



993 *Additional notes about interpretation of screening*

994 Citations were excluded if the study population comprised exclusively neonatal, dairy, veal, or sick  
995 calves (i.e., if they were treatment studies rather than metaphylactic/prophylactic studies) or if  
996 antimicrobials were only administered before the cattle arrived at the feedlot (i.e., preconditioning  
997 studies). In vitro-only citations were also excluded, as were citations for which the antimicrobials  
998 were given solely via feed or water. Studies of acute bovine pulmonary edema and emphysema  
999 (ABPE, also known as fog fever) were excluded, because that disease is treated using oral medica-  
1000 tions. Citations were also excluded if they did not include at least one arm with an antimicrobial  
1001 registered for the control or prevention of BRD or any injectable oxytetracycline. Although the  
1002 protocol stipulated the inclusion only of studies that examined at least one arm in which animals  
1003 received an antibiotic within 48 h of arrival at the feedlot, we opted to include outbreak studies  
1004 in which animals did not receive a metaphylactic injection of antibiotic until a certain proportion  
1005 of the feedlot animals began to exhibit clinical signs of BRD (provided that the animals receiving  
1006 metaphylaxis were clinically healthy), regardless of the elapsed time since the arrival of the cattle at  
1007 the feedlot. We did not exclude citations that only mentioned nasopharyngeal flora as an outcome  
1008 because the full text of such studies might have indicated that BRD was also an outcome.

1009 For the citation screening, Question 1 (Q1) of the abstract/title screening form was edited from the  
1010 protocol to specify primary research so that literature reviews could be excluded at this level. Ques-  
1011 tion 2 (Q2) was edited from the protocol to specify that reviewers were to assess a given reference  
1012 using only the title and/or abstract, even if the full text was available. For the full-text screening,  
1013 two reviewers independently evaluated the full-text articles for relevance, and any disagreements  
1014 were resolved by discussion. If consensus could not be reached, a third reviewer (AOC) was con-  
1015 sulted. Question 1 (Q1) was not in the protocol but was added to identify non-English language  
1016 citations, citations for which the full text could not be obtained, and conference abstracts that were  
1017 considered too short to constitute a full-text report (less than 500 words). Likewise, Question 2  
1018 (Q2) and Question 3 (Q3) were not in the protocol but were added so that the full texts could  
1019 be assessed based on the same two questions used for the title/abstract assessment (which was  
1020 especially important when a citation had no abstract). For Question 4 (Q4), we included studies of  
1021 stocker cattle unless the authors explicitly reported that the animals were kept on pasture/paddock.  
1022 Question 5 (Q5) was modified from the protocol to specify that at least one arm of the study must

1023 utilize a registered antibiotic for the prevention/control of BRD (or an injectable oxytetracycline),  
1024 and an answer option was added for studies for which that information was unclear.

Search Number	Search String	Number of hits
1	Cattle/ or Cattle Diseases/	331164.00
2	(cow or cows or cattle or heifer\$ or steer or steers or bull or bulls or calf or calves or youngstock\$ or young-stock\$ or beef or veal or bovine\$ or bovinæ or buiatric\$).ti,ab,kf.	349370
3	1 or 2	452936
4	exp Bovine Respiratory Disease Complex/	719.00
5	Pasteurella multocida/ or Mannheimia haemolytica/ or Haemophilus somnus/	2690
6	(respiratory disease\$ or respiratory tract disease\$ or respiratory virus\$ or respiratory tract virus\$ or shipping fever\$ or undifferentiated fever\$ or BRD or BRDC or pasteurellosis or pasteurella multocida or p multocida or mycoplasma or pneumonia\$ or pleuropneumonia\$ or pneumonitis or pneumonitides).ti,ab,kf	209216.00
7	(mannheimia haemolytica or mannheimia hemolytica or m haemolytica or m hemolytica or pasteurella haemolytica or pasteurella hemolytica or p haemolytica or p hemolytica or mannheimios\$).ti,ab,kf.	1889
8	(haemophilus somn\$ or hemophilus somn\$ or histophilus somn\$ or h somnus or h somni).ti,ab,kf.	475
9	or/4-8	210506
10	exp Chemoprevention/	17894
11	post-exposure prophylaxis/ or primary prevention/ or pre-exposure prophylaxis/	18743
12	(prophyla\$ or chemoprophyla\$ or chemoprevent\$ or chemo-prevent\$ or metaphyla\$ or meta-phyla\$ or premedicat\$ or pre-medicat\$).ti,ab,kf.	182924
13	exp anti-infective agents/ or exp anti-bacterial agents/	1497359
14	(population wide or whole population or mass or blanket or prevent\$ or preemptiv\$ or pre-emptiv\$).ti,ab,kf.	2035095
15	(arrival\$ or arrive\$ or arriving or entry or enter\$).ti,ab,kf.	530163
16	13 and (14 or 15)	186101
17	((mass or blanket or prevent\$ or preemptiv\$ or pre-emptiv\$) adj5 (treat\$ or therap\$ or antimicrobial\$ or anti-microbial\$ or antibiotic\$ or anti-biotic\$ or antibacterial\$ or anti-bacterial\$ or antiinfect\$ or anti-infect\$ or bacteriocid\$ or bactericid\$ or microbicid\$ or anti-mycobacteri\$ or antimycobacteri\$)).ti,ab,kf.	199978
18	((population wide or whole population\$) adj5 (treat\$ or therap\$ or antimicrobial\$ or anti-microbial\$ or antibiotic\$ or anti-biotic\$ or antibacterial\$ or anti-bacterial\$ or antiinfect\$ or anti-infect\$ or bacteriocid\$ or bactericid\$ or microbicid\$ or anti-mycobacteri\$ or antimycobacteri\$)).ti,ab,kf.	136
19	((mass or blanket) adj5 (medicat\$ or dosing or administration)).ti,ab,kf.	2937
20	((mass or blanket or prevent\$ or preemptiv\$ or pre-emptiv\$) adj5 (amoxicillin or amoxycillin or ampicillin or erythromycin or ceftiofur or cloxacillin or danofloxacin or enrofloxacin or florfenicol or gentamycin or gentamicin or lincomycin or oxytetracycline or penicillin or spectinomycin or sulfamethoxazole or tilmicosin or trimethoprim or tulathromycin or tylosin or gamithromycin or tildipirosin)).ti,ab,kf	1442
21	((arrival\$ or arrive\$ or arriving or entry or enter\$) adj5 (medicat\$ or antimicrobial\$ or anti-microbial\$ or antibiotic\$ or anti-biotic\$ or antibacterial\$ or anti-bacterial\$ or antiinfect\$ or anti-infect\$ or bacteriocid\$ or bactericid\$ or microbicid\$ or anti-mycobacteri\$ or antimycobacteri\$ or amoxicillin or amoxycillin or ampicillin or erythromycin or ceftiofur or cloxacillin or danofloxacin or enrofloxacin or florfenicol or gentamycin or gentamicin or lincomycin or oxytetracycline or penicillin or spectinomycin or sulfamethoxazole or tilmicosin or trimethoprim or tulathromycin or tylosin or gamithromycin or tildipirosin)).ti,ab,kf.	8404
22	(or/16-21) or 10 or 11 or 12	544569
23	3 and 9 and 22	370
24	exp Bovine Respiratory Disease Complex/pc and (exp anti-infective agents/ or exp anti-bacterial agents/ or post-exposure prophylaxis/ or primary prevention/ or pre-exposure prophylaxis/ or exp chemoprevention/)	41
25	Cattle Diseases/pc and Respiratory Tract Infections/ and (exp anti-infective agents/ or exp anti-bacterial agents/ or post-exposure prophylaxis/ or primary prevention/ or pre-exposure prophylaxis/ or exp chemoprevention/)	23
26	Cattle Diseases/ and Respiratory Tract Infections/pc and (exp anti-infective agents/ or exp anti-bacterial agents/ or post-exposure prophylaxis/ or primary prevention/ or pre-exposure prophylaxis/ or exp chemoprevention/)	19

Search Number	Search String	Number of hits
27	or/23-26	395
28	remove duplicates from 27	395

Table S1: Search string results for Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) , conducted on 05/07/18. Interface : OVID, Database coverage dates: 1946 to current (Updated daily)

Search Number	Search String	Number of hits
# 14	#13 AND #5 AND #1	1147
# 13	#12 OR #11 OR #10 OR #9 OR #8 OR #7 OR #6	142691
# 12	DE=("disease prevention") AND TS=(antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR "anti-infect*" OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri* OR amoxicillin" OR amoxycillin" OR ampicillin" OR erythromycin" OR ceftiofur" OR cloxacillin" OR danofloxacin" OR enrofloxacin" OR florfenicol" OR gentamycin" OR gentamicin" OR lincomycin" OR oxytetracycline" OR penicillin" OR spectinomycin" OR sulfamethoxazole" OR tilmicosin" OR trimethoprim" OR tulathromycin" OR tylosin" OR gamithromycin" OR tildipirosin"))	5784
# 11	TS=((arrival* OR arrive* OR "arriving" OR "entry" OR enter*) NEAR/5 (medicat* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR "anti-infect*" OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri* OR amoxicillin" OR amoxycillin" OR ampicillin" OR erythromycin" OR ceftiofur" OR cloxacillin" OR danofloxacin" OR enrofloxacin" OR florfenicol" OR gentamycin" OR gentamicin" OR lincomycin" OR oxytetracycline" OR penicillin" OR spectinomycin" OR sulfamethoxazole" OR tilmicosin" OR trimethoprim" OR tulathromycin" OR tylosin" OR gamithromycin" OR tildipirosin"))	3900
# 10	TS=("mass" OR "blanket" OR prevent* OR preemptiv* OR pre-emptiv*) NEAR/5 ("amoxicillin" OR amoxycillin" OR ampicillin" OR erythromycin" OR ceftiofur" OR cloxacillin" OR danofloxacin" OR enrofloxacin" OR florfenicol" OR gentamycin" OR gentamicin" OR lincomycin" OR oxytetracycline" OR penicillin" OR spectinomycin" OR sulfamethoxazole" OR tilmicosin" OR trimethoprim" OR tulathromycin" OR tylosin" OR gamithromycin" OR tildipirosin"))	651
# 9	TS=("mass" OR "blanket") NEAR/5 (medicat* OR "dosing" OR "administration"))	1741
# 8	TS=("population wide" OR "whole population*") NEAR/5 (treat* OR therap* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR anti-infect* OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri*))	47
# 7	TS=("mass" OR "blanket" OR prevent* OR preemptiv* OR pre-emptiv*) NEAR/5 (treat* OR therap* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR anti-infect* OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri*))	51631
# 6	TS=(prophyla* OR chemoprophyla* OR chemoprevent* OR "chemo-prevent*" OR metaphyla* OR "meta-phyla*" OR premedicat* OR "pre-medicat*"))	87438
# 5	#4 OR #3 OR #2	110884
# 4	TS=("haemophilus somn*" OR "hemophilus somn*" OR "histophilus somn*" OR "h somnus" OR "h somni")	981
# 3	TS=("mannheimia haemolytica" OR "mannheimia hemolytica" OR "m haemolytica" OR "m hemolytica" OR "pasteurella haemolytica" OR "pasteurella hemolytica" OR "p haemolytica" OR "p hemolytica" OR mannheimios*)	3388
# 2	TS=("respiratory disease*" OR "respiratory tract disease*" OR "respiratory virus*" OR "respiratory tract virus*" OR "shipping fever*" OR "undifferentiated fever*" OR "BRD" OR "BRDC" OR "pasteurellosis" OR "pasteurella multocida" OR "p multocida" OR "mycoplasma" OR pneumonia* OR pleuropneumonia* OR "pneumonitis" OR "pneumonitides")	109540
# 1	TS=("cow" OR "cows" OR "cattle" OR heifer* OR "steer" OR "steers" OR "bull" OR "bulls" OR "calf" OR "calves" OR "youngstock*" OR "young-stock*" OR "beef" OR "veal" OR bovine* OR "bovinae" OR buiatric*)	738516

