**Review: The influence of probiotic use in sows and neonatal piglets on performance measures and diarrhoea in suckling piglets.**

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**Background**

The European ban on antibiotics use as a growth promoter in feed, has left the pig industry seeking viable alternatives to prevent losses due to illness and suboptimal growth. Probiotics are already in widespread use in the livestock, poultry and companion animal sectors as an aid in treatment and as a promoter of intestinal health (Chaucheyras-Durand2010). In humans, the efficacy of probiotics has been described with evidence of effects for certain strains of organisms under specific circumstances, such as acute diarrhoea (Allen2010, Parkes2009). Dietary changes can result in major adjustments of the bacterial composition, morphology and micro-flora of the intestinal tract as seen in piglets after weaning often resulting in compromised health (Castillo2007, Konstantinov2006). In piglets, prevention of post-weaning diarrhoea using probiotics has therefore been the focus of much research but is not the only growth phase that could benefit from its use.

*Lactobacilli spp, Bacillus spp, Enterococcus faecium and Saccharamyces cerevisiae* have dominated the research in pig probiotic use. Yeast cultures and fermentation products, though not included in this review, have demonstrated tendencies to improve performance parameters (Kim2010, Shen2011) although Veum et al. (1995) found no effect in a trial. Proposed mechanisms of action of probiotics include: competition with pathogenic bacteria for nutrients and absorption sites; competition for intestinal epithelium binding sites; production of compounds that are toxic to pathogens and by stimulating the immune system (Cho2010, Heo2012). The effect of the probiotics have been measured with bacterial counts in faeces and the intestinal tract, bacterial composition analysis including lactic acid bacteria: coliform ratios, morphological changes to the intestinal villus and immunological changes including inflammatory reactions to infection challenges. Practical applications with effects on performance parameters such as average daily gains, feed conversion, morbidity and mortalities are of great importance to the pig industry.

The gastrointestinal tract of new-born piglets is sterile and the initial colonization takes place through environmental bacteria, primarily from the dam. Thompson et al. (2008) reported that a stable micro-flora occurs after roughly 5 weeks in the piglet and the developmental window in which the gut community is in a transition phase is relatively short. Colonization of the neonatal gut is random and even within the same environment, animals will develop unique bacterial compositions (Thompson2008). Early development of the microbiota is shown to have a long-term influence on intestinal parameters (Jansman2012, Schultz2004) and Harvey et al. (2005) conducted a study with a single dose of probiotic in the neonate and showed lasting effects post weaning. Buddington et al. (2010) showed persistence of L. acidophilus and B. lactis 14 days after birth in piglets with mothers fed probiotics and separated immediately after birth. In the healthy neonate, *Lactobacillus spp* dominant the gastrointestinal tract by day 10 after birth (Petri2010). It is hypothesized that addition of probiotics early in the piglet's life will decrease the colonization of pathogenic bacteria and promote health and growth on a long-term basis by altering the bacterial composition. Germ-free piglets fed a *Lactobacillus* probiotic had lower colonization densities with *Cl. perfringens* (Siggers2008). Demeckova et al. (2002), demonstrated a change in the Lactic acid bacteria:coliform ratio in the faeces of the dam after feeding a *L. plantarum* fermented feed during gestation. This reduces the faecal contamination of the environment by pathogens.

The objective of this systematic review was to search the published literature to evaluate the effect of probiotic use in gestating sows and neonates on performance and health outcomes in piglets up until weaning.

**Methods**

*Search methods*

The literature search was conducted using Pubmed and CAB abstracts on 15 April 2013.The search terms used were limited to title and abstract as follows: (probiotic OR probiotics OR bifidobacteri\* OR pediococc\* OR lactobacil\* OR enterococc\* OR bacill\* OR saccharomyces) AND (pig OR pigs OR sow OR sows OR piglet OR piglets). The results were transferred to EndNote X5 ®, duplicate entries were removed (n=820) and entries before 1990 were removed (n=2981). Titles were screened for relevance, followed by two rounds of abstract screening. Full texts were obtained for the remaining articles deemed to be relevant.

Screening of titles was done by one individual and the removed articles were cross-checked with key-word searches for studies excluded in error. Publications were excluded if considered not relevant to the topic – not related to probiotics (eg. tuberculosis or anthrax), wrong species, later growth phases, in vitro studies and preliminary identification of potential probiotics. During abstract screening, publications were excluded if not clinical trials (intervention with comparator), not in English or Dutch, wrong growth phase (post-weaning), liquid feeds or fermentation cultures, in vitro or isolation studies, wrong species, reviews and non-peer reviewed papers. Full publications were obtained, where possible, using the internet and Utrecht University resources.

