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Scotland's Rural College

#### Evidence for Farming Initiative: Assessment of practices to reduce post-weaning diarrhoea in pigs without using zinc oxide

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February 2023



**Final report** 

# Evidence for Farming Initiative: Assessment of practices to reduce post-weaning diarrhoea in pigs without using zinc oxide

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There were no conflicts of interest in the writing of this report.

#### Contributions

The opinions expressed in this publication are not necessarily those of AHDB. Responsibility for the views expressed remains solely with the authors.

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#### List of acronyms

- AA(s) Amino acid(s)
- AHDB Agriculture and Horticulture Development Board
- AST Antimicrobial Susceptibility Testing
- EFI Evidence for Farming Initiative
- EFSA European Food Safety Authority
- ETEC Enterotoxigenic Escherichia coli (E. coli)
- EU European Union
- NADIS National Animal Disease Information Service
- n.d. no date
- PRRS Porcine Reproductive and Respiratory Syndrome
- PWD Post-weaning diarrhoea
- REA(s) Rapid Evidence Assessment(s)
- ROI Return of investment
- SDP Spray dried plasma
- SID Standardised Ileal Digestible
- UK United Kingdom
- VMD Veterinary Medicines Directorate
- ZnO Zinc oxide

## 1 Summary

Weaning is an important transitional stage in pigs, and it is associated with environmental, social, and dietary challenges. Post-weaning diarrhoea (PWD) is a common health problem and one of the greatest challenges in pig production. Zinc oxide (ZnO) at therapeutic doses has been used since the early 1990s to reduce colonisation of pathogenic diarrhoea-causing bacteria during post-weaning of pigs in many parts of the world (Barbosa et al., 2019). However, there are concerns regarding the therapeutic use of ZnO due to its association with the development and spread of antimicrobial resistance and with the potential risk to the environment. Hence, the EU has prompted the withdrawal of market authorisation of ZnO at therapeutic levels from the pig industry as of July 2022, with the UK set to follow in this direction. Indeed, the marketing authorisation has been removed in the UK as well as Europe, but a product that had been manufactured at the date of the withdrawal can be used in the UK until expired. Thus, alternative measures are being investigated to replace ZnO use in the control of PWD in pigs.

Here, rapid evidence assessments were conducted to identify existing practices in pig production which have the potential and may be explored alone or supplemented with other practices to replace the therapeutic use of ZnO. To do this, systematic searches using PubMed, Web of Science, and Scopus databases were carried out to identify relevant scientific review articles published from 2010 to 2022. Manual searches in Google and Google Scholar targeted original research, grey literature, and technical information to complement the evidence that was collated from the reviews. Recovered publications were grouped into nutritional changes, management practices and immune status. In-depth analyses of the publications resulted in the identification of practices for each group to include nutritional changes (reduced crude protein intake, alternative sources of proteins, dietary fibre, feed additives), management practices (stress reduction, housing and pen layout, water quality, hygiene and biosecurity, delayed weaning and feeding regimes), and immune status (colostrum management, vaccination and antibiotic usage for *Escherichia coli*). Feed additives identified included probiotics, prebiotics, synbiotics, amino acids, enzymes, essential oils and plant extracts. Impact and narrative summaries for each practice were produced, and where appropriate, a return on investment was also developed.

First and foremost, it is important to stress that, from the work conducted, it is evident that no other practices were as effective and inexpensive as ZnO in feed at therapeutic levels (2500ppm) in treating PWD in pigs. Put together, our analyses suggest that there are feed additives and nutritional changes that may be combined with other strategies to potentially (or at least partially) replace ZnO use in feed. The cost and effectiveness of the methods to mitigate against ZnO removal would largely depend on the degree of challenge and could differ from farm to farm, with better successes in one farm than another. On the other hand, management practices are comparatively more complex to implement but have the potential to prevent other diseases in addition to PWD, further impacting survival and increasing growth rates. Immune status improvements, including colostrum management, are very effective in preventing PWD caused by pathogenic *E. coli* but can be costly due to the diagnostic workup and labour involved in its

implementation. It is probable that the application of more than one practice at once has a synergistic effect, especially in the case of management practices.

Further additional practices, such as phage therapy and genetic selection, have good prospects as alternatives for ZnO, albeit they are still in experimental stages and are not commercially available yet.

Selection of the most appropriate practice(s) to implement would depend on the most significant factor causing PWD (i.e. nutritional vs infectious, or both) on each farm. Consequently, due consideration is required for the potential cost implications of the practice to be adopted. Hence, a working calculator is developed to allow farmers to make an informed decision for each practice.

# 2 Background

Weaning is known to be a challenging time for pigs with common health problems linked to enteric (intestinal) disease leading to diarrhoea (or scour). The disease starts after weaning and frequently affects the first two weeks after weaning and beyond. Piglets develop diarrhoea, become dehydrated, and growth is reduced or non-existent. This results in poor welfare and severe economic impact with mortality rates which can increase by up to 20% in the subsequent weeks. Mortality can be directly related to infectious pathogens causing diarrhoea or the inadvertent consequences of disease, such as malabsorption and an impaired immune system. PWD is a multi-factorial disease with multiple causes. Risk factors include the sow and the maternal immunity acquired by piglets, the environment in the farrowing house and pressure of infection by *E. coli* and other pathogens, management, and cleaning and disinfection (Rhouma et al., 2017).

In the last two decades, and in response to the need for more responsible use of antimicrobials in livestock production, PWD has been largely controlled with ZnO. This has been largely due to the cheap cost and efficacy. Zinc is an essential mineral nutrient for the health and growth of pigs. The use of ZnO in feed at therapeutic levels (2,500 ppm of inclusion rate for zinc; 3,100 ppm ZnO; for up to 14 days as per the product market authorisation), typically during the first two weeks after weaning, is associated with good control of PWD.

The mechanism of action of ZnO has been investigated over the years, and it has been demonstrated that this substance has an antimicrobial effect. Indeed, an *in vitro* study mimicking the conditions of the stomach demonstrated that ZnO has an antibacterial effect, particularly against *E. coli* (Aarestrup & Hasman, 2004). While seeking a better understanding of the antimicrobial effect of ZnO, researchers discovered that ZnO reduced the adherence of the pathogenic *E. coli* (K88 or F4), and it also blocked the bacterial invasion of the intestine by decreasing the permeability of tight junctions in the gut and modulating inflammatory responses (Roselli et al., 2003). Taking this into account, it is possible that ZnO may not have a direct antimicrobial effect as previously believed but rather an indirect antimicrobial effect.

Over the years, it has been noted that the use of ZnO in weaner pigs' feed at therapeutic levels risks environmental contamination and leads to the development of bacterial resistance. Since June 2022, the European Union (EU) has been enforcing legislation that withdraws the market authorisation of the use of ZnO at therapeutic levels in pig diets. The UK is implementing a phased withdrawal with effect from mid-2024. There is, therefore, an urgent need to find an alternative to ZnO for the control of PWD in pigs.

This work was commissioned by the Agriculture and Horticulture Development Board (AHDB) to prepare Rapid Evidence Assessments (REAs) of research studies and evidence syntheses on the assessment of practices to reduce PWD in pigs in response to the withdrawal of therapeutic ZnO from pig diets.

# 3 Project aims and objectives

### 3.1 Aim

The aim of this project was to conduct REAs on practices to reduce PWD in pigs without using ZnO. These REAs aim to provide AHDB with an overall picture of the evidence landscape.

### 3.2 Objectives

The objectives of this project were to:

- a. Provide REAs on practices that reduce PWD according to AHDB's draft Evidence Standards. These practices were listed in the Evidence for Farming Initiative (EFI) request for quote and were grouped into nutritional changes, management practices, and immune status.
- b. Outline where there are existing evidence syntheses and the nature of these syntheses.
- c. Translate REAs into narrative summaries for each practice that can be presented to producers through the EFI.
  - a. Much of what has already been reviewed was summarised if possible.
  - b. Conduct returns on investment (ROI) which was discussed and agreed upon with AHDB.
- d. Outline where there are gaps in the evidence base that the EFI might seek to address through the commissioning of primary research.
- e. Outline where there are future data developments and technologies (such as big data and AI for predictive analytics) that may give greater insights than current research and data methods.
- f. Provide feedback on the EFI framework and the generation and application of evidence standards.

#### 3.3 Report structure

Following the introductory parts, sections 1–3, this report is presented in subsequent sections:

- Section 4 presents the methodology used for conducting the REAs, including the steps conducted for the systematic literature search
- Section 5 presents an overview of practices to control PWD without using ZnO and explains the scoping exercise conducted to select the practices included in this report. A global critical review of these practices is also presented
- Sections 6,7 and 8 present the results for the nutritional changes, management practices, and immune status, respectively
- In **sections 9** and **10**, the practices with insufficient evidence to progress to REA are briefly discussed, with recommendations for future work where applicable.
- In section 12, the work conducted and its results are discussed

- Section 13 contains the references cited in this report. It is divided into two main sections: references retrieved during the systematic search and references retrieved during the manual searches
- Finally, **section 14** presents the following appendices:
  - **Section 14.1** Evidence for Farming Initiative Draft Standards that provided the basis for assessment
  - Sections 14.2, 14.3 and 14.4 contain the narrative summaries for the nutritional changes, management practices, and immune status, respectively

# 4 Rapid evidence assessment methodology

Rapid evidence assessments (REAs) offer a structured and methodical search and quality assessment of the evidence when compared to a standard literature review but are not as exhaustive as a systematic review. Generally, they can be used to give an overview of the volume and quality of evidence on a particular issue, to support decision-making by providing evidence on key topics, and to support the commissioning of further research by identifying knowledge gaps (Rapid evidence assessments – GOV.UK (www.gov.uk). REAs are often used when time and other resources are scarce, and a quality summary of the evidence is necessary. While employing similar methods to systematic reviews by compromising only on the depth and breadth of the search, REAs offer timely and much-needed answers for optimal industry uptake (Townsend & Douglas, 2021).

Please insert the below, which highlights REAs are a useful way of synthesising contradictory information quickly when there is a need to deliver approaching legislation changes:

REAs bring together fragmented knowledge and evidence on the farming industry to provide a coordinated central point for the delivery of quality-assured advice. The evidence base is being developed through sector-specific rapid evidence assessments (REAs). REAs are used to provide a systematic and transparent basis to identify, critically appraise and synthesise evidence that reduces the potential for bias. As stated above, there is already considerable scientific literature on alternative farrowing systems, but it is often contradictory.

In this report, the REAs proceeded as follows:

- 1) First, a systematic search to retrieve reviews on practices to control PWD was conducted.
- 2) Second, the reviews found were categorised, and syntheses of the evidence were performed.
- 3) Third, manual searches were made to address the knowledge gaps identified and to seek additional (practical) information not documented in scientific literature.
- 4) Finally, the syntheses of evidence were refined.

The systematic search step aimed to ensure that the evidence retrieved had the highest quality and to ensure that all relevant aspects of the various practices were retrieved, as well as to minimise bias when reporting. Figure 1 illustrates this process. A search string with keywords was built and adapted to each of the databases selected. All results were

extracted to EndNote (version X8) and later to Microsoft Excel®. Inclusion and exclusion criteria were defined to assist with the title and abstract screenings as well as with the full-text assessments. For training purposes, an initial sampling of 30 records was performed. The records' titles and abstracts were screened by two assessors in parallel to validate the application of the inclusion and exclusion criteria. After this step, the assessors discussed and synchronised the results and refined the established criteria. Title and abstract screenings were conducted (with each assessor reviewing half), and the records selected were then assessed in full after their retrieval. All full-text assessments were performed by two members of the research team (both assessed all full texts), which were blinded to each other's assessment. Disagreements were discussed before rejecting any review.

