Non-antibiotic approaches for disease prevention and control in beef and veal production

Appendix 2. Relevance screening questions and guide.

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|  | **Question** | **Answer Options** | **Action within Distiller**  **Included (rationale)** | **Action within Distiller**  **Excluded (rationale)** |
| 1 | Is this primary research involving cattle? | Yes | clinical trial, Experiment, challenge trial (i.e., the pathogen is given to the comparative groups), outbreak report, case study, case series, observational study including a survey (if risk factors assessed) |  |
|  |  | Unclear | Unclear – kept for look at full text |  |
|  |  | No [review, SR, MA, risk, analysis, erratum/correction] [and SUBMIT]\* |  | Narrative reviews, systematic review (SR), meta-analysis (MA). |
|  |  | No, other  [and SUBMIT] |  | NOT:   * *In vitro* study (e.g., Rusitec fermenter) * Rumen contents alone even if taken from live cattle. * Other document types: [Comm.entary, testimonials, business reports * product reports UNLESS a trial is described * prevalence/ incidence studies * Another species |
| 2 | Does the study involve beef herds OR beef cattle of any age? | Yes | cow-calf OR "beef calves" OR "grazing calves" OR "veal calves" OR "male dairy calves" OR "dairy beef steers" OR "stocker cattle" OR "backgrounders" OR "feedlot cattle" OR "finishing cattle" OR "fattening cattle" OR "feeder cattle" OR "finishing steers" OR "fattening steers" OR "Holstein bulls" OR "Holstein steers" OR "beef heifers" OR "feedlot heifers" OR "finishing heifers" OR "fattening heifers" OR "beef steers" OR "feedlot calves" OR "beef herds" OR "feedlot animals" OR "Holstein calves" OR "feeder calves" OR "sale barn-origin calves" OR "sale barn origin calves" OR "sales-barn origin calves" OR "sales barn origin calves"  dairy calves if they are male or sex unknown  [Bos traus or bos Indicus type breeds are included with some exceptions]  Also include producers/veterinarians/farm mangers that are making decisions about what interventions/management measures are used |  |
|  |  | Unclear | Unclear – kept for look at full text |  |
|  |  | No |  | NOT:   * dairy cows/Holstein cows * dairy replacement heifers * dairy heifers * Friesian heifers * Holstein heifers * Female dairy calves * Female Holstein calves * Holstein breeding bulls * Bison * Buffalo * yaks   NOT the following breeds:  Japanese, Korean [e.g., Hanwoo], other Asian breeds, including ‘Chinese Holsteins’ for example |
| 3 | Does the study report on a targeted risk factor, intervention, vaccine, feed additive or targeted management practice? | Yes | Intervention:   * Something that is fed directly or as a feed additive or administered to the cattle by injection, implant, or in the water [e.g., probiotic, DFM, plant extracts, Ractopamine, minerals, vitamins, amino acids, feed enzymes, urea, others] * Include vaccines and adjuvants * Any antibiotics * growth promotants in feed [e.g., Rumensin, lasalocid, others] * hormones for AI or growth promotion   Management practice:  Weaning practice  Housing  Density  Stress reduction  Feed type/feed stuff/pasture type  Feeding frequency/feed energy  Producer education  Genetics/breeding/cross-breeding/breed type  Genetic markers/candidate genes [for disease prevention or performance characteristics]  Artificial Insemination protocols  biosecurity/infection control  animal introductions |  |
|  |  | Unclear | Unclear – kept for look at full text |  |
|  |  | No, other  [and SUBMIT] |  | NOT:   * Dewormers/anthelminthics   Anticoccidial drugs, pyrethroid,   * Test technology/test comparisons/ BLUP evaluations [accuracy/sensitivity/specificity] * Detection of sick cattle |
| 4. | Does the study measure one of the targeted health outcomes? | Yes | Antimicrobial/antibiotic use, vaccine efficacy or serologic/immune/humoral response, mediators of inflammation interleukins [ IL-2, IL-8, IFN-γ, etc.], tumor necrosis factor (TNF), acute-phase response, oxidative burst of leucocytes, natural killer cells, neutrophil bactericidal activity, animal health/calf health, risk of disease, mortality/morbidity, bovine respiratory disease, diarrhea, fecal score, scours, bovine viral diarrhea, bacterial diseases, survival to weaning, treatment cost, return on treatment cost, treatment rate, condemnations, liver abscesses, rumenitis, acidosis/subacute ruminal acidosis, dietary cation-anion difference (DCAD), metabolic acid load/urine pH, grain overload, total tract barrier function, Abomasal ulcers, rumen development, mastitis, injection site lesions regardless of injection type,  and  Lameness if it could be related to an infection [viral or bacterial infections],  Abortions related to infection [viral or bacterial infections],  IF IT SAYS ‘HEALTH’ in the abstract  Any outbreak reports of viral or bacterial conditions [not parasites, not toxins, not fungal] |  |
|  |  | Unclear | Unclear outcome |  |
|  |  | No, outcome is an animal performance parameter  [and SUBMIT] | * weight gain, days in feed , finished weight, average daily gain (ADG), dry matter intake (DMI), feed cost per unit of gain, feed to gain ratio/feed conversion ratio/feed efficiency/residual feed intake,(RFI) * weaning body weight in calves on cow-calf farms * carcass weight or grade, marbling, intramuscular fat, fat thickness * farm profitability, break even cost |  |
|  |  | No, other  [and SUBMIT] |  | NOT:   * Mechanistic studies * prevalence/ incidence studies [if no risk factors of interest] * Gene expression * rumen fermentation/nutrient digestibility/rumen pH * clinicopathologic variables (i.e., blood parameters, heart rate) * fertility/reproductive efficiency/ pregnancy rate/estrus/ovulation, reproductive efficiency [age at first calving (AFC), first calving interval (FCI) and non-return rate (NRR) * antimicrobial/antibiotic resistance (AMR) * meat nutrients [e.g., fatty acids, Omega-3 fatty acids] * meat tenderness * parasitic [worms/nematodes, ticks, lice] and protozoan diseases * Methane production * Milk production * Asymptomatic food-borne pathogen carriage/shedding [e.g., Campylobacter, Salmonella, E. coli (EHEC) grp.] * Body condition score or weight gain in breeding beef cows or heifers * Lameness or ill health associated with toxin or congenital disease * Abortions related to toxicosis * Immunity to fertility hormones OR growth hormone |
| 5 | Was the study conducted in a country of interest? | Yes | Canada, USA, EU [include Eastern European countries and Switzerland] and Britain, Australia/NZ, Mexico, Brazil, Argentina, Uruguay, Russia |  |
|  |  | Unclear | unclear |  |
|  |  | No  [and SUBMIT] |  | NOT:  [Asian or African countries, Kurdistan or other ‘…stans’, Middle Eastern countries or Turkey]  also NOT Greece, not Alaska |

