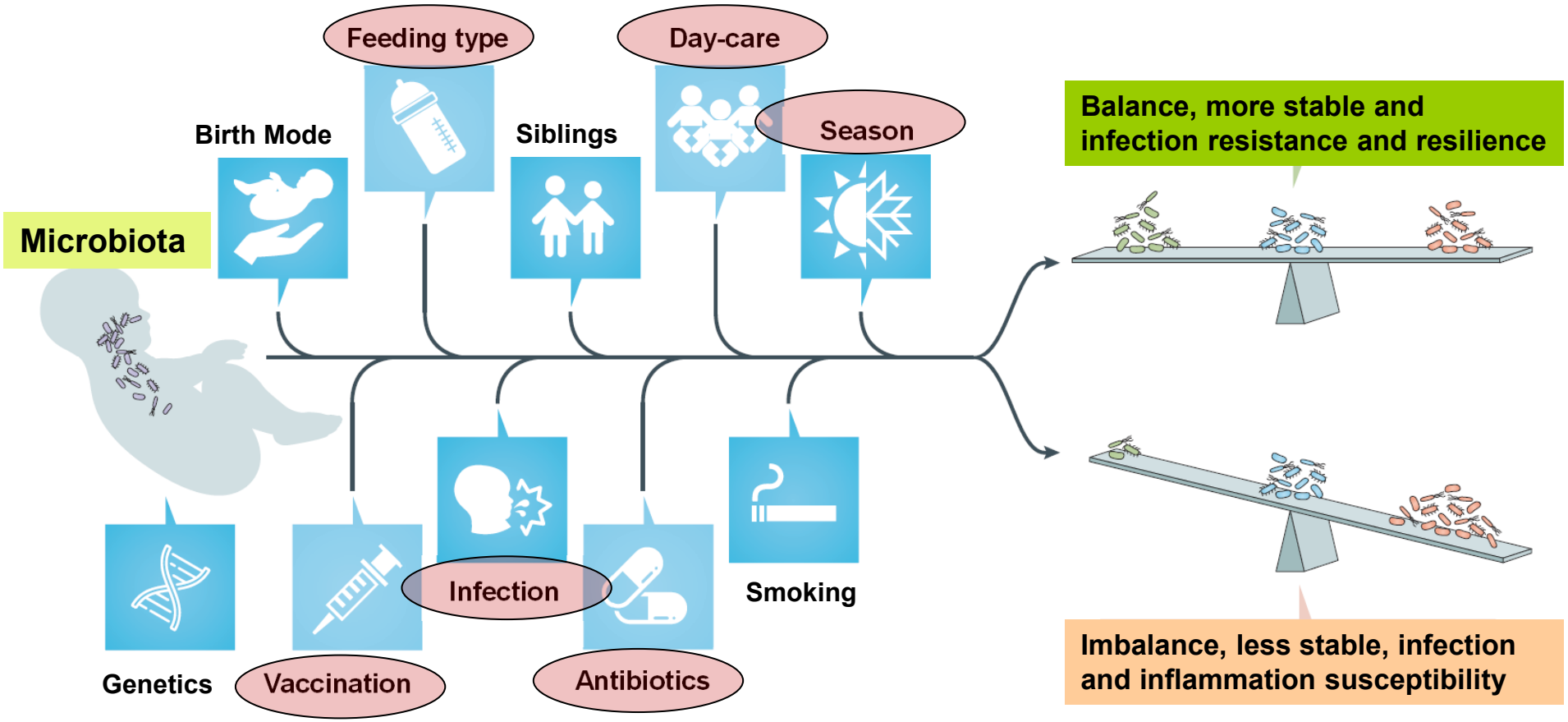
Comparison of health performance during the first 28 days of feed at a feedlot for the 3 types of calves:

	Conventional	Vaccinated	Preconditioned
Number of calves	6018	5651	644
BRD treatement rate	20.20%	13.70%	3.90%

- Compared to Conventional calves:
  - Vaccinated were 0.68 times likely to be treated for BRD
  - Preconditioned were 0.22 times as likely to be treated

→ Management strategies will be important to reducing antimicrobial use (know what you're buying)

Future work: in humans host and environmental factors influence the respiratory microbiota → many similar factors in beef industry



