**A systematic literature mapping and meta-analysis of animal-based traits as indicators of production diseases in pigs**

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animal journal

**Supplementary materials**

# Supplementary Material S1. Search terms used in Web of Science Core collection

**Splayleg**

(TS=(pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR boar OR boars OR porcine OR gilt OR gilts OR pork) NOT TS=("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*")) AND LANGUAGE: (English OR French) AND DOCUMENT TYPES: (Article)(TS=("splay$leg\*" OR "splayleg\*" OR "myofibrillar hypoplas\*")) AND LANGUAGE: (English OR French) AND DOCUMENT TYPES: (Article)

**Osteochondrosis**

(TS=((((osteochondrosis) OR (osteochondros\*)) OR (osteochondritis)) OR (osteochondrist\*)) AND LANGUAGE: (English OR French) AND DOCUMENT TYPES: (Article)(TS=(pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR boar OR boars OR porcine OR gilt OR gilts OR pork) NOT TS=("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*")) AND LANGUAGE: (English OR French)

**Arthrosis (osteoarthrosis)**

(TS=(arthrosis OR arthrose OR arthroses)) AND LANGUAGE: (English OR French) AND DOCUMENT TYPES: (Article)(TS=(pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR boar OR boars OR porcine OR gilt OR gilts OR pork) NOT TS=("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*")) AND LANGUAGE: (English OR French)

**Pododermatitis**

TS= (pododerma\* OR pododermatitis) AND TS= (pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR boar OR boars OR porcine OR gilt OR gilts OR pork) NOT TOPIC: ("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*") Refined by: LANGUAGES: ( ENGLISH )

**Arthitis-polyarthritis-osteoarthritis**

(TS=(polyarthritis OR "poly$arthritis" OR polysarthrit\* OR "poly$arthrit\*" OR arthritis or arthrit\*) AND (TS=(pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR boar OR boars OR porcine OR gilt OR gilts OR pork) NOT TS=("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*"))) AND DOCUMENT TYPES: (Article) AND LANGUAGE: (English OR French)

**Panaritum (Foot Rot)**

(TS=(panaritium OR whitlow OR panaritum\* OR panari\* Or whitlow\*) AND (TS=(pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR boar OR boars OR porcine OR gilt OR gilts OR pork) NOT TS=("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*"))) AND DOCUMENT TYPES: (Article) AND LANGUAGE: (English OR French)

**Rectal prolapse**

"TOPIC: (""rectal\*$prolaps\*"" OR ""prolapsus of the rectum"" or ""rectum$prolaps\*"") AND TOPIC: (pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR porcine OR gilt OR gilts OR pork) NOT TOPIC: (""guinea$pig"" OR ""guinea$pigs""OR ""pig$nosed turtle\*"")

Refined by: LANGUAGES: ( ENGLISH OR FRENCH ) AND DOCUMENT TYPES: ( ARTICLE ) "

**Organ torsion**

TOPIC: (torsion\*) AND TOPIC: (organ\* OR splenic OR spleen OR digestive OR "gastro$intestinal$tract\*" OR "intestin\*" OR liver OR digest\*) AND TOPIC: (pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR porcine OR gilt OR gilts OR pork) NOT TOPIC: ("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*") Refined by: LANGUAGES: ( ENGLISH OR FRENCH ) AND DOCUMENT TYPES: ( ARTICLE )

**Colitis**

TOPIC: (colitis or colitides) AND TOPIC: (pig OR pigs OR piglet OR piglets OR swine OR swines OR porcine OR pork) NOT TOPIC: ("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*")efined by: LANGUAGES=( ENGLISH OR FRENCH ) AND DOCUMENT TYPES=( ARTICLE )Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, CCR-EXPANDED, IC Timespan=All years

**Ulcers**

TOPIC: (ulcer OR ulcers) AND TOPIC: (pig OR pigs OR piglet OR piglets OR swine OR swines OR porcine OR pork) NOT TOPIC: ("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*") NOT TOPIC: ("skin$ulcer$")Refined by: LANGUAGES: ( ENGLISH OR FRENCH ) AND DOCUMENT TYPES: ( ARTICLE )Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, CCR-EXPANDED, IC Timespan=All years

**Post-weaning diarhea**

TOPIC: ("post$weaning" OR "post$wean\*") AND TOPIC: (diarrhoea\* OR syndrom\* OR diarrhea\*) AND TOPIC: (pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR porcine OR gilt OR gilts OR pork) NOT TOPIC: ("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*" OR "post$weaning multi$systemic?wasting?syndrom\*" OR "circovirus") Refined by: LANGUAGES: ( ENGLISH ) AND DOCUMENT TYPES: ( ARTICLE )

**Porcine Respiratory Disease Complex**

TOPIC: ("porcine respiratory disease complex" OR "porcine respirator\* disease\* complex\*" OR "porcine$respirator\*$disease\*$complex\*" OR "respirator\* disease\* complex\*") AND TOPIC: (pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR porcine OR gilt OR gilts OR pork OR boar OR boars OR weaner OR grower\* OR finisher\*) NOT TOPIC: ("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*") Refined by: LANGUAGES: ( ENGLISH ) AND DOCUMENT TYPES: ( ARTICLE OR PROCEEDINGS PAPER OR CORRECTION ) Timespan: 1976-2015. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH.

**Pleuropneumonia**

TOPIC: ("Pleuropneumonia" AND "Actinobacillus pleuropneumoniae" AND "respirator\*") AND TOPIC: (pig OR pigs OR sow OR sows OR piglet OR piglets OR swine OR swines OR porcine OR gilt OR gilts OR pork OR boar OR boars OR weaner OR grower\* OR finisher\*) NOT TOPIC: ("guinea$pig" OR "guinea$pigs"OR "pig$nosed turtle\*") Refined by: DOCUMENT TYPES: ( ARTICLE ) AND LANGUAGES: ( ENGLISH ) Timespan: 1976-2015. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH.

# Supplementary Material S2. Description of the type of interventions applied in studies included in the database

# Management interventions: management practices such as stocking density, climate, ventilation, hygiene and litter conditions directly affect the development of production diseases. As such, studies that employed different management procedures inducing a production disease were included.

# Nutritional interventions: quantitative or qualitative unbalance of feed or nutrient intake are strongly associated with the risk of production diseases. Namely, vitamins A, B, C, D and K, Ca and P dietary supplementation levels are crucial for bone health and abnormalities. As such, studies might employ different nutritional procedures to induce a production disease.

# Administration of pathogens: many production diseases are characterized by the presence of pathogens that being either opportunistic or the causative factor. Administration of pathogens can be used to experimentally reproduce those diseases and can provide meaningful results in relation to their effect on production traits. Those studies were included when the inoculation of the pathogen was used to reproduce the specific production disease of interest. In these studies, the pathogens inoculation was often associated with other etiological factors (animal density, hygiene degradation, and coinfection).

