Turkish Journal of Veterinary and Animal Sciences

http://journals.tubitak.gov.tr/veterinary/

Research Article

Turk J Vet Anim Sci
(2022) 46: 58-66
© TÜBİTAK
doi:10.3906/vet-2103-35

# Effects of probiotic supplementation for piglets in a nursery: a meta-analysis of controlled randomized studies

**Isabella Cristina de Castro LIPPI*, Larissa Braganholo VARGAS, Fabiana Ribeiro CALDARA, Henrique Biasotto MORAIS, Jean Kaique VALENTIM, Janaína Palermo MENDES**

Department of Animal Science, College of Agricultural Sciences, Federal University of Grande Dourados, Dourados, Brazil

**Received:** 10.03.2021 • **Accepted/Published Online:** 21.11.2021 • **Final Version:** 23.02.2022

**Abstract:** The objective of this article was to evaluate the effect of probiotic addition on average daily gain and feed conversion on the final piglet nursery phase. This study used a systematic review by meta-analysis to contrast the effect of piglets supplementation without antibiotics (negative control) and with antibiotics (positive control). These results archived a dichotomy that suggests a need for different statistical treatments to evaluate these outcomes obtained by articles. Because of this, a metaanalysis evaluation is justified to identify the animal performance on probiotic or antibiotic supplementation conditions. The use of probiotics improved the feed conversion in the experiments that used NC and PC, as well as improved the weight gain in those that used NC. It is concluded that the restoration of the intestinal flora by the supply of probiotics with a positive effect on the intestinal tract decreases the risk of diarrhea and causes better absorption of nutrients.

**Key words:** Forest plot, intestine, Lactobacilli, microflora, microorganisms, weaning

## 1. Introduction

In intensive systems of pig production, piglets are weaned early at the 3rd and 4th week of life, which is characterized as one of the most critical periods in production. During that time, piglets face different stress situations, such as complex social changes, separation of their mothers and their litter of origin, cohabitation with different litters, high housing density, changes in diet and environment, leading to the occurrence of a variable period of hyporexia or anorexia [1]. In addition, this drastic series of changes occurs when animals still have the immature immune system, low thermoregulation capacity, limited digestive capacity with incomplete digestion of nutrients [2], unstable intestinal microbiota, and changes in the intestinal epithelium [3].

Weaning consists, therefore, a phase that the performance of the piglets is seriously compromised [4], and the animals are predisposed to the excessive growth of opportunistic pathogens like Salmonella or Escherichia coli [5]. This process and changes in this period are called post-weaning syndrome and have been extensively studied and revised once that, besides compromising the welfare of the pigs, it causes extensive economic losses [2, 6].

To overcome the adversities of the post-weaning syndrome, the use of antibiotics in the diet has traditionally been used. However, regions such as Europe prohibit the use of antibiotics as growth promoters (Regulation (EC) No 1831/2003), and world authorities are pressuring to limit the use of antibiotics as additives. Due to this scenario, the pig industry and researchers are making great efforts to find strategies of biosafety, management [6], and feeding [4] in order to help and mitigate the challenges suffered by piglets at weaning.

Among the various weaning aid strategies, nutritional care has received increasing attention in recent years, and the use of probiotics to supplement the beneficial microbiota of the gastrointestinal ecosystem [7] has been widely documented due to its ability to reduce digestive disturbances and improve performance rates, ensuring the development and health of the animals [8, 9]. However, not all the research conducted with pigs showed beneficial effects of the addition of probiotics [10, 11]. The results of the use of probiotics have been characterized as inconsistent and of low applicability in the commercial farms' scenario. Thus, although some studies point to the use of probiotics in the diet as a potential substitute for antibiotics, many producers do not consider them reliable.

Considering the increase in research evaluating the use of probiotics as performance enhancers observed in recent years, this study aims to provide an in-depth

* Correspondence: Kaique.tim@hotmail.com

analysis of published scientific data. The dichotomy of the results achieved in such studies needs to be reviewed and treated with statistical techniques, which allow a quantitative evaluation of the results, so it is justified to perform a meta-analysis. Systematic reviews accompanied by a metaanalysis can reduce multiple biases inherent in traditional verifications and should clearly indicate the criteria used in the selection and evaluation of selected scientific articles in the subject under review [12].

The objective of this systematic review using metaanalysis was to evaluate the effect of probiotic addition on the average daily gain and feed conversion in pigs supplemented with probiotics in the post-weaning phase, contrasting the results with the use of negative control (without the addition of antibiotics - NC) and positive control (with the addition of antibiotics - PC).

## 2. Materials and Methods

### 2.1. Criteria for Selecting Articles

Initially, bibliometric research was conducted, which directs bibliographical research to the production of a metaanalysis [13]. This step consisted of defining the databases and the keywords to be used in the search of the articles used in the metaanalysis.

Therefore, the following electronic databases of scientific data were searched: *Science Direct, Web of Science, Google Scholar,* and *Scopus*, using the associated terms in plural or singular form as follows: "Probiotics, piglets and weaned" and "Probiotics, antibiotics, piglets and weaned".