Appendix 3. Clinical trials of vaccine interventions for beef cattle and veal calf populations.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Disease type** | **Description of vaccination pathogen** | **Production stage population type** | **Outcomes of interesta** | **Refid** |
| Gastro-intestinal | *Salmonella dublin* | Veal calves Comm.b (n=1) | Diarrhea (n=1)  Morbidity c (n=1)  Mortality (n=1)  Surrogate measuresd (n=1)  Treatments for illnesse (n=1)  Respiratory disease (n=1) | 11359 |
| Respiratory disease | *Bovine viral diarrhea virus* (BVD), *Bovine Herpes Virus-*1 (BoHV-1), commercial culture supernatant vaccine, *Pasteurella haemolytica,* *Mycoplasma bovis,* trivalent [IBR, BVD, *Bovine respiratory syncytial virus* (BRSV)] vaccine, unspecified bovine respiratory disease (BRD) vaccines with biological response modifiers, intranasal modified live virus (MLV) BRD vaccine 1 dose vs. 2 doses | Veal calves  Exp.f (n=5)  Comm. (n=2)  Unclear (n=1) | Respiratory disease (n=4)  Mortality (n=3)  Morbidity (n=3)  Surrogate measures (n=8)  Non-specific immunityg (n=2)  Treatments for illness (n=2)  Treatment cost (n=1)  Pathologyh (n=3)  Diarrhea (n=1) | 10332  13337  13503  11307  13870  14281  13661  40291  11132 |
| Respiratory disease | Commercial inactivated commercial MLV vaccine [BVBV, BVH-1, BRD pathogens], combined *Pasturella haemolytica* and *Haemophilus somnus*, BRD antigens, commercial inactivated BVDV and BRD vaccinations | Cow-calf  Exp. (n=2)  Comm. (n=4) | Respiratory disease (n=1)  Mortality (n=2)  Morbidity (n=1)  Surrogate measures (n=6)  Non-specific immunity (n=1)  Treatments for illness (n=1)  Pathology (n=1) | 13785  13679  10812  40291  12676  16249 |
| Respiratory disease | BRSV, Somnu-Star Ph, *P. haemolytica*, BRDV vaccines, BVD and IBRV with needle free device, priming with a MLV BRD vacc, commercial BRSV given at various stages of production, Experimental BRD vaccines, BRD revaccination | Beef calves  Exp. (n=4)  Comm. (n=7) | Respiratory disease (n=6)  Mortality (n=3)  Morbidity (n=7)  Surrogate measures (n=4)  Non-specific immunity (n=2)  Treatments for illness (n=2)  Treatment cost (n=2)  Pathology (n=2) | 16306  14311  40264  10839  10978  16517  12180  11659  12215  11925 |
| Respiratory disease | BRSV, Somnu-Star Ph, *M. bovis* and various adjuvants, *M. bovis* cytotoxin, BRD vaccines, novel combinations and routes of BRD vaccines, inactivated vs. MLV BRSV, *Mannheimia haemolytica*, various recombinant interleukin vaccines with MLV BRD and killed BVD vaccines, *P. haemolytica*, commercial BRD vaccines | Stockers  Exp. (n=12)  Comm. (n=2) | Respiratory disease (n=2)  Mortality (n=2)  Morbidity (n=8)  Surrogate measures (n=9)  Non-specific immunity (n=2)  Treatments for illness (n=2)  Pathology (n=1) | 16306  11095  12573  40264  40282  13841  10936  14014  11808  13336  12215  19852  14175 |
| Respiratory disease | *Infectious bovine rhinotracheitis virus* (IBR), *Parainfluenza virus-*3 (PI-3), BVD, BRSV, Re-17 mutant *Salmonella typhimurium* bacterin-toxoid, *P. haemolytica*, *H. somnus,* BRD vaccines, IBR-P1-3, novel combinations and routes of BRD vaccines, *M. haemolytica*, commercial BRD vaccines, *M. bovis* [novel route and adjuvants], BRD vaccine timing, priming with a MLV BRD vacc, commercial BRSV given at various stages of production, revaccination of sick calves with BRD [IBR,PI-3,BRSV), revaccination with MLV BRD, BRD with BVD, Experimental BRD vaccines, BRD revaccination, MLV BRD vaccine with killed BVD, MVL BRD vaccine timing, BVDV type-1 vs. type-2, MLV bovine rota/corona viruses | Feedlot  Exp. (n=21)  Comm. (n=10)  Unclear (n=2) | Respiratory disease (n=17)  Mortality (n=18)  Morbidity (n=23)  Surrogate measures (n=16)  Non-specific immunity (n=6)  Treatments for illness (n=12)  Treatment cost (n=5)  Pathology (n=6) | 12814  20309  14311  40264  16253  14074  40282  13503  10336  13901  10160  16233  40300  10978  16517  13959  10376  10936  40281  11726  12210  12180  11948  11919  11659  11969  11925  13103  11961  14711  12607 |
| Liver abscesses/  Acidosis | *Fusobacterium necrophorum* bacterin (n=1), *F. necrophorum* leukotoxin and *Acranobacterium pyogenes* polysin at high or low levels (n=1), *F. necrophorum* leukotoxin (n=1) | Feedlot  Exp. (n=1)  Comm. (n=2) | Mortality (n=2)  Liver abscess (n=3)  Lameness (n=2)  Surrogate measures (n=1)  Acidosis (n=0) | 12418  12683  34484 |

Refid (reference identity number) is linked to citation information in Excel spreadsheet Appendix 7

a Outcomes of interest included: surrogate measures of disease and susceptibility, indices of nonspecific immunity, non-specific morbidity, mortality, respiratory disease, diarrhea, treatments for illness, other disease (e.g. non-diarrheal, non-respiratory infectious disease), pathology (e.g. post mortem findings), rumen or abomasum development, acidosis, liver abscesses, lameness or foot lesions total farm-level antibiotic use, injection site lesions, gene expression of immunity, abortion and treatment cost.

b Comm. (i.e. populations living under commercial farm settings)

c Morbidity (i.e. non-specific illness or pyrexia)

d Surrogate measures of disease and disease susceptibility (i.e. pathogen detection or indices of specific immunity such as serology and cell mediated immunity)

e Treatments for illness (i.e. sequential treatments administered to sick animals)

f Exp. (i.e. populations living under experimental research farm settings)

g Indices of non-specific immunity (i.e. immunoglobulins to non-infectious agents and immune biomarkers such as acute-phase proteins and tumor necrosis factor)

h Pathology (i.e. post mortem findings excluding liver abscesses)