*Inclusion criteria*

*Types of studies*

Controlled trials reporting the effect of a probiotic on health or performance measures in the pre-weaned piglet. Trials measuring only immunological, blood parameters or bacterial composition of the gut were not included.

*Types of interventions*

Intervention: Specific, identified probiotic excluding fermented feeds and cultures. Probiotics must have been administered during gestation in sows and/or given to neonates within seven days. Initial exposure of piglets to probiotics should therefore be within 7 days of birth, either directly, or indirectly through the dam.

Comparator: Placebo or no probiotic. Feeding, housing and management the same as for the intervention group.

*Outcome measures*

Primary outcomes: Piglet health or performance measures – pre-weaning mortality, diarrhoea score, weaning weight, average daily gain to weaning.

Secondary outcomes: Sow health or performance measures – litter size and weight, body weight loss during lactation, milk fat and protein content.

*Quality of publication*

Proceedings, theses and books were excluded. Unrecognised journals were investigated online to check if they were peer-reviewed. If it was not explicitly stated on the journal website, then the paper was not considered to be peer-reviewed and was excluded. Papers were evaluated for the quality and completeness of reporting. Only randomised controlled trials were included; if the methodology was not described or the outcomes were not quantified, the paper was excluded.

*Data extraction*

Data was extracted using tables with the predetermined outcome measures. Significant differences were reported where available. Due to the varied nature of the interventions, no meta-analysis was conducted.

**Results**

The initial search resulted in n=2235 potential papers after duplicates had been removed. After the title and abstract screening, a potential 85 full text articles remained. Additional reasons for exclusion were: non-peer reviewed (n=31), incorrect growth phase (n=2), prebiotic or non-specified probiotic (n=9), germ-free piglets (n=3), alternate outcomes (n=7), multiple papers for same trial (n=4) and no full text available (n=13). Three additional papers were found with cross-referencing the main articles. No cross-referenced trials published before 1990 met the inclusion criteria.

Nineteen clinical trials met the inclusion criteria and were included in this report to examine the effects of probiotics in sows during gestation and piglets in their first week of life. Probiotic type, timing and duration of administration, outcome measures and hygiene status varied among the studies. Four studies administered probiotics only to the dam; seven studies to the dam and in the creep feed to the piglets; in seven studies probiotics were given to the piglet within 7 days of birth; and in one study a combination of all three scenarios was used. A summary of the studies can be seen in Table 1, showing product, dose, number of animals and type of farm. Of the nineteen studies, 10 reported at least one outcome to be statistically significant in favour of the probiotic, one reported significance in favour of the control (Taras et al., 2005), one was borderline significant (p=0.057) for one outcome in favour of the control group (Martin et al., 2012), and 7 studies reported no statistically significant effects on these outcomes.

The type of probiotics used varied widely and only two strains were used in more than study, namely, *Bacillus cereus var. toyoi* (Toyocerin), n=2 and *Enterococcus faecium NCIMB 10415* (Cylactin), n=3. The remaining probiotics were *Bacillus cereus CIP5832* (Paciflor), *Enterococcus faecium DSM 7134* (Bonvital), *Saccharomyces cerevisiae*, *B. cereus* (CenBiot), *Lactobaccillus brevis IEI*, *Pediococcus acidilactici MA 18/5M*, *S. cerevisiae boulardi CNCM 1-1077, B. subtilis MP9* and *MP10, Clostridium difficile JGS753.* Combinations of probiotics administered were: *B. licheniformis DSM 5749* and *B. subtilis DSM 5750 (Bioplus 2B); L. acidophilus, B. subtilis and S. cerevisiae* (Farm Pack Y); *L. acidophilus, L. casei, L. plantarum and E. faecium* (Probios)*; L. acidophilus, L. bulgaris, B. subtilis and S. cerevisiae* (Economix).

Figures 2 and 3 show the duration of probiotics given, separated for sows and piglets, indicating studies that gave probiotics to both sows and piglets. The probiotics were administered to sows beginning from 90 days ante partum to 5 days ante partum, and was continued until weaning in all cases. Probiotics were mixed into the feed of sows. In piglets, the beginning of probiotic administration varied from within 24 hours of birth until 7 days in piglet-only studies. In studies where sows and piglets were administered probiotics, the starting day usually coincided with giving creep feed (day 5-15). In two piglet studies, only one dose of probiotics was given within 24 hours of birth (Estienne et al., 2005, Songer et al., 2007). Maneewan et al. (2011) administered probiotics from day 3 till 10 and the remainder of the studies administered probiotics until weaning. The probiotics were administered either directly in a gel or liquid form, or combined in the creep feed. Weaning age differed from 21-28 days of age.