The search period was between 2000 and 2018. After the selection of articles through the bibliographic search, a test of relevance was applied: a questionnaire in which criteria for inclusion or exclusion of the articles was established, consisting of questions related to the characteristics of the work, which generated an affirmative or negative response [14]. The answers to the questions were made through the reading of the title, materials and methods, and part of the results of the articles of the bibliographic search. Three reviewers independently answered "yes" or "no" to the questions. The questions asked for the relevance test were as follows:

- Is the article published in the period 2000 to 2018?
- Was the article found in one of the four databases selected for research?
- Does the article contain negative and/or positive control?
- Does the article analyze the variable weight gain and/or feed conversion?
- Does the article use pigs in the nursery phase?

Through the keywords searched within the databases, were found an amount of approximately 12206 files that matched the theme. Using the questionnaire mentioned above were initially selected 60 articles that studied the use of probiotics for piglets in the nursery phase. By increasing the selection criteria and considering whether all the works contained the necessary information that answered the problem and corresponded to the objectives of the study, 19 articles were found out (Table).

### 2.2. Data analysis

Through spreadsheets in Excel, the relevant data corresponding to the objective for performing the statistical analysis were separated. These data involved feed conversion and weight gain rates of piglets that were submitted to probiotic supplementation and negative control (no probiotic) and probiotic and positive control (antibiotic) treatments.

### 2.3. Statistical analysis

Statistical analyses were performed in the RStudio.Ink program, using the *meta* package and *metacont* command for continuous data. Because the analysis performed was based on continuous variable data, the effect measured on the results was the difference of means (DM) between the treatment with probiotics and the controls, with a confidence interval of 95% using effects model by chance. The heterogeneity of effect size across trials was tested by I2 statistic. Generating forest plots is the next step after extracting data from studies eligible for metaanalysis; a forest plot displays the effect estimates and confidence intervals of individual studies and their meta-analysis.

## 3. Results

Among the 36 studies used to evaluate the effect of probiotics on feed conversion, three studies were conducted before 2010 and the remainder after. Twenty-five experiments were conducted using only one species of probiotic microorganism to evaluate feed conversion, while eleven used various strains of microorganisms.

On the other hand, thirty experiments could be included to evaluate the impact of probiotic supplementation on weight gain, with three studies conducted before 2010 and the remainder after. Among these, nineteen experiments were performed with single species of probiotic microorganism, while eleven used different strains of microorganisms.

### 3.1. Feed conversion

Among the 19 articles that met the inclusion criteria for feed conversion evaluation, 23 experiments (778 animals) used probiotic treatment and negative control, without the addition of antibiotics, while 13 experiments (330 animals) conducted the research with probiotic supplementation and positive control (with antibiotic).

Observing the summarized effect, the probiotics significantly improved the feed conversion of the pigs when compared to the negative control (MD = –0.1492 kg food/kg of body weight gain, 95% CI: -0.1699 to –0.1305 kg food/kg body weight, ($p < 0.0001$) in the mean difference

**Table**. Selected articles for metaanalysis.

| *Paper Reference* | *Year of publication* | *Journal* |
|---|---|---|
| Xuan et al. *Study on the development of a probiotics complex for weaned pigs* | 2001 | *Asian-Australasian Journal of Animal Sciences* |
| Huang et al. *Effects of Lactobacilli on the Performance, Diarrhea Incidence, VFA Concentration and Gastrointestinal Microbial Flora of Weaning Pigs* | 2003 | *Asian-Australasian journal of animal sciences* |
| Broom et al. *Effects of zinc oxide and Enterococcus faecium SF68 dietary supplementation on the performance, intestinal microbiota and immune status of weaned piglets* | 2005 | *Research in Veterinary Science* |
| Giang et al. *Growth performance, digestibility, gut environment and health status in weaned piglets fed a diet supplemented with potentially probiotic complexes of lactic acid bacteria* | 2010 | *Livestock Science* |
| Mair et al. *Impact of inulin and a multispecies probiotic formulation on performance, microbial ecology and concomitant fermentation patterns in newly weaned piglets* | 2010 | *Journal of Animal Physiology and Animal Nutrition* |
| Vrotniakienė et al. *Effects of probiotics dietary supplementation on diarrhea incidence, fecal shedding of Escherichia coli and growth performance in post-weaned piglets* | 2013 | *Veterinarija ir Zootechnika* |
| Ahmed et al. *Evaluation of Lactobacillus and Bacillus-based probiotics as alternatives to antibiotics in enteric microbial challenged weaned piglets* | 2014 | *African Journal of Microbiology Research* |
| Dong. et al. *Effects of dietary probiotics on growth performance, faecal microbiota and serum profiles in weaned piglets* | 2014 | *Animal Production Science* |
| Prieto et al. *Evaluation of the Efficacy and Safety of a Marine-Derived Bacillus Strain for Use as an In-Feed Probiotic for Newly Weaned Pigs* | 2014 | *Plos One* |
| Hu et al. *Dietary Enterococcus faecalis LAB31 Improves Growth Performance, Reduces Diarrhea, and Increases Fecal Lactobacillus Number of Weaned Piglets* | 2015 | *Plos One* |
| Liu et al. *Effects of Lactobacillus brevis preparation on growth performance, fecal microflora and sérum profile in weaned pigs* | 2015 | *Livestock Science* |
| Qiao et al. *Effects of Lactobacillus acidophilus dietary supplementation on the performance, intestinal barrier function, rectal microflora and serum immune function in weaned piglets challenged with Escherichia coli lipopolysaccharide* | 2015 | *Antonie van Leeuwenhoek* |
| Jorgensen et al. *Effects of a Bacillus-based probiotic and dietary energycontent on the performance and nutrient digestibility of wean to finish pigs* | 2016 | *Animal Feed Science and Technology* |
| Peréz et al. *Effect of probiotic strain addition on digestive organ growth and nutrient digestibility in growing pigs* | 2016 | *Revista Facultad Nacional de Agronomía Medellín* |
| Li et al. *Effects of Lactobacillus acidophilus and zinc oxide on the growth performance, jejunal morphology and immune function of weaned piglet following an Escherichia coli K88 challenge* | 2017 | *Italian Journal of Animal Science* |
| Chen et al. *Effects of dietary Clostridium butyricum supplementation on growth performance, intestinal development, and immune response of weaned piglets challenged with lipopolysaccharide* | 2018 | *Journal of Animal Science and Biotechnology* |
| Dowarah et al. *Selection and characterization of probiotic lactic acid bacteria and its impact on growth, nutrient digestibility, health and antioxidant status in weaned piglets* | 2018 | *Plos One* |