Each practice was summarised in light of i) the evidence retrieved, and ii) the impact these practices had on the reduction of PWD, the reduction of post-weaning mortality, and on pig growth. All selected papers were classified as of primary interest – papers presenting a review of two or more of the practices listed (i.e. fibre and protein nutritional strategies) or as of secondary interest - papers offering insights into one of the practices listed. Knowledge gaps were identified.

Manual searches were included to counteract the lack of scientific documentation within the search parameters of the benefits of some practices, such as management practices. The syntheses were refined with the information retrieved in this second search. Experts were consulted to complement the information gathered and validate the practical aspects of the narrative summaries.

The systematic search process for the REAs is detailed below.

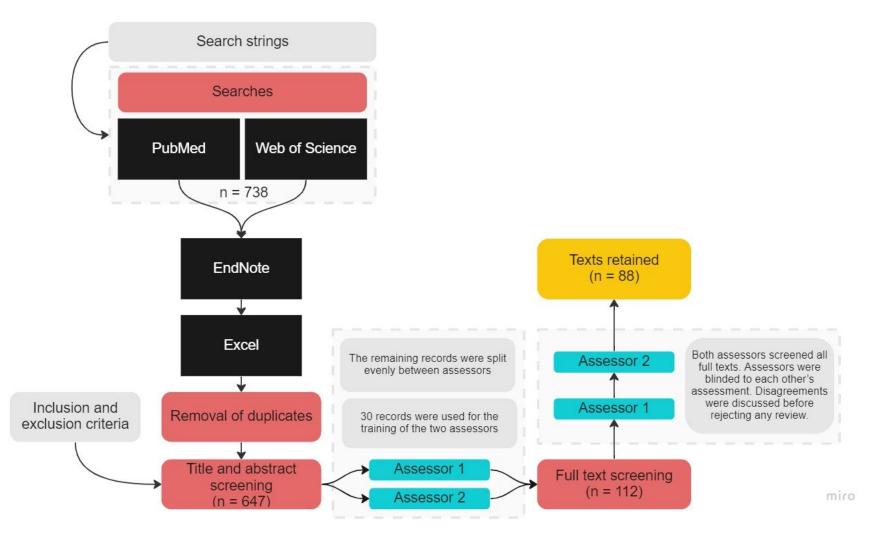


Figure 1. Tools and methods employed during the systematic search process

## 4.1 Defining search terms and databases

An initial set of 16 practices to reduce PWD were proposed by AHDB. Table 1 shows these practices grouped into nutritional changes, management practices, and immune status. For each practice, a search string was built and adapted to each database in the systematic searches.

Nutritional changes	Management practices	Immune status
Inert fibres	Stress reduction	Vaccination
Acidification of feed and water	Housing/pen layout	Colostrum
Fermentation	Water quality	Antibiotic usage
Feed additives	Hygiene and biosecurity	Phages
Reduce crude protein intake	Delayed weaning	
Use of alternative protein/or impact	Feeding regimes (e.g.	
on gut development/inflammation of	mat and gruel feeding)	
alternates to soya meal		

Table 1. Practices to reduce PWD – alternatives to the use of ZnO

Three databases were used: PubMed, Web of Science, and Scopus. One systematic search per database was conducted. Google and Google Scholar were used in the forward and backward searches to seek additional information on the knowledge gaps identified. Table 2 shows the list of search terms employed in the systematic searches, the databases used, and the filters applied. Only reviews in English published after 2010 were selected. Searches were restricted to titles and abstracts.

Database	Search string used
PubMed	(pig OR wean* OR nursery) AND (diarr* OR scour)
	AND (control OR intervention OR strategy OR practice
	OR reduction OR treat* OR preven*)
Web of Science	ALL=((pig OR wean* OR nursery) AND (diarr* OR
	scour) AND (control OR intervention OR strategy OR
	practice OR reduction OR treat* OR preven*))
Scopus	(pig OR wean* OR nursery) AND (diarr* OR scour)
	AND (control OR intervention OR strategy OR practice
	OR reduction OR treat* OR preven*) AND <limitations></limitations>
	(see full search string in annex XX, documenting
	searches excel sheet)
Filters applied	Review papers
	Peer reviews and grey literature
	Searches restricted to title and abstract
	Reviews after 2010*
	English

Table 2. Search strings used in the systematic searches and filters applied

\* The 2010 time limit dictated that only more recent reviews were returned. However, we still covered relevant research papers published before 2010 because reviews summarise evidence from older research papers.

## 4.2 Screening and selection of evidence

The eligibility criteria used during the screening and selection process were as follows:

#### • Inclusion criteria:

- Reviews, peer-reviewed or not, gathering and synthesising evidence on practices to control PWD in pigs
- Field and laboratory trials
- It refers to nutritional practices, including inert fibres, acidification of feed and water, fermentation, feed additives, reduced crude protein intake, use of alternative protein/or impact on the gut, and development/inflammation of alternates to soya meal
- It refers to management practices, including stress reduction, housing/pen layout, water quality, hygiene and biosecurity, delayed weaning, and feeding regimes (e.g. mat and gruel feeding)
- It refers to immune status, including vaccination, colostrum management, antibiotic usage, and phages
- It includes information on the effect of the treatment or intervention on PWD, mortality rate, and or growth rate
- Papers and grey literature providing economic information that may be used to estimate economic effects of practices

#### • Exclusion criteria

- Treatments or interventions using ZnO need to be excluded
- Early weaning strategies (21 or 28 days) should not be considered

The number of reviews found, retrieved, and selected in the systematic searches performed is shown in Figure 2. The number of reviews of primary interest (summarising more than one practice) and secondary interest (summarising only one practice) are also shown.

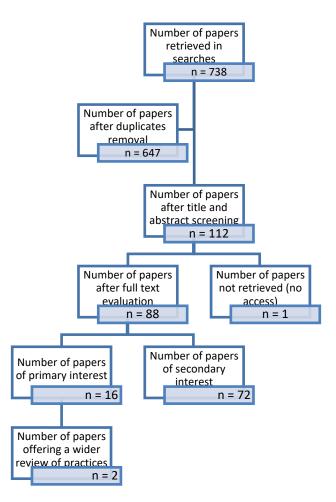


Figure 2. Number of reviews retrieved, assessed and retained after steps one and two of the REAs

The number of reviews extracted with the searches was larger than expected (n=647). Of these, 112 reviews were selected after the title and abstract screenings. All but one of the 112 reviews were screened in the full-text evaluation, out of which 88 were selected. Overall, only two of the papers retained offered a wider review of practices to reduce PWD in pigs, covering all three groups of practices. The papers selected were classified into primary (n=16) or secondary interest (n=72) (Figure 2). All papers were cross-referenced against the list of nutritional (Table 3), management (Table 4) and immune status practices (Table 5) to control PWD.

The two papers offering a wider review of all practices to control PWD were Rhouma et al. (2017); Wisener et al. (2021).

Listed	Total	Reference category
practices	number	(Primary or secondary)
General	9	All primary: (Vondruskova et al., 2010; Xiong et al.,
nutritional		2019; Babatunde et al., 2021; Bonetti et al., 2021; Klein
changes		et al., 2021; Laird et al., 2021; Lopez-Galvez et al., 2021;
0		Wei et al., 2021; Zheng et al., 2021)
Fibre <sup>a</sup>	9	All secondary:
		(Jha & Berrocoso, 2016; Flis et al., 2017; Gao et al.,
		2019; Babatunde et al., 2021; Bonetti et al., 2021;
		Hussein et al., 2021; Huting et al., 2021; Klein et al.,
		2021; H. Li et al., 2021)
Acidification	6	All secondary:
of feed and		(Suiryanrayna & Ramana, 2015; Ferronato & Prandini,
water		2020; Nguyen et al., 2020; Pearlin et al., 2020; Tugnoli et
		al., 2020; Nowak et al., 2021)
Fermentation	2	Primary: (H. L. Zhang et al., 2020)
		Secondary: (Pieper et al., 2016)
Feed	46	All secondary:
additives		(Campbell et al., 2010; Torrallardona, 2010; Ulgheri et al.,
		2010; Cho et al., 2011; Halas & Nochta, 2012; Heo et al.,
		2013; Pluske, 2013; Subramaniam & Kim, 2015; Xiao et
		al., 2015; Sweeney & O'Doherty, 2016; Gresse et al.,
		2017; Liao & Nyachoti, 2017; Liu et al., 2017; O'Doherty
		et al., 2017; Sun & Kim, 2017; Karuppannan &
		Opriessnig, 2018; W. C. Liu et al., 2018; Y. Liu et al.,
		2018; Barba-Vidal et al., 2019; Bogere et al., 2019;
		Corino et al., 2019; Mou et al., 2019; Shannon & Hill,
		2019; Genova et al., 2020; Girard & Bee, 2020;
		Lauridsen, 2020; Nguyen et al., 2020; Babatunde et al.,
		2021; Balan et al., 2021; Blavi et al., 2021; Bonetti et al.,
		2021; Caprarulo et al., 2021; Corino et al., 2021;
		Espinosa & Stein, 2021; Huting et al., 2021; Jahan et al.,
		2021; Klein et al., 2021; Laird et al., 2021; Lallès &
		Montoya, 2021; Lauridsen et al., 2021; O'doherty et al.,
		2021; Tan et al., 2021; Zamojska et al., 2021; Zhao et al.,
		2021; Adli et al., 2022; Luise et al., 2022; Su et al., 2022),
Proteins <sup>b</sup>	13	Primary: (H. L. Zhang et al., 2020)
		Secondary: (Jezierny et al., 2010; Ayrle et al., 2016; Jha
		& Berrocoso, 2016; Pieper et al., 2016; Gilbert et al.,
		2018; Gao et al., 2019; Humphrey et al., 2019;
		Babatunde et al., 2021; Bonetti et al., 2021; Klein et al.,
		2021; Laird et al., 2021; Xia et al., 2021)

Table 3. Papers retrieved in the systematic literature searches assigned to each of the listed nutritional practices to reduce PWD in pigs

<sup>a</sup> including inert fibres; <sup>b</sup> including: reduce crude protein intake and use of alternative protein/or impact on gut development/inflammation of alternates to soya meal.

Table 4. Papers retrieved in the systematic literature searches assigned to each of the listed management practices to reduce PWD in pigs

Listed Practices	Total	Reference category	
	number	Primary references	Secondary references
Stress reduction	3	(Pluske et al., 2018b)	(Pluske et al., 2018a;
			Klein et al., 2021)
Housing/pen	1	-	(Gebhardt et al., 2020)
layout			
Water quality	0	-	-
Hygiene and	2	-	(Jacobson et al., 2010;
biosecurity			Jayaraman & Nyachoti,
			2017)
Delayed weaning	1	-	(Al Masri et al., 2015)
Feeding regimes	3	-	(Pluske et al., 2019;
a			Cullen et al., 2021;
			Huting et al., 2021)

<sup>a</sup> e.g. mat and gruel feeding.