The outcomes for this review (Table 2 and 3) are the piglet health and performance factors of weaning weight, number weaned, mortality during the suckling period, diarrhoea scores and average daily gains (ADG) until weaning. Secondary outcomes for the dam include weight loss during lactation, milk fat and protein percentages. These outcomes were not reported for all studies and in many cases, specific values were not given. For this reason, the table shows significant differences (p<0.05) between treatment and control groups (increase/decrease) or indicates if there was no statistical significance or borderline significance, but does not give actual values for these differences.

The weaning weight was reportedly increased in 5/14 studies and decreased in 1/14 studies when comparing treatment and control groups. 3/12 studies reported an increased number of piglets weaned in the treatments groups. 3/10 studies reported a decrease in piglet mortality in the treatment group prior to weaning. Number weaned and mortality rate are correlated but both are shown in this review due to reporting and methodological differences of the studies. Diarrhoea scores were decreased in the treatment group in 5/8 studies that reported this outcome. Although the study of Taras et al. (2006) was not significant with regard to diarrhoea outcomes during the entire suckling period, it showed a trend in the treatment group (p=0.09) of decreasing diarrhoea in piglets within the first three days after birth. Considering a p-value <0.1 for the ADG before weaning, four studies show an increase, one a decrease and two have no effect.

Regarding the studies in which probiotics were fed to sows, litter size at birth was found to be significantly increased in the treatment groups in 2/10 studies and litter weight increased in one study and decreased in another of these ten studies. Weight loss of the sows during lactation was decreased in the treatment group in 3/8 studies with an additional study of borderline significance. Where milk content was analysed, milk fat percentage (3/4) and milk protein percentage (2/3) were increased in the treatment group. The sampling of the milk in the study with no effect was taken one week later than the other three studies (day 21 vs. day 14/15) and this may have influenced the result.

This was a summary to give an overview of the results reported in the papers. Interpretation of the effect of probiotics as a whole based on these summaries should be made with caution. Due to the variety of probiotics and methodologies, each study needs to be individually evaluated for its merits even though sub-grouping can help identify trends in the effects.

**Additional results**

The performance and health outcomes summarised in Table 2 and 3, were not necessarily the primary outcomes in these studies. Reproductive factors, immunological factors and bacterial counts or identification were performed.

*Reproductive factors*

A decreased weaning-to-service interval was reported in the treatment group by Alexopoulos et al. 2001, however there was no effect seen by three other studies (Alexopoulos et al., 2004, Baker et al., 2013, Stamati et al., 2006). A decreased incidence of MMA was seen in treated sows in the Alexopoulos et al. 2004 and Stamati et al. (2006) studies. In the Jurgens et al. (1997) study, even though there was no significant difference in fat or protein content of milk, there was increase in milk solids and gamma gobulins (p=0.06) which they stated could have a local protective effect on the intestinal mucosa.

*Immunological factors*

Trials exploring the effects of probiotics on the immune system have been included in this review where they met the criteria of reporting performance factors, and is only a limited representation of the studies exploring these factors further. The two studies that examined these outcomes had opposing results but both reported that probiotics can modulate immune cells in pigs.

Mafamane et al. (2011), a Salmonella challenge trial with probiotic *E. faecium*, reported a reduction of CD8+ T cells in the epithelium of probiotic pigs, similar to results found by Schareck et al. (2005). They stated that this decreased the cellular immunity impairing the integrity of the intestinal walls, favouring infection. Despite this immune effect, there was still a decline in pathogens with use of the probiotic *E. faecium* ( Pollmann2005, Schareck2007). Mafamane et al. (2011) theorised that previous exposure to pathogens would result in a competent antibody response that would prevent the new infection, despite the inadequate cellular immunity. However, in the challenge trial, a Salmonella free herd was used and when piglets were exposed to the infection, severe infection resulted with a trend of increased diarrhoea in the treatment group within one month after infection (Szabo et al., 2009, Mafamane et al., 2011). Taras et al. (2006), argued that this decrease in CD8 cells could be indicative of a lower exposure to non-pathogenic microbes and thus represent a healthier gut.

Lessard et al. (2009), reported an increase in CD8+ cells in the ileum when using the probiotic *Pediococcus acidilactici,* possibly boosting cellular immunity. This effect was seen before weaning, but not after weaning, during which time there was a marked decrease in cells. Lessard et al., (2009) commented that the difference in effect compared to the Mafamane et al., (2011) study could be due to the probiotic organism used, administration or sampling methodology between the studies. Lessard et al., (2009) also reported a possible interaction between *P. acidilactici* and *S. cerevisiae* seen by a reduction in CD8 cells. The effectiveness of each probiotic organism should be evaluated individually and in combination, as interactions can have unexpected results.