Appendix 4. Clinical trials of non-vaccine, non-antibiotic interventions for beef cattle and veal calf populations presented in decreasing order of frequency.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Intervention type** | **Intervention description** | **Production stage population type** | **Outcomes of interesta** | **Refid** |
| Feed additive non-antibiotic  Total (n=121) | Se supplement above recommended levels (n=1), crude protein (n=1), yeast extract (n=1), yeast culture (n=5), plant extracts [flavonoid and catchins] (n=1), cation and calcium level (n=2), probiotic products (n=1), prebiotic mannanoligosaccharide (MOS) (n=1), commercial blend of essential oils (n=1), Vit. E supplement (n=1), cotton seed hulls (n=1), fermentation extract of Aspergillus (n=1), molasses (n=1), two roughages [wheat straw vs. beet pulp] (n=1) | Veal calves  Exp.b (n=16)  Comm.c (n=2) | Respiratory disease (n=4)  Diarrhea (n=15)  Mortality (n=1)  Morbidityd (n=5)  Surrogate measures e (n=3)  Non-specific immunityf(n=2)  Abomasum/rumeng (n=6)  Treatments for illnessh (n=1)  Treatment cost (n=3)  Pathologyi (n=1)  Liver abscesses (n=1)  Acidosis (n=5) | 10735  23882  11507  14425  13073  11627  11962  24977  11989  14265  11830  27542  20829  12635  26308  29480  12457  23523  37061 |
|  | Mineral supplement (n=1), selenium source (n=1), level and source of selenium (n=2), selenium subclinical toxicosis (n=1), trace mineral [organic vs. inorganic] (n=3), late gestation protein and mineral supplement (n=1), Vit E supplement (n=1), beta-carotene (n=1), molasses with added urea or protein meal (n=1), prebiotic Mannan-oligosaccharides **(**MOS) and urea (n=1), rumen protected methionine (n=1), supplemental fat [safflower seed, cotton seed] (n=1), omega-3 fatty acids (n=1), supplemental feed level (n=1) | Cow-calf  Exp. (n=14)  Comm. (n=3) | Respiratory disease (n=4)  Diarrhea (n=2)  Mortality (n=7)  Morbidity (n=7)  Surrogate measures (n=10)  Non-specific immunity (n=3)  Treatments for illness (n=1)  Treatment cost (n=1)  Lameness (n=1)  Gene expression (n=1)  Abortion (n=1)  Other diseasej: infectious bovine keratitis (IBK) (n=1) | 20632  19664  40262  10836  23253  10211  13413  40289  40276  13378  13011  25982  19728  11610  12093  25499  26253 |
|  | Dietary cation-anion difference [molasses with or without buffer] (n=1), selenium (n=1), saturated and unsaturated fatty acid (n=1) | Cows/heifers  Exp. (n=3)  Comm. (n=1) | Morbidity (n=1)  Surrogate measures (n=1)  Non-specific immunity (n=1)  Acidosis (n=1) | 11631  11382  11640 |
|  | Pre-weaning concentrates (n=1), Vit. E, selenium, copper (n=1) | Beef calves  Exp. (n=2) | Morbidity (n=1)  Surrogate measures (n=1)  Non-specific immunity (n=2) | 23064  19727 |
|  | Vit A level (n=1), Vit. E level (n=4), Vit E or cysteine-rich feather meal (n=1), Vit E with various fatty acids (n=1), Vit E and/or selenium (n=1), Vit E, selenium source (n=1), selenium, copper (n=1), selenium enriched hay (n=1), chromium with urea-corn vs. soybean meal (n=1), chromium (n=5), chromium source (n=2), inorganic chromium with or without niacin vs. organic chromium (n=1), trace minerals with iodine (n=1), trace mineral [organic vs. inorganic] (n=2), magnesium (n=1), trace mineral sources of Cu and Zn (n=1), copper level and source (n=1), zinc level and source (n=1), zinc source (n=1), calcium oxide level (n=1), mineral supplement with or without an ionophore (n=1), late gestation protein and mineral supplementation (n=1), dry distillers grains with moderate vs. high sulfur content (n=1), bicarbonate (n=1), sodium bicarbonate [free choice or part of total mixed ration (TMR) (n=1), potassium level (n=1), exogenous fibrolytic enzyme (n=1), anti-phospholipase antibody (n=2), polyclonal antibody (n=2), yeast (n=2), yeast [live or cell wall extract] (n=1), yeast [active dried vs. killed] (n=1), enterococcus faecium with or without yeast (n=1), direct-fed microbial (DFM) product (n=1), lactobacillus (n=1), commercial feed additives [Prime Purge, Organo-Pro, Convert calf gel containing probiotics and/or feed enzymes] (n=1), pre-biotic oligofructose (n=1), Tasco-Forage® a brown seaweed extract (n=2), essential oils (n=4), Ground flax seed (n=1), RummNext® plant extract product (n=2), de-sugared molasses (n=1), rumen modifier (n=1), lipid source (n=1), fish oil (n=1), fatty acid supplementation (n=4), organic acids (n=1), metabolizable protein supply (n=1), molasses and urea (n=1), urea concentration (n=1), glycerin partial roughage replacement (n=1), ractopamine or zilpaterol (n=4) | Feedlot  Exp. (n=67)  Comm. (n=10) | Respiratory disease (n=14)  Diarrhea (n=3)  Mortality (n=17)  Morbidity (n=35)  Surrogate measures (n=23)  Non-specific immunity (n=18)  Abomasum/rumen (n=2)  Treatments for illness (n=14)  Treatment cost (n=5)  Pathology (n=1)  Liver abscesses (n=11)  Acidosis (n=15)  Lameness (n=1)  Gene expression (n=1) | 14157  12915  34739  21601  16301  13654  26669  26498  40279  29662  27753  33073  12139  19727  10740  40262  12449  20176  15654  23503  19613  10836  26382  12961  11942  28517  27479  40281  12771  16233  13664  14302  12615  10809  40275  40269  14031  27695  11302  15930  11757  10837  20828  11530  11651  40295  23472  40304  14128  16239  12132  11885  33551  10355  10557  36893  11640  12287  26413  12877  40286  10804  29766  12055  26595  13758  13901  27047  19519  26540  26777  39570  12311  11883 |
| Feed type  Total (n=111) | Milk replacer type (n=1), milk replacer plus solid feed of barley grain or ground wheat straw (n=1), milk replacer plus access to hay (n=2), milk replacer plus corn and wheat straw mixtures (n=1), milk replacer plus concentrate of corn silage and barley straw started early or late (n=1), conventional vs. organic pasture with or without concentrate (n=1), concentrate type/roughage source (n=8), roughage particle length (n=1), corn processing type (n=1), high fibre vs. ground corn (n=1), starter format [ground, pelleted, texturized, flakes, meal] (n=6), pelleted starter with or without oats (n=1), varying protein, fat and calcium concentrations or starter diets (n=2), protein level of starter diet started early or later (n=1), early vs. late concentrate (n=1), corn diet contaminated with Fusarium mycotoxin (n=1) | Veal calves  Exp. (n=23)  Comm. (n=6) | Respiratory disease (n=5)  Diarrhea (n=11)  Mortality (n=3)  Morbidity (n=9)  Surrogate measures (n=4)  Non-specific immunity (n=2)  Abomasum/rumen (n=17)  Treatments for illness (n=8)  Treatment cost (n=1)  Pathology (n=1)  Acidosis (n=13) | 12897  30045  26849  33421  27762  12469  27157  23882  11507  23523  24077  26426  29890  32423  15834  27566  23465  24018  26429  27371  23078  26660  28457  38988  28517  26199  29809  29327  27156 |
|  | Rotational feed management (n=1), late gestation dry-lot rations (n=1), rangeland with or without complementary forage (n=1), grazed forage type and endophyte (n=1), grass vs. straw silage late gestation (n=1) | Cow-calf  Exp. (n=5) | Mortality (n=3)  Morbidity (n=1)  Surrogate measures (n=3) | 11888  26214  31264  26263  25520 |
|  | Dry lot weaning vs. pasture (n=1), creep feeding vs. supplement feeding after weaning (n=1), preconditioning program (n=1) | Beef calves  Exp. (n=3)  Comm. (n=2) | Respiratory disease (n=1)  Mortality (n=1)  Morbidity (n=2)  Non-specific immunity (n=2) | 40263  23272  16524 |
|  | Dry lot weaning vs. pasture (n=1), forage infected with endophyte fungus (n=1), 4 types of pasture treatments (n=1), level of concentrate with hay ad lib (n=1), anti-phospholipase antibody in a forage-based vs a grain-based diet (n=1), preconditioning program (n=1), wet brewer’s grains at 2 supplementation rates and frequencies (n=1), conventional or natural beef production maintained on grass (n=1) | Stockers  Exp. (n=7)  Comm. (n=3) | Respiratory disease (n=2)  Mortality (n=1)  Morbidity (n=4)  Surrogate measures (n=1)  Non-specific immunity (n=1)  Liver abscesses (n=1) | 40263  13349  40283  31388  26498  16524  14340  26595 |
