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# **Effect of prebiotic supplementation on performance and health of dairy calves: protocol for a systematic review and meta-analysis**

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## **INTRODUCTION**

### **Rationale**

In the dairy industry, the treatment of sick calves is commonly based on the antibiotic use by systematic therapy or addition into the milk (Foutz et al., 2018; Urie et al., 2018). The overuse and misuse of antibiotics contribute to the development of antimicrobial resistance, which is a threat to both animal and human health. Thus, it is fundamental to investigate preventative strategies, such as prebiotics, to reduce the incidence of diseases and consequently the use of antibiotics. According to the International Scientific Association for Probiotics and Prebiotics, prebiotic is a “substrate that is selectively utilized by host microorganisms conferring a health benefit” (Gibson et al., 2017). The use of prebiotics may promote the enhancement of beneficial microbiota, which can prevent the adhesion of pathogens to mucosa and modulate the immune response (Uyeno et al., 2015). The literature on prebiotic supplementation for dairy calves is inconsistent, while some studies reported increased body weight (Heinrichs et al., 2003) and intestinal health (Roodposhti and Dabiri, 2012), other observed no improvement on performance or health of calves (Heinrichs et al., 2009; Hill et al., 2008). To the best of our knowledge there is no systematic review or meta-analysis published on prebiotic supplementation on dairy calves. A systematic identification, appraisal, and synthesis of the available literature on this field can contribute to the decision making of veterinarians and dairy consultants.

**Objective:**

The objective of this protocol is to specify the method for a systematic review and meta-analysis to address the following research question: Does the prebiotic supplementation affects performance or health of dairy calves younger than 6 months?

- a) Population: dairy calves (up to 6 months of age) of both sexes
- b) Intervention: prebiotic supplementation (only as prophylactic)
- c) Comparator: placebo or no prebiotic supplementation
- d) Outcomes: any performance measurement [e.g. body weight, average daily gain, body traits (heart girth, wither height, hip width, or body length), feed efficiency, dry matter intake, gastrointestinal tract measurements (volatile fatty acid concentration, rumen pH, papilla length and papilla width)] or any health measurement [e.g. fecal score, diarrhea incidence, serum metabolites (glucose and beta-hydroxybutyrate), immunoglobulins, cytokines, pneumonia incidence, mortality, days on treatment, microbiota and microbiome].

**METHODS**

**Eligibility criteria:** Besides the PICO elements described above, the proposed review will include only primary research including randomized and non-randomized controlled trials; observational studies will be excluded. Studies written in English, Spanish or Portuguese will be included in the review. No restriction for publication date will be imposed. The eligible studies can be published or unpublished, which include peer-reviewed manuscripts, theses and dissertations. Conference abstracts will be excluded.

**Information sources:** The Electronic databases that will be searched are the following: Biosis (Web of Science), CAB Abstracts (CAB Direct), Medline (PubMed), and Scopus (Scopus). Grey literature will be searched using Dissertations and Theses Database (ProQuest). The bibliography of relevant studies will be hand-searched by RBL.

**Search strategy:** Based on the PICO elements, a preliminary search conducted on August 18<sup>th</sup> of 2020 is described on the Appendix 1.

**Data management:** Searches results will be uploaded to the reference manager Sciwheel (Faculty of 1000 Limited, London, UK) and duplicates will be removed by EDF. The de-duplicated results will be exported to the Covidence systematic review management software (Veritas Health Innovation, Melbourne, AU).

**Selection process:** Title and abstract manuscripts will be screened by two independent reviewers (RBL and CBC), using the following questions:

- 1) Does the title or abstract describe a study involving dairy calves?
- 2) Does the title or abstract describe a study with prebiotic supplementation?
- 3) Does the title or abstract describe a primary intervention study?
- 4) Does the title or abstract describe one or more of the measurements in performance (e.g., average daily gain, feed efficiency) or health (e.g., fecal score, diarrhea incidence)?

If both reviewers answer “no” for one of the questions the study will be excluded. Only studies with “maybe” or “yes” answers will be selected for full manuscript screening. Conflicts between the two reviewers will be discussed until a consensus will be reached.

A full manuscript screening will be performed by RBL on the remnant studies. This screening included the 4 questions plus:

- 5) Is the study a controlled trial with negative control group?
- 6) Is the study written in English, Spanish, or Portuguese?
- 7) Is the prebiotic a supplementation strategy (prophylactic, not treatment, for sick animals)?
- 8) Is the study population (dairy calves) equal or less than 6 months old?