From: Nat. Rev. Microbiol. 2017, 15:259

Evidence for respiratory microbiota impacting cattle health

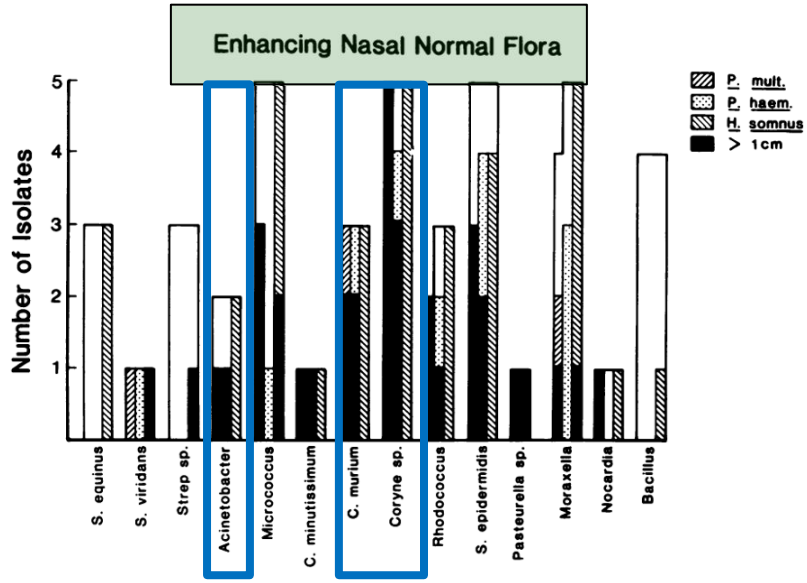
JOURNAL OF CLINICAL MICROBIOLOGY, May 1985, p. 803–807
0095-1137/85/050803-05$02.00/0
Copyright © 1985, American Society for Microbiology
Vol. 21, No. 5

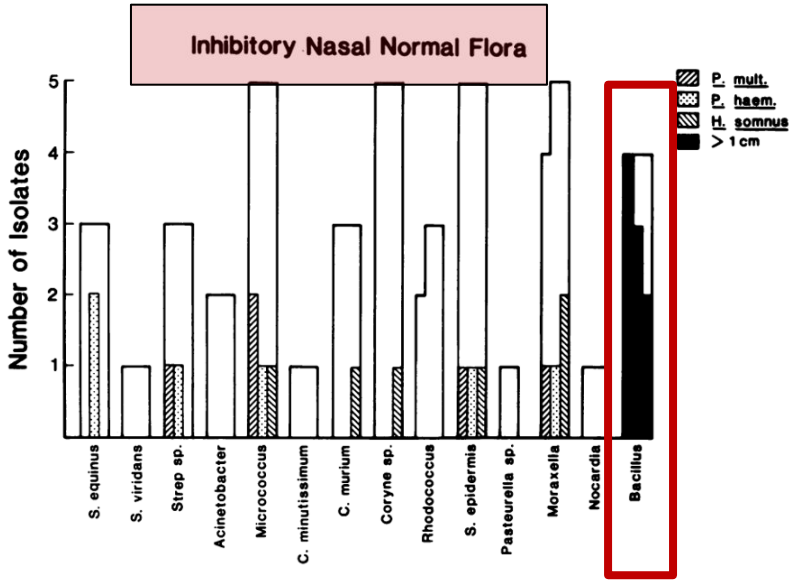
Bacterial Interactions in Bovine Respiratory and Reproductive Infections†

L. B. CORBEIL,[1]* W. WOODWARD,[1] A. C. S. WARD,[2,3] W. D. MICKELSEN,[4] AND L. PAISLEY[4]

Department of Veterinary Microbiology and Pathology,[1] Washington Animal Disease Diagnostic Laboratory,[2] and Department of Veterinary Medicine and Surgery,[4] Washington State University, Pullman, Washington 99164-7040, and Department of Veterinary Science, University of Idaho, Moscow, Idaho 83843[3]

- Commensals in the cattle respiratory tract can enhance or inhibit pathogens *in vitro*





Acinetobacter + *Cornynebacter*

Bacillus spp.