Table S2: Search string results for CAB Abstracts and Global Health, Search date: 04/07/18 , Interface: Web of Science, Database coverage dates: 1910-03/07/18

Search Number	Search String	Number of hits
# 13	#12 AND #5 AND #1	351
# 12	#11 OR #10 OR #9 OR #8 OR #7 OR #6	346969
# 11	TS=((arrival* OR arrive* OR "arriving" OR "entry" OR enter*) NEAR/5 (medicat* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR "anti-infect*" OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri* OR "amoxicillin" OR "amoxycillin" OR "ampicillin" OR "erythromycin" OR "ceftiofur" OR "cloxacillin" OR "danofloxacin" OR "enrofloxacin" OR "florfenicol" OR "gentamycin" OR "gentamicin" OR "lincomycin" OR "oxytetracycline" OR "penicillin" OR "spectinomycin" OR "sulfamethoxazole" OR "tilmicosin" OR "trimethoprim" OR "tulathromycin" OR "tylosin" OR "gamithromycin" OR "tildipirosin"))	8446
# 10	TS=(("mass" OR "blanket" OR prevent* OR preemptiv* OR pre-emptiv*) NEAR/5 ("amoxicillin" OR "amoxycillin" OR "ampicillin" OR "erythromycin" OR "ceftiofur" OR "cloxacillin" OR "danofloxacin" OR "enrofloxacin" OR "florfenicol" OR "gentamycin" OR "gentamicin" OR "lincomycin" OR "oxytetracycline" OR "penicillin" OR "spectinomycin" OR "sulfamethoxazole" OR "tilmicosin" OR "trimethoprim" OR "tulathromycin" OR "tylosin" OR "gamithromycin" OR "tildipirosin"))	1251
# 9	TS=(("mass" OR "blanket") NEAR/5 (medicat* OR "dosing" OR "administration"))	3059
# 8	TS=(("population wide" OR "whole population*") NEAR/5 (treat* OR therap* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR anti-infect* OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri*))	139
# 7	TS=(("mass" OR "blanket" OR prevent* OR preemptiv* OR pre-emptiv*) NEAR/5 (treat* OR therap* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR anti-infect* OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri*))	171222
# 6	TS=(prophyla* OR chemoprophyla* OR chemoprevent* OR "chemo-prevent*" OR metaphyla* OR "meta-phyla*" OR premedicat* OR "pre-medicat*")	177323
# 5	#4 OR #3 OR #2	219711
# 4	TS=("haemophilus somn*" OR "hemophilus somn*" OR "histophilus somn*" OR "h somnus" OR "h somni")	607
# 3	TS=("mannheimia haemolytica" OR "mannheimia hemolytica" OR "m haemolytica" OR "m hemolytica" OR "pasteurella haemolytica" OR "pasteurella hemolytica" OR "p haemolytica" OR "p hemolytica" OR mannheimios*)	2531
# 2	TS=("respiratory disease*" OR "respiratory tract disease*" OR "respiratory virus*" OR "respiratory tract virus*" OR "shipping fever*" OR "undifferentiated fever*" OR "BRD" OR "BRDC" OR "pasteurellosis" OR "pasteurella multocida" OR "p multocida" OR "mycoplasma" OR pneumonia* OR pleuropneumonia* OR "pneumonitis" OR "pneumonitides")	218289
# 1	TS=("cow" OR "cows" OR "cattle" OR heifer* OR "steer" OR "steers" OR "bull" OR "bulls" OR "calf" OR "calves" OR "youngstock*" OR "young-stock*" OR "beef" OR "veal" OR bovine* OR "bovinae" OR buiatric*)	526226

Table S3: Search string results for Science Citation Index (SCI), Search date: 04/07/18, Interface: Web of Science, Database coverage dates: 1900-03/07/18

Search Number	Search String	Number of hits
# 13	#12 AND #5 AND #1	20
# 12	#11 OR #10 OR #9 OR #8 OR #7 OR #6	30937
# 11	TS=((arrival* OR arrive* OR "arriving" OR "entry" OR enter*) NEAR/5 (medicat* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR "anti-infect*" OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri* OR "amoxicillin" OR "amoxycillin" OR "ampicillin" OR "erythromycin" OR "ceftiofur" OR "cloxacillin" OR "danofloxacin" OR "enrofloxacin" OR "florfenicol" OR "gentamycin" OR "gentamicin" OR "lincomycin" OR "oxytetracycline" OR "penicillin" OR "spectinomycin" OR "sulfamethoxazole" OR "tilmicosin" OR "trimethoprim" OR "tulathromycin" OR "tylosin" OR "gamithromycin" OR "tildipirosin"))	508
# 10	TS=(("mass" OR "blanket" OR prevent* OR preemptiv* OR pre-emptiv*) NEAR/5 ("amoxicillin" OR "amoxycillin" OR "ampicillin" OR "erythromycin" OR "ceftiofur" OR "cloxacillin" OR "danofloxacin" OR "enrofloxacin" OR "florfenicol" OR "gentamycin" OR "gentamicin" OR "lincomycin" OR "oxytetracycline" OR "penicillin" OR "spectinomycin" OR "sulfamethoxazole" OR "tilmicosin" OR "trimethoprim" OR "tulathromycin" OR "tylosin" OR "gamithromycin" OR "tildipirosin"))	69
# 9	TS=(("mass" OR "blanket") NEAR/5 (medicat* OR "dosing" OR "administration"))	215
# 8	TS=(("population wide" OR "whole population*") NEAR/5 (treat* OR therap* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR anti-infect* OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri*))	6
# 7	TS=(("mass" OR "blanket" OR prevent* OR preemptiv* OR pre-emptiv*) NEAR/5 (treat* OR therap* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR anti-infect* OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri*))	13915
# 6	TS=(prophyla* OR chemoprophyla* OR chemoprevent* OR "chemo-prevent*" OR metaphyla* OR "meta-phyla*" OR premedicat* OR "pre-medicat*")	17255
# 5	#4 OR #3 OR #2	15244
# 4	TS=("haemophilus somn*" OR "hemophilus somn*" OR "histophilus somn*" OR "h somnus" OR "h somni")	19
# 3	TS=("mannheimia haemolytica" OR "mannheimia hemolytica" OR "m haemolytica" OR "m hemolytica" OR "pasteurella haemolytica" OR "pasteurella hemolytica" OR "p haemolytica" OR "p hemolytica" OR mannheimios*)	82
# 2	TS=("respiratory disease*" OR "respiratory tract disease*" OR "respiratory virus*" OR "respiratory tract virus*" OR "shipping fever*" OR "undifferentiated fever*" OR "BRD" OR "BRDC" OR "pasteurellosis" OR "pasteurella multocida" OR "p multocida" OR "mycoplasma" OR pneumonia* OR pleuropneumonia* OR "pneumonitis" OR "pneumonitides")	15199
# 1	TS=("cow" OR "cows" OR "cattle" OR heifer* OR "steer" OR "steers" OR "bull" OR "bulls" OR "calf" OR "calves" OR "youngstock*" OR "young-stock*" OR "beef" OR "veal" OR bovine* OR "bovinae" OR buiatric*)	39515

Table S4: Search string results for Conference Proceedings Citation Index Science (CPCI-S), Search date: 04/07/18, Interface: Web of Science, Database coverage dates: 1990-03/07/18



Search Number	Search String	Number of hits
#1	NOFT(cow OR cows OR cattle OR heifer* OR steer OR steers OR bull OR bulls OR calf OR calves OR youngstock* OR "young-stock*" OR beef OR veal OR bovine* OR bovinæ OR buiatric*)	352207.00
#2	NOFT("respiratory disease*" OR "respiratory tract disease*" OR "respiratory virus*" OR "respiratory tract virus*" OR "shipping fever*" OR "undifferentiated fever*" OR BRD OR BRDC OR pasteurellosis OR "pasteurella multocida" OR "p multocida" OR mycoplasma OR pneumonia* OR pleuropneumonia* OR pneumonitis OR pneumonitides)	26624
#3	NOFT("mannheimia haemolytica" OR "mannheimia hemolytica" OR "m haemolytica" OR "m hemolytica" OR "pasteurella haemolytica" OR "pasteurella hemolytica" OR "p haemolytica" OR "p hemolytica" OR mannheimios*)	1239
#4	NOFT("haemophilus somn*" OR "hemophilus somn*" OR "histophilus somn*" OR "h somnus" OR "h somni")	325
#5	S2 OR S3 OR S4	27306
#6	NOFT(prophyla* OR chemoprophylla* OR chemoprevent* OR "chemo-prevent*" OR metaphyla* OR "meta-phylla*" OR premedicat* OR "pre-medicat*")	10397
#7	NOFT((mass OR blanket OR prevent* OR preemptiv* OR "pre-emptiv*") NEAR/5 (treat* OR therap* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR "anti-infect*" OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri*))	12821
#8	NOFT(("population wide" OR "whole population*") NEAR/5 (treat* OR therap* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR "anti-infect*" OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri*))	7
#9	NOFT((mass OR blanket) NEAR/5 (medicat* OR dosing OR administration))	392
#10	NOFT((mass OR blanket OR prevent* OR preemptiv* OR "pre-emptiv*") NEAR/5 (amoxicillin OR amoxycillin OR ampicillin OR erythromycin OR ceftiofur OR cloxacillin OR danofloxacin OR enrofloxacin OR florfenicol OR gentamycin OR gentamicin OR lincomycin OR oxytetracycline OR penicillin OR spectinomycin OR sulfamethoxazole OR tilmicosin OR trimethoprim OR tulathromycin OR tylosin OR gamithromycin OR tildipirosin))	153
#11	NOFT((arrival* OR arrive* OR arriving OR entry OR enter*) NEAR/5 (medicat* OR antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR "anti-infect*" OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri* OR amoxicillin OR amoxycillin OR ampicillin OR erythromycin OR ceftiofur OR cloxacillin OR danofloxacin OR enrofloxacin OR florfenicol OR gentamycin OR gentamicin OR lincomycin OR oxytetracycline OR penicillin OR spectinomycin OR sulfamethoxazole OR tilmicosin OR trimethoprim OR tulathromycin OR tylosin OR gamithromycin OR tildipirosin))	490
#12	mainsubject.Exact("disease prevention") OR mainsubject.Exact("disease control")	33624
#13	NOFT(antimicrobial* OR "anti-microbial*" OR antibiotic* OR "anti-biotic*" OR antibacterial* OR "anti-bacterial*" OR antiinfect* OR "anti-infect*" OR bacteriocid* OR bactericid* OR microbicid* OR "anti-mycobacteri*" OR antimycobacteri* OR amoxicillin OR amoxycillin OR ampicillin OR erythromycin OR ceftiofur OR cloxacillin OR danofloxacin OR enrofloxacin OR florfenicol OR gentamycin OR gentamicin OR lincomycin OR oxytetracycline OR penicillin OR spectinomycin OR sulfamethoxazole OR tilmicosin OR trimethoprim OR tulathromycin OR tylosin OR gamithromycin OR tildipirosin)	83529
#14	S12 AND S13	2030
#15	S14 OR S11 OR S10 OR S9 OR S8 OR S7 OR S6	25266
#16	S15 AND S5 AND S1	183