Table 5. Papers retrieved in the systematic literature searches assigned to each of the listed immune status practices to reduce PWD in pigs

Listed practices	Total	Reference categories	
	number	Primary references	Secondary references
General	1	(Pluske et al., 2018a)	-
Vaccination <sup>a</sup>	7	(Melkebeek et al.,	(X. Li et al., 2015;
		2013)	Hedegaard & Heegaard,
			2016; Sun & Kim, 2017;
			Vlasova et al., 2017;
			Dubreuil, 2021; Laird et
			al., 2021)
Colostrum	1	-	(Blavi et al., 2021)
management			
Antibiotic usage	4	-	(Jacobson et al., 2010;
			Karuppannan &
			Opriessnig, 2018;
			Caprarulo et al., 2021;
			Lallès & Montoya, 2021)
Phages	5	(J. Zhang et al., 2015)	(Gigante & Atterbury,
			2019; O'Sullivan et al.,
			2019; Dec et al., 2020;
			Bonetti et al., 2021)

<sup>a</sup> One publication from Bearson (2022) was unable to be accessed

## 4.3 Assessment of evidence and narrative summaries

The evidence selected was critically assessed, taking into account the EFI standards. Each practice was reviewed to assess its effectiveness, cost, speed of change, and strength of evidence, with information being retrieved from the bulk of reviews cross-referenced to each practice and from the manual searches (Appendices 14.2, 14.3, 14.4). Considerations and recommendations for each practice were added to complement the REAs and narrative summaries.

Practices with sufficient technical and scientific evidence were included in the narrative summaries, with an exception for spray-dried plasma (SDP). This practice has limited applicability in the UK: the use of blood products and pig-derived nutritional products, including SDP, is not allowed under quality assurance schemes like Red Tractor. Practices not applicable to farmers directly were discussed as areas for future research and potential industry development. Practices identified in the reviews as promising interventions but lacking technical and/or scientific evidence were discussed as knowledge gaps (see section 'Sector-wide evidence gaps').

The steps conducted thus far generated scientific and technical evidence, which were then translated into narrative summaries. These aimed to help farmers understand each practice, its pros and cons, and how to implement it well. Each narrative summary includes an impact summary and a table summarising the weighted scores for evidence quality and support for each practice. Included are also explanations of what the practice is, how effective it is, in which contexts it works, costs to be considered and, where possible, an estimated cost of implementation. Further, they include what good practice looks like, the strength of the evidence base, and links to further information.

# 5 Practices to reduce PWD without using ZnO

## 5.1 Scoping exercise

The systematic search exercise aimed to find reviews of the practices to control PWD without using ZnO at therapeutic levels in the UK pig sector. We identified many reviews on nutritional changes, whereas evidence on immune status and management practices was limited within our search terms. This suggested that the industry is attempting to replace an in-feed treatment (ZnO) with another in-feed treatment. Indeed, there were multiple types of feed practices, feed additives and sub-groups within them, with multiple reviews targeting the same areas. Thus, cross-referencing the evidence retrieved against the initial list of practices proposed was challenging. A re-arrangement of the practices was therefore necessary in light of the evidence found in the literature, and this new structure is shown in section 5.3.

In most of the reviews retained, feed additives were discussed in detail. However, the different products, dosages and delivery methods dictate the mixed results observed in the literature. As Modina et al. (2019) notes, "the efficiency of each additive depends on the diet itself, the state of health, and the age of the animals". Hence varying types of feed additives at different concentrations are available on the market to address specific needs. It should be noted that commercial feed companies have been trialling many products and generating a lot of trial data on the use of diets and feed additives as

alternatives to the use of ZnO to control PWD in pigs. However, most of these data are commercially sensitive and have not been published for that reason.

For each nutritional change, there was extensive scientific literature available. Yet, while nutritional changes may represent the most straightforward alternative to ZnO, it became apparent that using these practices in isolation might not be sufficient to minimise risk factors for PWD. Its effectiveness varied substantially depending on the most significant contributor to PWD on each farm.

On the other hand, the implementation of management practices (discussed below in section 7) and immune status changes (discussed below in section 8) seemed to substantially tackle most of the risk factors for PWD, preventing its development. There was, however, a clear lack of scientific evidence for management practices and immune status in scientific literature within the parameters of our searches. These two groups of practices, especially management practices, often require more structural approaches and rethinking of the farm operations. They are also typically presented in combination with other measures, making them more difficult to endorse in published reviews. The evidence gathered on these practices was complemented with expert advice and technical information gathered from manual searches.

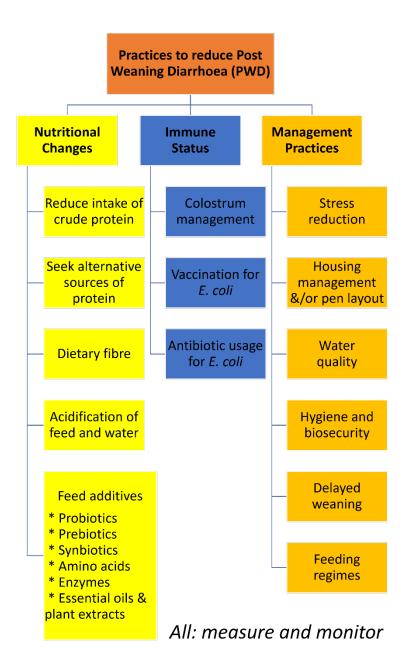
Finally, an interesting but predictable observation was that most publications had been published in the last few years, denoting the urgency to find alternatives to ZnO. With the withdrawal of ZnO at therapeutic levels already taking effect in European countries, effective practices to control PWD will become more evident in the near future.

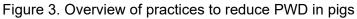
## 5.2 Critical review

Having extracted the review articles, each was critically reviewed and analysed based on content and relevance to the field, followed by assigning them to the practices identified. Other manual searches conducted on Google yielded additional references, which, for unknown reasons, were not captured by the limit of the databases and search strings. Further grey literature was identified and added, and all references were collated to build content for each practice. This was done by structuring and linking each article to a practice with primary literatures providing an overview of the relevant practices in a group. All other articles that provided specific evidence for a particular practice were classified as secondary articles. Where needed, additional relevant research papers which were cited in the reviews were consulted to further strengthen the evidence. After examination of the initial groups of practices provided (see section 5) and evidence obtained from the literature, it was logical to restructure the practices to those provided in Figure 3 for clarity and in-depth comparisons.

## 5.3 Practices Included in REAs

As shown in Figure 3, 14 practices aiming to reduce PWD were included for investigation and grouped under nutritional changes (5), immune status (3) and management practices (6).





# 6 Nutritional changes

Within nutritional changes, we considered:

- Reductions in crude protein intake
- Alternative protein sources
- Dietary fibre
- Acidification of feed and water

We also considered feed additives, including probiotics, prebiotics, synbiotics, amino acids, enzymes, essential oils and plant extracts.

## 6.1 Reduce crude protein intake

Protein supplies amino acids, which are essential for muscle growth and repair. Adequate protein is therefore important for daily weight gain of growing pigs. Sources of protein for diet formulation originate from plant or animal origins, with plant-origin ingredients being the largest component of pig diets. The level of crude protein is important for weaned pigs and is usually under 200g/kg. High protein diets (~230g) are difficult for piglets to digest due to their immature digestive tracts and can cause diarrhoea (Heo et al., 2013; Pluske, 2013; Lopez-Galvez et al., 2021). ZnO was used to offset some of these undesirable effects. In the absence of ZnO, high protein content in feeds of weaned piglets need to be adjusted to levels which would provide sufficient protein source for growth but not detrimental to piglet health (Heo et al., 2013; Lopez-Galvez et al., 2021). The negative impacts of high crude protein diets in weaning pigs are detailed below, with emphasis on potential methods to mitigate the effects during this challenging transitional weaning time in piglets.

High protein diets can lead to high protein fermentation resulting from residual undigestible proteins and the generation of corresponding metabolites such as biogenic amines, ammonia and indole and phenolic compounds, mostly in the large intestines (Heo et al., 2013; Jha & Berrocoso, 2016). These metabolites can cause detrimental changes in the morphology and permeability of the intestines of weaning piglets (H. L. Zhang et al., 2020). High protein feeds are also associated with high pro-inflammatory cytokines in the intestinal wall and disruption of levels of beneficial gut microbiota, which in turn affect nutrient utilisation, bioavailability, energy status and proliferation of pathogenic bacteria causing diarrhoea (Pluske, 2013). The intestine of piglets is still developing and constantly changing (Heo et al., 2013). The transition from liquid feed (milk) to solid feeds during weaning is particularly challenging to piglets and can be further compounded by the effects of high protein feeds, as described above. As a result, high protein feeds are potentially harmful and have been associated with decreased faecal consistencies and increased incidence of diarrhoea in weaning piglets (Pluske, 2013; H. L. Zhang et al., 2020). These further complicate the weaning stage leading to reduced growth, low performance, and increased mortality rate in piglets (Heo et al., 2013). Whether the feeds are formulated in-house or are commercially sourced, it is important to opt for feeds which have low crude protein content to minimise the negative effects during post-weaning.

Using low crude protein diets during weaning has other advantages, such as reduced feed cost, low nitrogen excretion through urine and reduced odour production. These are also beneficial to piglet growth and welfare and advantageous to farmers and the environment (Gao et al., 2019). However, lowering crude proteins significantly in feeds can typically affect productivity. Therefore, it is essential to balance the nutrition of piglets during weaning through increasing insoluble fibre and moderately fermentable carbohydrate intakes (Pluske, 2013). This would help divert nitrogen from urine to faeces and provide a more preferred substrate for microbial fermentation over proteins. The overall aim is to reduce the generation of protein fermentation metabolites and maintain a healthy microbial community in the gut environment, preventing PWD (Wang et al., 2018). Also, supplementation of low crude protein diets with sources of branched-chain amino acids could reduce protein metabolites and the concomitant impact on gut

microbiome profiles, which is beneficial in reducing the prevalence of PWD in pigs (Spring et al., 2020).

## 6.2 Alternative protein sources

Protein levels are important factors in controlling PWD, maintaining healthy piglets and improving productivity, as discussed in the previous section. The need to provide a cheap and accessible protein to pigs has created an over-dependence on soyabean meal as a protein source for pig feeds. It has also created an unnecessary competition in food, biofuel, and bioprocessing industries, which have resulted in a continual rising cost of pig feeds and a reliance on importation in the UK and EU. Furthermore, soyabean is often obtained from genetically modified cultivars, which may be a concern for consumers who prefer organic production (Babatunde et al., 2021). In addition, soyabeans contain anti-nutritional factors such as protease inhibitors or trypsin inhibitors (TI), which inhibit the activity of enzymes that digest protein in the digestive tract of the pig. Thus, to improve the nutritional content of soya, levels of trypsin and other enzyme inhibitors can be reduced through various processing methods such as dehulling, soaking, boiling, roasting, autoclaving, micronisation, microwave cooking, extrusion cooking, fermentation and germination (Shi et al., 2017). For example, extrusion has been shown to destroy over 90% of trypsin inhibitor activity in soya (Romarheim et al., 2005). These enzyme inhibitors affect the pig's digestion contributing to diarrhoea. These issues have triggered the need for alternative sources of protein to cater for the growing needs of the swine industry. Since many farmers procure their feeds commercially, little emphasis is given to alternative sources of proteins in this assessment, with the focus, instead, on readily sourced ingredients and their generalised nutritional potentials as an alternative to soyabean in feeds during the post-weaning stage in pigs.

To set a foundation for comparison, it is important to understand that the nutritional composition of a soyabean meal is an attractive source of protein in pigs and a potential reason why alternative replacement are needed. Soyabean meals are rich in limiting amino acids lysine, threonine and tryptophan and are generally low in other food sources such as cereal (Babatunde et al., 2021). In addition, the amino acids present in soyabeans have greater digestibility than those found in other protein sources and are digestible and metabolisable energy sources comparable to corn. However, soyabean use in pig feeds is not always positive as it contains anti-nutritional factors that could limit growth, although different technologies have been employed to reduce the impacts of these factors (Babatunde et al., 2021). Soyabean also contains phosphorus bound to phytic acid, which has low digestibility unless it is supplemented with microbial phytase.