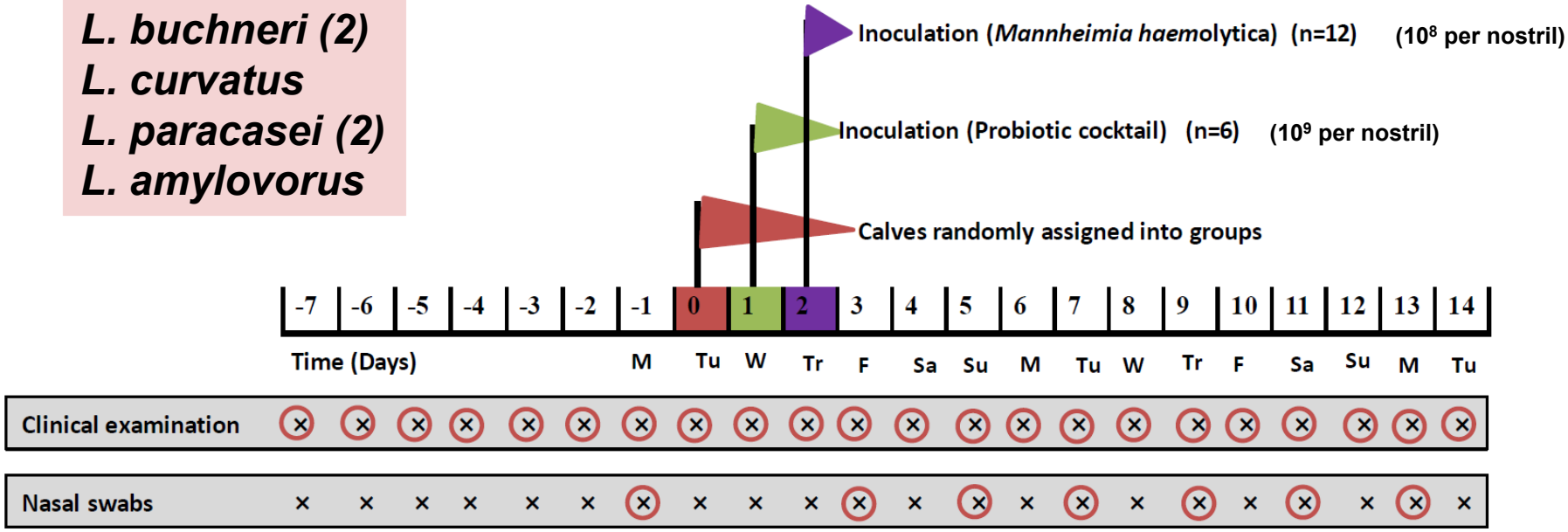
Future work - can we alter the respiratory microbiota to enhance pathogen resilience?

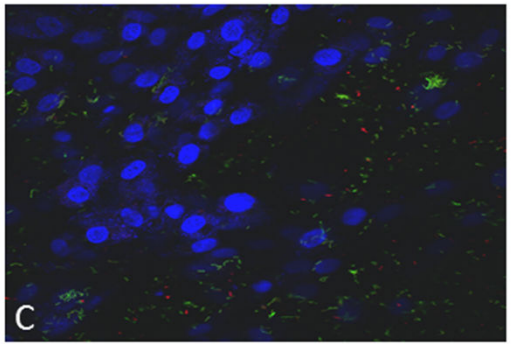
- Pathogen proliferation in the upper respiratory tract can lead to infection in the lungs
- Metaphylactic antimicrobials are used at feedlot entry to control pathogen growth

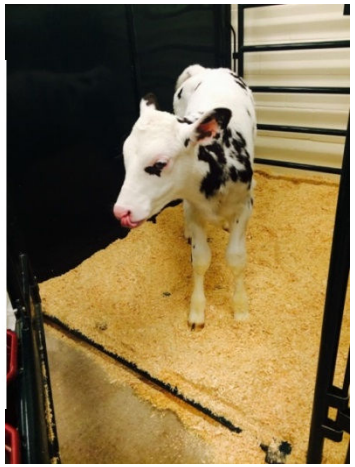
→ Our studies have shown that ***Lactobacillus*** are involved in bovine respiratory health. Are they useful as **nasal probiotics to reduce BRD pathogens**?