*Bacterial composition and intestinal morphology*

The numbers of bacteria in the intestine of the piglets was evaluated in a number of studies, the majority of which are not reported here as they did not meet the criteria for the review. Villus length and crypt depth, as an indicator for intestinal health were also measured.

Bohmer et al. 2006 reported no differences in bacterial counts in the piglets. Conversely, four studies reported a lower number of coliforms in the treatment groups. Firstly, Baker et al. (2013), using a terminal restriction fragment technique, reported an increase of *L. gasseri* and *L. johnsonii* in the treatment groups on day three. By ten days of age, the piglets in the control group had increased *Cl. perfringens* and the treatment groups had an increase in *Lactobacillus sp.* Secondly, Gerbert et al. 2011 reported a lower ileal *E. coli* number in the treatment group and in a second experiment saw a lower percentage of *E. coli* in both the ileum and jejunum compared to the control group. In this study, no effects were seen on villus height or crypt depth. Thirdly, at day 7 of age, Maneewan et al. (2011), saw reduced *E.coli* in piglets after the use of probiotic strain *B. subtilis* MP9. By day 11, both strains *B. subtilis* MP9 and MP10 had reduced *E.coli* and *Salmonella spp*. levels compared to the control. *Lactobacillus spp.* and *B. subtilis MP* were higher at both sampling points for both probiotic strains. Lastly, Shim et al. 2005 reported a higher number of *Bifidobacteria* and lower numbers of coliforms in the treatment group. Crypt depth or villus height were unaffected. Martin et al. 2012 also reported no difference in jejunal villus length or crypt depth. Songer et al. 2007 measured toxins for Clostridia as there had been a high correlation between toxin detection in faecal swabs and typhlocolitis in a previous study (Songer2000). Toxin detection was decreased as a result of the use of a non-toxogenic *Clostridium spp.*

**Discussion**

The aim of this review was to identify the piglet performance and health effects after feeding probiotics to sows or to piglets in the first week of life. The hypothesis was that initial exposure to a beneficial micro-flora will influence the intestinal health, and thus performance parameters in a positive way. The criteria for a trial to be included in this review, was that first exposure to the probiotic should take place in the first week of life. An end point for this probiotic use was not initially defined and more than half of the trials continued probiotics in the piglet until weaning. Both Taras et al. (2005) and Taras et al. (2006), showed decreased post-weaning diarrhoea in the treatment group of piglets, but it is difficult to evaluate the contribution to the effect made by the probiotics fed to the dam, as piglets received probiotics in their feed until weaning. The direct effect of probiotics in piglets around weaning has been explored (Kyriakis1999, Heo2012, Turner2001) and this may mask whether early probiotic use, or use in the gestating sow, has added benefit.

For the purpose of answering our research question and excluding the effect of maintaining probiotic use, a subgrouping was made of the sow-only studies and the piglet studies that stopped probiotic use within ten days of birth (n=8). Regarding piglet outcomes in the treatment group, 4/6 studies reported an increased weaning weight in the litters, 2/6 reported decreased mortality, 2/4 reported decreased diarrhoea scores and 3/6 reported increased number of piglets weaned. Two additional papers also reported borderline significance for an increased weaning weight (p=0.06).

Probiotic strains of bacteria were detected in the faeces of piglets prior to directly feeding probiotics to the piglets in the second week of life (Taras et al., 2005, Taras et al., 2006). The probiotics were therefore ingested from the environment or from the dam. It is difficult to measure if this was in sufficient numbers to impact the intestinal health of the piglets. *Bacillus spp.* probiotics tended to have a positive effect on the outcomes, even when only fed to the sow (Alexopoulos et al., 2001, Alexopoulos et al., 2004, Baker et al., 2013, Stamati et al., 2006, Maneewan et al., 2011). The success of the *Bacillus spp*. might be related to the survival of the organism through the intestinal tract of the dam and subsequent uptake by the piglets. The study by Alexopoulos et al. (2001), demonstrates the indirect/ direct effect clearly, as the study consisted of a control group, a group where only sows received probiotics, a group of only piglets receiving probiotics and a fourth group of both sow and piglets receiving probiotics. The mortality and diarrhoea outcomes were only significantly reduced when piglets received probiotics directly from day 5 until weaning and the effect was compounded if both piglets and sows were receiving probiotics. In the group where only sows received probiotics, there was a decrease in these outcomes but it was not statistically significant. Mortality in this study was reported as wasting due to diarrhoea in 92% of the cases.