Table S5: Search string results for AGRICOLA, Search date: 05/07/18, Interface: ProQuest, Database coverage dates: 1970 to 05/07/18

Study	Country	Feedlot type	Year	Pens	Concurrent treatments
(Food and Drug Administration Accessed September 2018. <i>d</i> )	USA	Unspecified feedlot	Not reported	NR	NR
(Food and Drug Administration Accessed September 2018. <i>d</i> )	USA	Unspecified feedlot	NR	NR	NR
(Booker et al. 2006)	USA	Commercial feedlot	NR	10	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Booker et al. 2007)	Canada	Commercial feedlot	NR	10	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Blasi et al. 2010)	USA	Research/University feedlot	2008	8	BRD vaccines, antiparasitic treatment(s)
(Amrine et al. 2014)	USA	NR, Research/University feedlot	2013-2014	12	Antiparasitic treatment(s)
(Baggott et al. 2011)	France	Rearing unit	NR	NR	BRD vaccines, antiparasitic treatment(s), implants (hormones) except bacterial BRD vaccines unclear
(Baggott et al. 2011)	Italy	Rearing unit	NR	NR	BRD vaccines, antiparasitic treatment(s), implants (hormones) except bacterial BRD vaccines unclear
(Baggott et al. 2011)	Italy	Rearing unit	NR	NR	BRD vaccines, antiparasitic treatment(s), implants (hormones) except bacterial BRD vaccines unclear
(Step et al. 2007)	USA	Backgrounding lot	NR	8 (588 animals, 3 treatment groups, 24-27 calves per pen)	BRD vaccines, antiparasitic treatment(s)
(McClary & Vogel 1999)	USA	Research/University feedlot	NR	10	BRD vaccines, antiparasitic treatment(s)
(Gill et al. 1986)	USA	NR	1984	4	Antiparasitic treatment(s)
(Morck et al. 1993)	Canada	Commercial feedlot	NR	9	BRD vaccines, antiparasitic treatment(s), antibiotics (decoquinatone, monensin)
(Food and Drug Administration Accessed September 2018. <i>f</i> )	USA	Unspecified feedlot	NR	NR	NR
(Food and Drug Administration Accessed September 2018. <i>b</i> )	USA	Unspecified feedlot	2006	6	BRD vaccines, antiparasitic treatment(s)
(Food and Drug Administration Accessed September 2018. <i>b</i> )	USA	Unspecified feedlot	2008	22	BRD vaccines, antiparasitic treatment(s)
(Janzen & McManus 1980)	Canada	Commercial feedlot	NR	6	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Timsit, Workentine, Crepieux, Miller, Regev-Shoshani, Schaefer & Alexander 2017)	Canada	Commercial feedlot	2014	1	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Erickson & R. 2008)	USA	Research/University feedlot	2006	26	BRD vaccines, antiparasitic treatment(s)
(Schumann et al. 1991)	Canada	Research/University feedlot	1989	8	BRD vaccines, antiparasitic treatment(s)
(Schumann et al. 1990)	Canada	Research/University feedlot	1988	12	BRD vaccines, antiparasitic treatment(s)
(Brazle 1997)	USA	NR	NR	4	BRD vaccines, antiparasitic treatment(s), implants (hormones)

Study	Country	Feedlot type	Year	Pens	Concurrent treatments
(Hanzlicek et al. 2016)	USA	Research/University feedlot	2011	12	BRD vaccines, antiparasitic treatment(s)
(Duff et al. 2000)	USA	Research/University feedlot	1997	3	BRD vaccines, antiparasitic treatment(s)
(Duff et al. 2000)	USA	Research/University feedlot	1998	8	BRD vaccines, antiparasitic treatment(s)
(Frank & Duff 2000)	USA	Research/University feedlot	NR	3	BRD vaccines, antiparasitic treatment(s)
(Martin et al. 2007)	Spain	Commercial feedlot	NR	NR	NR
(Vogel et al. 1998)	USA	Commercial feedlot	NR	8	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Lofgreen et al. 1978)	USA	NR	NR	NR	BRD vaccines, antiparasitic treatment(s)
(Regev-Shoshani et al. 2017)	Canada	Commercial feedlot	2013-2014	4	BRD vaccines
(Glynn et al. 2002)	USA	Unspecified feedlot	NR	8	BRD vaccines, antiparasitic treatment(s)
(Glynn et al. 2002)	USA	Unspecified feedlot	NR	6	BRD vaccines, antiparasitic treatment(s)
(Food and Drug Administration 2003)	USA	Unspecified feedlot	NR	NR	NR
(Schipper & Kelling 1974)	USA	Unspecified feedlot	NR	NR	BRD vaccines
(Schipper & Kelling 1971)	USA	Unspecified feedlot	NR	1	BRD vaccines, antibiotics (tetracycline in feed)
(Stegner et al. 2013)	USA	Commercial feedlot	2009-2010	8	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (chlortetracycline)
(Hawley et al. 2016)	USA	Receiving Unit	2012-2013	12	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Brown et al. 1989)	USA	Research/University feedlot	NR	4	BRD vaccines, antiparasitic treatment(s)
(Nickell et al. 2008)	USA	Commercial stocker facility	2007	12	BRD vaccines, antiparasitic treatment(s)
(Gonzalez-Martin et al. 2011)	Spain	Commercial feedlot	2006-2007	NR	Antiparasitic treatment(s)
(van Donkersgoed & Merrill 2012)	Canada	Commercial feedlot	2010-2011	10	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (chlortetracycline, monensin)
(van Donkersgoed & Merrill 2013a)	Canada	Commercial feedlot	2012-2013	10	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (monensin, tylosin)
(van Donkersgoed & Merrill 2013b)	Canada	Commercial feedlot	2012	10	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (monensin, tylosin)
(van Donkersgoed et al. 2017)	Canada	Commercial feedlot	2016	10	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (monensin, tylosin)
(John et al. 2008)	USA	Commercial feedlot	2006-2007	7 (MP), 14 (no MP)	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(White et al. 2015)	USA	NR	2013-2014	8	BRD vaccines
(Food and Drug Administration Accessed September 2018.c)	USA	NR	2007	NR	NR
(Food and Drug Administration Accessed September 2018.a)	USA	NR	1999	NR	NR
(van Donkersgoed et al. 2008)	Canada	Commercial feedlot	2007-2008	10	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (chlortetracycline in feed)
(DeDonder et al. 2016)	USA	Research/University feedlot	NR	3	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Sturgess & Renter 2017)	USA	Commercial feedlot	2012-2013	12	BRD vaccines, antiparasitic treatment(s), implants (hormones)

Study	Country	Feedlot type	Year	Pens	Concurrent treatments
(Rooney et al. 2005)	USA	Research/University feedlot	2003	5	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Rooney et al. 2005)	USA	Research/University feedlot	2001-2002	5	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Rooney et al. 2005)	USA	Research/University feedlot	2001-2002	5	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Fazio et al. 2015)	Argentina	Commercial feedlot	NR	10	BRD vaccines, antiparasitic treatment(s)
(Corbin et al. 2009)	USA	Commercial feedlot	2006-2007	4 or 8	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (monensin, tylosin)
(Corbin et al. 2009)	USA	Commercial feedlot	2006-2007	4 or 8	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (monensin, tylosin)
(Galyean et al. 1995)	USA	Research/University feedlot	NR	3	BRD vaccines, antiparasitic treatment(s)
(Galyean et al. 1995)	USA	Research/University feedlot	NR	4	BRD vaccines, antiparasitic treatment(s)
(Montague et al. 1996)	USA	NR	1994-1995	NR	BRD vaccines, antiparasitic treatment(s)
(Food and Drug Administration Accessed September 2018.e)	USA	NR	2010	NR	NR
(van Koevering et al. 1992)	USA	Research/University feedlot	1991-1992	10	BRD vaccines, antiparasitic treatment(s)
(Meeuwse & Hibbard 2002)	USA	Commercial feedlot, Research/University feedlot	2002	NR	NR
(Schunich et al. 2002)	Canada	Commercial feedlot	1995-1997	20	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Cusack 2004)	Australia	Commercial feedlot	2001	3	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Guichon et al. 1993)	Canada	Commercial feedlot	1991-1992	6	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Compiani et al. 2014)	Italy	Commercial feedlot	NR	NR	BRD vaccines, antiparasitic treatment(s)
(Breeze et al. 1982)	Canada	Unspecified feedlot	1979-1980	8	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Harland et al. 1991)	Canada	Commercial feedlot	1986-1987	7	BRD vaccines, antiparasitic treatment(s)
(Hibbard et al. 2002)	USA	Commercial feedlot	NR	NR	NR
(Montgomery et al. 2008)	USA	Unspecified feedlot	NR	14	BRD vaccines, antiparasitic treatment(s)
(Food and Drug Administration Accessed September 2018.g)	USA	NR	2013	NR	NR
(Siddhartha et al. 2013)	USA	Commercial feedlot	2010-2011	17	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Hendrick et al. 2013)	Canada	Commercial feedlot	2007, 2008	15	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Stokka & Kreikemeier 1996)	USA	Research/University feedlot	1995-1996	8	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Guthrie et al. 2004)	USA	Commercial feedlot	1998	4	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (monensin, tylosin)
(Bryant et al. 2008)	USA	Commercial feedlot	2004-2005	22	BRD vaccines, antiparasitic treatment(s), implants (hormones), antibiotics (monensin, tylosin)
(Tennant et al. 2014)	USA	Commercial feedlot	2009-2010	8	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Crepieux et al. 2016)	Canada	Commercial feedlot	2014-2015	2	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Miller et al. 2016)	USA	Research/University feedlot	NR	10	BRD vaccines, antiparasitic treatment(s), implants (hormones)