|  | Grain adaptation protocol (n=1), dried distillers grains (n=1), corn or wheat dried distillers grains (n=1), varied proportion of wheat dried distillers grains with solubles, barley grain vs. barley silage (n=2), triticale dried distillers grains with solubles (n=1), effects of Sulfur concentration on dried distillers grains with solubles (n=1), wet distillers grains with solubles (n=2), level of dry or modified wet corn distillers grains plus solubles in whole corn grain-based finishing diets (n=1), modified wet distillers grains plus solubles fed high fat (n=1), wet corn gluten (n=2), high-lipid by-product pellets (n=1), dietary crude protein concentration (n=2), metabolizable protein supply (n=1), corn silage with various grains (n=1), grain concentrate plus barley straw vs. silage based total mixed ration (TMR) (n=1), corn processing method (n=2), grain processing methods (n=2), mixed ration vs. pelleted (n=1), critical roughage part (n=1), various roughage content and roughage timing (n=1), steam-flaked corn and dietary roughage concentration (n=2), increasing straw intake by adding molasses (n=1), levels of concentrate with ad lib hay (n=1), effect of the inclusion of different levels and sources of dietary roughage (n=1), levels of barley concentrate vs. barley silage (n=1), sliced vs. baled alfalfa hay (n=1), limit fed grain based diet vs. access to ad lib forage (n=2), maize silage and 4 isofibrous diets (n=1), chop length of barley silage with or without an esterase-producing inoculant (n=1), alkaline hydrogen peroxide treated wheat straw vs. corn silage (n=1), self-selection of dietary ingredients vs. total mixed ration (TMR) (n=2), grain mix as corn, barley or both (n=1), barley-based vs. oat-based diet (n=1), hulless barley vs. conventional covered barley (n=1), dietary starch and energy concentration (n=1), concentrate level (n=1), sunflower seed forage replacement and effect of its processing method (n=1), backgrounding or a finishing diet (n=1), anti-phospholipase antibody (aPLA-2) during change from forage to grain-based diet (n=1), conventional vs. natural pasture raised (n=1) | Feedlot  Exp. (n=41)  Comm. (n=7)  Unclear (n=1) | Respiratory disease (n=7)  Mortality (n=4)  Morbidity (n=9)  Surrogate measures (n=3)  Non-specific immunity (n=4)  Abomasum/rumen (n=3)  Treatments for illness (n=4)  Pathology (n=2)  Liver abscesses (n=22)  Acidosis (n=18)  Lameness (n=3) | 27151  12477  27529  34739  33421  27651  34137  26712  33430  23893  12418  40263  25272  23272  26413  27865  28517  23339  33670  26669  23145  28587  26845  26658  23472  25277  31388  25677  28573  29021  26588  23721  30018  28872  10318  26498  26111  14190  11888  16524  16524  27753  20956  10337  26595  40295  23171  28579  29168  29766  25231  34317 |
| Medications  Total (n=46)  [Medication as any medication, vitamin, mineral, or antibodies administered directly to individual animals] | Hormone cocktail (n=2), recombinant bST (n=1), parapox ovis based immunomodulation (n=1), Tween 80® (n=1), zinc methionine or zinc oxide (n=1), selenium yeast (n=1),  Non-pathogenic E. coli starin Nissle 1917 (n=1), probiotics and seaweed extracts (n=1), mycobacterium cell wall fraction [Immunoboost®] (n=1) | Veal calves  Exp. (n=5)  Comm. (n=3)  Unclear (n=1) | Respiratory disease (n=3)  Diarrhea (n=4)  Mortality (n=3)  Morbidity (n=6)  Surrogate measures (n=4)  Non-specific immunity (n=3)  Treatments for illness (n=3)  Treatment cost (n=1) | 12036  11966  16134  34430  14186  10817  12560  40308  40311  10735 |
|  | Heifers implanted with zeranol (n=1) | Cow-calf  Exp. (n=1) | Mortality (n=1)  Abortion (n=1) | 31160 |
|  | GnRH controlled release (n=1) | Cows/heifers  Exp. (n=1) | Non-specific immunity (n=1) | 14723 |
|  | Timing of estrogenic implant relative to weaning (n=1), meloxicam at castration (n=1) | Beef calves  Exp. (n=3) | Morbidity (n=1)  Surrogate measures (n=1)  Non-specific immunity (n=1) | 14341  26417 |
|  | Flunixin meglumine (n=1), prolactin (n=1), meloxicam (n=2), meloxicam at castration (n=1), trace mineral injection (n=2), vitamin and mineral drench (n=1), timing of estrogenic implant relative to weaning (n=1), trenbolone actetate and estradiol (n=1), forage:concentrate diet with selenium and Vit E injection (n=1) | Stockers  Exp. (n=10)  Comm. (n=2) | Respiratory disease (n=1)  Morbidity (n=3)  Surrogate measures (n=2)  Non-specific immunity (n=6)  Liver abscess (n=1)  Lameness (n=1)  Other disease (n=1) [scrotal infection] | 10831  12576  32017  13515  14341  19520  40283  27553  26417  11128  26595 |
|  | Nitric oxide releasing solution (n=4), ancillary NSAID treatment (n=8), trace mineral injection (n=2), Zinc drench or nasal spray (n=1), Vitamins A,D, C and E injection (n=1), Vitamin A and C (n=1), delayed implantation of steroid/growth implant (n=2), timing of estrogenic implant relative to weaning (n=1), beta-adrenergic agonists (n=1), trenbolone actetate and estradiol (n=1), Zelnate® immunostimulant (n=2), mycobacterium cell wall fraction [Immunoboost®] (n=1), Convert calf gel® mix of direct-fed microbial (DFM) and organic acids (n=1) | Feedlot  Exp. (n=14)  Comm. (n=10)  Unclear (n=3) | Respiratory disease (n=15)  Diarrhea (n=1)  Mortality (n=12)  Morbidity (n=18)  Surrogate measures (n=6)  Non-specific immunity (n=7)  Abomasum/rumen (n=)  Treatments for illness (n=12)  Treatment cost (n=4)  Pathology (n=3)  Liver abscesses (n=2)  Acidosis (n=)  Lameness (n=1)  Genes (n=)  Abortion (n=)  Other disease (n=1) [scrotal infections] | 10192  10854  10376  40297  10687  13515  10737  27347  27553  29835  10228  40267  11973  40298  40310  40286  26417  25226  10137  11270  40268  30890  10711  26595  10358  32017  14341 |
| Colostrum or milk replacer additive  Total (n=40) | Yeast or yeast extract (n=5), mannanoligosaccharide (n=4), probiotic (n=4), prebiotic (n=2), pre and pro-biotic combination product (n=3), clonoptilite adsorbent (Zeolite) (n=4), milk-free vs. milk based (n=1), added IgG (n=1), commercial lacteal-derived colostrum replacer (n=1), commercially available plasma derived colostrum replacer (n=2), spray-dried animal plasma (n=1), whey protein with or without spray-dried animal plasma (n=1), level of concentrations of Vit A and Vit. E (n=1), Vit.E (n=2), Vit. A (n=2), fatty acid supplement (n=2), clenbuterol (n=1), chromium (n=1), source of trace minerals (n=1), lactoferrin (n=2), excess Selenium supplementation (n=1), plane of nutrition (n=1), roughage supplement (n=1), essential oils (n=1) | Veal calves  Exp. (n=39)  Comm. (n=2) | Respiratory disease (n=10)  Diarrhea (n=29)  Mortality (n=4)  Morbidity (n=12)  Surrogate measures (n=19)  Non-specific immunity (n=4)  Abomasum/rumen (n=6)  Treatments for illness (n=6)  Treatment cost (n=2)  Pathology (n=3) | 10735  12182  12457  15558  10870  11830  11605  29327  13911  11248  28528  27542  15394  14265  12036  13350  12932  10688  12897  12733  37061  15111  12503  13118  14237  12469  13849  26308  11059  32423  24018  24977  29853  11627  15507  11520  27293  12918  25660  27186 |
| Feeding regime  Total (n=35) | Milk fed vs. concentrate and early weaned vs. late weaned (n=2), high vs. low plane of nutrition of milk replacer or concentrate (n=1), conventional weaning vs. concentrate dependent (n=1), once daily vs. twice daily feeding and weaning timing (n=1), milk replacer for various periods (n=1), low protein starter diet (n=1), various milk replacer allowances (n=1) | Veal calves  Exp. (n=9) | Respiratory disease (n=1)  Diarrhea (n=3)  Morbidity (n=1)  Surrogate measures (n=1)  Non-specific immunity (n=2)  Abomasum/rumen (n=5)  Treatments for illness (n=1)  Acidosis (n=3) | 30480  23078  32423  11059  23240  23117  26872  23882  23343 |
|  | Feed amounts at various periods of gestation and lactation (n=3), timed nutrient or amount of limitation (n=4), energy restriction and calf management systems (n=1), proportion dried distillers grains with solubles and soybean hulls (n=1) | Cow-calf  Exp. (n=7)  Unclear (n=1) | Mortality (n=3)  Surrogate measures (n=4)  Gene expression that may impact immunity (n=1) 10372 | 29402  23546  32970  10157  23743  25520  10372  23940 |
|  | Negative energy balance (n=1) | Cows/heifers  Exp. (n=1) | Non-specific immunity (n=1) | 31900 |
|  | Rate of body gain during winter grazing (n=1), wet brewers grains at different supplementation rate and frequency (n=1), nutrient supplement ad libitum vs. range delivered 3 times weekly (n=1) | Stockers  Exp. (n=3)  Comm. (n=1) | Mortality (n=1)  Morbidity (n=1)  Surrogate measures (n=1) | 33703  14340  25239 |
|  | Amount and timing of feed delivered (n=2), previous rate of body weight gain during winter grazing (n=1), nutrient supplement ad libitum vs. range delivered 3 times weekly (n=1), limit fed grain vs. ad libitum (n=2), proportion dried distillers grains with solubles and soybean hulls (n=1), wet corn gluten feed fed ad libitum vs. restricted (n=1), grain adaptation protocol (n=1), ad libitum forage vs. limit fed high grain diet (n=1), self-selection of feed ingredients (n=1), dietary crude protein concentration (n=1), amount of roughage fed (n=1) | Feedlot  Exp. (n=12)  Comm. (n=2)  Unclear (n=1) | Mortality (n=2)  Morbidity (n=2)  Surrogate measures (n=1)  Non-specific immunity (n=1)  Abomasum/rumen (n=1)  Treatments for illness (n=1)  Treatment cost (n=1)  Liver abscesses (n=5)  Acidosis (n=5)  Gene expression (n=1)10372 | 23484  10304  33703  25239  12418  10372  23721  12477  27178  23339  27865  34739  23893 |
| Weaning  Total (n=34) | Reared with or without various level of contact with the dam (n=1), feeding regime pre-weaning vs. post weaning (n=1), concentrate dependent weaning (n=1), early vs. late weaning with milk vs. concentrate feeding (n=2), Jersey vs. Holstein calves gradually weaned (n=1) | Veal calves  Exp. (n=7) | Respiratory disease (n=1)  Diarrhea (n=1)  Morbidity (n=2)  Surrogate measures (n=1)  Non-specific immunity (n=3)  Abomasum/rumen (n=3)  Treatments for illness (n=1)  Acidosis (n=2)  Genes (n=1) | 30480  28345  23117  23118  23240  29327  25976 |