Studies will be excluded if RBL answer “no” for one or more of the questions. The exclusion reason will be recorded at this screening level.

**Data collection process:** Data from eligible studies will be extracted by RBL into an electronic spreadsheet and it will be reviewed by CBC. Data extraction forms, adapted from previous studies, will be tested on 5 studies randomly selected by RBL. Data extracted will include:

1. General information: journal name, language, country, author’s name and affiliation, year of publication, funding information.
2. Population characteristics: breed, sex, age, housing system, type production system, assessment of passive transfer, commercial or research herd.
3. Intervention and comparator: commercial name of prebiotic, scientific name, concentration, dose, via of administration (e.g. whole milk, milk replacer), duration of supplementation.
4. Outcomes: type, number of experimental units for each treatment level, least square or contrast means for each treatment level, mean differences from control, unit of results, lower/upper 95% CI, 6) standard error, standard deviation, P-value, and time point of each measurement.

For dichotomous outcomes (e.g. occurrence of diarrhea) information: number of positive experimental units per treatment group, proportion of positive experimental units per treatment group, total number of experimental units per treatment group, unit of results, odd ratio, relative risk, lower/ upper 95% CI, P-value, and time point of each measurement.

## **Data items**

**Outcomes and prioritization:** The definitions of outcomes for performance and health are described in table 1. The main performance outcomes are average daily gain and feed efficiency, and the secondary performance outcomes are body weight, body traits (heart girth, wither height, hip width, or body length), dry matter intake and rumen development indicators (volatile fatty acid concentration, ruminal pH, papilla length and papilla width). The main health outcomes are fecal score and diarrhea incidence and the secondary health outcomes are serum metabolites (glucose, beta-hydroxybutyrate), immunoglobulins, cytokines, pneumonia incidence, mortality, days on treatment, and rumen and gut microbiota and microbiome. The outcomes prioritization was based on their impact on calf growth and intestinal health as well as the economical responses of dairy farms.

**Risk of bias assessment:** The Risk of bias will be assessed at outcome level by one reviewer (RBL), using the Cochrane risk of bias 2.0 tool (Sterne et al., 2019) with the necessary adaptations to fit the specific review question.

**Data synthesis:** Meta-analysis will be conducted if more than 3 studies investigated similar treatments with the same outcome. A random effects meta-analysis will be conducted, and studies will be weighted using the inverse variance method. Heterogeneity between studies will be assessed using Cochran's  $Q$  statistic and  $I^2$  statistic. If there are more than 10 studies, publication bias will be investigated using funnel plots, Begg's adjusted rank correlation, and Egger's test.

## APPENDIX 1: Complete Search Strategy

### Databases and Interfaces Searched:

Database	Interface	Date Coverage	Date Searched
Medline	PubMed	1966 to Present	18 Aug 2020
CAB Abstracts	CAB Direct	1973 to Present	18 Aug 2020
Biosis	Web of Science	1926 to Present	18 Aug 2020
Scopus	Scopus	1996 to Present	18 Aug 2020
Dissertations and Theses Database	Proquest	1861 to Present	18 Aug 2020