Study	Country	Feedlot type	Year	Pens	Concurrent treatments
(Reece & Smith 1996)	USA	Backgrounding lot	1994	NR	BRD vaccines, antiparasitic treatment(s), implants (hormones)
(Kilgore et al. 2005)	USA	Research/University feedlot	NR	NR	BRD vaccines, antiparasitic treatment(s)
(Rossi et al. 2010)	Italy	Commercial feedlot	NR	NR	BRD vaccines, antiparasitic treatment(s)
(Rossi et al. 2010)	Italy	Commercial feedlot	NR	NR	BRD vaccines, antiparasitic treatment(s)
(Rossi et al. 2010)	Italy	Commercial feedlot	NR	NR	BRD vaccines, antiparasitic treatment(s)

Table S6: Characteristics of relevant studies identified by the systematic review for Bovine Respiratory Disease; NR= Not reported; MP= Metaphylaxis

Study	Status	BRD cases at arrival
(Food and Drug Administration Accessed September 2018. <i>d</i> ) (Booker et al. 2006)	Included in meta-analysis Excluded due to data issues	Excluded from study Treated for BRD,randomly assigned to experimental group after initial treatment on day 0
(Booker et al. 2007)	Excluded due to data issues	Not reported
(Blasi et al. 2010)	Risk period unclear or not appropriate	Not reported
(Amrine et al. 2014)	Included in meta-analysis	Excluded from study
(Baggott et al. 2011)	Included in meta-analysis	Treated for BRD
(Step et al. 2007)	Included in meta-analysis	Excluded from study
(McClary & Vogel 1999)	Included in meta-analysis	No sick animals at arrival
(Gill et al. 1986)	Included in meta-analysis	Not reported
(Morck et al. 1993)	Included in meta-analysis	Excluded from study
(Food and Drug Administration Accessed September 2018. <i>f</i> )	Excluded due to data issues	Not reported
(Food and Drug Administration Accessed September 2018. <i>b</i> )	Included in meta-analysis	Excluded from study
(Janzen & McManus 1980)	Excluded due to data issues	Excluded from study,Treated for BRD
(Timsit, Workentine, Crepieux, Miller, Regev-Shoshani, Schaefer & Alexander 2017)	Excluded due to data issues	Excluded from study
(Erickson & R. 2008)	Included in meta-analysis	Not reported
(Schumann et al. 1991)	Included in meta-analysis	Excluded from study
(Schumann et al. 1990)	Included in meta-analysis	Excluded from study
(Brazle 1997)	Excluded due to data issues	Not reported
(Hanzlicek et al. 2016)	Included in meta-analysis	Not reported
(Duff et al. 2000)	Included in meta-analysis	Not reported
(Frank & Duff 2000)	Included in meta-analysis	Not reported
(Martin et al. 2007)	Included in meta-analysis	Excluded from study
(Vogel et al. 1998)	Included in meta-analysis	Excluded from study
(Lofgreen et al. 1978)	Included in meta-analysis	Not reported
(Regev-Shoshani et al. 2017)	Included in meta-analysis	Excluded from study
(Glynn et al. 2002)	Included in meta-analysis	Not reported
(Food and Drug Administration 2003)	Included in meta-analysis	Not reported
(Schipper & Kelling 1974)	Excluded due to data issues	No sick animals at arrival
(Schipper & Kelling 1971)	Risk period unclear or not appropriate	No sick animals at arrival
(Stegner et al. 2013)	Risk period unclear or not appropriate	Excluded from study
(Hawley et al. 2016)	Included in meta-analysis	Not reported
(Brown et al. 1989)	Excluded due to data issues	Not reported
(Nickell et al. 2008)	Included in meta-analysis	Not reported
(Gonzalez-Martin et al. 2011)	Included in meta-analysis	Excluded from study
(van Donkersgoed & Merrill 2012)	Risk period unclear or not appropriate	Treated for BRD,randomly assigned to experimental group after initial treatment on day 0
(van Donkersgoed & Merrill 2013 <i>a</i> )	Risk period unclear or not appropriate	Treated for BRD,randomly assigned to experimental group after initial treatment on day 0
(van Donkersgoed & Merrill 2013 <i>b</i> )	Risk period unclear or not appropriate	Treated for BRD
402	(van Donkersgoed et al. 2017)	Risk period r or not appropriate
Treated for BRD, Randomly assigned to experimental group after initial treatment on day 0		
(John et al. 2008)	Risk period unclear or not appropriate	Treated for BRD
73	(White et al. 2015)	Included in analysis
Excluded from study		
(Food and Drug Administration Accessed September 2018. <i>c</i> )	Included in meta-analysis	Excluded from study
(Food and Drug Administration Accessed September 2018. <i>a</i> )	Included in meta-analysis	Excluded from study
(van Donkersgoed et al. 2008)	Risk period unclear or not appropriate	Not reported
(DeDonder et al. 2016)	Included in meta-analysis	Excluded from study
(Sturgess & Renter 2017)	Risk period unclear or not appropriate	Excluded from study
(Rooney et al. 2005)	Included in meta-analysis	Excluded from study
(Fazzio et al. 2015)	Excluded due to data issues	Not reported
(Corbin et al. 2009)	Risk period unclear or not appropriate	Excluded from study
(Galyean et al. 1995)	Excluded due to data issues	Not reported
(Montague et al. 1996)	Excluded due to data issues	Not reported
(Food and Drug Administration Accessed September 2018. <i>e</i> )	Included in meta-analysis	Excluded from study
(van Koeveing et al. 1992)	Excluded due to	Not reported
(Meeuwse & Hibbard 2002)	Included in meta-analysis	Not reported
(Schunich et al. 2002)	Risk period unclear or not appropriate	Not reported
(Cusack 2004)	Risk period unclear or not appropriate	Not reported
(Guichon et al. 1993)	Excluded due to data issues	Excluded from study
(Compiani et al. 2014)	Risk period unclear or not appropriate	Not reported
(Breeze et al. 1982)	Included in meta-analysis	Excluded from study
(Harland et al. 1991)	Included in meta-analysis	Excluded from study
(Hibbard et al. 2002)	Excluded due to data issues	Not reported
(Montgomery et al. 2008)	Included in meta-analysis	Not reported
(Food and Drug Administration Accessed September 2018. <i>g</i> )	Included in meta-analysis	Excluded from study
(Siddhartha et al. 2013)	Included in meta-analysis	Excluded from study
(Hendrick et al. 2013)	Risk period unclear or not appropriate	Excluded from study,Treated for BRD
(Stokka & Kreikemeier 1996)	Risk period unclear or not appropriate	Not reported
(Guthrie et al. 2004)	Included in meta-analysis	No sick animals at arrival
(Bryant et al. 2008)	Risk period unclear or not appropriate	Not reported
(Tennant et al. 2014)	Risk period unclear or not appropriate	Not reported
(Crepieux et al. 2016)	Excluded due to data issues	Excluded from study
(Miller et al. 2016)	Excluded due to data issues	Not reported
(Reece & Smith 1996)	Excluded due to data issues	Not reported
(Kilgore et al. 2005)	Included in meta-analysis	Excluded from study
(Rossi et al. 2010)	Included in meta-analysis	Not reported

Table S7: Exclusion criteria for BRD cases in the studies determined to be relevant to the review

Study	Status	BRD Outcome Definition
(Food and Drug Administration Accessed September 2018. <i>d</i> )	Included in meta-analysis	"Morbidity was based on clinical appearance, rectal temperature, respiratory rate, dyspnea, cough, and nasal discharge."
(Booker et al. 2006)	Excluded due to data issues	"The case definition for UF (undifferentiated fever) was an elevated rectal temperature ( $\geq 104.5$ degrees F), a lack of abnormal clinical signs referable to body systems other than the respiratory system, eligibility for UF treatment based on the predefined postallocation intervals for each experimental group, and no previous treatment history for SA (sick on arrival) or no fever."
(Booker et al. 2007)	Excluded due to data issues	The case definition for UF (undifferentiated fever) was an elevated rectal temperature ( $\geq 105.0$ degrees F), lack of abnormal clinical signs referable to body systems other than the respiratory system, and no previous treatment history for no fever.
(Blasi et al. 2010)	Risk period unclear or not appropriate	BRD morbidity definition was not reported.
(Amrine et al. 2014)	Included in meta-analysis	"BRD morbidity data (animals with CIS $> 1$ and rectal temperatures $> 40$ degrees C [104.0 degrees F])"
(Baggott et al. 2011)	Included in meta-analysis	Cattle were diagnosed with BRD if they fulfilled the clinical criteria of BRD (depression score $\geq 0$ , respiratory character score $\geq 0$ , and rectal temperature $\geq 40.0$ degrees C) for one day, or showed clinical signs of BRD which, while not fulfilling all the clinical criteria of BRD, were considered severe enough by the attending veterinarian to justify removal on welfare grounds starting on day 1 (following treatment).
(Step et al. 2007)	Risk period unclear or not appropriate	Calves with a CAS of 1 or 2 were pulled and treated for BRD only if their rectal temperature exceeded $40.0 > C$ (104 degrees F); calves with a CAS of 4 were pulled and treated regardless of rectal temperature.
(McClary & Vogel 1999)	Included in meta-analysis	BRD morbidity (clinical signs observed by human and remote early disease identification system)
(Gill et al. 1986)	Included in meta-analysis	If the body temperature exceeded 104 F the animal was considered sick.
(Morck et al. 1993)	Included in meta-analysis	Morbidity attributable to pneumonia: Those calves that had signs of respiratory tract infection; including depression, anorexia, fever ( $> 40$ degrees C), and an absence of clinical signs attributable to other body systems; were considered to have pneumonia and were treated with the standard protocol for this particular feedlot.
(Food and Drug Administration Accessed September 2018. <i>f</i> )	Excluded due to data issues	Calves were observed daily for 30 days for signs such as poor general appearance, depressed attitude, and reluctance to move. Rectal temperature was measured in animals displaying such signs, and calves with temperatures $\geq 104$ degrees F were treated with Micotil (single 10 mg/kg dose SQ) and returned to the pen.
(Food and Drug Administration Accessed September 2018. <i>b</i> )	Included in meta-analysis	Treatment failure was defined as any one of the following: Mortality/euthanasia due to BRD (confirmed by necropsy); Any animal with a depression score $\geq 1$ OR a respiratory score $\geq 2$ , AND rectal temperature $\geq 104.0$ degrees F; Any animal with a respiratory score = 3 (regardless of rectal temperature); or Any animal with a depression score $\geq 3$ (regardless of rectal temperature).
(Janzen & McManus 1980)	Excluded due to data issues	Cattle were treated for shipping fever or undifferentiated bovine respiratory disease based on the following signs: a) elevated temperature $> 40.0$ degrees C, b) anorexia, c) increased respiratory rate, d) depression.
(Timsit, Workentine, Crepieux, Miller, Regev-Shoshani, Schaefer & Alexander 2017)	Excluded due to data issues	Heifers with visual BRD signs $\geq 1$ and a rectal temperature $\geq 40$ degrees C were diagnosed with BRD and given tulathromycin (2.5 mg/kg, SQ, Draxxin, Zoetis) as per standard feedlot procedures.
(Erickson & R. 2008)	Included in meta-analysis	BRD morbidity: Calves categorized as sick by the cattle crew were pulled, their symptoms assessed and rectal temperature recorded, and BRD cases were treated with Draxxin Injectable Solution (Pfizer Animal Health)