# Administration of toxins, adjuvants or other compounds: contamination of the feed by mycotoxins present is responsible for the development of production diseases. Only studies involving the administration of toxins that clearly induced the development of specific production diseases were included. Similarly studies where adjuvants, hormones or other compounds were administered to induce specific production diseases were included.

# Supplementary Material S3. List of published articles used in the meta-analyses

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**Table S1.** *Categorisation and examples of traits recorded in the database*

|  |  |  |
| --- | --- | --- |
| Groups of traits | General | Specific |
| Productive | Growth performance | Feed intake (daily or per period of measurement): As fed, Dry mater, Gross energy, Digestible energy, Total Nitrogen, Digestible Nitrogen, Digestible dry matter)  Average daily gain, BW, Empty BW, BW change  Feed conversion ratio  Digestibility (DM, Organic matter, Gross energy, Protein, Amino acids, Crude fibre) |
|  | Production performance | Morbidity, Mortality |
|  | Reproductive performance | Cyclicity (Return to œstrus)  Litter characteristics : Survivability, BW, BW gain, Size |
| Entire animal | Anatomical | Back fat thickness and change |
|  | Digestive tract characteristic | Digestive tract weight |
|  | Leg characteristic | Foot lift response to pressure, Thermal sensitivity, Front movement score, Front structure score, Rear hock structure score, Rear movement score, Rear toe size |
|  | Physiological | D mannitol absorption |
| Biochemical | Blood characteristic | Albumin, Globulin, Albumin/globulin ratio, Fibrinogen, Haemoglobin, Platelet  Erythrocyte, Lymphocyte, Macrophage  Total plasma concentration |
|  | Bone characteristic | Concentrations of calcium, of phosphorous |
|  | Enzyme activity | Acetylcholinesterase, Alanine amino transferase, Alkaline phosphatase, Butyryl-cholinesterase, Catalase, Cholinesterase, Creatine kinase, Glutathione peroxidase, Lactacte dehydrogenase, Matrix metalloproteinases-MMP 2 and 9, Myeloperoxidase, Superoxyde-dismutase |
|  | Hormone concentration | Insulin, Cortisol, Melatonin, Prostaglandin E2, 6-keto-prostaglandin F1a |
|  | Immune | Acute phase protein : C reactive protein, Haptoglobin  Immunoglobulins A, G, M  Interleukins, Lymphatic follicle number  lymphocytes : CD (Cluster of differentiation) 3, CD4, CD 4+CD5,CD 8a  Transforming growth factor -alpha, Tumor Necrosis Factor-alpha |
|  | Metabolite concentration | Total protein, Amino acids (Total, Aromatic, Branched chain, Essential, No essential, individual), Urea, Nitrogen from urea  Glucose, Lactic acid, Phospholipid fatty acid, Choline, D-xylose  Minerals : Phosphorus, Potassium, Sodium  Vitamins A, C, E, D  Osteocalcine  Carboxy-terminal telopeptide of type II collagen, Comp cartilage oligomeric matrix protein, C-propeptide of type II collagen, Chondritin sulfate epitope, Carboxy-terminal cross-linked telopeptide fragment of type II collagen, Ictp carboxy-terminal cross-linked telopeptide of type I collagen, Ntx amino-terminal telopeptide of type I collagen, Pyrodinoline cross-link |
|  | Microbiological count | Clostridia, Escherichia coli, Enterobacteriacae, Lactic acid bacteria, Lactobacillus |
|  | Mucus characteristic | Ratio : Fucose/galactose, GalNac/gal, GluNac/gal, Glycopeptides/protein  Mucin concentration, Protein concentration |
|  | Oxidative status | Hydroperoxydes  Blood antioxidant potential |
|  | Protein concentration | Claudine1 |
|  | Protein metabolism | Absolute or fractional synthesis rate of protein (albumin, fibrinogen), Protein turnover |
| Carcass | Bone characteristic | Cross sectional area, Density, Length, Mineral concentration, Weight, Width, Angle |
|  | Carcass yield | Back fat thickness, Length, Percent lean bone, Yield |
|  | Cells characteristic | Beta-adrenoreceptor affinity Kd, nb beta-adrenoreceptorn binding site  Cell apoptosis, Cell density, Cell proliferation |
|  | Digestive tract characteristic | Length, Weight empty, Weight full, Organ weight, Total or organ contents, pH, Mature and immature crypt cells/ratio, Endocrine cells density, Goblet cells, Crypt depth, Villus length, Ratio villus length/ crypt depth, Mucosal thickness, Muscle thickness, Epithelial erosion, Intra epithelial lymphocyte  Acetic, butyric, propionic acid branched chain fatty acid, Total acid concentrations, Nitric oxyde |
|  | Enzyme activity | Adenylate cyclase, Inducible nitric oxide synthase |
|  | Metabolite concentration | AMPc |
|  | Muscle characteristic | Myo fibre diameter, Weight, Length, Cross sectional area, Lean colour |
| Molecular | Gene characterisation | Matrix gamma-carboxyglutamate protein methylation |
|  | Gene expression | Numerous (as an example Caspase, Mucin, Mediators for immunity, NFYB, TLR, ZDHHC9…) |
|  | Protein expression | Interleukins, Tumor Necrosis factor-alpha |
|  | Protein metabolism | Phosphylated Akt, mTOR, S6K1 and Ribosomal protein S6 |

**Table S2** *Screening process of articles*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Physiological system and production disease | | | | | | | | | | | | | | | | | | |  | | |
|  | | | Locomotory system | | | | |  | | Digestive system | | | | |  | | Respiratory system | | |  | |
| Number of | | | Splay-leg | Osteo-chondrosis | Podo-dermatitis | Arthritis | Arthrosis/Osteoarthrosis |  | Rectal prolapse | | Organ torsion | Peptic ulcer | Colitis | PWD | |  | | PRDC | Pleuro-pneumonia | | Total | |
| Records identified through database searching | | | 45 | 178 | 5 | 573 | 32 |  | 22 | | 24 | 592 | 427 | 256 | |  | | 88 | 96 | | 2338 | |
| Records excluded after title and abstract examination | | | 9 | 79 | 5 | 502 | 28 |  | 12 | | 22 | 531 | 339 | 178 | |  | | 60 | 69 | | 1834 | |
| Full text articles assessed for eligibility | | | 36 | 99 | / | 71 | 4 |  | 10 | | 2 | 61 | 88 | 78 | |  | | 28 | 27 | | 504 | |
| Records excluded after full text examination | | | 30 | 88 | / | 66 | 4 |  | 10 | | 2 | 50 | 73 | 72 | |  | | 21 | 21 | | 437 | |
| Studies for construction of the systematic map | | | 6 | 11 | / | 5 | 0 |  | 0 | | 0 | 11 | 15 | 6 | |  | | 7 | 6 | | 67 | |

PWD: post weaning diseases; PRDC: Porcine Respiratory Disease Complex.