**Table**. (Continued).

| | | |
|---|---|---|
| Garcia et al. *Beneficial effects of Saccharomyces cerevisiae RC016 in weaned piglets: in vivo and ex vivo analysis* | 2018 | *Beneficial microbes* |
| Wang et al. *Effects of microencapsulated Lactobacillus plantarum and fructooligosaccharide on growth performance, blood immune parameters, and intestinal morphology in weaned piglets* | 2018 | *Food and Agricultural Immunology* |

model considering random effects (Figure 1). Significant heterogeneity was observed in the 23 experiments ($I^2$ = 99, 7%, Q-statistic: p = 0).

The same statistically positive effect of probiotic supplementation on feed conversion was observed when evaluating the summarized effect in the group of experiments using positive control (MD = –0.0624 kg food/kg body weight, 95% CI: –0.0996 to –0.0252 kg food/kg body weight, p = 0.0010) in the mean difference model considering random effects (Figure 2). Significant heterogeneity was observed in the 13 experiments ($I^2$ = 99.9%, Q-statistic: p = 0).

When evaluating the summary effect of probiotic supplementation, there was a significant improvement in feed conversion in experiments using negative control and only one strain of microorganism (MD = –0.1664 kg food/kg body weight, IC 95 %: –0.1891 to –0.1437 kg feed/kg body weight, p < 0.0001, $I^2$ = 99.8%, Q-statistic: p = 0). Similarly, the summary effect of the experiments that used negative control and more than one strain of microorganisms presented feed conversion values in the treatment group statistically lower than in the control group (MD = –0.1085 kg food/kg of body weight, 95% CI: -0.1381 to –0.0789kg of food/kg body weight, p < 0.0001, statistic $I^2$ = 98.9%, Q-statistic: p < 0.0001).

Experiments using positive control and single-strain microorganisms obtained statistically better results on probiotic treatment than on antibiotic use (MD = –0.0723 kg food / kg body weight, IC 95 %: –0.11150 to <0.0296 kg food / kg body weight, p = 0.0009, $I^2$ = 99.9%, Q-statistic: p = 0). Studies that also used antibiotics but used more than one strain of microorganism instead, presented a statistical difference between the control and probiotic groups, favoring the second (MD = –0.0328 kg of food / kg of body weight, 95% CI: –0.0646 to –0.0010 kg feed / kg body weight, p = 0.0432, $I^2$ = 96.5%, Q-statistic: p < 0.001).

Considering the probiotic species included in the studies, experiments using NC and *Lactobacillus spp*. resulted in a summary effect in favor of probiotic (MD = –0.1718 kg food / kg body weight, 95% confidence interval: –0.1987 to –0.1499 kg food / kg body weight, p <0.0001, $I^2$ = 99.7%, Q-statistic: p = 0), as well as the experiments using PC and *Lactobacillus spp*. (MD = –0.0607 kg food / kg body weight, 95% confidence interval: –0.0908 to –0.0307 kg food / kg body weight, p < 0.0001, statistic $I^2$ = 99, 6%, Q-statistic: p <0.0001). Likewise, experiments using NC and *Enterococcus spp.* achieved a probiotic-favorable summary effect (MD = -0.0938 kg food / kg body weight, 95% confidence interval: –0.1272 to –0.0603 kg of food / kg of body weight, p < 0.0001, statistic $I^2$ = 99.8%, Q-statistic: p = 0). On the other hand, the experiments with PC and *Enterococcus spp.* did not present a significant summary effect, and there was no statistical difference between the means of the treatments of the probiotic and control groups (n = 2; DM = -0.0750 kg of food / kg body weight , 95% confidence interval: -0.22220 to -0.0720 kg food / kg body weight, p = 0.3173, $I^2$ = 100% statistic, Q-statistic: p = 0).