The hygiene and general disease status on the farm has been reported to have an influence on the effect of probiotics. Janczyk et al. (2010) demonstrated that feed additives have a greater effect on lower hygiene farms. Of our 19 reviewed studies, 7 were field studies, 5 at research institutes and 7 were not specifically reported but are most likely at a high status facility. Of the 7 studies on a commercial farm, 5 reported disease problems on the farm with high diarrhoea or piglet mortalities. 6/7 on-farm studies reported a significant effect on the piglet outcomes, reinforcing the previous reports.

Weaning weight of piglets is influenced by a number of factors including feed. Higher milk fat percentage and a higher milk protein percentage could account for the increased weaning weights of piglets seen by the indirect effect of probiotics fed to the dam (Alexopoulos et al., 2004, Stamati et al., 2006). The increased milk fat percentage is associated with a decreased loss of weight by the sow during the lactation period. Weight changes are, however, also influenced by other factors, and individual weaning weight is correlated to litter size and weight at birth (Beaulieu 2010). Taras et al. (2005), reported a higher piglet birth weight in the control groups and a subsequent higher weaning weight. Reporting on statistical methodology was limited in the majority of studies and it was not always clear if litter size and birth weights were considered when individual weaning weights were reported. In all studies, randomisation to the treatment or control groups was done at the sow or litter level. This resulted in some variation between litter groups with regard to litter size and weight at birth, even though these differences were on average not significant in all but two studies. Cross-fostering within treatment groups to standardise litter size would rule-out the litter size effect as a confounder on individual weaning weight, but would not alter the effect of birth weight. For those studies in which litters were standardised within three days of farrowing, 3/6 studies reported an increase in weaning weight of the piglets.

A significant increase of number of live born piglets were seen in the treatment groups of Baker et al. (2013) and Bohmer et al. (2006); both studies reported no difference in number of stillborn piglets. Litter size is determined by a host of reproductive factors, most of which occur around the conception period, when probiotics were not being fed and therefore, it cannot be assumed that the difference is due to the probiotic. The increase is most likely related to an unobserved effect. It should be noted however, that sow body weight and litter size had been adjusted for in these studies using mixed models.

The organisms, methodologies and reporting for the studies were diverse. Variation in detail of reporting and in methodological factors such as cross fostering and duration of treatment, make comparisons invalid. The quality of the reporting, in many cases, also made review challenging. Evaluation of confounding or bias in the trials was not always clear as experimental setup, blinding, medication use and cross contamination were often not reported.

Publication bias could be present for this study. Even though 10/19 studies reported at least one statistically significant outcome, there were only two studies that reported negative outcomes. The remainder tended to show positive performance results, even though these were not significant. Also, the outcomes examined for this review were not always the primary focus or extensively reported in all papers. Immune modulation, microbial changes or post-weaning effects, which were beyond the scope of this review, were significant in 7/8 papers which had reported no effect for the performance outcomes, reinforcing the possibility of a publication bias.

**Author conclusions**

Specific probiotics such as *Bacillus spp* bacteria show positive results on performance measures in piglets. An association was seen between probiotic use and piglet weaning weight and number of piglets weaned in more than 50% of the studies that fed probiotics to sows or only neonatal piglets. There are differences in the strain of bacterium used and interactions can modify the effects of the bacteria; these and other external influences can impact the results of the probiotics. The limited number of studies per strain do not allow for definitive conclusions, as it is preferable to have multiple studies to corroborate the evidence.

With the decreased use of antibiotic growth promoters, alternatives will be sought by farmers and practitioners alike, even with insufficient evidence. Probiotics are not without risk and the negative effects on the disease course as reported by Mafamane2011, should not be ignored. Cillieborg et al. (2011) reported an increase in necrotising enterocolitis in neonatal piglets with probiotic use and in a human multicentre trial in the Netherlands for probiotic use in acute pancreatitis, a significant increase in mortality was seen in the treatment arm of the study (Besselink2008). Probiotics should not be indiscriminately applied until evidence of the effect is obtained for a specific organism.

Future studies should include detailed descriptions of the probiotic used to the strain level. Testing for CFU levels in the feed of both treatment and control groups should be conducted to rule-out cross-contamination and calculate effective dose. Outcomes need to be well defined, ideally testing for effectiveness against specific pathogens and identifying the reasons for mortality and the pathogens responsible for disease. Statistical analysis should be described in detail. More studies on using probiotics as a potential farm level treatment for an identified problem pathogen are needed. To establish the effectiveness of feeding probiotics to sows and neonatal piglets, further studies are needed that reduce the confounding effect of maintaining probiotic feed until weaning. Immune modulation and changes to micro-flora have been demonstrated. The implications of these changes on pig health and performance need to be expanded further in additional field trials.

Figure 1. Flow diagram depicting the literature search, listing exclusion criteria for papers to the right of the boxes.

Figure 2. Graph showing duration of probiotic used in the sow groups. Day 0 is farrowing and the end point is weaning.