**Table S3** *Number of occurrence of traits by trait group for each pig disease*

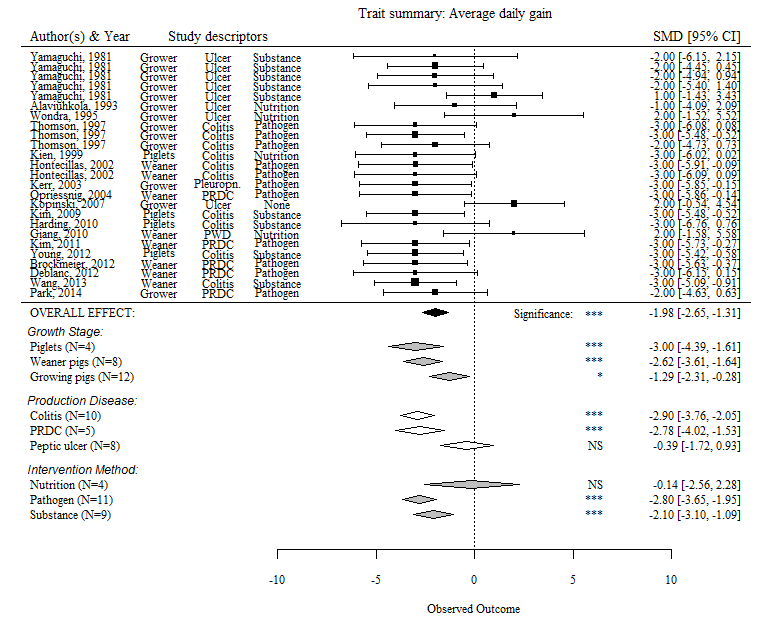
|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Physiological system and  disease | Group of traits | | | | |  | |
| Productive | Entire Animal | Biochemical | Carcass | Molecular | | Total |
| Locomotor system  Arthritis  Lameness  Leg weakness  Osteochondrosis  Splayleg | 2  /  /  4  / | /  4  /  5  / | 9  /  2  16  6 | /  /  17  4  6 | 6  /  /  12  16 | | 17  4  19  41  28 |
| Total | 6 | 9 | 33 | 27 | 34 | | 109 |
| Digestive system  Colitis  Post-weaning diarrhoea  Peptic ulcer | 36  25  58 | 4  /  3 | 87  33  15 | 27  25  13 | 45  /  / | | 199  83  89 |
| Total | 119 | 7 | 135 | 65 | 45 | | 371 |
| Respiratory system |  |  |  |  |  | |  |
| Respiratory disease complex | 9 | / | / | / | 10 | | 19 |
| Pleuropneumonia | 3 | / | 10 | / | 12 | | 25 |
| Total | 12 | 0 | 10 | 0 | 22 | | 44 |

**Table S4** *Categorization of traits recorded across studies for each physiological system of the pig*

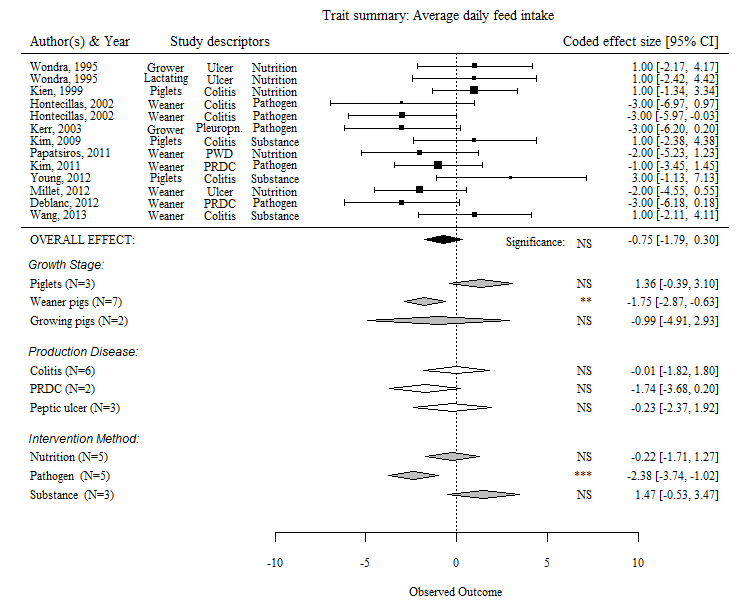
|  |  |  |  |
| --- | --- | --- | --- |
|  | Physiological system | | |
| Groups of traits | Digestive | Locomotor | Respiratory |
| Productive |  |  |  |
| Growth performance | 108 | 6 | 12 |
| Production performance | 1 | / | / |
| Reproductive performance | 8 | / | / |
| Total | 119 | 6 | 12 |
| Entire animal |  |  |  |
| Anatomical | 3 | / | / |
| Digestive tract characteristic | 3 | / | / |
| Leg characteristic | / | 9 | / |
| Physiological | 1 | / | / |
| Total | 7 | 9 | 0 |
| Biochemical |  |  |  |
| Blood characteristic | 15 | 2 | 4 |
| Bone characteristic | / | 2 | / |
| Enzyme activity | 17 | 7 | 2 |
| Hormone concentration | 10 | / | 2 |
| Immunological | 14 | 8 | / |
| Metabolite concentration | 38 | 13 | 2 |
| Microbiological count | 7 | / | / |
| Mucus characteristic | 6 | / | / |
| Oxidative status | 4 | / | / |
| Protein concentration | 1 | / | / |
| Protein metabolism | 23 | 1 | / |
| Total | 135 | 33 | 10 |
| Carcass |  |  |  |
| Bone characteristic | / | 13 | / |
| Carcass yield | 2 | 4 | / |
| Cells characteristic | / | 2 | / |
| Digestive tract characteristic | 62 | / | / |
| Enzyme activity | / | 1 | / |
| Metabolite concentration | / | 1 | / |
| Muscle characteristic | 1 | 6 | / |
| Total | 65 | 27 | 0 |
| Molecular |  |  |  |
| Gene characterisation | / | 1 | / |
| Gene expression | 36 | 26 | 22 |
| Protein expression | 4 | 7 | / |
| Protein metabolism | 5 | / | / |
| Total | 45 | 34 | 22 |
| Total | 371 | 109 | 44 |