Study	Status	BRD Outcome Definition
(Schumann et al. 1991)	Included in meta-analysis	Respiratory disease: The calves were checked twice daily by the feedlot staff for signs of disease, and any calves that appeared depressed, gaunt, or distinctly different from their penmates were taken to the treatment pen. A tentative diagnosis of respiratory disease was made on the above criteria, and an increased respiratory rate plus a rectal temperature $\geq 40$ degrees C and absence of clinical signs attributable to dysfunction of any other body system were used to confirm the diagnosis.
(Schumann et al. 1990)	Included in meta-analysis	Calves that appeared depressed, gaunt, and distinctly different from their penmates were taken to the treatment chute. A diagnosis of BRD was made on the above criteria, an increased respiratory rate plus a rectal temperature $\geq 40$ degrees C, and an absence of clinical signs attributable to dysfunction of any other body system.
(Brazle 1997)	Excluded due to data issues	BRD morbidity definition was not reported.
(Hanzlicek et al. 2016)	Included in meta-analysis	At the end of the moratorium, a clinical illness scoring system of 1 to 4 (1, normal; 2, mild depression, gaunt; 3, severe depression, labored breathing; and 4, moribund, near death, little response to human approach) was used to determine health status. Calves with a score $> 1$ were taken to the working facility for examination. Those calves with a clinical illness score $\geq 1$ and a rectal temperature $\geq 40$ degrees C taken during the examination and not presenting signs indicative of nonrespiratory disease were determined to be experiencing BRDC.
(Duff et al. 2000)	Included in meta-analysis	Cattle were monitored daily for signs of BRD, including nasal or ocular discharge, labored breathing, lethargy, and(or) emaciated body condition. Cattle displaying symptoms were removed from their pens, and rectal temperature was measured. Cattle with a rectal temperature $> 39.7$ degrees C received medical treatments, which included tilmicosin phosphate (10 mg/kg BW) and 10 mL penicillin.
(Frank & Duff 2000)	Included in meta-analysis	"Cattle were monitored daily for signs of BRD, including nasal or ocular discharge, labored breathing, lethargy, and(or) emaciated body condition. Cattle displaying symptoms were removed from their pens, and rectal temperature was measured. Cattle with a rectal temperature $> 39.7$ degrees C received medical treatments, which included tilmicosin phosphate (10 mg/kg BW) and 10 mL penicillin.
(Martin et al. 2007)	Included in meta-analysis	BRD morbidity definition was not reported.
(Vogel et al. 1998)	Included in meta-analysis	Steers were monitored daily for signs of respiratory tract disease. Signs monitored included nasal or ocular discharge, labored breathing, lethargy, or emaciated body condition. Cattle that had signs of respiratory tract disease were removed from their pens and taken to a processing facility; the rectal temperature of each steer then was measured. Steers with an increased rectal temperature ( $> 39.7$ degrees C) received medical treatments.
(Lofgreen et al. 1978)	Included in meta-analysis	BRD morbidity: Texas Criteria for removing and treating cattle for BRD included abnormal respiratory patterns, lethargy, and abnormal nasal discharge. Colorado: In Colorado, a clinical impression scoring system, using criteria similar to those for the cattle in Texas, was used to categorize cattle with clinical signs of BRD. Cattle were observed daily by an investigator and scored as follows: 1 = healthy, 2 = slightly ill, 3 = moderately ill, 4 = severely ill, or 5 = moribund. Calves with a score of 2 or more were taken to the hospital for additional evaluation. When rectal temperature of a calf at the hospital was $\geq 40$ degrees C, a diagnosis of BRD was made and the animal was treated. calves with a clinical impression score $\geq 3$ and a rectal temperature $> 40$ degrees C were treated for BRD at the discretion of the investigator.
(Regev-Shoshani et al. 2017)	included in meta-analysis	The judgment of the investigators of the clinical condition of the calf, not just a temperature $\geq 104$ degrees F, determined initiation of antimicrobial treatment.



Study	Status	BRD Outcome Definition
(Glynn et al. 2002)	Included in meta-analysis	Steers were monitored daily for signs of RTD. Signs monitored included nasal or ocular discharge, labored breathing, lethargy, and emaciated body condition. Steers that had signs of RTD were moved to a processing facility, and those with rectal temperature $\geq 39.7$ degrees C received antibiotics.
(Food and Drug Administration 2003)	Included in meta-analysis	Study calves with depression and abnormal respiration (after Day 2) were administered standard feedlot therapy and were considered arrival treatment failures.
(Schipper & Kelling 1974)	Excluded due to data issues	Detection of illness was based on fence observation and subsequent temperature evaluation.
(Schipper & Kelling 1971)	Risk period unclear or not appropriate	Calves were considered to be clinically ill when depression and anorexia, dyspnea, and coughing was noticed. Temperatures ranged from 102 to 107 degrees F (38.941.7 degrees C).
(Stegner et al. 2013)	Risk period unclear or not appropriate	A heifer was clinically diagnosed with BRD if it scored a CAS $\geq 2$ and had a rectal temperature $\geq 40.0$ degrees C or had a CAS $\geq 3$ (regardless of rectal temperature).
(Hawley et al. 2016)	Included in meta-analysis	To be considered 'a case' of BRD, calves had to meet one of the two following definitions based on presenting clinical signs: 1) Clinical Impression Score (CIS) $\geq 1$ and RT $\geq 104.0$ degrees F (40.0 degrees C), or 2) CIS $\geq 2$ regardless of RT.
(Brown et al. 1989)	Excluded due to data issues	Non-randomized study. Information not extracted.
(Nickell et al. 2008)	Included in meta-analysis	Calves registering rectal temperatures $\geq 40$ degrees C ( $\geq 104$ degrees F) were classified as experiencing BRD and were treated according to a predesigned treatment protocol.
(Gonzalez-Martin et al. 2011)	Included in meta-analysis	Diagnostic criteria for BRD were the following: calves with a disease score $> 1$ on a 0 to 4 scale (0, healthy; 1, mild depression; 2, moderate to marked depression; 3, severe depression; 4, unable to rise) were individually evaluated and considered sick if they showed rectal temperature $\geq 40$ degrees C and presented at least one respiratory sign (tachypnea greater than 40 bpm, dyspnea, purulent nasal discharge, or cough).
(van Donkersgoed & Merrill 2012)	Risk period unclear or not appropriate	A diagnosis of an initial case of BRD was made on an animal if the following criteria were satisfied: 1) the case abstract, which appeared on the computer screen, indicated no previous treatment history for BRD; 2) there was an absence of clinical signs referable to organ systems other than the respiratory tract; and 3) animals meeting the temperature criteria ( $\geq 104.0$ degrees F or 40 degrees C). If all criteria were met, the animal was treated and designated as UF (Undifferentiated Fever). Animals not meeting the temperature criteria were treated and designated as NF (No Fever).
(van Donkersgoed & Merrill 2013a)	Risk period unclear or not appropriate	A diagnosis of an initial case of BRD was made on an animal if the following criteria were satisfied: 1) the case abstract, which appeared on the computer screen, indicated no previous treatment history for BRD; 2) there was an absence of clinical signs attributable to organ systems other than the respiratory tract; and 3) animals met the temperature criteria ( $\geq 104.0$ degrees F or 40 degrees C). If all criteria were met, the animal was designated as UF (undifferentiated fever). Animals not meeting the temperature criteria were designated as NF (no fever).
(van Donkersgoed & Merrill 2013b)	Risk period unclear or not appropriate	A diagnosis of an initial case of BRD was made on an animal if the following criteria were satisfied: 1) the case abstract, which appeared on the computer screen, indicated no previous treatment history for BRD; 2) there was an absence of clinical signs attributable to organ systems other than the respiratory tract; and 3) animals met the temperature criteria ( $\geq 104.0$ degrees F or 40 degrees C). If all criteria were met, the animal was designated as UF (undifferentiated fever). Animals not meeting the temperature criteria were designated as NF (no fever).

Study	Status	BRD Outcome Definition
(van Donkersgoed et al. 2017)	Risk period unclear or not appropriate	A diagnosis of an initial case of UF (Undifferentiated Fever) was made on an animal if the following criteria were satisfied: 1) the case abstract, which appeared on the computer screen, indicated no previous treatment history for BRD (UF or NF (no fever)); 2) there was an absence of clinical signs attributable to organ systems other than the respiratory tract as described above; 3) animals met the temperature criteria ( $\geq 104.0$ degrees F; 40 degrees C). Animals with clinical signs of BRD and a rectal temperature $> 104.0$ degrees F (40 degrees C) were treated and designated as NF (No-Fever). Bovine respiratory disease cases included both UF and NF.
(John et al. 2008)	Risk period unclear or not appropriate	BRD was defined as calves with a CAS of 1 or 2 and pyrexia (rectal temperature $\geq 40$ degrees C or $\geq 104.0$ degrees F) or with a CAS of 3 or 4 regardless of rectal temperature.
(White et al. 2015)	Included in meta-analysis	For the REDI group (did not receive metaphylaxis at arrival), a BRD diagnosis was based on a computer algorithm (not described in detail) that ignored rectal temperature. For the metaphylaxis group: After the post-metaphylaxis interval, CONV cattle (received metaphylaxis at arrival) deemed to exhibit signs of BRD by the observer were taken to the chute, and if rectal temperature was elevated ( $> 40.0$ degrees C) and posttreatment eligibility requirements were met as described in the treatment protocol, the calf was treated.
(Food and Drug Administration Accessed September 2018.c)	Included in meta-analysis	BRD morbidity (attitude score = 1 or 2 and rectal temperature $\geq 104.0$ degrees F, or respiratory score = 2 and rectal temperature $\geq 104.0$ degrees F, or respiratory score = 3 regardless of rectal temperature, or attitude score $\geq 3$ regardless of rectal temperature.)
(Food and Drug Administration Accessed September 2018.a)	Included in meta-analysis	Any calf developing BRD (respiration score = 1 and attitude score $\geq 1$ and rectal temperature $\geq 104$ degrees F) was classified as a non-responder and removed from the study. The primary variable was the determination of failure rate through Day 14. Failures included calves classified as non-responders and calves that died or were euthanized for severe BRD.
(van Donkersgoed et al. 2008)	Risk period unclear or not appropriate	Animals that had a rectal temperature $\geq 104$ degrees F, an absence of clinical signs referable to organ systems other than the respiratory system, and no previous treatment history for NF (no fever) or UF (undifferentiated fever) were designated as first UF treatments. Animals not meeting the rectal temperature criterion but having signs of BRD (e.g., depression, inappetence, nasal discharge, cough, abnormal respiration) and no previous treatment history for UF or NF were designated as first NF treatments. First BRD treatments included first UF treatments and first NF treatments.
(DeDonder et al. 2016)	Included in meta-analysis	Cattle having a rectal temperature $\geq 104.0$ degrees F ( $\geq 40.0$ degrees C) and a clinical score of $\geq 1$ were diagnosed with BRD and included in the study.
(Sturgess & Renter 2017)	Risk period unclear or not appropriate	Once the respective PMI (post-metaphylaxis interval) had passed and a steer was observed to have a CAS $\geq 2$ , it was taken to the hospital for evaluation. The rectal temperature of calves pulled to the hospital was recorded but was not used as part of the case definition.
(Rooney et al. 2005)	Included in meta-analysis	From day 3 to day 28, a calf was deemed a nonresponder if it had a CAS of 1 or 2 and a rectal temperature of 104 degrees F (40 degrees C) or higher or a CAS of 3 or 4. After day 28, cattle were observed according to existing feedlot practice, and all calves exhibiting signs of BRD were pulled and classified as nonresponders.
(Fazio et al. 2015)	Excluded due to data issues	Animals showing signs of BRD (depression, eye or nose discharge, anorexia, dyspnea, cough, rectal temperature $\geq 39.5$ degrees C, orthopneic posture) received a rescue therapeutic treatment with tilmicosin SC 10 mg/kg (Micotil, Elanco Animal Health) plus meloxicam 0.5 mg/kg (Metacam 20% Boehringer Ingelheim).
(Corbin et al. 2009)	Risk period unclear or not appropriate	Calves with a CIS greater than or equal to 2 and a rectal temperature $\geq 104$ degrees F were treated for BRD.