*\*Studies where probiotics were fed to both sows and piglets. ^At least one performance measure significant (p<0.05)*

Figure 3. Graph showing the duration of probiotic fed to piglets. Day 0 is birth and the day of weaning ranges from 21-28 days.

*\*Studies where probiotics were fed to both sows and piglets. ^At least one performance measure significant (p<0.05)*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study** | **Probiotic** | **Dose** | **First day of treatment for piglet** | **Standardized litter size <3 days** | **Farm status (Disease problem)** | **Number of animals** | | **F/u post weaning** |
| **Sows only probiotics** | | | | | | **Control** | **Probiotic** |  |
| Alexopoulos 2001 | ***1.*** *Bacillus cereus CIP5832 (Paciflor)* | 8.5x105 cfu/g feed | Indirect | Yes | Field study  (MMA) | 30 sows | 30 sows | Yes |
| Alexopoulos 2004 | *Bacillus licheniformis DSM5749 + Bacillus subtilis DSM5750 (Bioplus 2B)* | 1.28x106 spores/g feed | Indirect | Yes | Field study  (E.coli diarrhoea) | 55 sows | 54 sows | No |
| Baker 2013 | *Bacillus subtilis (two strains Baker 2008)* | 3.75x105 cfu/g feed | Indirect | Yes | Field study  (High health status) | 102 sows | 103 sows | No |
| Bohmer 2006 | *Enterococcus faecium DSM 7134 (Bonvital)* | 5x108 cfu/g feed | Indirect | *NR* | *NR* | 16 gilts | 17 gilts | No |
| Stamati 2006 | *Bacillus cereus var toyoi (Toyocerin)* | 5x108 spores/g feed | Indirect | Yes | Field study  (E.coli diarrhoea) | 79 sows | 79 sows | No |
|  |  |  |  |  |  |  |  |  |
| **Sows and piglets probiotic** | | | | | | | | |
| Alexopoulos 2001 | ***2****. Bacillus cereus CIP5832 (Paciflor)* | G 3.75x105; P 1x106 cfu/g feed | d5 | Yes | Field study  (MMA) | 15 sows | 15 sows | Yes |
| Jurgens 1997 | ***1****. Saccharomyces cerevisiae* | G 0.1%, L 0.15%, P 0.2% | d12 | Yes | *NR* | 20 sows | 20 sows | Yes |
|  | ***2.*** *Saccharomyces cerevisiae* | G 0.2%, L 0.3%, P 0.4% | d12 |  |  |  | 20 sows | Yes |
| Mafamane 2011 | *Enterococcus faecium NCIMB 10415 (Cylactin)* | G 2.2 x106, L 1.4 x106,  P 7.5x106 cfu/g feed | d15 | *NR* | Research institute (High health status) | 10 sows | 10 sows | Yes |
| Martin 2012 | *Enterococcus faecium NCIMB 10415 (Cylactin)* | G 4.2x106; P 5.1x106 cfu/g feed | d12 | *NR* | Research institute (High health status) | 8 sows | 8 sows | Yes |
| Milenkovic 2011 | ***1****. L. acidophilus + B. subtilis + S. cerevisiae (Farm pack Y)* | 0,10% | d5 | *NR* | Field study | 10 sows | 10 sows | No |
|  | ***2.*** *(Farm pack Y)* | 0,20% | d5 |  |  |  | 10 sows |  |
| Taras 2005 | *Bacillus cereus var toyoi (Toyocerin)* | G 2.6x105, L 4x105,  P 1.3x106 cfu/g feed | d15 | No | (>10% diarrhoea) | 10 sows | 10 sows | Yes |
| Taras 2006 | *Enterococcus faecium NCIMB 10415 (Cylactin)* | G 1.6x106, L 1.2x106,  P 0.17x106 cfu/g feed | d15 | No | (>10% diarrhoea) | 13 sows | 13 sows | Yes |
| Zani 1998 | *Bacillus cereus (CenBiot)* | 0.5-1x106 spores/g feed | d0 | *NR* | Field study (E.coli, rotavirus diarrhoea) | 7 sows | 7 sows | No |
| **Study** | **Probiotic** | **Dose** | **First day of treatment for piglet** | **Standardized litter size <3 days** | **Farm status (Disease problem)** | **Number of animals** | | **F/u post weaning** |
| **Piglets only probiotic** | | | | | | | | |
| Alexopoulus 2001 | ***3.*** *Bacillus cereus CIP5832 (Paciflor)* | 1x106 cfu/g feed | d5 | Yes | Field study  (MMA) | 150 piglets | 150 piglets | Yes |
| Estienne 2005 | *Lactobaccilus + Streptococcus (Probios – Lactobacillus acidophilus, L. casei, L. plantarum, Entercoccus faecium)* | 10x106 cfu/pig/day  Oral suspension | d0 | *NR* | Research institute | 87 piglets | 94 piglets | No |
| Gerbert 2011 | ***1****. Lactobacillus brevis IEI* | 5x109 cfu/pig/day  Milk supplement | d0 | *NR* | Research institute | 5 litters | 4 litters | Yes |
|  | ***2****. Lactobacillus brevis IEI* |  |  |  |  | 9 litters | 9 litters | Yes |
| Lessard 2009 | ***1****. Pediococcus acidilactici MA 18/5M* | 109 cfu x3 per week Lavage | d0 | Yes | Research institute (High health status) | 6 litters | 6 litters | Yes |
|  | ***2****. S. cerevisiae boulardi CNCM 1-1077* | 109 cfu x3 per week Lavage | d0 |  |  |  | 6 litters |  |
|  | ***3****. Pediococcus acidilactici + S. cerevisiae boulardi* | 109 cfu x3 per week Lavage | d0 |  |  |  | 6 litters |  |
| Maneewan 2011 | ***1****. Bacillus subtilis MP9* | 10x1011 cfu/pig/day Suspension | d3 | *NR* | *NR* | 20 piglets | 20 piglets | No |
|  | ***2****. Bacillus subtilis MP10* | 10x1011 cfu/pig/day |  |  |  |  | 20 piglets |  |
| Shim 2005 | *L. acidophilus + L. bulgaris + B. subtilis + S. cerevisiae (Economix)* | 0,30% | d7 | Yes | *NR* | 50 piglets | 50 piglets | No |
| Songer 2007 | ***1****. Clostridium difficile JGS753* | 106 spores/ pig Suspension | d0 | Yes | Field study (Diarrhoea) | 26 litters | 29 litters | No |
|  | ***2****. Clostridium difficile JGS753* | 15x106 spores  Sprayed on teats | d0 |  |  |  | 29 litters | No |
| Zeyner 2006 | *E. faecium NCIMB 10415* | 2.8x109 cfu/g as oral gel | d0-3 | *NR* | *NR* | 60 litters | 54 litters | No |
|  |  | 1.26x109 cfu/pig  Suspension | d4 |  |  |  |  |  |