**Figures S1 – S14**

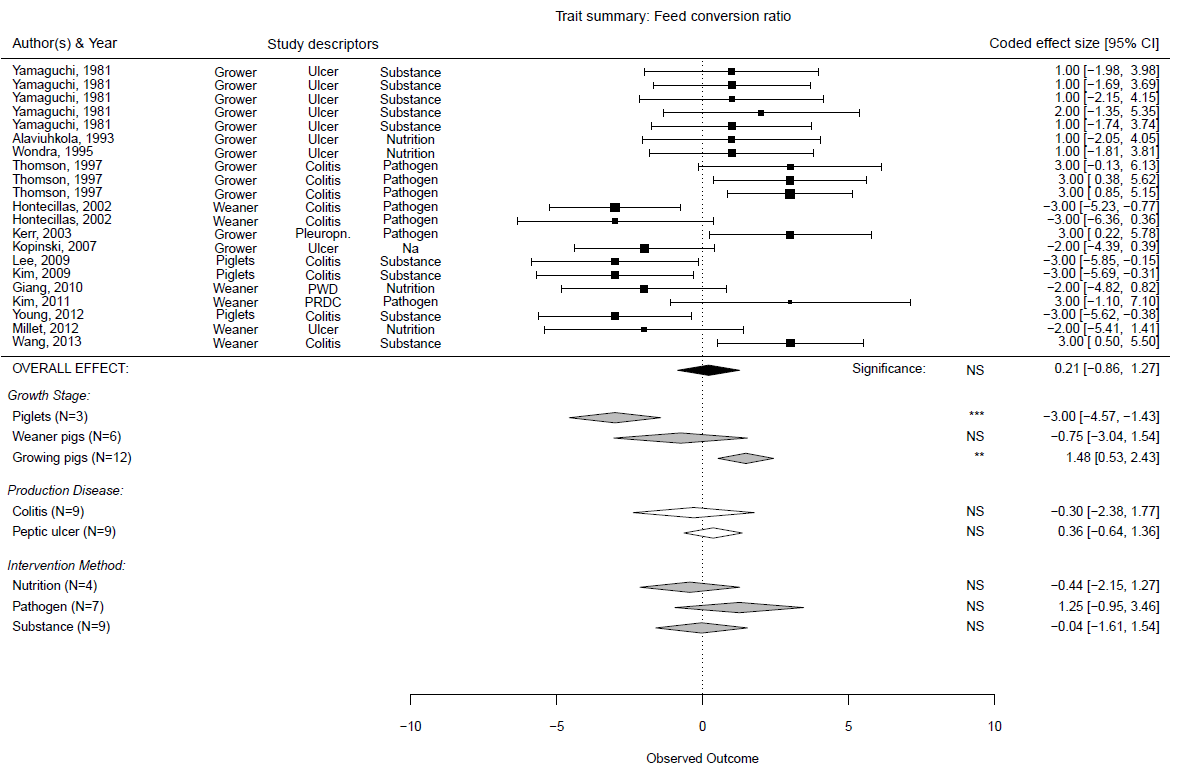
Forest plot showing the results of the comparison of traits between infected and healthy using coded effect size with 95% confidence intervals (CI), for studies included in meta-analysis. The coded effect size for each studies and overall effect for different product groups are indicated at the right of the figures. SMD is the Standardized Mean Difference between infected and healthy groups of pigs and corresponds to the summary effect size. The effect size was coded as 1 when the difference was between 0 and 5%, 2 when it was between 5 and 15% and 3 when it was greater than 15%. Sign of the effect size indicates if the analysed parameter is higher (+) or lower (-) in infected pigs. \*\*\* *P* < 0.001, \*\* *P* < 0.01, \* *P* < 0.05, NS: no significant