Study	Status	BRD Outcome Definition
(Galyean et al. 1995)	Excluded due to data issues	In all trials, calves were evaluated daily for symptoms of BRD (nasal/ocular discharge, depression, anorexia). Suspect calves were subsequently brought to the working facility, and their rectal temperature was measured. In Trial 1, calves with a rectal temperature $\geq 39.4$ degrees C were treated with either Naxcel (Upjohn, Kalamazoo, MI; 1 mL per 45.4 kg of BW) or Micotil (10 mg tilmicosin phosphate per kg BW) on an alternate basis.
(Montague et al. 1996)	Excluded due to data issues	BRD morbidity criteria were not reported.
(Food and Drug Administration Accessed September 2018.e)	Included in meta-analysis	Calves meeting the treatment failure criteria (depression score = 1 or 2 or respiratory score = 2, and a rectal temperature $\geq 104.0$ degrees F; or a depression or respiratory score = 3 regardless of rectal temperature)
(van Koeveering et al. 1992)	Excluded due to data issues	Calves were monitored twice daily for sickness (rectal temperature $> 104$ degrees F, or visually depressed)
(Meeuwse & Hibbard 2002)	Included in meta-analysis	Cattle were eligible for additional treatment (Standard Feedlot Therapy) when they had clinical signs of BRD (abnormal respiration and depression) and a rectal temperature $> 104$ degrees F after the assigned PMI (post-metaphylaxis interval).
(Schunich et al. 2002)	Risk period unclear or not appropriate	In these studies, the case definition for UF (undifferentiated fever) was a lack of abnormal clinical signs referable to body systems other than the respiratory system and an elevated rectal temperature (40.3 degrees C).
(Cusack 2004)	Risk period unclear or not appropriate	A diagnosis of BRD was based on the absence of clinical signs referable to systems other than the respiratory system, and two or more of the clinical signs of dyspnoea, nasal and/or oral discharge, lethargy, and inappetance.
(Guichon et al. 1993)	Excluded due to data issues	The case definition for bovine respiratory disease (BRD) was an elevated rectal temperature ( $\geq 40.3$ degrees C) and a lack of abnormal clinical signs referable to organ systems other than the respiratory system.
(Compiani et al. 2014)	Risk period unclear or not appropriate	Morbidity due to BRD was defined as animals showing mild to severe depression and/or respiratory signs and having rectal temperature $\geq 104$ degrees F (40 degrees C).
(Breeze et al. 1982)	Included in meta-analysis	Calves with clinical respiratory disease had the following clinical signs: oculo-nasal discharge, increased respiratory rate, cough, dullness, and fever.
(Harland et al. 1991)	Included in meta-analysis	Calves were selected as tentative BRD cases when they appeared depressed, inappetent, or showed specific signs of respiratory disease. Such animals were taken to the treatment chute, and those with a temperature $\geq 40.5$ degrees C were treated.
(Hibbard et al. 2002)	Excluded due to data issues	Pen riders, who remained blinded to the assigned treatment groups throughout the study, observed the cattle daily for 28 days for clinical signs of BRD, signs of ear swelling, or any other problems. Cattle with clinical signs of BRD received a standard feedlot therapy and were considered preemptive treatment failures.
(Montgomery et al. 2008)	Included in meta-analysis	Heifers were monitored for clinical signs of UBRD including depression, lethargy, anorexia, coughing, rapid breathing, and nasal or ocular discharge and were not showing clinical signs associated with any other organ system at the time of their classification.
(Food and Drug Administration Accessed September 2018.g)	Included in meta-analysis	"Treatment Success on Day 10 if animal met the following criteria: 1. It was alive; 2. It had not been identified as a treatment failure; 3. It had not been removed for non-BRD reasons.
(Siddhartha et al. 2013)	Included in meta-analysis	BRD morbidity criteria were not reported.
(Hendrick et al. 2013)	Risk period unclear or not appropriate	The case definition of BRD was an elevated rectal temperature ( $\geq 40.0$ degrees C) and an absence of abnormal clinical signs directly attributable to organ systems other than the respiratory system.
(Stokka & Kreikemeier 1996)	Risk period unclear or not appropriate	Sick cattle were pulled based on visual unthriftiness and treated if rectal temperature was $\geq 103$ degrees F.

Study	Status	BRD Outcome Definition
(Guthrie et al. 2004)	Included in meta-analysis	
(Bryant et al. 2008)	Risk period unclear or not appropriate	BRD morbidity criteria were not reported.
(Tennant et al. 2014)	Risk period unclear or not appropriate	Case definition of BRD was a CAS = 1 and rectal temperature $\geq 40$ degrees C or a CAS = 2 or 3 regardless of rectal temperature.
(Crepieux et al. 2016)	Excluded due to data issues	
(Miller et al. 2016)	Excluded due to data issues	Any animal removed from the pen with a combined morbidity score $\geq 3$ regardless of rectal temperature.
(Reece & Smith 1996)	Excluded due to data issues	Calves showing signs of nasal discharge, labored breathing, difficulty in locomotion, or depression were clinically diagnosed as having BRD and treated with tilmicosin at the label dose.
(Kilgore et al. 2005)	Included in meta-analysis	Calves with respiratory scores of 1 or attitude scores of at least 1 were removed from study pens for rectal temperature measurement. Calves with rectal temperatures of 104 degrees F or higher were considered BRD morbidities; they were given antimicrobial therapy according to the site standard procedures and returned to their study pens to maintain animal density within the pens.
(Rossi et al. 2010)	Included in meta-analysis	Any animals that were seen to be affected by BRD during the 14-day observation period were examined clinically and treated individually, at the discretion of the veterinarian, with antibiotics and non-steroidal anti-inflammatory agents (NSAIDs).

Table S8: Definitions of Bovine Respiratory Disease (BRD) used in studies relevant to the review.

Citation	Random Sequence	Sequence Concealment	Baseline Imbalances	Intended Interventions	Missing Outcome Data	Mismeasured Outcomes	Selective Outcome Reporting
(Guichon et al. 1993)	No information random	No information	No information	Low	Low	Low	Some concerns
(Harland et al. 1991)	Probably no	No information	No information	Low	Some concerns	Low	Some concerns
(Schumann et al. 1990)	No information random	No information	Probably no	Low	Low	Low	Some concerns
(Timsit, Workentine, Crepieux, Miller, Regev-Shoshani, Schaefer & Alexander 2017)	Yes	No information	No information	Low	Low	Low	Low
(Regev-Shoshani et al. 2017)	Yes	No information	No information	Some concerns	Low	Low	Some concerns
(Crepieux et al. 2016)	Yes	No information	No	Low	Low	Low	Some concerns
(DeDonder et al. 2016)	No information random	No information	No information	Low	Low	Low	Some concerns
(White et al. 2015)	Yes	No information	No	Low	Some concerns	Low	Some concerns
(Tennant et al. 2014)	No information random	No information	No	Low	Low	Low	Some concerns
(Hendrick et al. 2013)	Probably no	No information	No	Low	Low	Low	Some concerns
(Siddartha et al. 2013)	Yes	Yes	No	Low	Low	Low	Some concerns
(Baggott et al. 2011)	Probably yes	No information	Probably yes	Low	Low	Low	Some concerns
(van Donkersgoed et al. 2008)	No information random	No information	No	Low	Some concerns	High	Some concerns
(Nickell et al. 2008)	Yes	No information	No	Low	Low	Low	Some concerns
(John et al. 2008)	Probably yes	No information	No information	Low	Low	Low	Some concerns
(Booker et al. 2007)	No information random	No information	Yes	Low	Low	Low	Some concerns
(Step et al. 2007)	No information random	No information	No information	Low	Low	Low	Some concerns
(Booker et al. 2006)	Yes	No information	No	Low	Low	Low	Some concerns
(Rooney et al. 2005)	No information random	No information	No information	Low	Low	Low	Some concerns
(Cusack 2004)	No	No information	No	Low	Low	Low	Some concerns
(Hibbard et al. 2002)	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed

Citation	Random Sequence	Sequence Concealment	Baseline Imbalances	Intended Interventions	Missing Outcome Data	Mismeasured Outcomes	Selective Outcome Reporting
(Schunich et al. 2002)	Yes	No information	No	Low	Some concerns	Low	Some concerns
(Glynn et al. 2002)	No information random	No information	No information	Low	Low	Low	Some concerns
(Frank & Duff 2000)	No information at all	No information	No information	Low	Low	Low	Some concerns
(Duff et al. 2000)	No information random	No information	No	Low	Low	Low	Some concerns
(Vogel et al. 1998)	No information random	No information	No	Low	Low	Low	Some concerns
(Galyean et al. 1995)	No information at all	No information	Probably no	Low	Low	Low	Some concerns
(Morck et al. 1993)	Yes	No information	No information	Low	Some concerns	Low	Some concerns
(Schumann et al. 1991)	No information random	No information	No	Low	Low	Low	Some concerns
(Schipper & Kelling 1974)	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed
(Schipper & Kelling 1971)	No information random	No information	No information	Low	Some concerns	Low	Some concerns
(van Donkersgoed et al. 2017)	Yes	No information	No	Low	Low	Low	Some concerns
(Sturgess & Renter 2017)	Yes	No information	No	Low	Low	Low	Some concerns
(Miller et al. 2016)	No information random	No information	No	Low	Low	Low	Some concerns
(Hawley et al. 2016)	No information but said clusters were randomly allocated	Probably no	No	Low	Low	Low	Some concerns
(Hanzlicek et al. 2016)	Yes	Probably no	No information	Low	Low	Low	Some concerns
(Fazio et al. 2015)	No information random	Yes	No information	Low	Low	Low	Some concerns
(Compiani et al. 2014)	No information random	No information	No	Low	Low	Low	Some concerns
(van Donkersgoed & Merrill 2013b)	Yes	No information	No	Low	Low	Some concerns	Some concerns
(van Donkersgoed & Merrill 2013a)	Yes	No information	No	Low	Low	Low	Some concerns
(Stegner et al. 2013)	No information random	No information	No	Low	Low	Low	Some concerns