Table 1. Summary table of included papers showing probiotic used, dosage, method of administration, number of animals in the study and farm type.

*Multiple treatment groups in one study are indicated with 1,2,3 differing by dose, route of administration or probiotic type. NR – not reported; G- gestation feed, L- lactation feed, P- piglet feed.*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study** |  | **Piglet factors** | | | | |
| **Sow only** |  | **Number weaned** | **Weaning weight** | **Mortality** | **Diarrhoea** | **ADG till weaning** |
| Alexopoulos 2001 | ***1.*** *Bacillus cereus CIP5832* | Increase | - | *NS* | *NS* | - |
| Alexopoulos 2004 | *B. licheniformis + B. subtilis* | Increase | Increase | Decrease | Decrease | - |
| Baker 2013 | *Bacillus subtilis* | Increase\* | Increase $ | *NS* | - | Increase\* |
| Bohmer 2006 | *Enterococcus faecium* | Increase\* | *NS* | *NS* | - | - |
| Stamati 2006 | *Bacillus cereus var toyoi* | Increase | Increase | Decrease | Decrease | - |
|  |  |  |  |  |  |  |
| **Sows and piglets** |  |  |  |  |  |  |
| Alexopoulos 2001 | ***2.*** *Bacillus cereus CIP5832* | - | - | Decrease | Decrease | - |
| Jurgens 1997 | ***1.*** *Saccharomyces cerevisiae* | - | *NS* | - | - | - |
| Jurgens 1997 | ***2.*** *Saccharomyces cerevisiae* | - | *NS* | - | - | - |
| Mafamane 2011 | *Enterococcus faecium NCIMB 10415* | *NS* | - | *NS* | - | - |
| Martin 2012 | *Enterococcus faecium NCIMB 10415* | - | *NS* | - | *NS* | Decrease\* |
| Milenkovic 2011 | ***1.*** *L. acidophilus + B. subtilis + S. cerevisiae* | *NS* | Increase | - | *NS* | Increase |
| Milenkovic 2011 | ***2.*** *L. acidophilus + B. subtilis + S. cerevisiae* | *NS* | Increase | - | Decrease | Increase |
| Taras 2005 | *Bacillus cereus var toyoi* | *NS* | Decrease | *NS* | - | - |
| Taras 2006 | *Enterococcus faecium NCIMB 10415* | *NS* | - | *NS* | - | - |
| Zani 1998 | *Bacillus cereus* | - | *NS* | - | Decrease | - |
|  |  |  |  |  |  |  |
| **Piglets** |  |  |  |  |  |  |
| Alexopoulos 2001 | ***3.*** *Bacillus cereus CIP5832* | - | - | Decrease | Decrease | - |
| Estienne 2005 | *Lactobaccilus spp + E. faecium* | - | - | *NS* | - | - |
| Gerbert 2011 | ***1.*** *Lactobacillus brevis IEI* | *NS* | *NS* | *NS* | - | *NS* |
| Gerbert 2011 | ***2.*** *Lactobacillus brevis IEI* | *NS* | *NS* | *NS* | - | *NS* |
| Lessard 2009 | ***1.*** *Pediococcus acidilactici* | - | *NS* | - | - | - |
| Lessard 2009 | ***2.*** *S. cerevisiae boulardi* | - | *NS* | - | - | - |
| Lessard 2009 | ***3.*** *P. acidilactici + S. cerevisiae boulardi* | - | *NS* | - | - | - |
| Maneewan 2011 | ***1.*** *Bacillus subtilis MP9* | - | Increase | - | *NS* # | Increase |
| Maneewan 2011 | ***2.*** *Bacillus subtilis MP10* | - | Increase | - | *NS* | Increase |
| Shim 2005 | *Lactobacillus spp + B. subtilis + S.cerevisiae* | - | *NS* | - | - | *NS* |
| Songer 2007 | ***1.*** *Clostridium difficile JGS753* | *NS* | *NS* | - | - | - |
| Songer 2007 | ***2.*** *Clostridium difficile JGS753* | *NS* | *NS* | - | - | - |
| Zeyner 2006 | *E. faecium NCIMB 10415* | *NS* | - | - | Decrease | Increase |