In the light of the disadvantages of a soyabean meal, other plant-based and/or animalbased protein sources can be explored, such as faba beans, field peas, chickpeas, copra meal, rice, potato, whey/milk, pea, sunflower and palm kernel meal. Other alternatives like poultry meal, feather meal, blood meal and insect meal are not legal in the UK at the time of reporting (Jezierny et al., 2010; Babatunde et al., 2021; Bonetti et al., 2021; S. Kim et al., 2021). Some of the plant sources are nitrogen-fixing leguminous crops, rich in calcium, fat, crude protein, amino acids, energy, minerals, carbohydrates, fibre and non-starch polysaccharides but also contain some anti-nutritional factors such as trypsin as discussed above(Babatunde et al., 2021; S. Kim et al., 2021). Animal-based protein alternatives such as dicalcium and tricalcium phosphate can also be excellent ways of utilising waste.

## 6.3 Dietary fibre

Supplementing feeds with dietary fibres helps to maintain the digesta, and could greatly impact the ability of the piglets to navigate the challenging weaning period in many positive ways, depending on the fibre types, sources, levels/concentration and fermentation (Lopez-Galvez et al., 2021). Dietary fibres can affect gut health, growth performance, digestibility of nutrients, and prevent diarrhoea in weaning piglets, as discussed below (Lallès & Montoya, 2021).

Insoluble dietary fibres can act as prebiotics and can elevate mucosal integrity by increasing the villus length, reduce adhesion of pathogenic bacteria (such as *E. coli* F4) to epithelial cells and their retention in the gut (Gao et al., 2019; Bonetti et al., 2021), reducing the incidence of diarrhoea. Lowering the level of pathogenic bacteria also reduces competition for nutrients and space and could promote the proliferation of good bacteria in the gut, preventing diarrhoea in post-weaning pigs (Bonetti et al., 2021).

Dietary fibres also increase the bulk of diets, which help to promote intestinal development and integrity, gut movement and alleviate constipation, promoting intestinal health and function (Gao et al., 2019; Hussein et al., 2021; Huting et al., 2021; H. Li et al., 2021). Dietary fibres also provide energy in the form of volatile fatty acids and increase dietary fibre intake, balance low-protein diets and reduce protein fermentation metabolites (Gao et al., 2019; Huting et al., 2021).

The viscosity of dietary fibre affects the ileal digestibility of nutrients and could aid nutrient absorption and, consequently, weight gain and growth (Jha & Berrocoso, 2016; Flis et al., 2017). Also, fibre-degrading enzymes and microbes produce energy metabolites which prevent tissue breakdown and balance the anti-nutritional effects of fibres (Flis et al., 2017). Excessively high-fibre diets may have a conflicting impact by reducing growth and productivity associated with weaning but balancing with protein has been shown to improve the health of weaners (Flis et al., 2017).

## 6.4 Acidification of feed and water, including organic acids

Many classes and compositions of organic and inorganic acids have been studied, and their main activity in weaning piglets is associated with lowering the gastric pH, which has antimicrobial or disease-preventing abilities (Heo et al., 2013; Y. Liu et al., 2018; Nguyen et al., 2020). For reference, the gastric pH in weaned pigs ranges between 2.0 and 5.0. During the few weeks of life of piglets, the production of hydrochloric acid is not yet sufficient, and enzyme (pepsin) activity only increases from five to six weeks (one to two weeks post-weaning). Therefore, extra support to reduce stomach pH is likely to be beneficial during the first weeks following weaning to achieve adequate stomach acidification to support protein digestion (van Leeuwen, 2021). Low gastric pH prevents the multiplication of gut pathogenic bacteria responsible for diarrhoea, such as coliforms, *Salmonella* and *Clostridia* and improves immune response in weaners (Nguyen et al., 2020; Bonetti et al., 2021). Dietary supplementation of diets with lactic acid and citric acid prevents PWD in pigs (Sun & Kim, 2017).

In addition to bactericidal and bacteriostatic abilities, gastric acidification also helps digest nutrients such as dietary proteins and ensures feed efficiency, better growth performance and overall gut health of weaning piglets (Rhouma et al., 2017; Sun & Kim, 2017).

Low pH increases mineral utilisation and stimulates both endocrine and exocrine pancreatic secretions, which increases the proliferation of epithelial cells (Y. Liu et al., 2018; Jahan et al., 2021). Organic acids help with the formation of intermediary metabolic products which act as an energy source to be utilised, prevent tissue breakdown and enhance apparent total tract digestibility thus, improving growth performance (Sun & Kim, 2017; Y. Liu et al., 2018; Tugnoli et al., 2020). Their salts increase protein utilisation, especially in weaner pigs and improve production indices. While utilising organic acids, several factors such as types, dosage, feed formula and age of piglets play a critical role in the outcome of activity (Y. Liu et al., 2018; Jahan et al., 2021).

One of the constraints of this practice is the lack of infrastructure on some farms to deliver water-soluble acids and also the impact of such additions on existing infrastructure, resulting in possible water leaks. Acidification of feed, on the other hand, is more common in liquid-fed pigs and more easily implemented in such feed delivery systems.

## 6.5 Feed additives

Feed additives are products used in animal feed to achieve an effect either on the feed itself or on the animals. Additives may also be used to obtain an effect on meat or milk (animal products), or on the environment. In the scope of this work, feed additives will be substances enhancing the digestion of feed or with antimicrobial properties (European Food Safety Authority:EFSA, n.d., access year: 2022). Thus, they may enhance production and profitability under the right circumstances. Many additives have a target production phase, usage rate, and duration of use to be effective tools to enhance the production and profitability of the pig farm (Richert, 2006). Correct application according to the manufacturer's instructions is key to success.

There is very strict regulation around the use of feed additives in the EU and in the UK. Feed additives cannot be commercialised unless they have been authorised following a careful scientific evaluation carried out by EFSA/FSA, where it needs to be proven the additive has no harmful effects on human and animal health or on the environment (EFSA, n.d., access year: 2022).

#### 6.5.1 Probiotics

Probiotics are live microbial supplements which comprise of good or friendly bacteria which, when administered in optimal doses, could exert health benefits by improving intestinal microbial balance (Cho et al., 2011; Heo et al., 2013; Barba-Vidal et al., 2019; Lopez-Galvez et al., 2021). Many probiotic preparations containing varieties and doses of bacteria from genus *Lactobacillus*, *Lactococcus*, *Enterococcus*, *Streptococcus*, *Pediococcus*, *Bacillus*, *Bifidobacterium*, *Saccharomyces* and avirulent *E. coli* have been published and serve as an alternative to the use of antibiotics (Vondruskova et al., 2010; Bogere et al., 2019; Blavi et al., 2021; Laird et al., 2021). During post-weaning transition, there is a shift in the microbiome status of the young pigs, and this potentially provides an opportunity for colonisation of opportunistic pathogenic bacteria responsible for diarrhoea (Gresse et al., 2017; Zamojska et al., 2021). Probiotics modulate gut

microbiota and suppress the colonisation of pathogenic bacteria by competing for binding sites on intestinal epithelium surfaces and nutrients for growth (Gresse et al., 2017; Liao & Nyachoti, 2017; Laird et al., 2021; Su et al., 2022). They also stimulate the immune system and produce antagonistic substances against growth and proliferation of pathogens and toxin contents, reducing the incidence of diarrhoea and mortality in post-weaning piglets (Liao & Nyachoti, 2017; Bogere et al., 2019; Su et al., 2022). The overall intestinal health is also improved with probiotic usage leading to general health, better growth rate, feed efficiency and productivity (Gresse et al., 2017; Bogere et al., 2017; Bogere et al., 2019). Probiotics also have antioxidative activity by alleviating stress and can produce some vitamins and enzymes which can aid nutrient fermentation, digestion and uptake (Liao & Nyachoti, 2017).

## 6.5.2 Prebiotics, including seaweed

Prebiotics are selectively fermented components of feed such as seaweed extract, which are indigestible by pigs but could help maintain gut microbial balance to add benefit to health (Heo et al., 2013; Corino et al., 2021; Laird et al., 2021). Prebiotics can also support selective pressure for certain good bacteria, such as bifidobacteria and lactic acid bacteria, to prevent microbial imbalance. Non-starch polysaccharide by-products of soyabean meal hydrolysis interfere with pathogenic bacteria attachment sites and are beneficial in fluid retention during diarrhoeal infection (Rhouma et al., 2017; Y. Liu et al., 2018; Su et al., 2022).

#### 6.5.3 Synbiotics

Synbiotics are combinations of probiotics and prebiotic approaches used to achieve complementary or synergistic effects to improve microbial balance in the gut to prevent colonisation of pathogenic bacteria (Heo et al., 2013; Laird et al., 2021). The complementary synbiotic consists of a probiotic and a prebiotic selected independently to confer benefits to the host. The synergistic synbiotic comprised of prebiotics chosen specifically for the selected probiotics to enhance effects in the gut (Rhouma et al., 2017). An example is a combination of raw potato starch and a probiotic which was shown to increase microbial diversity and reduced diarrhoea in the gut of weaned pigs challenged with pathogenic Enterotoxigenic *E. coli* ETEC (Rhouma et al., 2017).

#### 6.5.4 Amino acids

Amino acids (AAs) are the structural units ('building blocks') of protein. AAs are absorbed in the body during digestion and used to build new proteins, like muscle, which in itself is composed of different AAs. It is not unusual to think that pigs need a certain level of protein to grow, but what is essential is an adequate provision of AAs. A pig's diet must include a certain amount of AAs to help it grow (Liu et al., 2017).

When attempting the reduction of protein levels in feed, it is crucial to ensure the pig receives all the AAs it needs and that a certain balance between the AAs is maintained. In order to give the weaned pigs what they need, the concept of ideal protein, defined as the AA profile that maximises nitrogen retention (i.e. muscle) and covers the pigs' physiological and growth needs, is applied when formulating diets (Cristobal et al., 2019). This is the key idea behind the use of AAs to prevent PWD: to allow the reduction of protein without the loss of performance. The availability of industrial AAs and the increased knowledge of AA requirements are now shedding light on how to formulate diets based on pig requirements for essential AAs. These new formulations should still

respect the ideal protein profile and focus less on protein levels (Cirera, 2016). Indeed, formulation to Standardised Ileal Digestible (SID) amino acid levels is now standard practice and follows the ideal protein concept. Diets are formulated using ratios of SID amino acid levels to SID lysine (the limiting AA in pigs, that which is the most needed). The ratio of SID lysine to energy is also an important consideration. The increased availability of other synthetic amino acids, such as isoleucine and leucine, has enabled more precise formulation and helped reduce protein further.

#### 6.5.5 Enzymes

Enzymes help in gut fermentation and have been proven to improve the digestibility and utilisation of nutrients and nutritional value of feeds, positively impacting growth performance in weaned piglets with comparable results to antibiotics as seen in multienzyme preparations (Lopez-Galvez et al., 2021). Enzymes also help maintain gut physiology and the immune system, aid metabolism and enhance small intestinal barrier function (Heo et al., 2013). Enzymes play a key role in the production of a variety of products of polysaccharide hydrolysis which favour the proliferation of good bacteria but inhibit the colonisation of pathogenic ones by competing with their attachment sites (Heo et al., 2013). Thus, enzymes act as prebiotics that can indirectly help in the modulation of gut microbiota levels and prevent PWD in pigs (Lallès & Montoya, 2021). Supplementing feeds with enzymes such as lysozyme showed improved gut health, enhanced non-specific immunity and low colonisation and shedding of enterotoxigenic *E. coli* in weaning piglets, preventing diarrhoea and improving growth and performance (Heo et al., 2013). Enzymes also have a positive effect on the antioxidant value in piglets and help in phosphorus and calcium excretion (Lallès & Montoya, 2021).