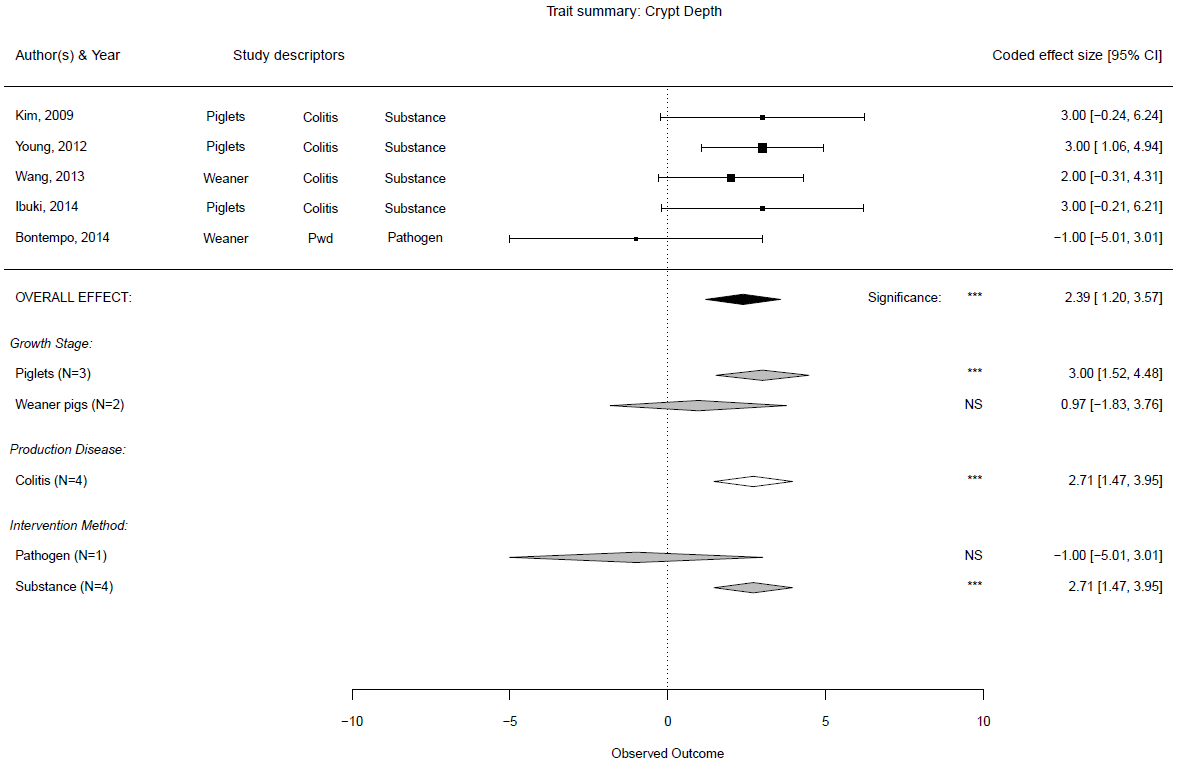
**Figure S1**



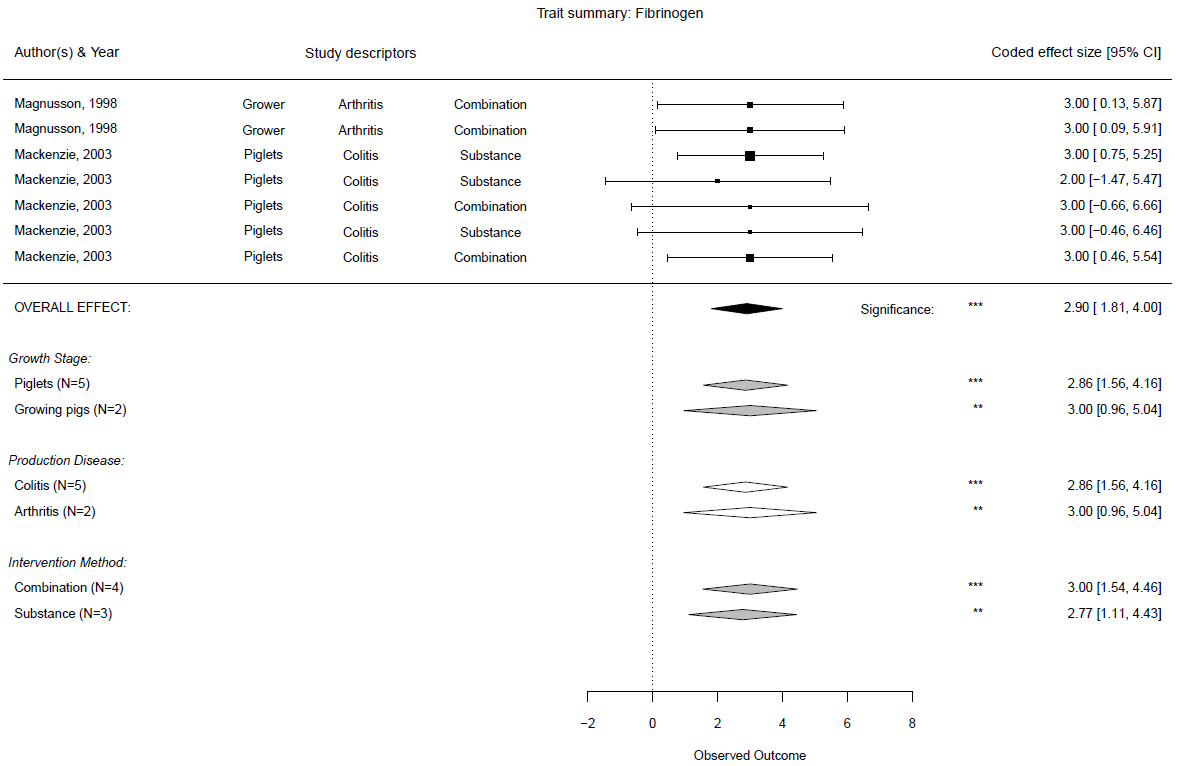
**Figure S2**



**Figure S3**

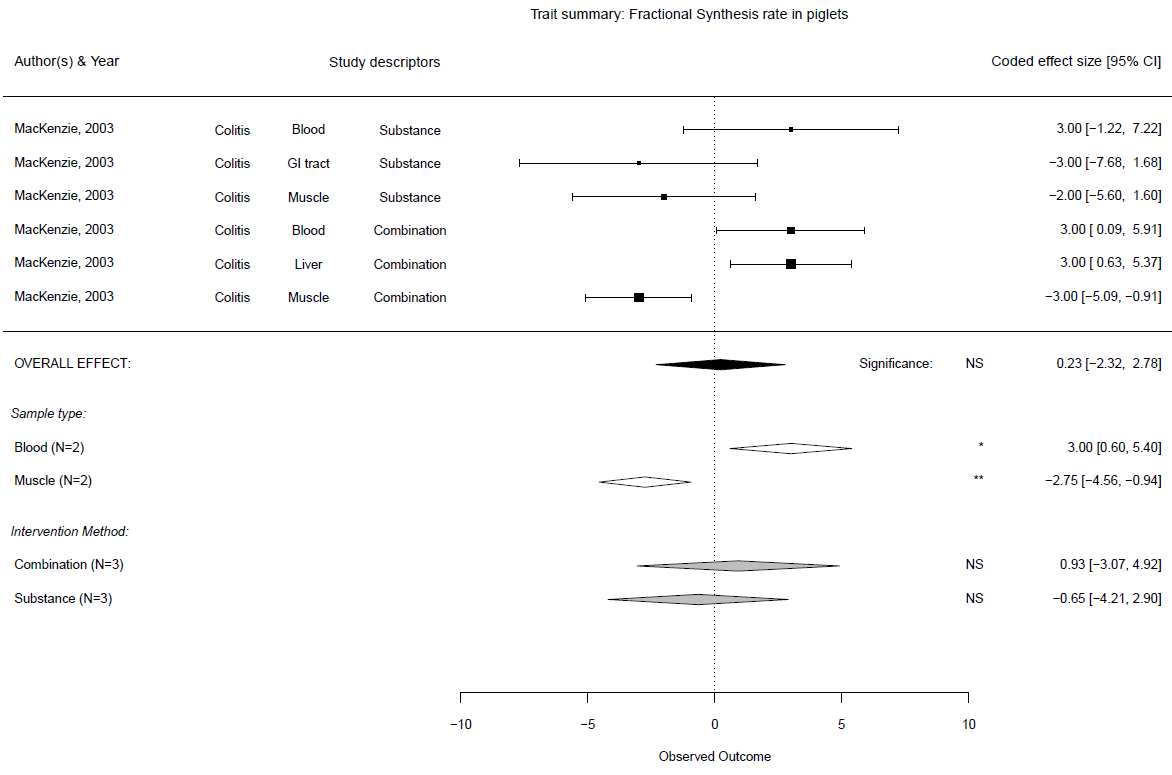