The effect of probiotic supplementation on feed conversion was higher when B*acillus spp.* was added in the diet compared to the negative control group (MD = –0.1523 kg food / kg body weight, 95% confidence interval: –0.2365 to –0.0682 kg food / kg body weight, p < 0.0004, $I^2$ statistic = 99.5%, Q-statistic: p < 0.0001). However, the inclusion of *Bacillus spp.* in the groups of experiments that used positive control was not able to lead to an improvement in feed conversion rates, with both treatments remaining without significant differences (MD = –0.0618 kg of food / kg body weight, 95% confidence interval: –0.1528 to –0.0292 kg food / kg body weight, p = 0.1834,$I^2$ statistic = 98.9%, Q-statistic: p < 0.0001).

### 3.2. Weight gain

Of the 22 articles that met the inclusion criteria for weight gain assessment, 10 experiments (270 animals) used probiotic and positive control, with the addition of antibiotics, while 20 experiments (724 animals) conducted the research with probiotic supplementation and negative control without the use of additives.

In the total effect (summarized), probiotics increased piglets weight gain when compared to the negative control (DM = 37.0232 g / day, 95% CI: 27.6763 to 46.3701 g / day, p < 0.0001) in the mean difference model considering effects at random (Figure 3). Significant heterogeneity was observed in the 20 experiments ($I^2$ = 99.4%, Q-statistic: p = 0).

When evaluating probiotic and positive control experiments, supplementation with microorganisms did not differ significantly in piglet weight gain when compared

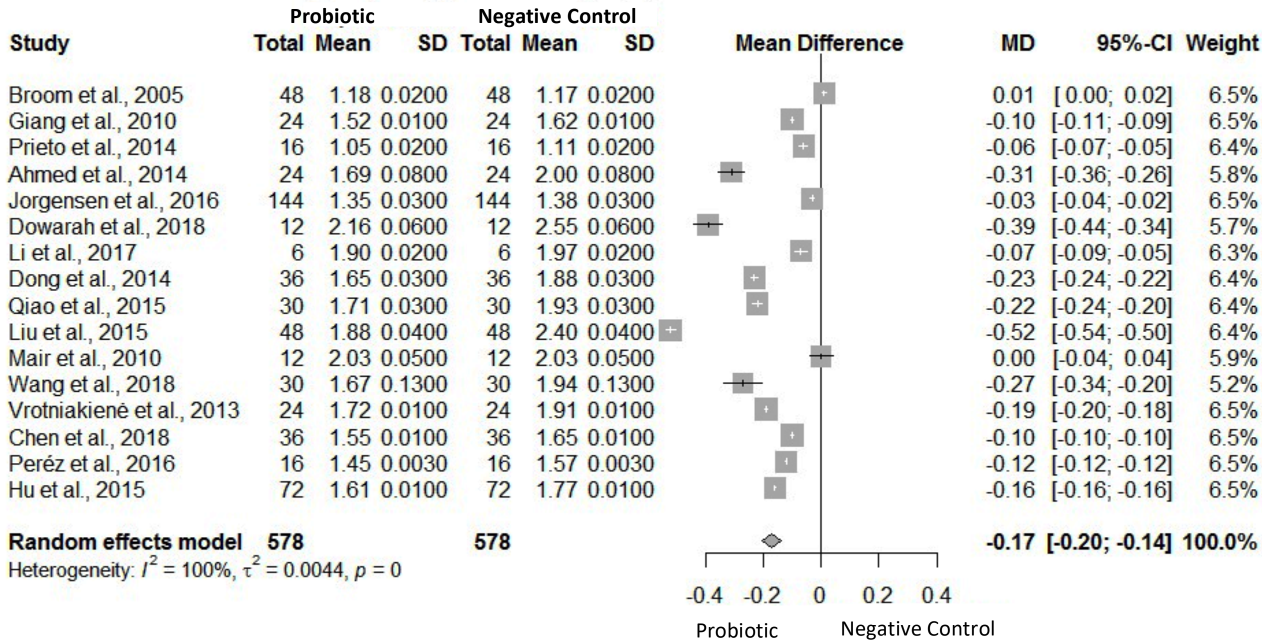


**Figure 1.** Forest plot for Feed conversion: Probiotic X Negative Control. SD: Standard Deviation; MD: Mean Difference; CI: Confidence Interval.