The effect of enzymes is related to the facilitation of digestion. Phytase is perhaps the most popular and most widely accepted and successful enzyme used in pig diets. It works by selectively breaking down (hydrolyses) the bonds that hold phosphorus to phytate, thus, increasing the digestibility of this nutrient and reducing dietary inclusion levels of inorganic phosphorus sources. Proteases attack proteins. Thus, they may be added to pig diets to help the pig digest proteins that are resistant to the digestive enzymes which naturally occur in the intestine of the pig. Enzymes like carbohydrase are widely used to improve nutrient digestibility and help with the transition from milk to plant-based feed. They are substrate-specific, meaning that its use is beneficial if the diet contains the specific substrate in a sufficient amount so the enzyme can work. Xylanases and beta-glucanases are the most used enzymes, and they improve the digestibility of the feed by acting on more or less indigestible fibre-rich raw materials (Giménez-Rico, 2014; Infinita - Biotech Private, 2018).

In a study designed to test the effect of  $\beta$ -mannanase feed supplementation on postweaning pig performance, Vangroenweghe *et al.* (2021) concluded that the use of a heattolerant  $\beta$ -mannanase allowed the use of reduced levels of expensive protein in diets fed post-weaning and a reduced net energy requirement in one of the post-weaning diets without adverse effects on intestinal health or overall performance. "In fact, the occurrence of PWD and number of individual treatments during the post-weaning period were significantly reduced on the  $\beta$ -mannanase supplemented diets", concluded the authors.

#### 6.5.6 Essential oils and plant extracts

There are claims for the antimicrobial, antioxidant and anti-inflammatory properties of selected essential oils and extracts of medicinal plants (W. C. Liu et al., 2018; Girard & Bee, 2020)(Liu 2018, Girard 2020). For example, treatment with essential oils and plant extracts has revealed a reduction in the colonisation of coliforms and total anaerobes such as *E. coli* F4, *Clostridium* spp, *Salmonella* in caecum, colon and rectum, which would help relieve PWD in piglets (W. C. Liu et al., 2018). Evidence has been reported in the downregulation of bacterial virulence factors such as toxins, adhesion to enterocytes, motility and quorum sensing with tea tree and cinnamon treatments (Lallès & Montoya, 2021). The extracts have also been shown to improve colonic microbial composition, intestinal morphology, enzyme activity, feed digestibility and growth performance, which could greatly help to relieve PWD (Lallès & Montoya, 2021). A decrease in intestinal oxidative stress has been recorded with treatment with essential oil blends. The activity of the essential oils and plant extract can be affected by plant species, composition, harvesting season, extraction method and stability (Bonetti et al., 2021).

# 7 Management practices

Commercially, pigs tend to be weaned at approximately four weeks of age. While this is associated with herd management benefits, it contrasts with weaning in nondomesticated pigs that occurs somewhere between 10-17 weeks of age. The faster growth rate of commercially reared pigs means they are more developed at four weeks than their counterparts in the wild. Nevertheless, their immune system is still developing, and they are susceptible to a range of challenges that may impact on appetite, growth rate and on their overall health. This happens not only in the period immediately postweaning but also with potentially lasting effects over the longer term (Moeser et al., 2017). While good management practice helps to mitigate the challenges impacting commercially reared pigs at weaning, it requires continual review to reflect the emergence of new challenges as patterns of disease evolve (Evans, 2001). Management practices are wide-ranging and may include, as illustrated in Figure 4, managing availability and intake of feed and water, managing the wider environment in terms of housing and hygiene, and management strategies to delay weaning and reduce stress. In practice, measures overlap, and benefits are optimised through a holistic or systemic approach to minimise the risk of gains in one area being offset by losses in another (Evans, 2001).



Figure 4. Wide-ranging management practices during weaning in pigs

Practices are interlinked and not mutually exclusive. For example, in the diagram, delayed weaning is associated with stress reduction; feeding regimes and water quality are connected as both refer to basic necessities, while a link is also made between housing and pen layout, and hygiene and biosecurity as both reflect aspects of farm management.

## 7.1 Stress reduction

Weaning requires that pigs adjust to the absence of maternal care and make the transition from suckling milk to eating solid diets. Accompanying management changes present young pigs with additional challenges (Sterndale *et al.*, 2022). For example, weaned pigs may be separated from littermates, mixed with new and unfamiliar pigs, and exposed to a new environment (Moeser *et al.*, 2017). The stress of weaning can contribute to intestinal and immune system dysfunctions that result in reduced pig health, growth, and feed intake, particularly during the first week after weaning but with impacts potentially enduring over the longer term.

To mitigate the challenges associated with weaning, various strategies have been described in the literature. As outlined in Table 6 below, these seek to reduce the stress arising from separation from littermates, mixing with new pigs, and exposure to a new environment. Biologically, it is plausible and likely that stress reduction positively affects all parameters (diarrhoea, mortality and growth).

Source of stress	Mitigation measure
Interruption of feeding patterns and	Ensuring pigs have prompt and regular access
change in diet	to fresh feed
Separation from littermates	Keeping pigs in their original litters at weaning

Table 6. Potential sources of stress at weaning and associated mitigation measures.

Mixing with new pigs	Familiarising batches of piglets through a multi- suckling environment
Exposure to a new environment	Close attention to environmental conditions and monitoring for behavioural indications of stress

#### • Interruption of feeding patterns and change of diet

The ease of access to feed for newly weaned pigs and the time interval of feed intake from removal from the sow to finding food in the new environment is critical. Before weaning, pigs feed every 2–4 hours and are called to do so by the dams through 'grunting'. Any increase in this time between feeds is stressful. Ensuring pigs have prompt and regular access to fresh feed is important. Most post-weaned pig feed has high milk content that risks going rancid at the high temperatures of the weaning accommodation. Pigs will be reluctant to eat rancid feed. Implementing systems where pigs are called to eat in the first week after weaning may be of benefit. Feeding practices such as creep feeding are discussed in the section Feeding regimes.

### • Separation from littermates

While keeping pigs in their original litter at weaning is a relatively simple measure that can be implemented with good results, it is not always possible or practical in the context of available space and established pig flow. Where it can be put into practice, maintaining litter groups minimises not only the circulation of disease across different litters but also reduces the upheaval associated with establishing new social hierarchies when pigs are mixed.

#### • Mixing with new and unfamiliar pigs

Introducing adjacent litters to one another before weaning may be implemented by lifting barriers between adjacent farrowing pens. This allows pigs to mingle before weaning while still having access to their mothers. At weaning, the mix of previously introduced litters eases the establishment of social hierarchies and reduces stress. It is important to notice that this practice increases the risk of disease spread between litters and may jeopardise the efforts put towards controlling diseases such as PRRS.

Work in Sweden (Šilerová *et al.*, 2010) and the Netherlands (Van Nieuwamerongen *et al.*, 2015) has explored the implications of multi-suckling compared with single-suckling production systems. On the one hand, the former found no significant differences between piglets reared either with individual sows or in a group setting in terms of their playing, fighting and biting behaviours observed around weaning. On the other hand, the latter found, among other things, that early socialisation experienced by piglets in a group environment and earlier interest in solid food appeared to help them adjust post-weaning. These benefits were, however, offset by raised mortality levels in the preweaning stages.

#### • Exposure to a new environment

It has been suggested that newly weaned piglets experience greater difficulties adjusting to a new environment rather than to a new social group (Puppe *et al.*, 1997). Furthermore, Colson et al. (2012) found that moving and mixing pigs at weaning is not only stressful but additive, concluding that there should be a greater focus on the environment at weaning to improve the welfare of piglets. Indeed, the environment for

weaned pigs in some intensive systems can be barren (Kelly et al., 2000; Bulens et al., 2016), with Kelly et al. (2000) observing less undesirable pen and pig-directed behaviours in straw-bedded rather than slatted systems. However, solid floor systems, including straw bedding, can increase the levels of enteric disease due to continued/prolonged exposure to faecal contents compared to slatted systems.

AHDB's leaflet on "Establishing the weaned pig" highlights the importance of managing the environment while paying close attention to the behaviours being exhibited (AHDB, 2020a). For example, excessive noise may indicate lack of access/ability to find fresh food stress. More specifically, chilling may prompt pigs to lie in huddles and to dung in the lying area. Avoid putting newly weaned pigs into a cold pen, allow sufficient time for pens to reach the required temperature before pigs are introduced. Emerging vices may reflect discomfort due to draughts, over-stocking or insufficient access to food and water. Maintaining a comfortable and consistent temperature; preventing draughts; stocking at an appropriate rate to avoid over-crowding; and ensuring ready access to fresh, clean water and an appetising diet are all advised.

## 7.2 Housing and pen layout

Only one publication describing interventions to control pathogens affecting postweaning mortality (not necessarily caused by diarrhoea) was retained. Depopulation was presented as an 'aggressive' intervention with proven results for pathogens like *Mycoplasma hyopneumoniae* or Porcine Reproductive and Respiratory Syndrome (PRRS). In the case of PWD, unless the problem is caused by a specific pathogen, it is not likely that drastic housing changes like depopulation will solve the problem. In the particular case of PWD associated with pathogenic *E. coli*, partial depopulation (of postweaned piglets) on a farm basis is not likely to be effective as sows are carriers of the pathogen. Differences in the incidence of diarrhoea between floor type and the supply of straw should be investigated.

Twenty years ago, reflecting on the housing and management of weaned pigs, Evans (2001) remarked that although the adoption of new production practices solves some problems associated with older systems, it will, in turn, give rise to new challenges as patterns of disease change. Some themes, however, are enduring. The need for a well-planned pig flow, close attention to detail and skilled stockpersons highlighted by Evans are echoed in the AHDB's current advice on 'Establishing the weaned pig' (AHDB, 2020a). Ensuring evenly-sized groups, handling piglets quietly and gently and working on an all-in/all-out basis to allow accommodation to be cleaned, disinfected and dried between batches are all advised.

In an early study into the effect of housing conditions on the behaviour of weaned pigs, Metz and Gonyou (1990) found little difference between piglets remaining in the farrowing unit after removal of the sow and those moved to weaning units. Similarly, Hötzel et al. (2011) were interested in better understanding interactions between housing and social change at weaning, and their studies led them to argue for an emphasis on ensuring that a solid diet is well-established before additional stressors of housing and social change are introduced. For Oostindjer *et al.* (2011), embedding social and foraging

behaviours in the pre-weaning environment and carrying these through to the postweaning environment may help piglets with this transition.

There are practical considerations as well. For example, National Animal Disease Information Service (NADIS) identifies low or variable temperatures and drafts among confounding factors that may increase the susceptibility of newly weaned pigs to PWD. In particular, the risk of chilling, which may prompt the blood supply to be diverted away from the gut and towards the vital organs, is highlighted. Writing in the Farmers Weekly, Hayley Chapman (1 February 2021) notes that while it is difficult to be absolute given variables of housing, vitality and appetite, as a general rule of thumb, a target temperature of 28–30°C, or 25°C in a straw system, is appropriate immediately postweaning. Dropping incrementally to 23°C once the animals reach a target weight of 20 kg.

## 7.3 Water quality

Drinking water is a critical point in preventing diarrhoea. Ensuring pigs have access to high-quality drinking water, both microbiological and physical-chemical, is essential to prevent the development of nutritional imbalances and bacterial and viral infections. Despite being a fundamental principle of livestock farming, it is one of the most often overlooked. In addition, water temperature, flow rate and pressure will also condition pigs' access to water and its consumption. Close attention to hygiene between batches and regular monitoring is advised, as any reduction in water consumption will lead to lower feed consumption.