|  | Early vs. late weaning and pasture rotational management of Neotyphodium-infected fescue at weaning (n=1), time from maternal separation and shipping (n=1), dam age (n=1), supplementation with dried distillers grains with solubles and soy hulls (n=1), 2-stage weaning with nose flaps (n=1), weaning age (n=2) | Cow-calf  Exp. (n=6)  Comm. (n=1) | Respiratory disease (n=3)  Diarrhea (n=1)  Mortality (n=2)  Morbidity (n=3)  Surrogate measures (n=3)  Treatments for illness (n=2)  Pathology (n=1)  Liver (n=1)  Lameness (n=1)  Genes (n=1)  Other disease (n=1) [IBK] | 11888  40266  10868  10372  10223  26253 |
|  | Weaned with access to creep feed before shipping or weaned at time of shipping (n=1), optimum time to wean fall calves grazing Neotyphodium infected fescue pasture (n=1), mingling with animals from multiple sources vs. single source (n=1),  yard weaning with or without feed-bunk training (n=1), calves weaning in presence of dam or not (n=2) [40263], weaned vs. not weaned (n=2), genetic effects on response to weaning (n=2) [29258], weaning concurrently or consecutively to castration (n=1), weaning at trucking or 30 days prior and weaning method (n=1), time between weaning and shipping (n=2), length of weaning period and timing of vaccination before weaning or on arrival (n=1) | Beef calves  Exp. (n=15)  Comm. (n=3) | Respiratory disease (n=6)  Mortality (n=2)  Morbidity (n=9)  Surrogate measures (n=2)  Non-specific immunity (n=8)  Treatments for illness (n=1)  Treatment cost (n=1)  Pathology (n=2)  Liver (n=2)  Lameness  Gene (n=1)  Abortion | 23336  40265  23136  12180  27894  19514  40270  23102  11886  29258  40263  23272  23235  12215  22976 |
|  | Weaned vs. not weaned (n=1), Regular weaning protocol vs. Michigan State University (MSU) protocol (n=1), early weaned vs. late weaned (n=1), weaning at trucking or 30 days prior and weaning method (n=1), time between weaning and shipping (n=1), calves weaning in presence of dam or not (n=2), optimum time to wean fall calves grazing Neotyphodium infected fescue pasture (n=1) [27894], weaned and housed or returned to pasture (n=1), weaned with or without a trainer cow (n=1), genetic effects on response to weaning (n=1) | Stockers  Exp. (n=8)  Comm. (n=3) | Respiratory disease (n=3)  Mortality (n=1)  Morbidity (n=6)  Surrogate measures (n=3)  Non-specific immunity (n=5)  Treatments for illness (n=1)  Pathology (n=1)  Liver (n=1)  Abortion | 40278  23446  40270  12215  27894  27875  40263  29258  25781  40266 |
| Breed  Total (n=32) | Holstein vs. Jersey calves (n=1) | Veal calves  Exp. (n=1) | Surrogate measures (n=1)  Non-specific immunity (n=1)  Gene expression (n=1) | 25976 |
|  | Pure bred vs. Heterosis (n=3), breed type/breed cross (n=2), 10 years of yearling weight selection (n=1) | Cow-calf  Exp. (n=6) | Mortality (n=5)  Surrogate measures (n=1) | 31523  31533  31558  31560  34780  31666 |
|  | BoLA type and sire effects (n=1) | Cows-heifers  Exp. (n=1) | Surrogate measures (n=1) | 20293 |
|  | Sire and dam breed and heterosis (n=2), genetic markers for BRSV susceptibility in Charolais-Holstein crosses (n=1), genetic markers of response to BRSV vaccine (n=1), immune response heritability and markers (n=1) | Beef calves  Exp. (n=5) | Respiratory disease (n=1)  Surrogate measures (n=2)  Non-specific immunity (n=2)  Pathology (n=1)  Gene expression (n=1) | 29258  23336  11166  12346  10880 |
|  | Sire and dam breed and heterosis (n=1), yearling weight selection approach to breeding (n=1) | Stockers  Exp. (n=2) | Mortality (n=1)  Non-specific immunity (n=1) | 29258  31666 |
|  | Sire and dam breed and heterosis (n=2),  vaccination against BRD in Mertolenga, Preta and mixed-breed calves (n=1), beef vs. dairy steers (n=1), breed cross effect on myostatin allele associated mortality (n=1) | Feedlot  Exp. (n=4)  Unclear (n=1) | Respiratory disease (n=1)  Mortality (n=2)  Morbidity (n=1)  Surrogate measures (n=1)  Non-specific immunity (n=2)  Pathology (n=1)  Liver abscesses (n=1) | 29258  23336  11919  13664  23466 |
| Transportation  Total (n=17) | Chromium supplement and transportation (n=1), transportation and co-mingling (n=1)  Transportation plus another intervention [23446, 32017, 29258] | Stockers  Exp. (n=2) | Non-specific immunity (n=2) | 29815  13515 |
|  | Space allowance during transportation (n=1), transport vs. not transported (n=2), long haul vs. short (n=1)  Transportation plus another intervention [23446, 29258, 10737, 10137, 32017, 23336, 26540, 12301, 13515, 27743, 28646 ] | Feedlot  Exp. (n=4) | Respiratory disease (n=1)  Mortality (n=1)  Morbidity (n=3)  Surrogate measures (n=2)  Non-specific immunity (n=3)  Treatments for illness (n=1)  Treatment cost (n=1) | 29254  12877  21187  25008 |
| Housing  Total (n=16) | Concentrate feeder design (n=1), single pen vs. group pen (n=3), pen density (n=1), hutches vs. pens in an open sided barn (n=1)  Housing plus another intervention [26308] | Veal calves  Exp. (n=5)  Comm. (n=1) | Respiratory disease (n=2)  Diarrhea (n=3)  Morbidity (n=2)  Surrogate measures (n=1)  Non-specific immunity (n=4)  Abomasum/rumen (n=1)  Treatments for illness (n=1)  Liver (n=1)  Acidosis (n=1)  Gene (n=1) | 38523  30026  23074  26435  12281  15507 |
|  | Tie stall vs. free stall housing (n=1), abrupt weaning and subsequent housing (n=1), insulated vs. uninsulated winter housing and outdoors with a rain shelter (n=1) | Cows-heifers  Exp. (n=2)  Comm. (n=1) | Morbidity (n=1)  Non-specific immunity (n=3)  Lameness (n=1) | 40302  15263  23361 |
|  | Housed or pastured after weaning (n=1) | Stockers  Exp. (n=1) | Morbidity (n=1)  Non-specific immunity (n=1) | 27875 |
|  | Manger space and flooring (n=1), bunk management [cleaned vs. traditional] (n=1), bare floor vs. mats (n=1), slats vs. mats (n=1)  Housing effect on another intervention [26674, tail docking or not in calves all living on slatted floors] | Feedlot  Exp. (n=2)  Comm. (n=2) | Mortality (n=1)  Morbidity (n=1)  Non-specific immunity (n=2)  Lameness (n=2)  Liver (n=1)  Acidosis (n=1) | 23470  29747  26241  31864 |
| Environment  Total (n=12) | Housed indoors vs. outdoors during high ambient temp. (n=1) | Veal calves  Exp. (n=1) | Morbidity (n=1)  Surrogate measures (n=1) | 10517 |
|  | Shade treatment (n=1), maternal heat stress and 2 planes of nutrition (n=1) | Cow-calf  Exp. (n=2) | Respiratory disease (n=1)  Diarrhea (n=1)  Morbidity (n=1)  Surrogate measures (n=2) | 23743  26634 |
|  | Efficacy of needle-free vaccine injection under cold and warm conditions (n=1) | Beef calves  Comm. (n=1) | Surrogate measures (n=1) | 10433 |
|  | Environmental conditions and spatial allowance during transportation (n=1) | Feedlot  Exp. (n=1) | Morbidity (n=1)  Non-specific immunity (n=1) | 29254 |
| Biosecurity  Total (n=8) | Regrouping and relocation (n=1) | Veal calves  Exp. (n=1) | Morbidity (n=1)  Abomasum/rumen(n=1) | 12971 |
|  | Specific education regarding biosecurity (n=1) | Cow-calf  Comm. (n=1) | Surrogate measures (n=1)  Other disease (n=1) [BVD] | 40273 |
|  | Multiple sources vs. single source ranch (n=1) | Beef calves  Exp. (n=1) | Respiratory disease (n=1)  Mortality (n=1)  Morbidity (n=1)  Surrogate measures (n=1)  Non-specific immunity (n=1)  Treatments for illness (n=1)  Treatment cost (n=1) | 11886 |
|  | Comingling and transportation (n=1),  regular weaning protocol vs. Michigan State University protocol (n=1) | Stockers  Exp. (n=1)  Comm. (n=1) | Mortality (n=1)  Morbidity (n=1)  Non-specific immunity (n=1) | 29815  40278 |
|  | Multiple sources vs. single source (n=2), regular weaning protocol vs. Michigan State University protocol (n=1), cattle source (n=1), comingled or not (n=1) | Feedlot  Exp. (n=2)  Comm. (n=4) | Respiratory disease (n=3)  Mortality (n=4)  Morbidity (n=3)  Surrogate measures (n=3)  Non-specific immunity (n=1)  Treatments for illness (n=2)  Treatment cost (n=2) | 12301  11886  26777  40310  40278 |
| Unspecified preconditioning  Total (n=3) | Preconditioning program (n=1), timing of vaccination before or after shipment (n=1), number of RBD vaccines prior to shipment (n=1) | Beef calves  Comm. (n=3) | Respiratory disease (n=2)  Mortality (n=3)  Morbidity (n=2)  Treatments for illness (n=1)  Treatment cost (n=1)  Pathology (n=1) | 16524  14311  11659 |
|  | Preconditioning program type (n=2), preconditioning nutrition (n=1) | Sockers  Exp. (n=2)  Comm. (n=2) | Respiratory disease (n=1)  Mortality (n=3)  Morbidity (n=3)  Treatments for illness (n=1)  Treatment cost (n=1) | 16524  11491  25239 |
|  | Preconditioning program type (n=2), preconditioning and length of transportation (n=1), branding method (n=1), preconditioning nutrition (n=1), timing of vaccination before or after shipment (n=1), number of RBD vaccines prior to shipment (n=1) | Feedlot  Exp. (n=4)  Comm. (n=4) | Respiratory disease (n=4)  Mortality (n=5)  Morbidity (n=7)  Surrogate measures (n=2)  Non-specific immunity (n=2)  Treatments for illness (n=3)  Treatment cost (n=4)  Pathology (n=1) | 16524  25913  25239  14311  11886  11659  21187 |