Citation	Random Sequence	Sequence Concealment	Baseline Imbalances	Intended Interventions	Missing Outcome Data	Mismeasured Outcomes	Selective Outcome Reporting
(van Donkersgoed & Merrill 2012)	Yes	No information	No	Low	Low	High	Some concerns
(Rossi et al. 2010)	No information random	No information	No information	Low	Some concerns	Low	Some concerns
(Corbin et al. 2009)	Yes	No information	No	Low	Low	Low	Some concerns
(Bryant et al. 2008)	Yes	Probably no	No information	Low	Low	Low	Some concerns
(Montgomery et al. 2008)	No information random	No information	No	Low	Low	High	Some concerns
(Martin et al. 2007)	Yes	No information	No information	Low	Some concerns	Low	High
(Kilgore et al. 2005)	Probably yes	Yes	No information	Low	Low	Low	Some concerns
(Guthrie et al. 2004)	Yes	No information	No	Low	Low	Low	Some concerns
(McClary & Vogel 1999)	Yes	No information	Probably yes	Low	Low	Low	Some concerns
(Montague et al. 1996)	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed
(Reece & Smith 1996)	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed
(van Koevering et al. 1992)	No information but said clusters were randomly allocated	Probably no	No information	Low	Low	Low	Some concerns
(Brown et al. 1989)	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed
(Gill et al. 1986)	No information but said clusters were randomly allocated	Probably no	Probably no	Low	Low	Low	Some concerns
(Breeze et al. 1982)	No information random	No information	No information	Low	Low	Low	Some concerns
(Janzen & McManus 1980)	No	No information	No information	Low	Low	Low	Some concerns
(Amrine et al. 2014)	Yes	No information	No	Low	Some concerns	Low	Some concerns
(Gonzalez-Martin et al. 2011)	No information random	Yes	Probably yes	Low	Low	Low	Some concerns
(Blasi et al. 2010)	No information random	No information	No	Some concerns	Low	Low	Some concerns
(Brazle 1997)	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed

Citation	Random Sequence	Sequence Concealment	Baseline Imbalances	Intended Interventions	Missing Outcome Data	Mismeasured Outcomes	Selective Outcome Reporting
(Food and Drug Administration Accessed September 2018. <i>d</i> )	Probably yes	No information	Probably no	Low	Low	Low	Some concerns
(Food and Drug Administration Accessed September 2018. <i>f</i> )	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed	Not assessed
(Food and Drug Administration Accessed September 2018. <i>a</i> )	Probably yes	No information	Probably no	Low	Low	Low	Some concerns
(Food and Drug Administration Accessed September 2018. <i>c</i> )	Probably yes	Yes	Probably no	Low	Low	Low	Some concerns
(Food and Drug Administration Accessed September 2018. <i>b</i> )	Yes	Yes	Probably yes	Low	Low	Low	Some concerns
(Food and Drug Administration Accessed September 2018. <i>g</i> )	Probably yes	Yes	Probably no	Low	Low	Low	Some concerns
(Food and Drug Administration Accessed September 2018. <i>e</i> )	Probably yes	Yes	Probably no	Low	Low	Low	Some concerns
(Food and Drug Administration 2003)	Probably yes	No information	Probably no	Low	Some concerns	Low	Some concerns
(Erickson & R. 2008)	No	No information	No	Low	Some concerns	Some concerns	Some concerns
(Meeuwse & Hibbard 2002)	Probably yes	No information	Probably no	Low	Low	Low	Some concerns
(Stokka & Kreikemeier 1996)	No information random	No information	No	Some concerns	Low	Low	Some concerns
(Lofgreen et al. 1978)	No information random	No information	Probably no	Some concerns	Low	Some concerns	Some concerns



Citation	Random Sequence	Sequence Concealment	Baseline Imbalances	Intended Interventions	Missing Outcome Data	Mismeasured Outcomes	Selective Outcome Reporting
(Food and Drug Administration Accessed September 2018. <i>d</i> )	Probably yes	No information	No	Low	Low	Low	Some concerns
(Food and Drug Administration Accessed September 2018. <i>b</i> )	Yes	Yes	Probably no	Low	Low	Low	Some concerns
(Baggott et al. 2011)	Probably yes	No information	Probably no	Low	Low	Low	Some concerns
(Baggott et al. 2011)	Probably yes	No information	Probably no	Low	Low	Low	Some concerns
(Rooney et al. 2005)	No information random	No information	No information	Low	Low	Low	Some concerns
(Fazio et al. 2015)	No information random	No information	No information	Low	Low	Low	Some concerns
(Galyean et al. 1995)	No information random	No information	Probably no	Low	Low	Low	Some concerns
(Glynn et al. 2002)	No information random	No information	No information	Low	Low	Low	Some concerns
(Rossi et al. 2010)	No information random	No information	No information	Low	Some concerns	Low	Some concerns
(Rossi et al. 2010)	No information random	No information	No information	Low	Some concerns	Low	Some concerns
(Corbin et al. 2009)	Yes	No information	No	Low	Low	Low	Some concerns

Table S9: Risk of bias (ROB) in relevant studies identified in the systematic review.

Citation	ROB1.1	ROB1.2
(Hawley et al. 2016)	Yes- the investigators used stratification or blocking	No information
(Hanzlicek et al. 2016)	Yes- the individual animals were randomized to clusters	No
(van Koevering et al. 1992)	No information	Yes
(Gill et al. 1986)	No- animals just assigned to clusters with no regard for individual characteristics	Probably no
(Duff et al. 2000)	No information	Probably no

Table S10: Risk of Bias (ROB) results for the extra two questions related to cluster-randomized trials

Comparison	Number.of.studies	Randomization	Blinding	Across.studies.bias	Imprecision	Heterogeneity
CCFA_P:GAM	1	No concerns	Some concerns	Undetected	No concerns	Some concerns
CCFA_P:TIL	2	No concerns	Some concerns	Undetected	Some concerns	Some concerns
FLO:TUL	2	Some concerns	Some concerns	Undetected	No concerns	No concerns
GAM:TUL	3	No concerns	Some concerns	Undetected	Some concerns	Some concerns
OXY_1:TMS	1	Major concerns	Some concerns	Undetected	Some concerns	Some concerns
TIL:TUL	3	No concerns	Some concerns	Undetected	No concerns	Some concerns
CCFA_P:DAN	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
CCFA_P:ENR	0	No concerns	Some concerns	Undetected	Major concerns	No concerns
CCFA_P:FLO	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
CCFA_P:OXY_1	0	Some concerns	Some concerns	Undetected	Major concerns	No concerns
CCFA_P:TILD	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
CCFA_P:TMS	0	Major concerns	Some concerns	Undetected	Some concerns	Some concerns
CCFA_P:TUL	0	No concerns	Some concerns	Undetected	No concerns	No concerns
DAN:ENR	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
DAN:FLO	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
DAN:GAM	0	No concerns	Some concerns	Undetected	Some concerns	Some concerns
DAN:OXY_1	0	No concerns	Some concerns	Undetected	Major concerns	No concerns
DAN:TIL	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
DAN:TILD	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
DAN:TMS	0	Major concerns	Some concerns	Undetected	Major concerns	No concerns
DAN:TUL	0	No concerns	Some concerns	Undetected	No concerns	Some concerns
ENR:FLO	0	No concerns	Some concerns	Undetected	Major concerns	No concerns
ENR:GAM	0	No concerns	Some concerns	Undetected	Some concerns	Some concerns
ENR:OXY_1	0	No concerns	Some concerns	Undetected	Major concerns	No concerns
ENR:TIL	0	No concerns	Some concerns	Undetected	Major concerns	No concerns
ENR:TILD	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
ENR:TMS	0	Major concerns	Some concerns	Undetected	Major concerns	No concerns
ENR:TUL	0	No concerns	Some concerns	Undetected	No concerns	No concerns
FLO:GAM	0	No concerns	Some concerns	Undetected	No concerns	Some concerns
FLO:OXY_1	0	Some concerns	Some concerns	Undetected	Major concerns	No concerns
FLO:TIL	0	Some concerns	Some concerns	Undetected	Some concerns	Some concerns
FLO:TILD	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
FLO:TMS	0	Major concerns	Some concerns	Undetected	Major concerns	No concerns
GAM:OXY_1	0	Some concerns	Some concerns	Undetected	Some concerns	Some concerns
GAM:TIL	0	No concerns	Some concerns	Undetected	Some concerns	Some concerns
GAM:TILD	0	No concerns	Some concerns	Undetected	Major concerns	No concerns
GAM:TMS	0	Major concerns	Some concerns	Undetected	No concerns	Some concerns
OXY_1:TIL	0	Some concerns	Some concerns	Undetected	Major concerns	No concerns
OXY_1:TILD	0	No concerns	Some concerns	Undetected	Major concerns	No concerns
OXY_1:TUL	0	Some concerns	Some concerns	Undetected	No concerns	Some concerns
TIL:TILD	0	No concerns	Major concerns	Undetected	Major concerns	No concerns
TIL:TMS	0	Major concerns	Some concerns	Undetected	Some concerns	No concerns
TILD:TMS	0	Major concerns	Some concerns	Undetected	Some concerns	Some concerns
TILD:TUL	0	No concerns	Some concerns	Undetected	Some concerns	Some concerns
TMS:TUL	0	Major concerns	Some concerns	Undetected	No concerns	No concerns

Table S11: The risk of bias judgment for randomization, blinding, across-study bias, imprecision, and heterogeneity. See Table 2 for definitions of the abbreviations.