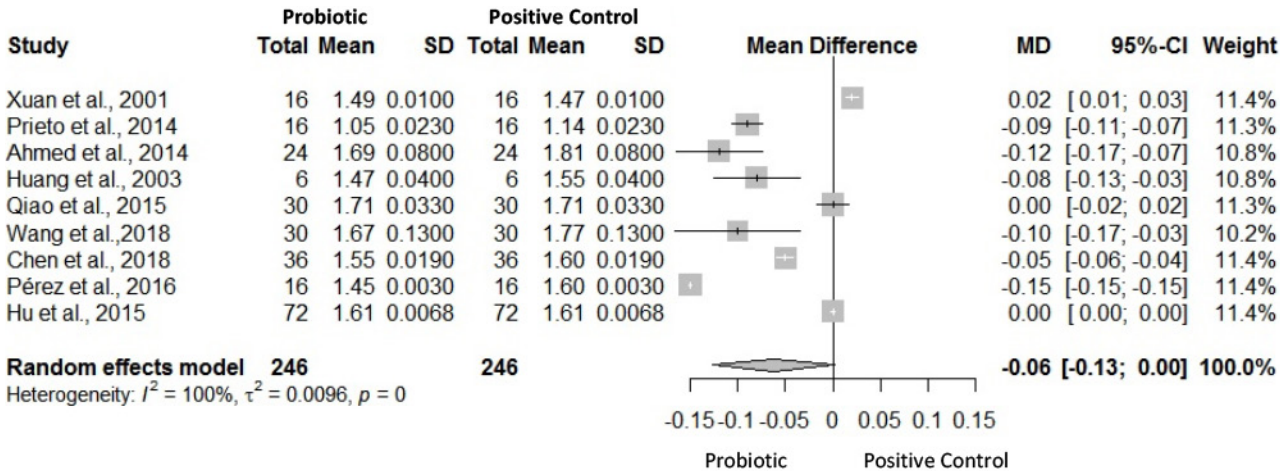


**Figure 2**. Forest plot for Feed conversion: Probiotic X Positive Control. SD: Standard Deviation; MD: Mean Difference; CI: Confidence Interval.

to a positive control (MD = 7.3038 g / day, 95% CI: -6.1546 to 20.7622 g / day, p = 0.2875) in the mean difference model considering random effects (Figure 4). Significant heterogeneity was observed in the 10 experiments ($I^2$ = 99%, Q-statistic: p <0.0001).

Supplementation with probiotic improved weight gain in experiments using negative control and single strain of microorganism (MD = 44.6293 g / day, 95% CI: 29.4146 to 59.8439 g / day, p < 0.0001, statistic $I^2$ = 99.6%, Q-statistic: p = 0), the same beneficial effect of probiotic addition could be observed in the studies using NC and multiple strains (MD = 23.5228 g / day, 95% CI: 19.6814 to 27.3642 g / day, p < 0.0001, statistic $I^2$ = 88.1%, Q-statistic: p < 0.0001)

There was significant improvement in piglet weight gain favoring probiotic supplementation, considering the experiments using PC and single-strain probiotic (MD = 24.0392 g / day, 95% CI: 12.9711 a 35.1073 g / day, p < 0.0001, $I^2$ statistic = 98.1%, Q-statistic: p < 0.0001). However, the use of multiple probiotic strains in the experiments in which the control group was positive provided no improvement in the animals' weight gain, maintaining results without significant differences

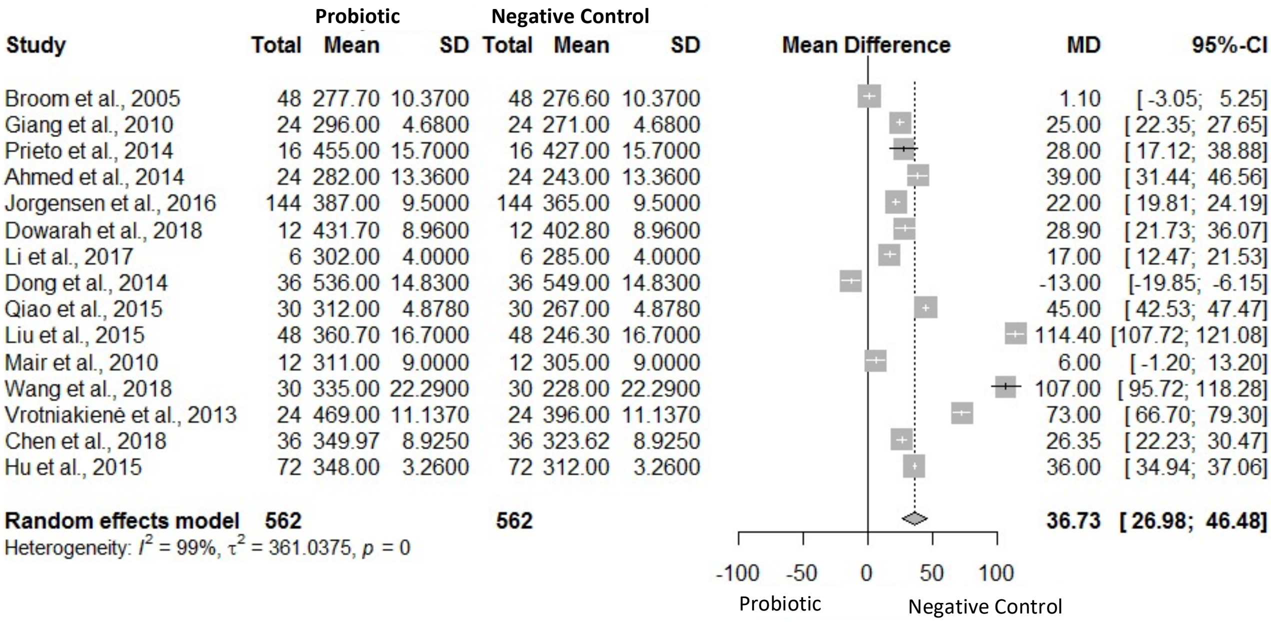


**Figure 3**. Forest plot for Weight Gain: Probiotic X Negative Control. SD: Standard Deviation; MD: Mean Difference; CI: Confidence Interval.