**Figure S4**

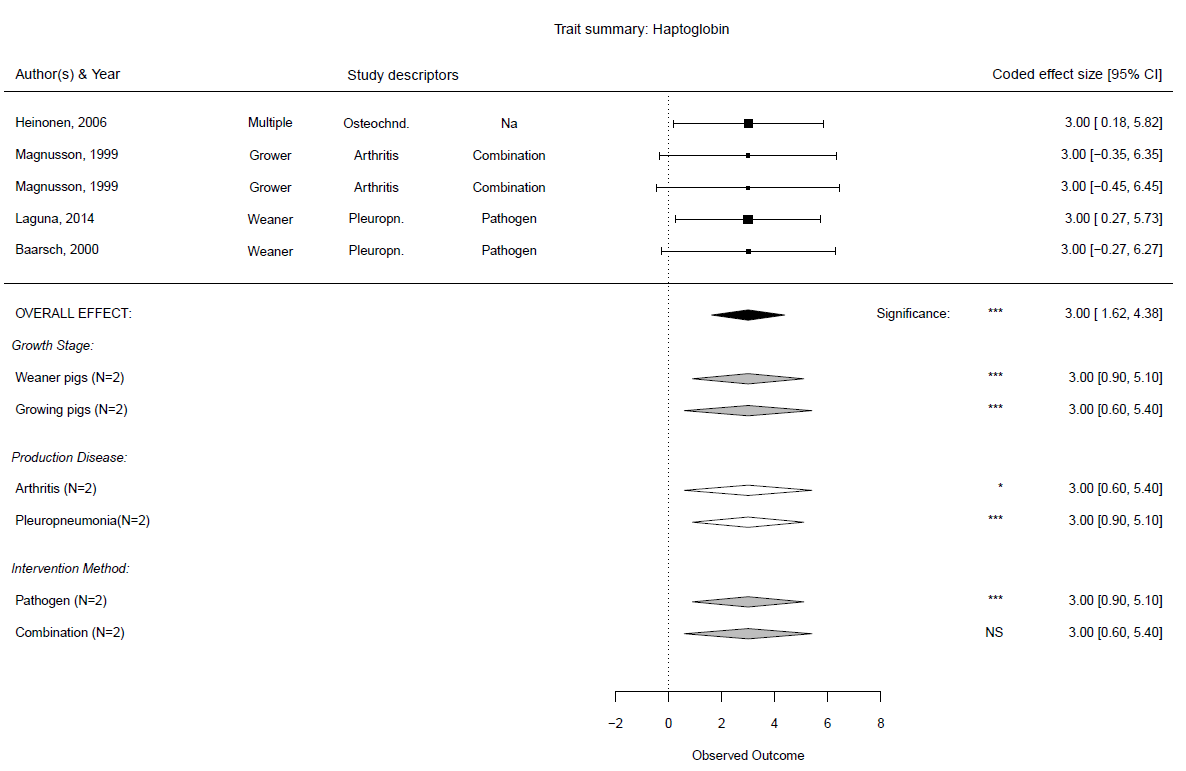


**Figure S5**

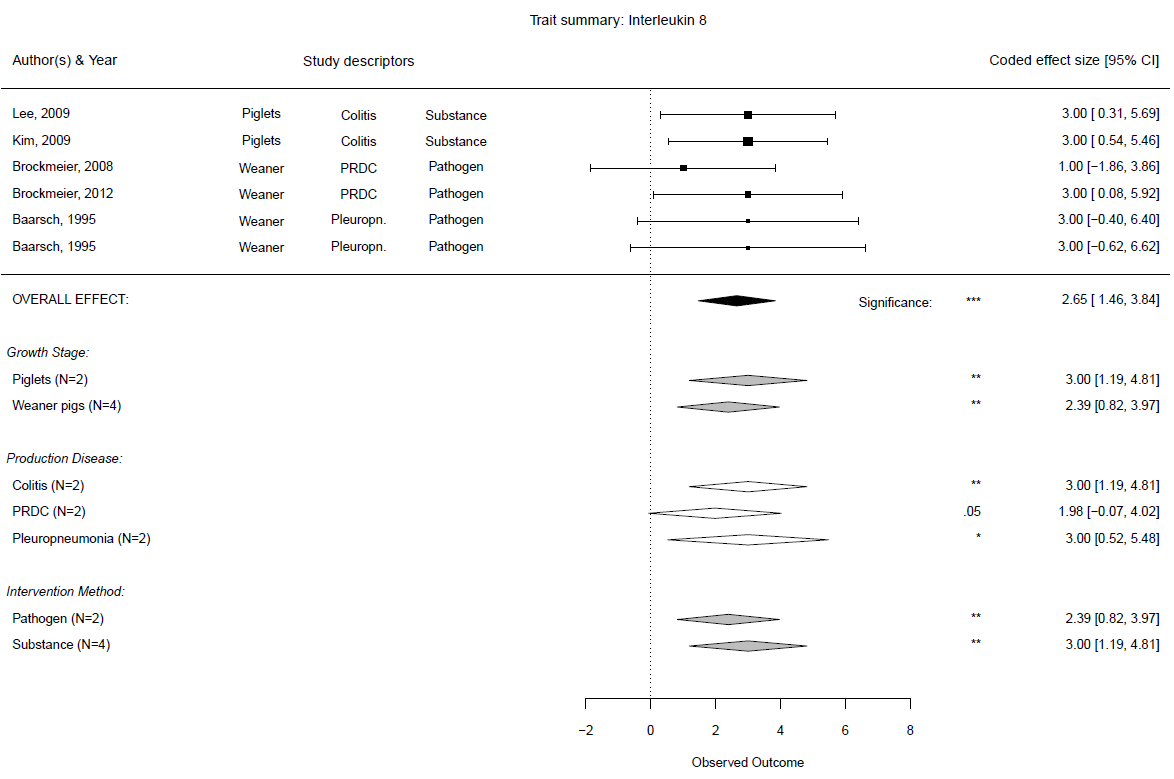
**Figure S6**



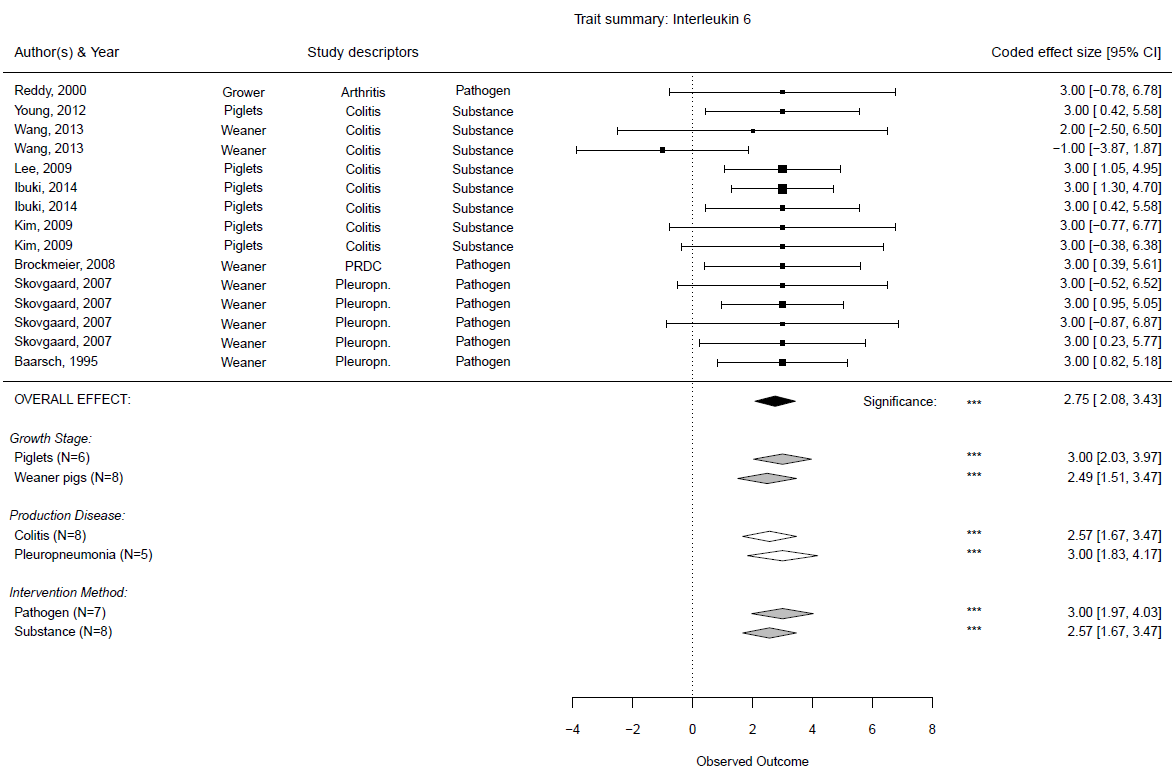