Refid (reference identity number) is linked to citation information in Excel spreadsheet Appendix 7

a Outcomes of interest included: surrogate measures of disease and susceptibility, indices of nonspecific immunity, non-specific morbidity, mortality, respiratory disease, diarrhea, treatments for illness, other disease (e.g. non-diarrheal, non-respiratory infections), pathology (e.g. post mortem findings), rumen or abomasum development, acidosis, liver abscesses, lameness or foot lesions total farm-level antibiotic use, injection site lesions, gene expression of immunity, abortion and treatment cost.

b Exp. (i.e. populations living under experimental research farm settings )

c Comm. (i.e. populations living under commercial farm settings)

d Morbidity (i.e. non-specific illness or pyrexia)

e Surrogate measures of disease and disease susceptibility (i.e. pathogen detection or indices of specific immunity such as serology and cell mediated immunity)

f Indices of non-specific immunity (i.e. immunoglobulins to non-infectious agents and immune biomarkers such as acute-phase proteins and tumor necrosis factor)

g Abomasum/rumen (i.e. abomasum or rumen development)

h Treatments for illness (i.e. sequential treatments administered to sick animals)

i Pathology (i.e. post mortem findings excluding liver abscesses)

j Other disease (i.e. non-diarrhea, non-respiratory infectious clinical disease)