### Search Database: PubMed

ID	Terms	Results
#1	"Calf"OR "calves"[tiab] OR "veal"[tiab] OR "preweaned dairy heifers"[tiab]	64,421
#2	"Fecal score"[tiab] OR "faecal score"[tiab] OR "weight gain"[tiab] OR "feed efficiency"[tiab] OR "diarrhea"[tiab] OR "diarrhoea"[tiab] OR "diarrheal"[tiab] OR "diarrhoeal"[tiab] OR "scours"[tiab] OR "scouring"[tiab] OR "intestinal development"[tiab] OR "intestinal bacterial community"[tiab] OR "microbiome"[tiab] OR "microbiomes"[tiab] OR "microbiota"[tiab] OR "microbial community"[tiab] OR "gut flora"[tiab] OR "intestinal flora"[tiab] OR "microbial flora"[tiab] OR "growth"[tiab] OR "health"[tiab] OR "mortality"[tiab] OR "Diarrhea/microbiology"[Mesh] OR "Diarrhea/mortality"[Mesh] OR "Diarrhea/veterinary"[Mesh] OR "Cattle/growth and development"[Mesh] OR "Microbiota"[Mesh] OR "gut health"[tiab] OR "Weight Gain"[Mesh]	3,987,048
#3	"Prebiotics"[Mesh] OR "dietary fiber"[tiab] OR "prebiotics"[tiab] OR OR "short-chain fatty acid"[tiab] OR "conjugated linoleic acid"[tiab] OR "conjugated linoleic acids"[tiab] OR "CLA"[tiab] OR "PUFA"[tiab] OR "polyunsaturated fatty acid"[tiab] OR "polyunsaturated fatty acids"[tiab] OR "fructooligosaccharides"[tiab] OR "polysaccharide"[tiab] OR "polysaccharides"[tiab] OR "galactooligosaccharide"[tiab] OR "galactooligosaccharides"[tiab] OR "xylooligosaccharides"[tiab] OR "xylooligosaccharide"[tiab] OR "oligosaccharides"[tiab] OR "mannanligosaccharide"[tiab] OR "mannanligosaccharides"[tiab] OR "glycans"[tiab] OR "inulin"[tiab] OR "phenolic acid"[tiab] OR "phenolic acids"[tiab] OR "phenolics"[tiab] OR "volatile fatty acids"[tiab] OR "volatile fatty acid"[tiab] OR "FOS"[tiab] OR "MOS"[tiab] OR "cellooligosaccharide"[tiab] OR "cellooligosaccharides"[tiab] OR "Dietary Supplements"[Mesh] OR "tannins"[tiab] OR "flavonoids"[tiab] OR "tannin"[tiab] OR "lignans"[tiab] OR "neolignans"[tiab] OR "terpenoids"[tiab] OR "terpenes"[tiab] OR "isoprenoids"[tiab] OR "carotenoids"[tiab] OR "carotenes"[tiab] OR "carotene"[tiab] OR "tetraterpene"[tiab] OR "tetraterpenes"[tiab] OR "Phytotherapy/veterinary"[Mesh] OR "Plant Extracts/therapeutic use"[Mesh] OR "Fatty Acids, Volatile"[Mesh] OR "Tannins/therapeutic use"[Mesh] OR "Polysaccharides"[Mesh] OR "Linoleic Acids, Conjugated/therapeutic use"[Mesh] OR "Polysaccharides/therapy"[Mesh] OR "Polysaccharides/veterinary"[Mesh] OR "Fatty Acids, Unsaturated/therapy"[Mesh] OR "phenolic acid" [Supplementary Concept] OR "Lignans/therapeutic use"[Mesh] OR "Terpenes/therapeutic use"[Mesh] OR "Carotenoids/therapeutic use"[Mesh]	1,009,725
#4	#1 AND #2 AND #3	1181

Search Database: CAB Direct

ID	Terms	Results
#1	title:(“Calf” OR “calves” OR “veal” OR “preweaned dairy heifers”) OR ab:(“Calf” OR “calves” OR “veal” OR “preweaned dairy heifers”) OR de:(“calf feeding” OR “calves” OR “veal calves”)	102,176
#2	(id:(“diarrhea” OR “fecal coliforms” OR “fecal flora” OR “feces” OR “gut flora” OR “intestinal micro-organisms” OR “microflora” OR “scouring” OR “death rate” OR “liveweight gains” OR “digestive tract contents”) OR (de:(“coliform count” OR “diarrhoea” OR “ faecal coliforms” OR "faecal flora" OR "intestinal microorganisms" ) OR de:(“microbial flora” OR “microorganisms” OR “growth rate” OR “liveweight gain” OR “animal health” OR “microbial flora” OR “liveweight” OR “weight gain” OR “faecal flora” OR “faeces”)) OR (ab:(“Fecal score”OR “faecal score” OR “feces score”OR “weight gain” OR “feed efficiency”OR “diarrheal” OR “diarrhea”OR “diarrhoea”OR “diarrhoeal” ) OR ab:(“intestinal development”OR “intestinal bacterial community”OR “microbiom*” OR “microbiota”OR “microbial community”OR “gut flora”OR “intestinal flora”OR “growth”OR “health”OR “mortality” OR “gut health”) OR ab:(“average daily gain” OR “ADG”)) OR (title:(“Fecal score”OR “faecal score” OR “feces score”OR “weight gain” OR “feed efficiency”OR “diarrheal” OR “diarrhea”OR “diarrhoea”OR “diarrhoeal” ) OR title:(“intestinal development”OR “intestinal bacterial community”OR “microbiom*” OR “microbiota”OR “microbial community”OR “gut flora”OR “intestinal flora”OR “growth”OR “health”OR “mortality” OR “gut health”) OR title:(“average daily gain” OR “ADG”))	2,297,396
#3	ti:(“Prebiotic*” OR “dietary fiber” OR “prebiotics” OR “conjugated linoleic acid*” OR “CLA” OR “PUFA” OR “polyunsaturated fatty acid*” OR “fructooligosaccharide*” OR “polysaccharide*” OR “glycan*” OR “galactooligosaccharide*” OR “xylooligosaccharide*” OR “oligosaccharide*” OR “mannanoligosaccharide*” OR “inulin” OR “phenolic acid*” OR “phenolic*” OR “volatile fatty acid*” OR “Dietary Supplement*” OR “tannin*” OR “flavonoid*” OR “tilbenes” OR “lignan*” OR “terpenoid*” OR “carotenoid*” OR “Phytotherap*” OR “Plant Extract*” OR “terpenoids” OR “terpenes” OR “carotenes” OR “carotene” OR “tetraterpene*” OR “isoprenoid*” OR “neolignan*” OR “FOS” OR “MOS” OR “cellooligosaccharide*”) OR ab:(“Prebiotics” OR “dietary fiber” OR “prebiotics” OR “conjugated linoleic acid*” OR “CLA” OR “PUFA” OR “polyunsaturated fatty acid*” OR “fructooligosaccharide*” OR “polysaccharide*” OR “galactooligosaccharide*” OR “xylooligosaccharide*” OR “oligosaccharide*” OR “mannanoligosaccharide*” OR “inulin” OR “phenolic acid*” OR “phenolic*” OR “volatile fatty acid*” OR “Dietary Supplement*” OR “tannin*” OR “FOS” OR “MOS” OR “cellooligosaccharide*” OR “flavonoid*” OR “tilbenes”[tiab] OR “lignan*” OR “terpenoid*” OR “carotenoid*” OR “Phytotherap*” OR “Plant Extract*” OR “terpenoids” OR “terpenes” OR “carotenes”[tiab] OR “carotene” OR “tetraterpene*” OR “isoprenoid*” OR “neolignan*”) OR de:(“prebiotics” OR “food supplements” OR “short chain fatty acids”)	419,482
#4	#1 AND #2 AND #3	1,109