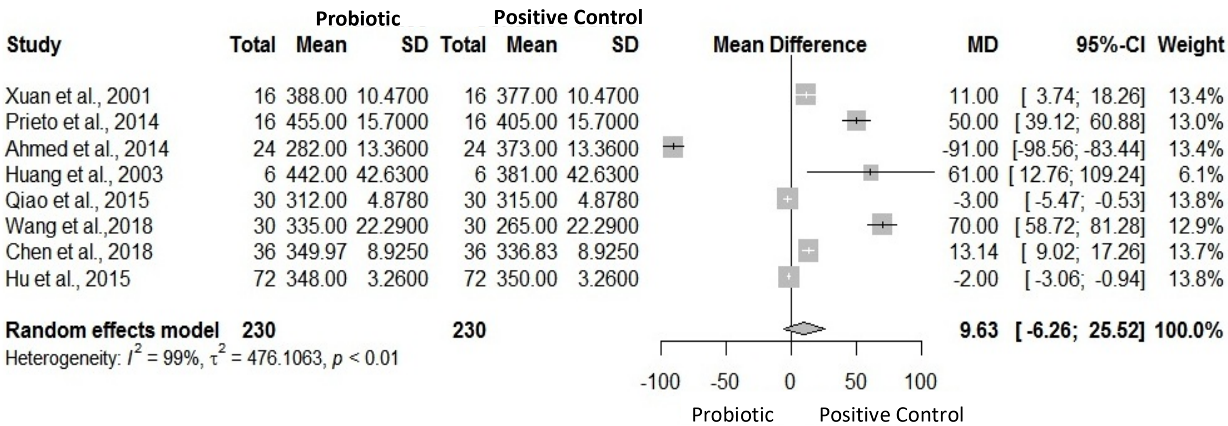


**Figure 4**. Forest plot for Weight Gain: Probiotic X Positive Control. SD: Standard Deviation; MD: Mean Difference; CI: Confidence Interval.

between treatment and control (MD = –12.6978 g / day, 95% CI: –63.5259 to 38.1302, g / day, p = 0.6244, statistic $I^2$ = 99.2%, Q-statistic: p < 0.0001).

In relation to the species of microorganisms that were added in the experiments, NC studies and the use of *Lactobacillus spp.* presented a significant improvement in weight gain with probiotic additive (n = 11, DM = 48.9982 g / day, 95% CI: 32.7749 to 65.22215g / day, p <0.0001, statistic $I^2$ = 99.5%, Q-statistic: p = 0), the same was demonstrated in the studies with PC and the above-mentioned microorganism ( n = 5, DM = 23.1414g / day, 95% CI: 0.0064 to 46.2764 g / day, p = 0.0499, statistic $I^2$ = 97.8%, Q-statistic: p < 0.0001 ). In contrast, the use of *Bacillus spp.* did not present favorable results to the probiotic treatment, and there were no statistically significant differences in means between supplementation and control group in both the negative control (MD = 15.9152 g / day, 95% CI: 3.5942 at 35.4246 g / day, p = 0.1098, statistic $I^2$ = 98.2%, Q-statistic: p <0.0001) and positive control (MD = –13.0680g / day, 95% CI: –91.6887 to 65.5526 g / day, p = 0.7446, statistic $I^2$ = 99.6%, Q-statistic: 0.0001).

## 4. Discussion

The meta-analysis of continuous data from randomized controlled trials showed that probiotic supplementation improved feed conversion in experiments using either negative control (-1.492kg food/kg weight gain) or positive control (- 624g food/kg of weight gain), but in the latter to a lesser magnitude, which is expected since the antimicrobials used as performance enhancers have mechanisms of action that are also linked to the better use of the diet by the animal [15].

Animals in intensive breeding systems are highly susceptible to infection by pathogenic enteric bacteria, which will result in low digestibility, poor nutrient uptake, and, therefore, changes in performance rates [16]. The use of strains of probiotic microorganisms may be associated with modulation of the immune system, also fulfilling a role as a barrier against pathogenic microorganisms and may potentiate zootechnical results, reflecting such benefits as the improvement of feed conversion [17].

The use of probiotics provided an improvement in weight gain in studies that used a negative control (37.0232 g more per day). However, there was no significant difference in weight gain for animals supplemented with probiotics when compared to those whose diets contained antibiotics (positive control). These results were also observed in other studies with antibiotic and probiotic-treated pigs, in which both treatments improved the mean daily weight gain and feed conversion of animals [18].

Using one or several strains of microorganisms may be a determining factor for the success of probiotic supplementation. This is because the activity exerted by different microorganisms may vary, so inoculation of multiple strains can provide more effective and consistent results than only one, since it allows the complementary effect of the probiotic properties of each strain; [19] proposed that multiple strains and multiple species of probiotics have a greater effect than single strains. Probiotic complexes using a mixture of lactic acid bacteria showed a positive effect, improving the performance of weaned piglets [20].

The present study, however, showed numerically better effects for both feed conversion and weight gain when a single strain of microorganisms was used in relation to the results observed for the negative control treatment. Considering the comparison of probiotic supplementation in relation to PC treatments, there was also favorable feed conversion to single-strain probiotics in relation to antibiotics, a result that was not obtained when antibiotics are used as compared to the use of multi-strains of microorganisms.

This divergent result can be explained due to the small number of studies used to obtain the result of this specific condition, so it must be interpreted with caution. It should also be considered that the effect of probiotics will depend not only on the combination of microorganism genera but on their doses and interactions with products added to the diet, food composition, storage, conditions, and technologies used for feeding [21].