Appendix 5. Studies of non-antibiotic interventions in beef and veal animals that included an antibiotic comparison group (n=21).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Study type | Intervention | Population | Outcomes of interesta | Ref id |
| Challenge trial  Total (n=2) | Fatty acid supplement non-antibiotic feed and milk replacer additive vs. milk replacer with neomycin sulfate and oxytetracycline antibiotic (n=1) | Veal calves  Exp.b (n=1) | Morbidityc (n=1)  Diarrhea (n=1)  Surrogate measuresd (n=1)  Non-specific immunitye (n=1) | 11298 |
|  | Acrobose non-antibiotic feed additive vs. monensin (n=1) | Feedlot  Exp. (n=1) | Acidosis (n=1) | 24221 |
| Clinical trial  Total (n=18) | Prebiotic and probiotic milk replacer additive vs. neomycin and oxytetracycline) (n=1), prebiotic and milk replacer additive vs. neomycin and oxytetracycline) (n=1) | Veal calves  Exp. (n=2) | Respiratory disease (n=1)  Diarrhea (n=2)  Morbidity (n=1)  Treatments for illnessf (n=1) | 12918  12733 |
|  | Mineral supplement plus nothing, monensin or chlorotetracyline (n=1) | Cow-calf  Comm.g(n=1) | Respiratory disease (n=1)  Morbidity (n=1)  Other diseaseh (n=1) [infectious bovine keratitis] | 20632 |
|  | Non-antibiotic feed additive [nutraceutical Actigen®] vs. chlortetracycline or Rumensin® (n=1), supplementation of anti-phospholipase A(2) vs. monensin and tylocin (n=1), rumen modifier vs. chlortetracycline (n=1) | Stockers  Exp. (n=3) | Non-specific immunity (n=3) | 40303  26498  26382 |
|  | Commercial DNA immune stimulant non-antibiotic medication [Zelnate®] vs. timlicocin medication (n=1) or tulathromycin (n=1), chromium non-antibiotic feed additive vs. long acting oxytetracycline medication (n=1), non-antibiotic feed additive anti-phospholipase A2 vs. monensin and tylocin (n=1), rumen modifier vs. chlortetracycline or monensin (n=1), Nitric oxide solution vs. tilmicocin (n=2), commercial plant extract [Rumnex®] feed additive vs. rumensin (n=1), sunflower seeds feed supplement vs. tylocin (n=1), commercial essential oil mixture non-antibiotic feed additive [NEXT ENHANCE®] vs. monensin/tylocin (n=1), avian derived polyclonal antibodies vs. monensin/tylocin (n=1), multivalent polyclonal antibodies vs. monensin (n=1), non-antibiotic feed additive zilpaterol hydrochloride with or without monensin and tylocin (n=1), non-antibiotic rumen modifier vs. chlortetracycline or monensin (n=1),  Fusobacterium necrophorum leukotoxin and Acranobacterium pyogenes polysin vaccine vs. tylocin (n=1) | Feedlot  Exp. (n=8)  Comm. (n=5)  Unclear (n=1) | Respiratory disease (n=4)  Mortality (n=7)  Morbidity (n=7)  Surrogate measures (n=2)  Non-specific immunity (n=2)  Treatments for illness(n=4)  Liver abscess (n=5)  Acidosis (n=2)  Pathology (n=1) | 40267  14157  26498  26382  12683  10192  40268  40295  11885  40269  12311  27479  33073  40297 |
| Observational  Total (n=1) | Non-antibiotic alternative treatment including homeopathy vs. conventional and intensive beef production systems (n=1) | Cow-calf, stockers, feedlot  Comm. (n=1) | Respiratory disease (n=1)  Mortality (n=1)  Morbidity (n=1)  Diarrhea (n=1)  Treatments for illness (n=1)  Liver abscess (n=1)  Lameness (n=1)  Pathology (n=1)  Abortion (n=1) | 25078 |

Refid (reference identity number) is linked to citation information in Excel spreadsheet Appendix 7

a Outcomes of interest included: surrogate measures of disease and susceptibility, indices of nonspecific immunity, non-specific morbidity, mortality, respiratory disease, diarrhea, treatments for illness, other disease (e.g. non-diarrheal, non-respiratory infectious disease), pathology (e.g. post mortem findings), rumen or abomasum development, acidosis, liver abscesses, lameness or foot lesions total farm-level antibiotic use, injection site lesions, gene expression of immunity, abortion and treatment cost.

b Exp. (i.e. populations living under experimental research settings)

c Morbidity (i.e. non-specific illness or pyrexia)

d Surrogate measures of disease and disease susceptibility (i.e. pathogen detection or indices of specific immunity such as serology and cell mediated immunity)

e Indices of non-specific immunity (i.e. immunoglobulins to non-infectious agents and immune biomarkers such as acute-phase proteins and tumor necrosis factor)

f Treatments for illness (i.e. sequential treatments administered to sick animals)

g Comm. (i.e. populations living under commercial settings)

h Other disease (i.e. non-diarrhea, non-respiratory infectious clinical disease)