Search Database: SCOPUS

ID	Terms	Results
#1	( TITLE-ABS-KEY ( diarrh* OR "fecal coliforms" OR "fecal flora" OR "feces" OR "gut flora" OR "intestinal micro-organisms" OR "microflora" OR scour* OR "death rate" OR "liveweight gains" ) OR TITLE-ABS-KEY ( "digestive tract contents" OR "coliform count" OR "faecal flora" OR "intestinal microorganisms" OR "microbial flora" OR "microorganisms" ) OR TITLE-ABS-KEY ( "growth rate" OR "animal health" OR "microbial flora" OR "liveweight" OR "weight gain" OR "faeces" "Fecal score" OR "faecal score" OR "feces score" OR "weight gain" OR "feed efficiency" ) OR TITLE-ABS-KEY ( "intestinal development" OR "intestinal bacterial community" OR microbiom* OR "microbiota" ) OR TITLE-ABS-KEY ( "microbial community" OR "gut flora" OR "intestinal	10,542,504

	flora" OR "growth" OR "health" OR "mortality" OR "gut health" OR "intestinal development" OR "average daily gain" OR "ADG" ) )	
#2	TITLE-ABS-KEY ( "Calf" OR "calves" OR "veal" OR "preweaned dairy heifers" )	96,600
#3	( TITLE-ABS-KEY ( prebiotic* OR {dietary fiber} OR "prebiotics" OR "conjugated linoleic acid*"OR "CLA" OR "PUFA" OR "polyunsaturated fatty acid*" OR "fructooligosaccharide*" OR "polysaccharide*" OR "glycan*" OR "galactooligosaccharide*" OR "xylooligosaccharide*" ) OR TITLE-ABS-KEY ("oligosaccharide*" OR "mannanligosaccharide*" OR "inulin" OR "phenolic acid*" OR "phenolic*" OR "volatile fatty acid*"OR"Dietary Supplement*" OR "tannin*" OR "flavonoid*"OR"tilbenes" OR "lignan*" OR "terpenoid*" OR "carotenoid*" OR "Phytotherap*" ) OR TITLE-ABS-KEY ( "Plant Extract*" OR "terpenoids" OR "terpenes" OR "carotenes" OR "carotene" OR "tetraterpene*" OR "isoprenoid*" OR "neolignan*" OR "FOS" OR "MOS" OR "cellooligosaccharide*" ) )	1,119,567
#4	#1 AND #2 AND #3	1,364
#5	#4 AND ( EXCLUDE ( SRCTYPE , "b" ) OR EXCLUDE ( SRCTYPE , "k" ) ) AND ( EXCLUDE ( DOCTYPE , "ed" ) OR EXCLUDE ( DOCTYPE , "no" ) )	1,351