**Figure S7**



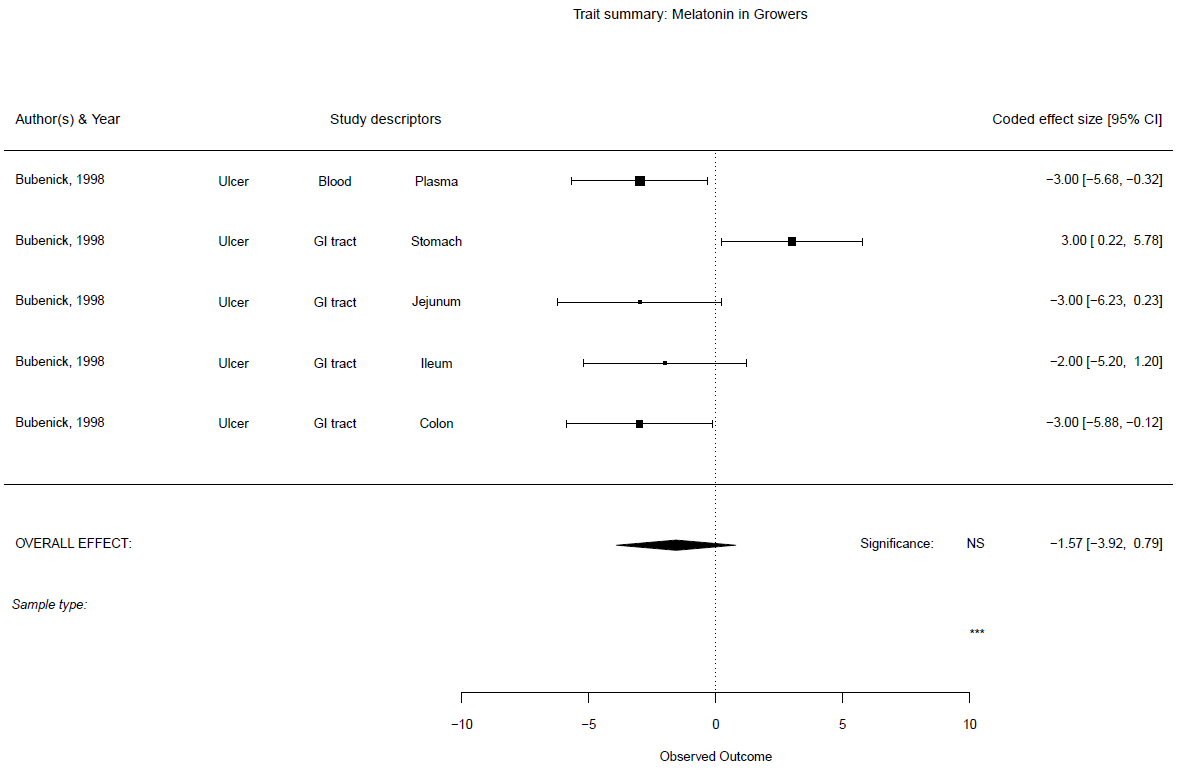
**Figure S8**



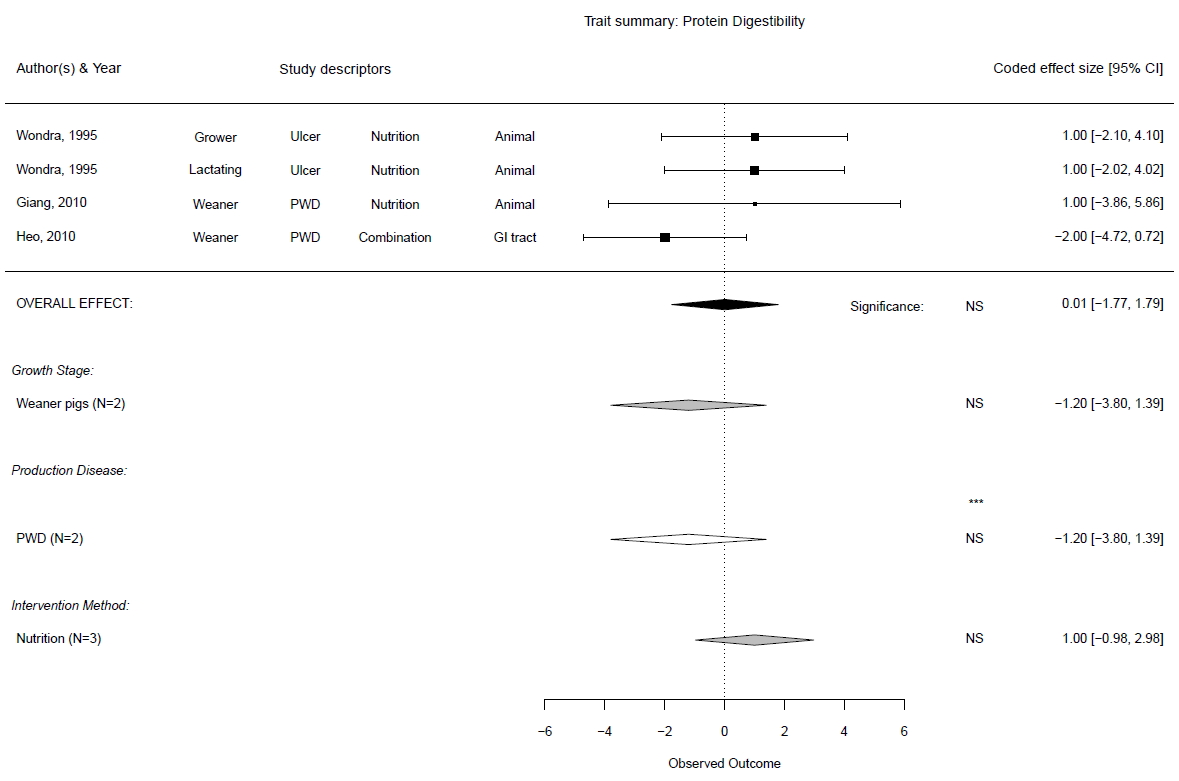
**Figure S9**