Appendix 6. Details of studies describing specific non-antibiotic interventions, specific populations and clinically important outcomesa in beef and veal animals from among the clinical trials (n=439) from January 1990 to October 2016 that may feasibly support systematic reviews.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Intervention | Intervention specifics | Population | Clinically important health outcomes | Refid |
| Vaccinations [bovine respiratory disease (BRD)]  (n=24) | *Vaccine types (n=12):*  Inactivated vaccine vs. modified live vaccine for specific pathogens (n=1),  univalent vs. multivalent vaccines (n=1),  various experimental and/or commercial multivalent vaccines containing various combinations of antigens with or without specific bacterial toxoids (n=10)  *Novel vaccine routes and novel combinations of viral-bacterial respiratory vaccines (n=1),*  *Vaccination site on animal (n=1):*  Clostridial vaccination at base of ear of neck (n=1)  *Vaccination-revaccination and vaccination schedules (n=10):*  BRD vaccination at weaning, followed by a revaccination [0, 1, 2, or 3 vaccinations] (n=1), BRD-vaccination treatment of 0, 1, 2, or 3 vaccinations (n=1), vaccination once or twice [modified-live virus vaccine containing BHV1, PI3V, BVDV1a, BVDV2a, and BRSV] (n=1), Pasteurella haemolytica and Haemophilus somnus vaccine given once or twice by IM or SQ route (n=1), vaccine timing [modified-live respiratory viral vaccine (bovine herpes virus-1, bovine viral diarrhea virus, bovine parainfluenza-3, bovine respiratory syncytial virus] given on d 0 or on d 14 of a receiving period (n=1), two vaccination timing treatments for multivalent modified live virus (MLV) BRD vaccine (n=1), modified-live infectious bovine rhinotracheitis virus (IBRV), bovine viral diarrhea virus types 1 (BVDV1) and 2 (BVDV2), parainfluenza type 3 virus and bovine respiratory syncytial virus vaccine and Mannheimia haemolytica and Pasteurella multocida bacterin-toxoid at 67, 167 days or 190 days of age (n=1), commercial bovine respiratory syncytial virus (BRSV) vaccine [given at various stages of production/ages (n=1), Pasteurella haemolytica bacterial extract before or after shipping (n=1), ancillary treatment revaccination with intranasal vaccination IBR­,PI3­,BRSV at time of treatment for BRD (n=1) | Feedlot cattle  Exp.b (n=15)  Comm.c (n=8)  Unclear (n=1) | Respiratory disease (n=16)  Morbidityd (n=22)  Mortality (n=15)  Treatments for illnesse (n=10) | 13103  11659  12180  12210  12814  40264  13503  11948  40300  11961  13901  11925  40281  40282  16517  13959  11919  11726  16233  10376  14311  14074  11886 |
| Feed additive  [probiotics]  (n=5) | Yeast culture live (n=2), yeast [live or cell wall extract] (n=1), DFM product [Bovamine Defend®] (n=1), commercial feed additives containing probiotics and/or feed enzymes] (n=1) | Feedlot cattle  Exp. (n=5)  Comm. (n=0) | Respiratory disease (n=3)  Morbidity (n=5)  Mortality (n=4)  Treatments for illness (n=3) | 40279  40281  40286  14128  12132 |
| Feed additive supplement  [Daily  Vitamin E]  (n=5) | Vit. E levels [285, 570, 1,140 IU] (n=1), Vit E 550 IU or cysteine-rich feather meal (n=1), Vit E 2,000 IU (n=1), Vitamin E with either flaxseed oil or safflower oil or alone (n=1), Vit E [2,000 IU] supplement for various lengths of time (n=1) | Feedlot cattle  Exp. (n=4)  Comm. (n=2) | Respiratory disease (n=1)  Morbidity (n=4)  Mortality (n=2)  Treatments for illness (n=3) | 12915  11651  12877  12449  12139 |
| Feed additive  [Chromium (Cr) supplement]  (n=6) | Various organically complexed Cr (n=1), chelated Cr (n=1), 0.14 ppm chelated Cr (n=1), unspecified chromium (n=1), inorganic or organic chromium (n=1), inorganic Cr with or without niacin vs. organic chromium (n=1) | Feedlot cattle  Exp. (n=6)  Comm. (n=0) | Respiratory disease (n=1)  Morbidity (n=6)  Mortality (n=1)  Treatments for illness (n=1) | 14031  13758  13901  20828  16233  16239 |
| Medications  NSAIDf  (n=5) | Flunixin meglumine (n=2), meloxicam at castration (n=2), flunixin, ketoprofen and carprofen as treatments for respiratory disease (n=1), meloxicam (n=1) | Feedlot cattle  Exp. (n=3)  Comm. (n=1)  Unclear (n=1) | Respiratory disease (n=4)  Morbidity (n=5)  Mortality (n=2)  Treatments for illness (n=2) | 30890  10376  26417  29835  27553 |
| Feed type  [roughage and grains]  (n=41) | *Forage format*  *Roughage type, processing methods and roughage levels (n=14)*  Feed presentation form (concentrate and straw offered separately or mixed in form of briquettes (n=1), sliced alfalfa hay vs. traditionally baled alfalfa (n=1), chop length and inoculation of barley silage [ensiled without or with an esterase-producing bacterial inoculant] (n=1), bulk densities of steam-flaked corn and dietary roughage concentration (n=1), effects of wet distillers grains with solubles and dietary concentration of alfalfa hay (n=1), critical roughage part (n=1), level of roughage 2% vs. 10% from day 22–84 with 10% fed to finish at day 133 (n=1),  maize silage as sole forage, four isofibrous diets were formulated with stepped substitution of wheat straw with maize silage (n=1), sunflower seeds [suitability as replacement for forage; the effect of processing before feeding] (n=1), barley (Hordeum vulgare L.) grain-based concentrate plus barley straw (CONC) and maize (Zea mays L.) silage-based total mixed ration (n=1), alkaline hydrogen peroxide-treated wheat vs corn silage, different supplemental CP sources and levels (n=1), increasing straw intake by adding molasses (n=1), different levels and sources of dietary roughage (n=1), conventional vs natural beef production systems (n=1)  *Forage protocols (n=3)*  Ad lib forage based diet vs. limit fed high grain diet (n=1), limit fed grain vs ad lib forage (n=1)  *Grain feeding protocols (n=3)*  Assess if self-selection of dietary ingredients modulates ruminal pH and improves rumen function of feedlot finishing cattle. (n=1), relative energy value of wet corn gluten feed vs corn when diets were ad lib or at restricted feed intake (n=1), grain adaptation protocol (n=1)  *Grain processing methods (n=9)*  Grain processing methods (grinding vs. pelleting) (n=1), effect of grinding or dry-rolling cereals in a concentrate based on maize or barley (n=1), steam-flaked grain sorghum in combination with steam-flaked, dry-rolled), or high-moisture corn (n=1), steam-rolled or ground corn supplemented with laidlomycin and chlortetracycline or monensin and tylosin (n=1), corn silage in combination with barley grain, corn or wheat distillers' grain or wheat middlings (n=1), inclusion or absence of wet distillers grains with solubles [steam-flaked form with or without corn] (n=1), dried distiller's grains vs dried distillers grains with solubles and corn silage (n=1), corn processing method used (n=1), increasing level of dry or modified wet corn distillers grains plus solubles in whole corn grain-based finishing diets (n=1)  *Grain type (n=6)*  Hulless vs conventional covered barley (n=1), wet corn gluten feed that replaced portions of steam-flaked corn (SFC), molasses, urea and soybean meal (n=1), barley-based diets containing wheat dried distillers grains with solubles (n=1), effects of sulfur concentration in dried distillers grains with solubles (n=1), diet grain mix (n=1), fed high fat, modified wet corn distiller's grains plus solubles (n=1)  *Replacing barley grain (n=6)*  Replacing barley and canola meal with high-lipid by-product pellets (n=1), corn or wheat dried distillers' grains with solubles to replace barley (n=1), varied in proportion of wheat dried distillers grains with solubles replacing barley grain or barley silage (n=1), substituting soft or hard wheat for barley grain (n=1), typical feedlot diets vs. oat treatment diet (n=1), triticale dried distillers grains with solubles as a replacement for barley silage in addition to a portion of the dry-rolled barley (n=1) | Feedlot cattle  Exp. (n=36)  Comm. (n=5)  Unclear (n=1) | Liver abscesses (n=26)  Acidosis (n=21) | 25272  23472  26595  27866  12477  33430  30018  23893  28872  29168  23171  26588  26712  28573  14190  34137  10318  26658  25231  26111  34317  12418  27651  26413  28579  25677  23145  20956  26669  27151  26616  28587  29021  10625  27529  27865  23721  23339  27753  28517  26845 |
| Milk replacer additive  [probiotics]  (n=14) | *Probiotics including yeasts (n=6)*  Probiotics containing different probiotic species of human origin, or a calf-specific probiotic (n=1), mixed microbial concentrate containing *Lactobacillus acidophilus*, *Lactobacillus lactis* and *Bacillus subtilis* (n=1), probiotic (n=1), 0.5 g of live yeast added to the milk and 0.5 g of live yeast added to the grain and to the milk (n=1), fermentation extract of *Aspergillus oryzae* (n=1), *Saccharomyces cerevisiae* (n=1),  *Prebioitcs (n=4)*  Mannanoligosaccharides [Bio-Mos®] (n=2),  prebiotic supplement (n=1), spray-dried animal plasma in milk replacer without or with the addition of additives containing fructooligosaccharides and spray-dried serum (n=1),  *Combination probiotic and/or prebiotic (n=4)*  Enteroguard® [blend of fructooligosaccharides, allicin and gut-active microbes] (n=1), mannanoligosaccharide, *Streptococcus faecium*, or a combination of both (n=1), live yeast product vs mannanoligosaccharide (n=1), combined prebiotics and probiotics product (Enterococcus faecium M74 with a non-digestible oligosaccharide (NDO) (n=1) | Veal calves  Exp. (n=14)  Comm. (n=0) | Diarrhea (n=14)  Mortality (n=2)  Morbidity (n=5) | 12918  11627  12733  27542  28528  11520  11830  11248  37061  12469  14237  12457  26308  12932 |

Refid (reference identity number) is linked to citation information in Excel spreadsheet Appendix 7

a Clinically important health outcomes (i.e. mortality, non-specific morbidity, respiratory disease, treatments for illness, liver abscesses and acidosis)

b Exp. (i.e. populations living under experimental research settings)

c Comm. (i.e. populations living under commercial settings)

d Morbidity (i.e. non-specific illness or pyrexia)

e Treatments for illness (i.e. sequential treatments administered to sick animals)

f NSAID (nonsteroidal anti-inflammatory medication)