#### Search Database: Biosis

ID	Terms	Results
#1	TITLE: (diarrh* OR "fecal coliforms" OR "fecal flora" OR "feces" OR "gut flora" OR "intestinal microorganisms" OR "microflora" OR scour* OR "death rate" OR "liveweight gains" OR "digestive tract contents" OR "coliform count" OR "faecal flora" OR "intestinal microorganisms" OR "microbial flora" OR "microorganisms") OR TITLE: ("growth rate" OR "animal health" OR "microbial flora" OR "liveweight" OR "weight gain" OR "faeces" OR "Fecal score" OR "faecal score" OR "feces score" OR "weight gain") OR TITLE: ("feed efficiency" OR "intestinal development" OR "intestinal bacterial community" OR microbiom* OR "microbiota" OR "microbial community") OR TITLE: ("gut flora" OR "intestinal flora" OR "growth" OR "health" OR "mortality" OR "gut health" OR "intestinal development" OR "average daily gain" OR "ADG")	984,443
#2	(Prebiotic*" OR "dietary fiber") OR "prebiotics") OR "conjugated linoleic acid*" OR "CLA") OR "PUFA") OR "polyunsaturated fatty acid*" OR "fructooligosaccharide*" OR "polysaccharide*" OR "glycan*" OR "galactooligosaccharide*" OR "xylooligosaccharide*" OR "oligosaccharide*" OR "mannanligosaccharide*" OR "inulin") OR "phenolic acid*" OR "phenolic*" OR "volatile fatty acid*" OR "Dietary Supplement*" OR "tannin*" OR "flavonoid*" OR "toluenes") OR "lignan*" OR "terpenoid*" OR "carotenoid*" OR "Phytotherap*" OR "Plant Extract*" OR "terpenoids") OR "terpenes") OR "carotenes") OR "carotene") OR "tetraterpene*" OR "isoprenoid*" OR "neolignan*" OR "FOS") OR "MOS") OR "cellooligosaccharide*")	179,860
#3	Title: ("Calf" OR "calves" OR "veal" OR "preweaned dairy heifers")	34,629
#4	#1 AND #2 AND #3	58

#### Search Database: ProQuest Dissertations and Theses

ID	Terms	Results
#1	ab("gut flora" OR "intestinal flora" OR "growth" OR "health" OR "mortality" OR "gut health" OR "intestinal development" OR "average daily gain" OR "ADG") OR ti("gut flora" OR "intestinal flora" OR "growth" OR "health" OR "mortality" OR "gut health" OR "intestinal development" OR "average daily gain" OR "ADG") OR ab("feed efficiency" OR "intestinal development" OR "intestinal bacterial community" OR microbiom* OR "microbiota" OR "microbial community") OR ti("feed efficiency" OR "intestinal development" OR	531,999