"Despite clear evidence that a high bacterial count in water is in itself a cause of postweaning diarrhoea, the French research showed it to be a RF for post- weaning diarrhoea in conjunction with other RFs. The water quality in many herds, based on counts of faecal contaminants and total bacteria, was poor. The World Health Organisation potable water standard for human consumption is zero faecal coliforms and zero faecal streptococci. This standard was used, and only 12 batches (22%) were drinking potable water." (Skirrow et al., 1997)

AHDB's guidelines, Water Guidance for Pig Farmers, address water quantity and quality, usage, waste and drainage, regulations applicable to pig units and supply issues. Under water quantity and quality, the estimated daily water requirement for newly weaned pigs is in the range of 1.0 - 1.5 litres/day rising over time to 5.0 - 6.0 litres/day as they approach finishing weight. In an Expert Guide to Feed and Water Requirements for Weaners, Farmers Weekly (2020) highlights the importance of ensuring the accessibility, cleanliness, and appropriate flow rate of water for weaners and also suggests practical measures to encourage water uptake that include ensuring consistency of nipple/bowl/trough across the farrowing and weaning environments.

Please see section 6.4, Acidification of feed and water, including organic acids, for more details on water acidification.

## 7.4 Hygiene and biosecurity

Hygiene measures work by reducing the pressure of infection and exposure to bacteria, viruses and parasites which may cause diarrhoea. Biosecurity measures will prevent

these pathogens from entering the farm or farm compartment and from spreading across different buildings/barns, breaking the disease transmission cycle. This is a practice with the potential to act as a preventive method against several pathogens. Different hygiene methods and biosecurity measures exist, and they are usually tested in combination with multiple measures.

In clean and disinfected barns, where pigs do not share the same air space as older pigs and do not access the same environment, pigs will be less challenged and have fewer outbreaks of PWD. Mortality is reduced due to less diarrhoea and other diseases. "Under poor sanitary conditions, piglets had depressed growth performance, stimulated immune system and a provoked inflammatory response which interferes with growth because of competition for nutrients between structural tissues and immune function." (Jayaraman & Nyachoti, 2017)

In its guidelines, Establishing the Weaned Pig (AHDB, 2020a) suggests an all-in-all-out approach by room-to-weaner accommodation to allow for thorough cleaning and disinfection between batches. To ensure the best results (Farmers Weekly, 2021), the cleaning and disinfection process should allow for i) removal of organic matter, ii) soaking with a mix of cold water and detergent, iii) washing, preferably with hot water and under pressure, iv) drying, v) disinfecting, with an approved product used at the recommended strength and applied at low pressure, and vi) drying.

## 7.5 Delayed weaning

Delayed weaning consists of delaying the weaning of the piglets to a later stage when pigs have more fully developed guts and are more resilient to the changes and stress associated with weaning. In the wild, pigs are weaned after 10 weeks of age, which is considerably later than at 4 weeks of age. Delayed weaning is not a practice implemented very often due to the farm performance losses associated with keeping the sows in lactation for longer periods of time. However, there are possible alternatives, such as split suckling, where sows are removed from the piglets for certain periods of time in order to induce heat but without stopping lactation (Gerritsen et al., 2008; Chen et al., 2017). This system allows the sow to come into heat and be inseminated while still nursing the piglets. The piglets can learn feeding behaviour with the sow and be weaned at a later age (Chen et al., 2017). Literature on these practices is scarce.

Al Masri et al. (2015) reviewed the influence of age at weaning and feeding regimes on the development of the small intestine. The results presented in this review are difficult to interpret since it mixes weaning age with diets after weaning. However, the authors state that "...delaying weaning from 3<sup>1</sup> to 4 weeks of age could reduce the post-weaning growth check while decreasing post-weaning mortality and faecal pathogenic bacterial counts and improving the intestinal barrier function". Another review agrees with this statement affirming that "(...) studies suggest that increasing weaning age reduces

<sup>&</sup>lt;sup>1</sup> Routine weaning at three weeks of age is not permitted in the UK. Weaning at three weeks of age is only permitted as an exception if the welfare of the piglets or the sow is compromised, and it requires the use of specialised housing for piglets. Such housing needs to be emptied, cleaned and disinfected before introducing a new batch of pigs, and it needs to be separate from housing where other sows are kept. Due to this provision, there are still units that wean piglets at around 23-24 days of age in the UK (<u>Caring for pigs - GOV.UK (www.gov.uk)</u>).

stress associated with this period and allows pigs to have a more mature gastrointestinal tract and become increasingly familiar with solid feed during lactation with an improvement in growth performance and in immune response" (Rhouma et al., 2017).

With the development of alternative farrowing systems, where sows are kept in loose crates or simply in a large farrowing pen, delayed weaning is a possibility to be considered. Writing in the Veterinary Times, Neville Gregory (2010) considers different approaches to weaning age. In healthy herds, weaning at a later age, say 35 days, may yield the highest gross margin per sow. This reflects i) the impact of higher sow feeding costs, given the extended suckling period but a reduced requirement for costly early weaning rations, and ii) reduced labour costs since pigs are more established at the time of delayed weaning and make lower demands on labour. An ADAS study (2005) found evidence of a growth check in four and six-week-old weaned pigs but not in 8 week-old weaned pigs, despite receiving a lower-specification diet at weaning. The study did not find that extended lactation adversely affected sow health.

## 7.6 Feeding regimes

In terms of stress, this is probably one of the most important aspects to address. Feeding regimes have briefly been addressed in the stress reduction section. To reiterate, the ease of access to feed for newly weaned pigs and the time interval of feed intake from removal from the sow to finding food in the new environment is critical. Before weaning, pigs feed every 2–4 hours and are called to do so by the dams through 'grunting'. Any increase in this time between feeds is stressful. Ensuring pigs have prompt and regular access to fresh feed is important. Reflecting the overlap between various management practices, feeding regimes and water quality may be considered as two sides of the same coin: with any reduction in water consumption leading to lower consumption of feed. Underpinning both good feeding and water management practice is attention to hygiene.

While there is often a growth check in newly weaned pigs, if this is not addressed, it risks giving rise to longer-term adverse effects on performance (AHDB, 2020b). Feeding regimes are plans for the provision of diets that will facilitate the transition of the pigs from nursing to eating solid feed. In other words, they can be seen as training programmes to support pigs as they learn how to feed. If pigs know how to eat and drink before weaning, the post-weaning fasting period is shortened, and with it, associated problems are reduced. Thus, training piglets to eat should start early during lactation. Most farms have creep and link feeds before introducing pigs to a 'weaner diet'. Creep feed is the first feed that piglets have access to. It is highly palatable and typically includes milk powder. This is important as pigs that eat solid feed before weaning tend to eat more post-weaning. Most reviews synthesised nutritional strategies as opposed to feeding practices or a mix between feed regimes and the nutritional composition of those regimes.

Feed regimes and feeding strategies can promote the development of the gut and the earlier adaptation of enzymes to the digestion of weaner diets. This training of the gut can reduce diarrhoea outbreaks. Mortality can be reduced indirectly by preventing diarrhoea outbreaks. Creep and link feeds are known to promote growth, also by preventing a lack of appetite and proportionating a smoother transition from milk to solids.

According to NADIS, good feeding practice begins by introducing a pre-weaning creep feed and further includes: avoiding the use of indigestible ingredients (for example, raw cereals) that may precipitate scours, ensuring that diets are fresh and free from contamination (for example, by paying attention to stock rotation and storage), and taking care to avoid gorging in the early stages (for example by offering feed little and often rather than on an ad lib basis). All these measures are supported by maintaining the highest possible standards of hygiene of troughs and feeders, ensuring sufficient trough space for piglets and ready access to fresh, clean water.

Continuing to offer creep feed for 24–48 hours post-weaning, ensuring that feed is visible, accessible and appetising, and 'calling' the piglets to feed three or four times per day in the days immediately after weaning (AHDB, 2020a) may all help with the transition.

# 8 Immune status

The immune system is the primary defence mechanism to fight off disease. It is well known that animals with an enhanced/better prepared immune system will prevent and combat infections more easily than naïve pigs and will not go off feed as a consequence of their better health. (Pluske et al., 2018a) Likewise, any practices to improve the pig's immune defences must be considered. In this section, we will cover three practices to improve the immune status of the pigs. Two of these are focused on the control of *E. coli* infections, the most important pathogen implicated in PWD.

PWD caused by *E. coli* is associated with strains that have adhesion factors allowing the bacteria to colonise the small intestine and to produce one or more exotoxins (toxins released by bacteria into its surroundings, which in this case will be the lumen of the intestine) (Fairbrother & Nadeau, 2019). These toxins will change the water and electrolyte flux/balance of the small intestine, leading to more water being drained to the lumen and causing diarrhoea. This can lead to dehydration as the intestine is not absorbing water and even drawing water to the lumen, to electrolyte disturbance which in turn can cause metabolic acidosis and result in death (Fairbrother & Nadeau, 2019).

## 8.1 Colostrum management

Colostrum is the first secretion from the mammary glands after farrowing, and it is rich in nutritional components, antibodies (also known as immunoglobulins), immune cells, growth and other factors. Its importance in pig production is accentuated because the placenta of the sow is not permeable to these components, meaning that it is only when piglets are born that they can acquire maternally derived antibodies (like IgG, IgM and IgA) through the ingestion of colostrum (Immunology Research Unit (IRU), 2018; Blavi et al., 2021).

Within 24 hours after birth, antibodies pass from mammary secretions to the lumen of the intestine, go through the intestinal absorptive cells (enterocytes), and then enter the newborn piglet's bloodstream. Once in the blood, IgG tend to act there and in other body fluids, whereas IgA's circulate and reach the intestinal and respiratory epithelia (cell lining forming the outer layer of a body surface). Other immune cells present in colostrum, like T and B lymphocytes, also reach the piglet's bloodstream. These cells can identify

(memory cells) viral and bacterial antigens and initiate the immune response to fight infection. B lymphocytes, for example, are known to contribute substantially to the production of mucosal IgA, which in turn inhibit pathogen colonisation (IRU, 2018).

The more circulating antibodies the sow has against *E. coli* and other pathogens, the higher the odds of boosting the piglet's immune system at birth via the ingestion of colostrum. Likewise, vaccinating sows against pathogenic strains of *E. coli* and other pathogens can increase the protection of piglets against those pathogens in the first weeks of life.

Managing access to colostrum using different techniques like split suckling, assisted suckling, cross-fostering to homogenise litter size and ensure access to the udder and ensuring those are done in the first few hours after birth can boost the immune status of the piglets and enhance their chances to fight off pathogenic bacteria and viruses which may cause diarrhoea before and after weaning (Muns et al., 2015).

Scientific literature was scarce on 'colostrum management' solely with the purpose of reducing PWD. Colostrum management reduces diarrhoea by reducing susceptibility to infectious agents causing PWD. However, pigs which had sufficient and timely access to colostrum are often healthier and present better growth rates compared to those which did not. This means that colostrum management also has the potential to reduce diarrhoea incidence by contributing to the general health of the piglets. As a consequence of reduced diarrhoea and less severe infections for the targeted pathogens, mortality decreases.

One of the limitations of this practice (colostrum management) is that maternal immunity against *E. coli* acquired via the ingestion of colostrum (mostly IgG) decreases as the pig ages. On the other hand, until piglets are weaned, the immune defences against local pathogens (i.e. in the lumen of the intestine), including *E. coli*, are mainly granted by milk (lactogenic immunity). This is because IgAs can still be passed on via milk and can act at the lumen of the piglet's gut, binding pathogens and protecting piglets against *E. coli*. Thus, milk withdrawal at weaning leads to the withdrawal of local immunity in the gut (IRU, 2018).