Feed conversion and weight gain benefited from the inclusion of *Lactobacillus spp*. in the diet of recently weaned piglets when compared to positive and negative controls. Bacteria of the genus Lactobacillus are natural inhabitants of the gastrointestinal tract of piglets. Its metabolites, which include lactic acid and digestive enzymes, stimulate gastrointestinal peristalsis and promote increased apparent digestibility of nutrients, leading to improved animal appetite [22].

After weaning, the population of lactobacilli drastically reduces [23], resulting in a dysregulated intestinal flora, digestive disorders, and a reduction in production levels. Thus, supplementation with products composed of lactobacilli may present positive results for the performance of pigs. The beneficial results found in the study may be associated with improved digestion of nutrients and the intestinal microbial population [22].

Addition of *Enterococcus spp*. improved the feed conversion in the experiments that used negative control, showing no differences in those who used the positive control. Again, as there were a small number of studies using the above-mentioned microorganism in comparison to the use of antibiotics (PC), such results should be interpreted carefully, deserving more attention in future studies. The effect on feed conversion observed in relation to NC may be related to the ability of this bacterium to reduce or inhibit the proliferation of coliforms and pathogenic bacteria due to its production of antimicrobial substances, such as lactic acid and acetic acid, thus, improving intestinal health and consequently performance [24].

Inclusion of *Bacillus spp*. only showed positive effects for feed conversion in the experiments with negative control; whereas, this same parameter did not present a significant difference in contrasting the effects of the positive and probiotic control. The same absence of significant mean difference was observed for all the experiments that evaluated the weight gain and used this microorganism. The results without significant effects agree with Kritas [25] who, likewise, did not find changes in the weight gain and feed conversion of weaned pigs supplemented with Bacillus spp.

Analyzing the sensitivity of this work, we discuss the high discrepancy of the number of animals (*n*) used in each study. As mentioned before, there were works with *n* of six animals, while others used 144 animals per treatment. A low *n* may negatively influence the statistical results, not demonstrating high reliability, as it happens in the studies with a greater number of animals. Accordingly, [12] found discrepancies between the number of animals of each work used in their metaanalysis.

The chosen theme was brought as a bibliometric result, already with the appropriate exclusions, 19 selected papers. Of these 19 studies, 15.8% were carried out before 2010 and the remainder after 2010. This confirms the idea of [26] that research on the subject was increasing, which in fact occurred. However, there are still many gaps to be filled in to support the replacement of antibiotics with probiotics as performance enhancers.

## 5. Conclusion

The result of this metaanalysis confirms the positive effect of the use of probiotics on weight gain and feed conversion of piglets after weaning. Positive or nonsignificant differences in antibiotics demonstrate the potential of probiotics as a substitute additive to synthetic antimicrobials. However, there is important heterogeneity between the experiments, and, therefore, studies should be conducted to identify the factors that lead to high heterogeneity, allowing greater contribution to demonstrate the positive effects of probiotic addition in the diet of piglets.

**Acknowledgments**
The authors are thankful to the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) for the financial support.

The authors have declared that no competing interests exist.