	<p>"intestinal bacterial community" OR microbiom* OR "microbiota" OR "microbial community") OR ab("growth rate" OR "animal health" OR "microbial flora" OR "liveweight" OR "weight gain" OR "faeces" OR "Fecal score" OR "faecal score" OR "feces score" OR "weight gain") OR ti("growth rate" OR "animal health" OR "microbial flora" OR "liveweight" OR "weight gain" OR "faeces" OR "Fecal score" OR "faecal score" OR "feces score" OR "weight gain") OR ab(diarrh* OR "fecal coliforms" OR "fecal flora" OR "feces" OR "gut flora" OR "intestinal micro-organisms" OR "microflora" OR scour* OR "death rate" OR "liveweight gains" OR "digestive tract contents" OR "coliform count" OR "faecal flora" OR "intestinal microorganisms" OR "microbial flora" OR "microorganisms") OR ti(diarrh* OR "fecal coliforms" OR "fecal flora" OR "feces" OR "gut flora" OR "intestinal micro-organisms" OR "microflora" OR scour* OR "death rate" OR "liveweight gains" OR "digestive tract contents" OR "coliform count" OR "faecal flora" OR "intestinal microorganisms" OR "microbial flora" OR "microorganisms")</p>	
#2	<p>ab("Prebiotic*" OR "dietary fiber" OR "prebiotics" OR "conjugated linoleic acid*" OR "CLA" OR "PUFA" OR "polyunsaturated fatty acid" OR "polyunsaturated fatty acids" OR "fructooligosaccharide" OR "fructooligosaccharides" OR "polysaccharide" OR "polysaccharides" OR "glycan*" OR "galactooligosaccharide" OR "galactooligosaccharides" OR "xylooligosaccharide" OR "xylooligosaccharides" OR "oligosaccharide" OR "oligosaccharides" OR "mannanoligosaccharide" OR "mannanoligosaccharides" OR "inulin" OR "phenolic acid" OR "phenolic*" OR "volatile fatty acid" OR "volatile fatty acids" OR "Dietary Supplement*" OR "tannin" OR "tannins" OR "flavonoid*" OR "tilbenes" OR "lignan" OR "lignans" OR "terpenoid*" OR "carotenoid*" OR "Phytotherapy" OR "phytotherapies" OR "phytotherapeutics" OR "Plant Extract" OR "Plant extracts" OR "terpenoids" OR "terpenes" OR "carotenes" OR "carotene" OR "tetraterpene*" OR "isoprenoid*" OR "neolignan*" OR "FOS" OR "MOS" OR "cellooligosaccharide" OR "cellooligosaccharides") OR ti("Prebiotic" OR "dietary fiber" OR "prebiotics" OR "conjugated linoleic acid" OR "CLA" OR "PUFA" OR "polyunsaturated fatty acid" OR "polyunsaturated fatty acids" OR "fructooligosaccharide" OR "fructooligosaccharides" OR "polysaccharide" OR "polysaccharides" OR "glycan*" OR "galactooligosaccharide" OR "galactooligosaccharides" OR "xylooligosaccharide" OR "xylooligosaccharides" OR "oligosaccharide" OR "oligosaccharides" OR "mannanoligosaccharide" OR "mannanoligosaccharides" OR "inulin" OR "phenolic acid" OR "phenolic*" OR "volatile fatty acid" OR "volatile fatty acids" OR "Dietary Supplement*" OR "tannin" OR "tannins" OR "flavonoid*" OR "tilbenes" OR "lignan" OR "lignans" OR "terpenoid*" OR "carotenoid*" OR "Phytotherapy" OR "phytotherapies" OR "phytotherapeutics" OR "Plant Extract" OR "Plant extracts" OR "terpenoids" OR "terpenes" OR "carotenes" OR "carotene" OR "tetraterpene*" OR "isoprenoid*" OR "neolignan*" OR "FOS" OR "MOS" OR "cellooligosaccharide" OR "cellooligosaccharides")</p>	35,368
#3	<p>ab("Calf" OR "calves" OR "veal" OR "preweaned dairy heifers") OR ti("Calf" OR "calves" OR "veal" OR "preweaned dairy heifers")</p>	5,669
#4	#1 AND #2 AND #3	79

Total Records	Total Records after deduplication
3,778	Not performed at this date



Table 1. Definition of main and secondary outcomes.

<b>Outcome</b>	<b>Definition</b>
Average daily gain	rate of weight gain per day over a specified period
Feed efficiency	ratio of feed intake to live weight gain
Body traits	indirect method to estimate the body weight
Heart girth	circumference of the animal just behind the withers
Body length	distance from the point of the shoulders to the ischium.
Hip width	distance between the left and right of femurs
Wither height	distance from the floor beneath the calf to the top of the withers directly above the center of the shoulder
Dry matter intake	amount of feed consumed per day on a moisture-free basis
Papilla length	distance from the tip to the base of the papilla along its axis
Papilla width	measure of the halfway of perpendicular papilla length
Ruminal pH	hydrogen ion concentration in rumen content
Volatile fatty acid concentration	concentration of acetate, propionate, and butyrate in the rumen content
Beta-hydroxybutyrate	measurement of the concentration of this ketone body in blood
Glucose	measurement of the concentration of this hexose in blood
Immunoglobulin	measurement of the concentration of IgG, IgA, IgM or IgE in blood
Fecal score	visual evaluation of the fecal consistency and an indirect indicator of the severity and the presence of diarrhea
Diarrhea incidence	proportion of the calves identified as diarrheic within a specified period
Pneumonia incidence	proportion of the calves identified with pneumonia within a specified period
Mortality	number of calf deaths during the specific time
Cytokines	concentration of signaling proteins that can be pro- or anti-inflammatory in blood
Days on treatment	the duration of systemic therapy that calves received during the experimental time
Microbiota	the microorganisms present in the rumen or gut
Microbiome	the total genome of microorganisms that reside in the rumen or gut

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