Question	Response and action
Title and abstract screening	
Q1) Does the study involve primary research on the assessment of a metaphylactic use of antibiotics for the prevention/control of bovine respiratory disease in feedlot cattle?	Yes/Unclear (proceed to next question)  No (exclude) No, but is a relevant review (exclude) Yes/Unclear (proceed to full-text assessment)
Q2) Based on the title/abstract is there a concurrent comparison group? (i.e., controlled trial with natural or deliberate disease exposure or analytical observational study)?	No (exclude)
Full text screening	
Q1) Is the full text available in English?	Yes (proceed to next question) Not in English (specify language) (exclude) Could not be procured (exclude) No (conference abstract < 500 words) (exclude) Yes/Unclear (proceed to next question)
Q2) Based on the full text, does the study involve primary research on the assessment of a metaphylactic use of antibiotics for the prevention/control of bovine respiratory disease in feedlot cattle?	No (exclude) Yes (proceed to next question)
Q3) Based on the full text, is there a concurrent comparison group? (i.e., controlled trial with natural or deliberate disease exposure or analytical observational study)?	No (exclude) Yes (proceed to next question)
Q4) Correct population: Is the study population, weaned cattle in a non-grazing situation that are at risk of developing BRD naturally, i.e., feedlot cattle?	No (exclude) Yes (proceed to next question)
Q5) Correct Interventions and Comparator: Does the study assess the use of at least one antibiotic, at a registered dose for metaphylaxis for prevention/control of BRD in feedlot cattle?	No (exclude) Yes (proceed to next question)
Q6) Correct outcome: Does the study report the risk of BRDC in the study groups?	No (exclude) Unclear if any arms are registered for BRD Yes (proceed to next question)  No (e.g. only reported outcome as nasopharyngeal flora) (exclude) Yes (proceed to data extraction)
Q7) Correct study design: Is the study a field trial, where an investigator is allocating animals to the intervention group (randomized or non-randomized)?	No - challenge study (indicate the antibiotic(s) studied) (exclude) No - observational study (the investigator did not allocate to the group allocation was chosen by producers or owner) (exclude)

Table S12: Screening questions, responses, and resulting actions for the title/abstract and full-text screens

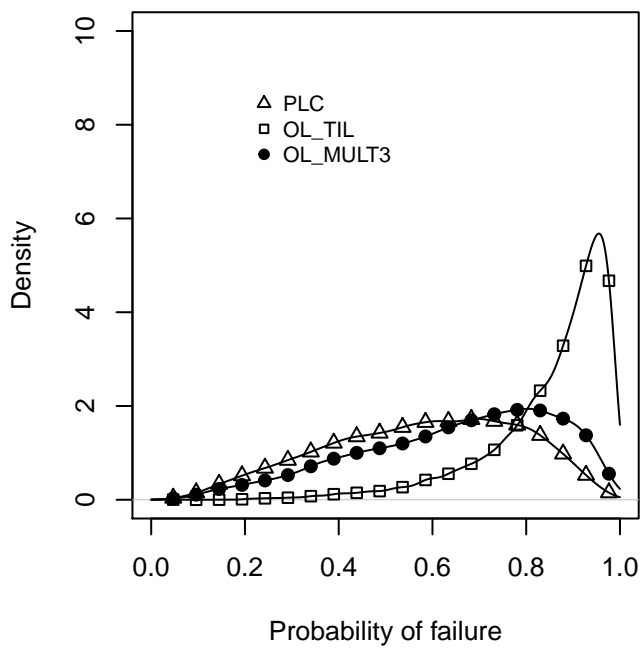
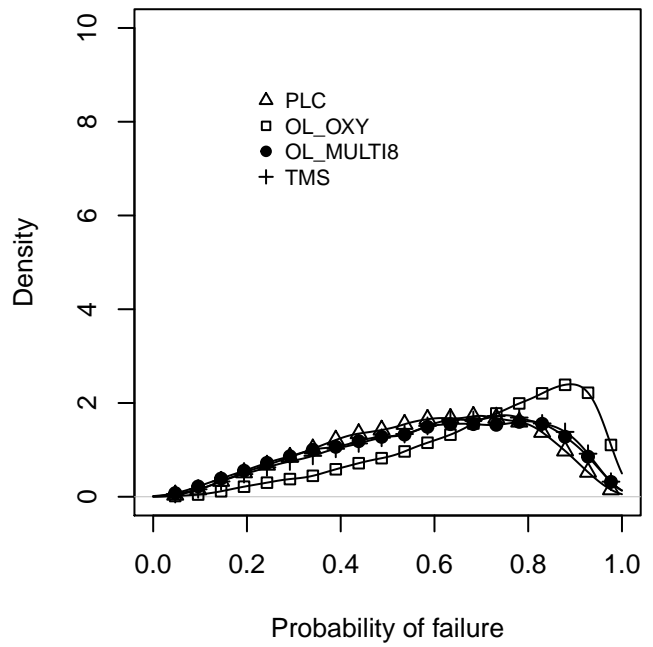
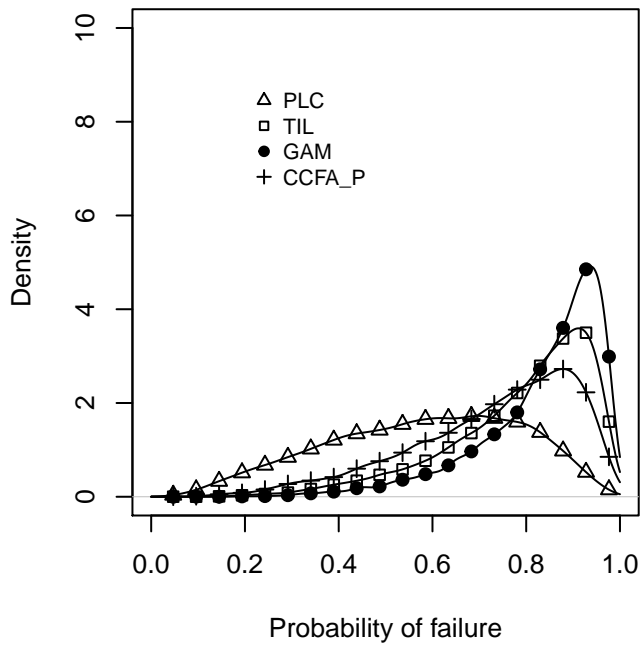


Figure S1: Distribution of the probability of response for each treatment.

Antibiotic	Abbreviation	Mean	Median	Min	Max	0.025 quantile	0.975 quantile
Tulathromycin	TUL	0.88	0.92	0.15	1.00	0.60	0.99
Gamithromycin	GAM	0.84	0.87	0.09	1.00	0.49	0.98
Tildipirosin	TILD	0.79	0.84	0.07	1.00	0.38	0.98
Tilmycosin	TIL	0.79	0.83	0.06	1.00	0.40	0.97
CeftiofurCFA (pinna)	CCFA_P	0.73	0.77	0.04	0.99	0.31	0.96
Florfenicol	FLO	0.72	0.76	0.05	0.99	0.30	0.96
Oxytetracycline_1	OXY_1	0.72	0.76	0.05	0.99	0.29	0.96
Danofloxacin	DAN	0.69	0.73	0.03	1.00	0.24	0.96
Enrofloxacin	ENR	0.67	0.71	0.02	0.99	0.21	0.95
Trimethoprim-sulfadoxine	TMS	0.61	0.63	0.03	0.99	0.17	0.93
Placebo (non-active control)	PLC	0.58	0.59	0.02	0.98	0.17	0.91

Table S13: Summary of the distribution of the probability of treatment response for the antibiotic with label dosing regimens. Ordered by median rank. See Table 1 for full regimens information

Antibiotic	Abbreviation	Ranked first	Ranked last
Tulathromycin	TUL	0.61	0.00
Tildipirosin	TILD	0.05	0.00
Gamithromycin	GAM	0.01	0.00
Danofloxacin	DAN	0.00	0.04
Enrofloxacin	ENR	0.00	0.06
Tilmycosin	TIL	0.00	0.00
Ceftiofur CFA in pinna	CCFA_P	0.00	0.00
Florfenicol	FLO	0.00	0.00
Oxytetracycline_1	OXY_1	0.00	0.00
Trimethoprim-sulfadoxine	TMS	0.00	0.18
Non-Active Control	PLC	0.00	0.16

Table S14: The probability of being ranked first or last for the antibiotics with label-dosing regimens. Ordered by the probability of being ranked first. See Table 1 for information about the full regimens

PLC	0	0	0	0.096	0	0	0.006	0.215	0.005	0.095	0.132	0.113	0.443	0.358	0	0.202
1	TIL	0.048	0.936	0.768	0	0.949	0.879	0.944	0.407	0.847	0.914	0.83	0.989	0.987	0.116	0.943
1	0.952	GAM	0.997	0.908	0.012	0.998	0.982	0.987	0.706	0.953	0.98	0.935	0.997	0.997	0.342	0.988
1	0.064	0.003	CCFA_P	0.544	0	0.545	0.534	0.801	0.172	0.615	0.722	0.596	0.921	0.921	0.038	0.789
0.904	0.232	0.092	0.456	OL_OXY	0.021	0.478	0.468	0.71	0.231	0.549	0.622	0.535	0.814	0.82	0.091	0.697
1	1	0.988	1	0.979	TUL	1	0.999	0.999	0.927	0.993	0.998	0.989	1	1	0.683	0.999
1	0.051	0.002	0.455	0.522	0	FLO	0.498	0.784	0.156	0.595	0.7	0.573	0.911	0.908	0.034	0.773
0.994	0.121	0.018	0.466	0.532	0.001	0.502	OXY_1	0.807	0.18	0.59	0.687	0.57	0.892	0.927	0.047	0.795
0.785	0.056	0.013	0.199	0.29	0.001	0.216	0.193	OR_Albon	0.087	0.343	0.413	0.34	0.671	0.646	0.022	0.483
0.995	0.593	0.294	0.828	0.769	0.073	0.844	0.82	0.913	TILD	0.828	0.879	0.806	0.962	0.962	0.235	0.91
0.905	0.153	0.047	0.385	0.451	0.007	0.405	0.41	0.657	0.172	DAN	0.581	0.491	0.797	0.779	0.055	0.649
0.868	0.086	0.02	0.278	0.378	0.002	0.3	0.313	0.587	0.121	0.419	ENR	0.413	0.752	0.722	0.035	0.571
0.887	0.17	0.065	0.404	0.465	0.011	0.427	0.43	0.66	0.194	0.509	0.587	OL_NO	0.802	0.772	0.065	0.649
0.557	0.011	0.003	0.079	0.186	0	0.089	0.108	0.329	0.038	0.203	0.248	0.198	OL_MULTIS	0.449	0.008	0.314
0.642	0.013	0.003	0.079	0.18	0	0.092	0.073	0.354	0.038	0.221	0.278	0.228	0.551	TMS	0.008	0.337
1	0.884	0.658	0.962	0.909	0.317	0.966	0.953	0.978	0.765	0.945	0.965	0.935	0.992	0.992	OL_TIL	0.977
0.798	0.057	0.012	0.211	0.303	0.001	0.227	0.205	0.517	0.09	0.351	0.429	0.351	0.686	0.663	0.023	OL_MULT3

Table S15: The probability that one antibiotic regimen is better than another, The probability that one antibiotic regimen is better than another (i.e., results in a lower BRD incidence during the study period). The upper quadrant provides the probability that the antibiotic in the column is better than the antibiotic in the row. For example, there is probability of zero that PLC (1st row) is better than TIL (2nd column) and a probability of 0.05 that TIL (2nd row) is better than GAM (3rd column). The lower quadrant provides the probability that the antibiotic in the row is better than the antibiotic in the column. For example the probability is 0.95 that GAM (3rd row) is better than TIL (2nd column). See Table 1 for information about the full regimens and definitions of the antibiotic abbreviations