## 8.2 Vaccination for *E. coli*

Before diving into the particulars of vaccination against pathogenic *E. coli*, it is important to understand a bit more about *E. coli*-associated disease and virulence factors. Some virulence factors of *E. coli* are enterotoxins (toxins produced in or affecting the intestine) and fimbria (hair/string-like appendages on the surface of the bacteria which allow attachment to receptors in the surface of the piglet's intestines). Pathogenic *E. coli* strains which produce enterotoxins are called enterotoxigenic E. coli (ETEC). These enterotoxins are secreted to the gut and can have local (i.e. hypersecretion of fluids, causing diarrhoea) or systemic effects (i.e. oedema disease). Typically, F4 (K88) and F18 intestine receptors to which fimbria can adhere to are present in pathogenic *E. coli* strains. F18 *E. coli* strains are associated with oedema disease, causing neurological signs and sudden deaths. This type of *E. coli* is also called Shiga toxin-producing *E. coli* (STEC).

Vaccines work by inducing the immune system of the sow or piglets in response to exposure to pathogenic bacteria or virus. The immune system then develops antibodies which will kill the invasive pathogen, preventing the development of infection. Vaccinating sows and/or piglets against *E. coli* strains prevent the development of disease and therefore reduces the incidence of PWD, and the severe outcomes of disease (reduces mortality).

Vaccination strategies, especially for neonatal infections, include the vaccination of pregnant sows, which will promote the passive immunisation of piglets through colostrum, and vaccination of piglets. Gilts should be vaccinated twice in the weeks before farrowing (usually at six and three weeks before farrowing) to allow the development of an immune response and the development of maternal antibodies suitable to be passed on to the piglets through the colostrum. Multiparous sows may only need a booster at three weeks before farrowing to develop an effective immune response. It must be noted, however, that sow vaccination against *E. coli* to control PWD is not licenced. This is because there is no guarantee that piglets at weaning still have protective levels of antibodies against the pathogen. After the disappearance of the maternal antibodies, the development of an active response of the piglet's mucosa (small intestine) is needed, with local production of antibodies against F4 and F18 factors. This kind of localised immunity can be achieved with the use of "subunit vaccines, live vaccines, killed vaccines or recombinant vaccines". Vaccines can be administered orally or parenterally (Piñeyro, 2016).

According to Melkebeek et al (2013), many oral enterotoxigenic *E. coli* (ETEC) vaccines have been successfully used in weaned pigs, including subunit vaccines as well as live oral vaccines (Melkebeek et al., 2013). However, to prevent PWD, piglets would have to be vaccinated before weaning during the suckling period. In the UK, at the time of writing this report, only one commercial vaccine to control ETEC-causing PWD was approved – Coliprotect® F4/F18 by Elanco. This oral vaccine contains live non-pathogenic *E. coli* strains expressing F4 and F18 factors. According to the manufacturer, it was designed for active immunisation of pigs from 3 weeks of age against ETEC expressing F4 and F18 in order to reduce the incidence of moderate to severe PWD caused by *E. coli* and to reduce the faecal shedding of pathogenic ETEC bacteria from infected pigs. Immunity starts seven days after vaccination and lasts for three weeks, covering the critical postweaning period.

Studies done on the efficacy of this vaccine relate that the "...*Coliprotec* vaccine significantly reduced colonisation of pig intestines after challenge with a virulent F4+ ETEC strain and consequently, that the duration and severity of diarrhoea, as well as the accumulation of fluids in the intestines after infection, were significantly reduced." (Melkebeek et al., 2013). As a consequence of reduced diarrhoea, and other *E. coli* effects, like oedema disease, and less severe infections for the targeted pathogens, mortality decreases. Other vaccines tested (though not available in the market) also demonstrated better growth rates in vaccinated pigs compared to non-vaccinated pigs (Nadeau et al., 2017; Correa et al., 2022). However, in real farm conditions, confounding factors like other infectious and risk factors for diarrhoea might translate into negligible improvements in growth performance.

For more details on the vaccination developments and research against ETEC, we recommend the reviews by Canibe et al. (2022), Melkebeek et al. (2013); and Dubreuil (2021).

The success of the vaccination programme will depend on the bacterial strains circulating and the characteristics of the vaccines employed. Likewise, isolation and identification of specific *E. coli* strains causing diarrhoea on farm is a good practice to ensure a correct choice of vaccine and its efficacy. Another issue to be considered is weaning age, as, on some farms, the timing of administration of the vaccine may not allow the development of a proper immune response before weaning. For example, Coliprotect® can be administered from 18 days of age, but if weaning occurs at 25 days, piglets may not have protective levels of antibodies circulating at weaning.

Finally, if commercially available vaccines are not effective in controlling the problem on farm and the problem has been correctly identified (i.e. it really is ETEC causing diarrhoea) and isolated, autogenous vaccines may be developed. Autogenous vaccines are vaccines produced from pathogens retrieved from pigs from a specific farm and used for the treatment of those pigs on that farm.

Vaccination is a highly specific practice, meaning that it will not be effective against other causes or pathogens causing diarrhoea. It also requires extra labour and can be expensive, especially when vaccinating piglets.

# 8.3 Antibiotic usage for *E. coli*

Treatment for PWD caused by *E. coli* is based on antibiotic therapy. Generally, sick pigs must be treated parenterally as they will eat little and drink little. However, antibiotics in feed (medicated feed) are generally the approach taken to prevent or treat large groups of weaner pigs from developing severe clinical signs.

Due to the development of antimicrobial resistance, any antibiotic treatment should be preceded by a positive diagnosis, followed by antimicrobial sensitivity testing before prescribing an effective drug. Historically, antibiotics that reach therapeutic concentrations in the small intestine, such as amoxicillin and clavulanic acid, fluoroquinolones, cephalosporins, apramycin, ceftiofur, neomycin, or trimethoprim, have been used. Antibiotics critically important to human medicine, such as fluoroquinolones and cephalosporins of 3rd and 4th generation, must only be used as a last resort (Fairbrother & Nadeau, 2019).

For many years, colistin has been widely used for the oral treatment (in-feed) of intestinal infections caused by *E. coli*, particularly of PWD in pigs. However, its widespread use is giving rise to concern about the development of resistance, meaning that future treatment effectiveness may be compromised. This is particularly worrying considering that colistin is an important drug used to fight multi-drug resistant bacteria in human medicine (Rhouma et al., 2017). In the UK, there is a general agreement to restrict the use of colistin and other critically important antibiotics for the treatment of infectious disease in pig production, and only use these as last-resort treatments.

Historically, in-feed antibiotics were the preferred administration mode when PWD caused by bacteria was diagnosed. However, the restrictions and the more prudent use of antibiotics mean that in-feed medication is not advisable due to the limitations of targeting only sick animals. In-water medication provides a more targeted treatment by allowing medication to single pens of piglets in a given building or barn. These systems, though more expensive, are now preferred.

**Disclaimer**: While most (if not all) of the practices listed thus far act mostly as preventative measures, the use of antibiotics to control diarrhoea is a therapeutic (curative) measure. Indeed, the use of antibiotics, especially under the new EU veterinary prescription rules (Munoz Madero, 2019) is only to be applied after a thorough diagnostic approach, including antibiotic sensitivity testing (AST) and only in batches with the identified problem. At the time of writing, this new EU legislation was being revised in the UK by the Veterinary Medicines Directorate (VMD) and out for <u>public consultation</u>.

Nevertheless, there are times in which the health and welfare of pigs are severely impacted, and antibiotics are still necessary.

# 9 Sector-wide evidence gaps

During the literature review, it became evident that there is still much to discover regarding the mechanisms of action of ZnO. Researching how ZnO works can provide useful insights into what works and which alternative practices have the potential to mimic its effects.

The authors are aware of two relevant projects on this topic, which may provide answers in the future. Working directly with farmers in anticipation of 'zero zinc', a one-year BBSRC-funded pilot study led by the Roslin Institute is investigating the impact of the withdrawal of ZnO at therapeutic levels on piglet health and growth. The study's goal is to identify practical measures that will make an on-farm difference to reduce disease while improving animal welfare and productivity. A range of biological measures are being studied to see which factors influence PWD in piglets. Pig faecal samples are being collected from participating farms in England, Scotland and Northern Ireland as they adjust to the withdrawal of ZnO supplementation with analysis of the type and numbers of microbes found. In particular, the composition of the 'friendly' gut bacteria, as well as disease-causing bugs, and levels of resistance to antibiotics are being examined. As well as biological data, management changes and the wider attitudes of livestock keepers are being explored to provide an all-around perspective of the pathway to change. A similar project has been conducted in Ireland (ZincO - Teagasc | Agriculture and Food Development Authority) and is now publishing its results (Sanjuán et al., 2022). This project studied the effects of ZnO on the pigs' microbiome, resistome and immune system in commercial conditions to help develop alternatives and has studied the implementation of different strategies to stop the use of ZnO on farm, providing Irish farmers with support when they have to remove ZnO.

During the analysis and synthesis of the evidence collected, we have identified the following sector-wide evidence gaps i) the impact of improved welfare standards on the reduction of PWD, ii) how do organic and outdoor systems compare to indoor systems

regarding PWD, iii) what is the impact of delayed weaning beyond five weeks of age, and iv) what are the interactions and synergistic effects between certain practices.

In this report, we discussed the benefits of stress reduction on the reduction of PWD, and it is known that improved welfare is necessarily related to stress reduction. However, improved welfare standards as defined by the industry and consumer expectations also include the provision of straw and other bedding materials. These materials may interfere with the diet (by inadvertently providing an additional source of fibre) and could disrupt the cleaning and disinfection (C&D) frequency and routine on farm (more organic matter to remove before starting the C&D process). Similar to this issue, there was no literature debating PWD in organic or outdoor settings and how they compare to indoor systems. It would be helpful to identify measures implemented in these systems that can be implemented in indoor pig farms. For example, a common feature of organic systems is delayed weaning. To what extent delayed weaning would mitigate or even eliminate the risk of PWD is unknown. There are records of 'intermittent suckling' systems in which four weeks after farrowing, sows are removed from the piglets for a few hours every day to induce heat but without stopping lactation. This means that piglets can be weaned at a later age without much or any reproductive performance losses (Gerritsen et al., 2008; Chen et al., 2017).

Finally, given that PWD is a multi-factorial problem, it is logical that its prevention and treatment are also multi-factorial. Little is known about the interactions and synergic effects between multiple practices when adopted simultaneously. It is difficult to assess these because every farm will have its own characteristics and a tailored plan is necessary. Knowing which combination of management practices has the best effects and which nutritional changes are most effective in stopping PWD caused by nutritional factors would be immensely helpful to most farmers (Barba-Vidal, 2022). More information on how nutrition can impact the immune status and on the reaction to vaccines is needed.

# 10 Additional practices and future development

Some areas in which evidence gaps were identified are also practices which should be developed in the future. We consider that intermittent suckling, the interactions between nutrition and health management, and attention to the management of the team running the farm (farmer, stockpersons, veterinarian, nutritionist, geneticist, etc.) should be further developed. In the latter, encouraging dialogue between all parties involved in the management of the farm is the key to ensuring the goals of the different sectors are aligned, and farm operations run smoothly.

From the literature review undertaken, two practices showed great promise for development: phages and genetic improvements. These two practices are summarised below.