**Funding**
This study was funded in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) Finance Code 001.

## References

1. Bruininx, EMAM, Van Der Peet-Schwering, CMC, Schrama JW, Den Hartog LA, Everts H, et al. The IVOG® feeding station: a tool for monitoring the individual feed intake of group-housed weanling pigs. Journal of Animal Physiology and Animal Nutrition 2003; 85 (3-4): 81-87. Doi: 10.1046/j.1439-0396.2001.00305.x
2. Lallès, JP, Bosi P, Smidt H, Stokes CR. Weaning a challenge to gut physiologists. Livestock Science, 2007; 108 (1-3): 82-93. Doi: 10.1016/j.livsci.2007.01.091
3. Wang M, Radlowski EC, Monaco MH, Fahey Jr GC, Gaskins HR et al. Mode of delivery and early nutrition modulate microbial colonization and fermentation products in neonatal piglets. The Journal of nutrition 2013; 143 (6): 795-803. Doi: 10.3945/jn.112.173096
4. Lallès JP, Bosi P, Smidt H, & Stokes CR. Nutritional management of gut health in pigs around weaning. Proceedings of the Nutrition Society 2007; 66 (2): 260-268. Doi: 10.1017/S0029665107005484
5. Fouhse JM, Zijlstra RT, Willing BP. The role of gut microbiota in the health and disease of pigs. Animal Frontiers 2016; 6 (3): 30-36. Doi: 10.2527/af.2016-0031
6. Heo JM, Opapeju FO, Pluske JR, Kim JC, Hampson DJ et al. Gastrointestinal health and function in weaned pigs: a review of feeding strategies to control post-weaning diarrhoea without using in-feed antimicrobial compounds. Journal of animal physiology and animal nutrition 2012; 97 (2): 207-237. Doi: 10.1111/j.1439-0396.2012.01284.x
7. Bomba A, Jonecová Z, Koščová J, et al. The improvement of probiotics efficacy by synergistically acting components of natural origin: a review. Biologia 2016; 61 (6): 729-734. Doi: 10.2478/s11756-006-0149-y
8. Meng QW, Yan L, Ao X , Zaho XT, Wang JP et al. Influence of probiotics in different energy and nutrient density diets on growth performance, nutrient digestibility, meat quality, and blood characteristics in growing-finishing pigs. Journal of animal science2010; 88 (10): 3320-3326. Doi: 10.2527/jas.2009-2308
9. Signorini ML, Soto LP, Zbrun MV, Sequeira GJ, Rosmini MR et al. Impact of probiotic administration on the health and fecal microbiota of young calves: a meta-analysis of randomized controlled trials of lactic acid bacteria. Research in Veterinary Science 2011; 93 (1): 250-258. Doi: 10.1016/j.rvsc.2011.05.001
10. Speiser S, Scharek-Tedin L, Mader A, Saalmüller A, Gerner W et al. Immune response of piglets on a PRRSV vaccination—Altered by different feed additives?. Livestock Science 2015; 174: 96-104. Doi: 10.1016/j.livsci.2015.01.010
11. Veizaj-Delia E, Piu T, Lekaj P, Tafaj M. Using combined probiotic to improve growth performance of weaned piglets on extensive farm conditions. Livestock Science 2010; 134 (1-3): 249-251. Doi: 10.1016/j.livsci.2010.06.155
12. Zimmermann JA, Fusari ML, Rossler E, Romero-Scharpen A, Astesana DM et al. Effects of probiotics in swines growth performance: a meta-analysis of andomized controlled trials. Animal Feed Science and Technology 2016; 219: 280-293. Doi: 10.1016/j.anifeedsci.2016.06.021
13. Subramanyam K. Bibliometric studies of research collaboration: A review. Journal of Information Science 1983; 6 (1): 33-38.
14. Uman, LS. Systematic reviews and meta-analyses. Journal of the Canadian Academy of Child and Adolescent Psychiatry, 20 (1): 57.
15. Shon, KS, Hong JW, Kwon OS, et al. Effects of Lactobacillus reuteri-based direct-fed microbial supplementation for growing-finishing pigs. Asian-australasian journal of animal sciences 2005; 18 (3): 370-374. Doi: 10.5713/ajas.2005.370

16. Nousiainen, J, Javanainen, P, Setälä, J, von Wright A. Lactic acid bacteria as animal probiotics. Lactic acid bacteria., 315-356. Doi: 10.1201/9780824752033

17. Baugher, JL, Klaenhammer TR. Invited review: Application of omics tools to understanding probiotic functionality. Journal of dairy science 2011; 94 (10): 4753-4765. Doi: /10.3168/jds.2011-4384

18. Wang S, Yang L, Tang X, Cai L, Liu G, et al. Dietary supplementation with high-dose Bacillus subtilis or Lactobacillus reuteri modulates cellular and humoral immunities and improves performance in weaned piglets. Journal of Food, Agriculture & Environment 2011; 9 (2 part 1): 181-187.

19. Timmerman HM, Mulder L, Everts H, van Espen DC, van dr Wal E et al. Health and growth of veal calves fed milk replacers with or without probiotics. Journal of Dairy Science, 88 (6): 2154-2165. Doi: 10.3168/jds.S0022-0302(05)72891-5

20. Wang W, Chen J, Zhou H, Wang L, Ding S et al. Effects of microencapsulated Lactobacillus plantarum and fructooligosaccharide on growth performance, blood immune parameters, and intestinal morphology in weaned piglets. Food and agricultural immunology 2018; 29 (1): 84-94. Doi: 10.1080/09540105.2017.1360254

21. Chen Y, Kwon O, Min B, Song S, Cho H et al. The Effects of Dietary Biotite V. Supplementation as an Alternative Substance to Antibiotics in Growing Pigs. Asian-Australasian Journal of Animal Sciences 2005; 18 (11): 1642-1645. Doi: 10.5713/ajas.2005.1642

22. Wang Y, Gong L, Wu YP, Wang YG, Huang Y et al. Oral administration of Lactobacillus rhamnosus GG to newborn piglets augments gut barrier function in pre-weaning piglets Journal of Zhejiang University-SCIENCE B 2019; 20 (2): 180-192. Doi: 10.1631/jzus.B1800022

23. Lähteinen T, Rinttilä T, Koort JM, et al. Effect of a multispecies lactobacillus formulation as a feeding supplement on the performance and immune function of piglets. Livestock Science 2015; 180: 164-171. Doi: 10.1016/j.livsci.2015.07.016

24. Saavedra L, Taranto MP, Sesma F, de Valdez GF. Homemade traditional cheeses for the isolation of probiotic Enterococcus faecium strains. International journal of food microbiology, 88 (2-3): 241-245. Doi: 10.1016/S0168-1605(03)00186-7

25. Kritas, SK, Morrison RB, Hermosilla C, Hetzel U, Bausch M et al. Evaluation of probiotics as a substitute for antibiotics in a large pig nursery. Veterinary Record-English Edition 2005; 156 (14); 447-447. Doi: 10.1136/vr.156.14.447

26. Vrotniakienė V, Jatkauskas J. Effects of probiotics dietary supplementation on diarrhea incidence, fecal shedding of Escherichia coli and growth performance in post-weaned piglets. Veterinarija ir Zootechnika 2013; 63 (85).