Table 2. Summary of evaluated outcomes showing change (increase/decrease) if significant (p<0.05) in treatment group (probiotics) compared to the control group for piglet performance factors.

\* p<0.1, *NS – not significant*

*Multiple treatment groups in one study are indicated with 1,2,3. differing by dose, route of administration or probiotic type.*

*# Number of days with diarrhoea significantly decreased*

*$ Subset 550 piglets no longer significant*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Study** |  | **Sow factors** | | | | |
| **Sow only** |  | **Lactation weight loss** | **Live litter size at birth** | **Piglet birth weight** | **Milk fat %** | **Milk protein %** |
| Alexopoulos 2001 | ***1.*** *Bacillus cereus CIP5832* | Decreased | *NS* | *NS* | Increased | - |
| Alexopoulos 2004 | *B. licheniformis + B. subtilis* | Decreased | *NS* | *NS* | Increased | Increased |
| Baker 2013 | *Bacillus subtilis* | Increased\* | Increased | Increased | - | - |
| Bohmer 2006 | *Enterococcus faecium* | *NS* | Increased | *NS* | - | - |
| Stamati 2006 | *Bacillus cereus var toyoi* | Decreased | *NS* | *NS* | Increased | Increased |
|  |  |  |  |  |  |  |
| **Sows and piglets** |  |  |  |  |  |  |
| Alexopoulos 2001 | ***2.*** *Bacillus cereus CIP5832* | - | - | - | - | - |
| Jurgens 1997 | ***1.*** *Saccharomyces cerevisiae* | *NS* | *NS* | *NS* | *NS* | Increased \* |
| Jurgens 1997 | ***2.*** *Saccharomyces cerevisiae* | *NS* | *NS* | *NS* | *NS* | *NS* |
| Mafamane 2011 | *Enterococcus faecium NCIMB 10415* | - | *NS* | *NS* | - | - |
| Martin 2012 | *Enterococcus faecium NCIMB 10415* | - | - | *NS* | - | - |
| Milenkovic 2011 | ***1.*** *L. acidophilus + B. subtilis + S. cerevisiae* | - | *NS* | *NS* | - | - |
| Milenkovic 2011 | ***2.*** *L. acidophilus + B. subtilis + S. cerevisiae* | - | *NS* | *NS* | - | - |
| Taras 2005 | *Bacillus cereus var toyoi* | *NS* | *NS* | Decreased | - | - |
| Taras 2006 | *Enterococcus faecium NCIMB 10415* | *NS* | *NS* | - | - | - |
| Zani 1998 | *Bacillus cereus* | - | - | - | - | - |
|  |  |  |  |  |  |  |

Table 3. Summary of evaluated outcomes showing change (increase/decrease) if significant (p<0.05) in treatment group (probiotics) compared to the control group for sow performance factors.

\* p<0.1, *NS – not significant*

*Multiple treatment groups in one study are indicated with 1,2,3. differing by dose, route of administration or probiotic type.*

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