In vivo colonization challenge study

L. buchneri (2)
L. curvatus
L. paracasei (2)
L. amylovorus

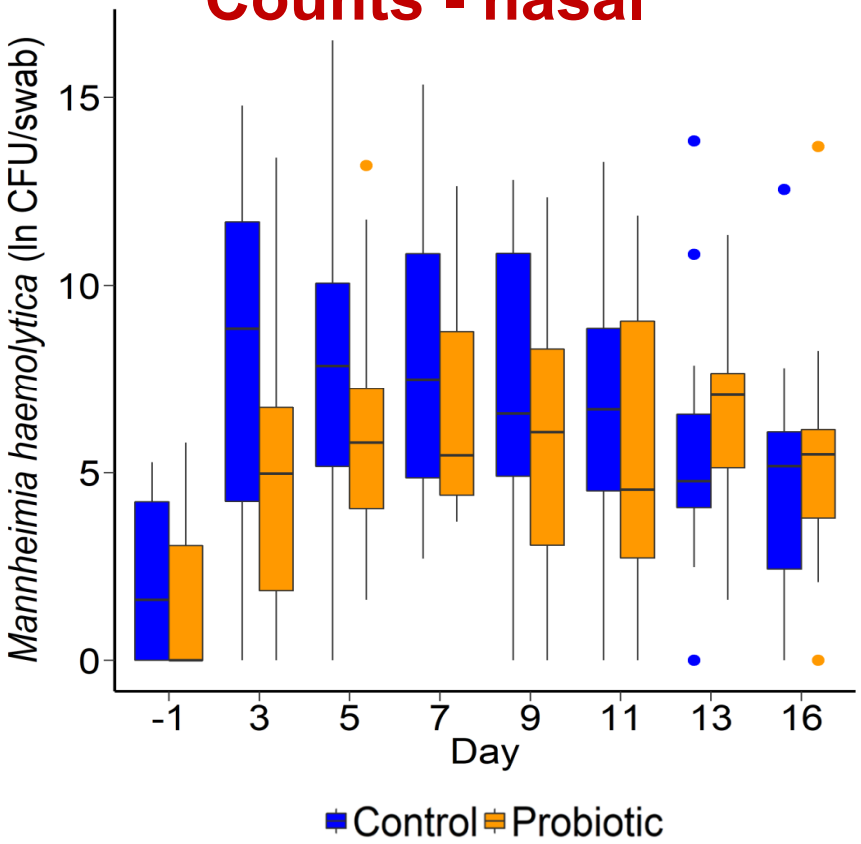




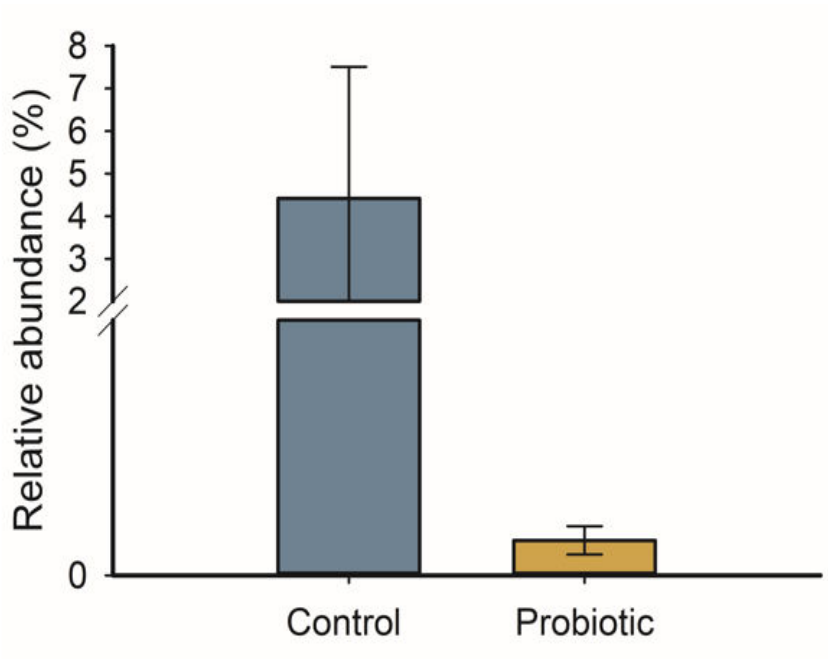


Prevalence of *M. haemolytica*

Counts - nasal



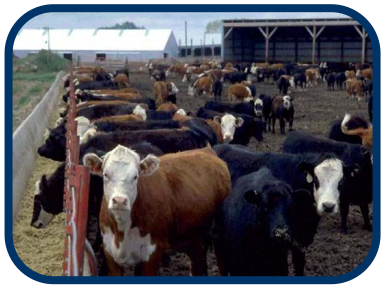
Abundance - lungs



Next step → synthetic bacterial communities to mitigate BRD pathogens

Summary of studies on antimicrobial resistance

1. Antimicrobial use (AMU)



- Resistance in BRD pathogens has increased substantially over the last decade
- Antimicrobial use, wherever it occurs, can promote resistance
- Antimicrobials used for metaphylaxis should be avoided for treatment

2. Antimicrobial administration

- While field data is limited, current commercial viral and bacterial vaccines have been shown to reduce BRD morbidity
- Vaccination may therefore reduce AMU by mitigating treatments required.

Summary of studies on antimicrobial resistance

3. Preconditioning

- Preconditioning has been shown to be effective in reducing BRD incidence and can also reduce AMU for treatment.
- Knowledge about purchased calves will help devise AMU strategies and potentially reduce AMU.

4. New technologies

- Using a targeted approach, bacteria were developed that could decrease colonization of the BRD pathogen *M. haemolytica*
- Nasal probiotics may be useful as part of a strategy to reduce metaphylactic antimicrobial use

Acknowledgements

- **Collaborators:**
  - Edouard Timsit (University of Calgary)
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  - Rima Menassa (AAFC – London)
  - Samat Amat (N. Dakota State University)
  - Murray Jelinski (University of Saskatchewan)
  - Calvin Booker (Feedlot Health Management Services)

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