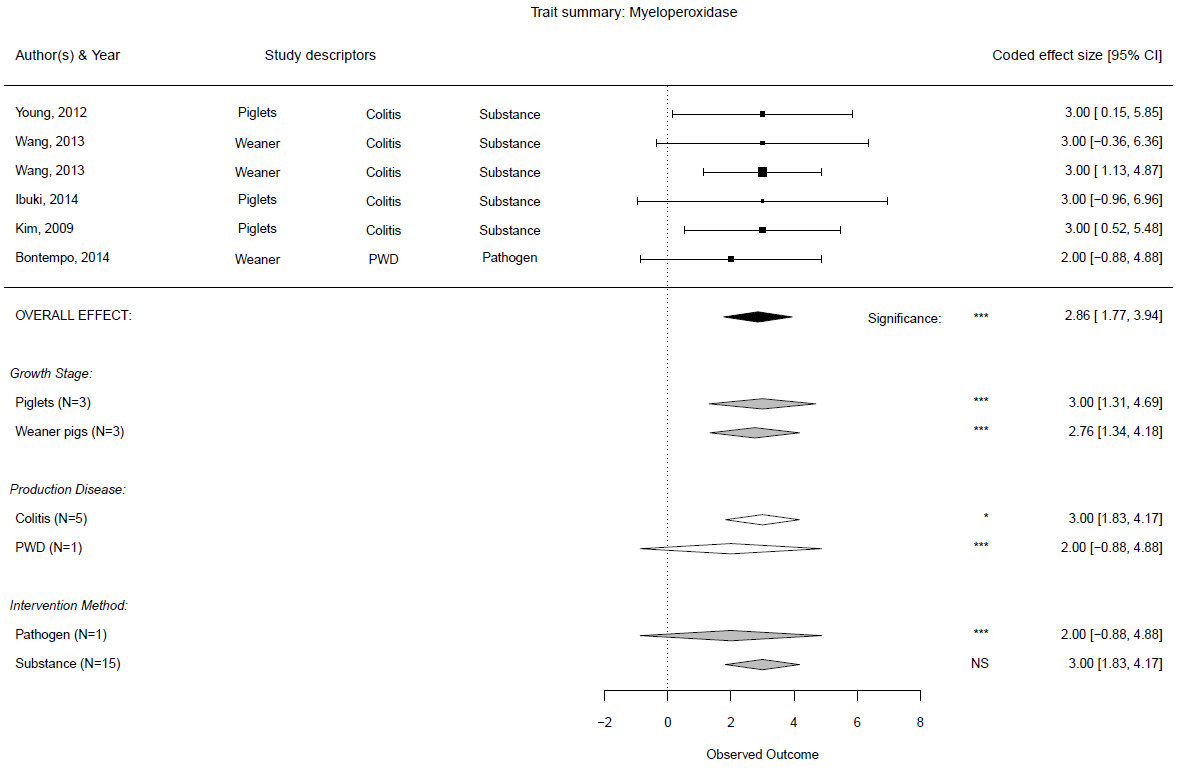
**Figure S10**



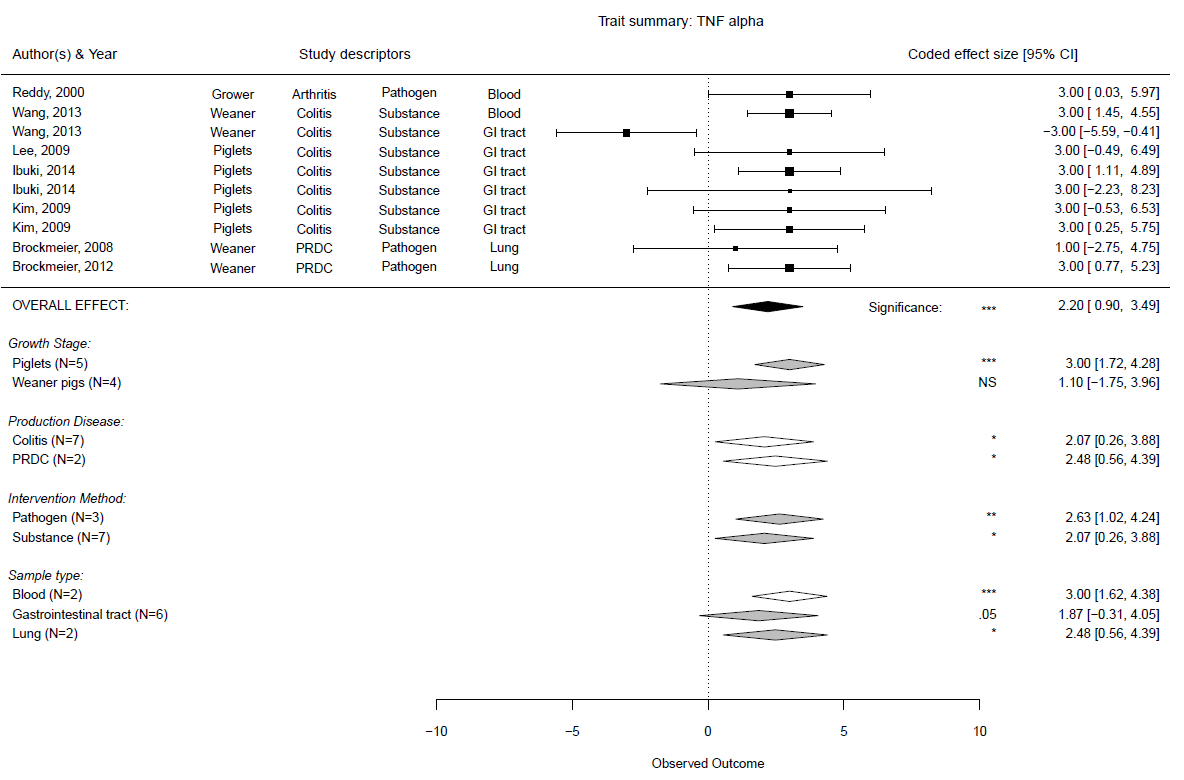
**Figure S11**



**Figure S12**



**Figure S13**



**Figure S14**