### **Bacteriophages**

Bacteriophages (phages) are viruses which target and kill bacteria, including multi-drug resistant strains with extreme specificity without damaging the natural gut microbiota. Being natural enemies of bacteria, phages have great advantages over antibiotic use in the livestock industry and food industry (Yan et al., 2012; O'Sullivan et al., 2019; Dec et

al., 2020). They are easy to isolate and develop, stable within most guts of animals and can amplify at infection sites to ensure a continuous dose supply of the anti-infectives. Although discovered over a century ago, phages are gaining more recognition lately due to increased awareness. Thus, many phage preparations that target and kill diarrhoeal pathogens are being investigated for therapeutic purposes in the pig industry (Dec et al., 2020).

Pertinent to PWD, phage therapy (application of phages to treat bacterial infections) has been shown to significantly reduce concentrations or colonisation of enteric or diarrhoeacausing pathogens in pigs (Desiree et al., 2021). For example, phage therapy experimental work conducted on *E. coli* F4 showed that pigs could be protected from the pathogen and cause a delay in the onset of symptoms of diarrhoea, and a reduction in colonisation and faecal shedding of the pathogen was observed (J. Zhang et al., 2015; Gigante & Atterbury, 2019; Bonetti et al., 2021). Therapeutic effectiveness of phage has also been demonstrated on other pig enteric pathogens, such as *Salmonella enterica* and *Clostridioides difficile* (Nale et al., 2018; Desiree et al., 2021). More recently, experimental studies have shown that the formulation of phages into spray-dried delivery forms can be incorporated into pig feeds and used to effectively reduce colonisation in pigs (Thanki et al., 2022). This can effectively be used to decrease PWD in pigs by targeting gut-pathogenic bacteria.

Phage therapy has also been shown to improve growth parameters, fecal consistency score, villi:crypt ratio, and goblet cell density and can enhance growth and better digestibility (Yan et al., 2012). Also, experimental evidence supports the safety of phage therapy on gut microbiota with a tendency to enhance the colonisation of good bacteria such as enterococci, lactobacilli and total anaerobes, exerting some probiotic properties (Nale et al., 2018; Byrne, 2022).

Despite the advantages and experimental evidence, however, currently, no phage preparations are commercially available for usage in pigs. Problems have mainly been on the possibility of the transfer of unwanted genes responsible for toxin production and antimicrobial resistance carried by phages through horizontal gene transfer (Villa et al., 2019). Also, preparing phages (i.e. amounts or dose, length of treatment, types of phages to target specific bacteria and their strains) and formulating phages for optimal pH delivery in the gut in various forms such as through feeds is still in developmental stages (Malik & Resch, 2020). Another issue with the use of phages is the consumer's unfamiliarity with them. Bacteriophages "as 'viruses' could be misinterpreted by the general public as being in some manner equivalent to viral pathogens that cause human disease" (Loc-Carrillo & Abedon, 2011). Finally, phage regulation, legislation and manufacturing are still in the infant stages in many parts of the world, and these create hurdles to their clinical development for therapeutic application (Huys et al., 2013).

## **Genetic selection**

We identified a very interesting review on the potential of genetic selection to control PWD in pig farms (Sinha et al., 2019). This contemplates the genetic selection of pigs resilient against *E. coli* infections, and it can be included as a promising alternative to the use of ZnO to control PWD. However, this can only be done at industry level, and it is not an option for individual farmers.

# 11 Considerations on the return of investments

The rate of return on investment (ROI) is a measure of the profitability of the investment made. It is computed by subtracting the initial cost of investment from the final value of the investment after a particular period divided by the initial cost of the investment. Thus, if an investor buys 10 shares in a company X at £1 per share and sells them at £2 per share one period later (being this period something that the analyst must determine prior to the computation of the ROI), obtains £0.5 per share during the period in which the investor holds the investment, and pays £2 for performing the transaction of buying the shares, the rate of return of this investment at the end of the period (which in this case is when the investor sells the shares) can be computed as:

$$ROI = \frac{\pounds 2*10 + \pounds 0.5*10 - \pounds 1*10 - \pounds 2}{\pounds 1*10} * 100$$
(1)

In the case of an investment in an agricultural practice that replace ZnO in the swine industry, the ROI is calculated similarly, but the quantities considered are the output and inputs of a pig farm. The following formulae can be employed:

$$ROI = \frac{(\pi_{np} - \pi_{op})}{\pi_{op}} * 100$$
 (2)

Where  $\pi_{np}$  is farm's profits with the new practice and  $\pi_{op}$  is the farm's profits with the old practice. A ROI computes the percentage change in the farm's profits when the new practice is adopted. As such, the computation of the ROI is farm-specific and depends on the initial layout and practices of the farm. It also depends on whether the practice under analysis changes the cost structure of the farm or not. Therefore, a ROI only can be computed when all the values associated with the profit function of the farm are known. Alternatively, the following measure can also be computed:

$$ROI2 = \frac{(\pounds P_z^{np} Z_{np} - \pounds P_z^{op} Z_{op})}{\pounds P_z^{op} Z_{op}} * 100$$
(3)

This measure computes the change in the costs of the farm with the new practice. A positive value means that the farm is expending more money with the new practice relative to the old practice, and a negative value means that the farm is expending less money with the new practice.

#### **Disclaimer:**

Commercial sensitivities around on-farm prices make the calculation of actual ROIs difficult. With the required information per pig unit, equation (2) may be used to calculate a ROI for each practice analysed in the narrative summaries.

Indicative ROIs have been calculated where price information is publicly available, or for practices where an estimated cost was provided by industry advisors. These calculations are, however, subject to significant uncertainties given the instability in global feed and energy markets at the time of reporting.

**Warning**: in all cases, ROIs are estimated comparing the use of ZnO in feed and the adoption of the new practice.

For farmers to effectively use the ROI calculator provided in this report, they need to request/have information on the following variables:

- Liveweight (LW) of the pig with old practice (kg), which in this case is under ZnO
- Liveweight (LW) of the pig with new practice (kg), which in this case is under any of the alternative practices analysed in this report
- LW pig price (£/kg), which is the price at which a piglet is sold after the weaning phase
- Price of ZnO (£/kg)
- Recommended use of ZnO for the whole treatment period (kg/treatment). This value is recommended by the EU to be 0.0105 kg of ZnO in total during 14 days of treatment
- Price of creep with ZnO (£/kg). It is the price of the feed creep that comes with ZnO in the mix. If farmers introduce ZnO themselves to the diet of the piglets, then please disregard the price of this feed once ZnO's price has already been taken into account as a standalone value (Price of ZnO (£/kg). Instead, provide the price of Creep without ZnO
- Price of link with ZnO (£/kg). It is the price of the feed link that comes with ZnO in the mix. If farmers introduce ZnO themselves to the diet of the piglets, then please disregard the price of this feed once ZnO's price has already been taken into account as a standalone value (Price of ZnO (£/kg). Instead, provide the price of link without ZnO
- Price of creep without ZnO (£/kg). It is the price of the feed creep that do not come with ZnO in the mix
- Price of link without ZnO (£/kg). It is the price of the feed link that comes with ZnO in the mix
- Quantity of creep (kg/treatment). It is the kg of creep that are fed to each piglet during the ZnO treatment period, even if ZnO is not being administered
- Quantity of link (kg/treatment). It is the kg of link that are fed to each piglet during the ZnO treatment period, even if ZnO is not being administered
- Price of new practice per unit (e.g. £/kg, £/gr, £/dose, etc). It is the price of any of the products introduced in this report as potential substitutes for ZnO
- Quantity of new practice per unit (e.g. £/kg, £/gr, £/dose, etc). It is the quantity of any of the products introduced in this report as potential substitutes for ZnO

# 12 Discussion

PWD is a topical problem that has been historically controlled with antibiotics or, more recently, with ZnO. Considering the withdrawal of ZnO as a control option, there is an urgent need to seek alternative practices to control PWD in pigs. The results of this work show that, unsurprisingly, the pig industry has responded to this need by researching and developing in-feed alternatives to ZnO. Within these alternatives, pre and probiotics exhibited a clear capacity to promote gut health or to reinforce the immune system, respectively, and therefore combat pathogenic *E. coli*.

From all the nutritional changes studied, while most reported positive effects, there were possible losses in performance. For example, pushing the pigs to perform by using high

crude-protein contents may exacerbate the PWD problem and lead to lower growth rates. In this context, allowing the gut to develop and accepting a lower performance periweaning may prove a better strategy in the long term. The effect of nutritional changes in reducing PWD and post-weaning mortality was largely dependent on the main cause behind PWD. If this was caused by nutritional deficiencies, imbalances, or indigestible ingredients, most nutritional practices were relatively effective in controlling diarrhoea. Anecdotally, one of the reasons for this positive effect may be the fact that before implementing any of these practices, a re-evaluation of the pig diets is necessary, which might then prompt the correction of any anomalies identified. None of the practices were singled out as the most effective or promising ZnO replacement.

Indeed, the efforts put into finding in-feed replacements of ZnO disregard the fact that ZnO as a treatment was not minimising the risk factors for the development of PWD but rather attenuating the problem or preventing the manifestation of severe outbreaks. If all facts surrounding the development of PWD were considered, we must acknowledge that the most important factors are the age at weaning and the underdevelopment of the gut. In the UK, as in the EU, pigs are widely weaned at 28 days of age<sup>2</sup>. Although this is an improvement on 21-day weaning practised in much of the rest of the world, this is still an early age compared to what would happen in the wild, with pigs being weaned from 10 weeks of age (Postma, 2019). This six-week difference is when piglets learn feeding behaviour from their mothers, and their gut gradually develops to digest solid feed and more complex ingredients. Later weaning ages also mean that piglets would be kept in their original litters for longer periods of time, and exposure to new environments would be progressive as the piglets gain independence and attempt to explore the surroundings of the nest. This is a very different situation compared to what happens in many commercial settings when piglets are weaned abruptly, mixed with other litters and moved to different facilities in the space of hours. Decisions about weaning age require farm-specific approaches to consider risks associated with PWD and other diseases.

Identifying the most important risk factors contributing to disease in each farm is, therefore, a crucial step for every farm before attempting to implement practices to control PWD. That will greatly impact the success of the practice chosen. A thorough diagnostic approach should be applied before deciding which therapeutic measures to implement. This includes the diagnosis of infectious agents but also investigation procedures around risk factors for PWD (for example, high protein content in the diet, poor cleaning and disinfection, etc.).

Good management is a key step for the prevention of any disease, and this is emphasised in light of the weaning challenges mentioned above. However, management will differ considerably between farms, making it difficult to test them, and most of the practices discussed in this report overlap considerably. For instance, stress reduction as a practice encompasses changes in different areas – such as nutrition, environment, feeding and management practices. Delayed weaning, early exposure and adaptation to

<sup>&</sup>lt;sup>2</sup> Legally, both in the EU and in the UK, it is still allowed to wean pigs at 21 days of age. However, this is only permitted if the welfare of the piglets or of the sow is compromised; and it requires the use of specialised housing for piglets. Such housing needs to be emptied, cleaned and disinfected before introducing a new batch of pigs, and it needs to be separate from housing where other sows are kept. Due to this provision, there are still units that wean piglets at around 23-24 days of age in the UK (<u>Caring for pigs - GOV.UK (www.gov.uk)</u>).

new (highly palatable) feeds, keeping pigs in their original litters after weaning, offering good and enriched environments (temperature, air quality, clean), and separating different age groups will all contribute to a reduction of the stress levels, less 'enteric' stress when digesting new feed, and less social stress when moving to a new environment. All management measures will act on the reduction of scours, but also on the decrease of post-weaning mortality caused by other infectious agents and on the improvement of growth performance (pigs less stressed and challenged will growth more). The effect of many practices is known empirically, whereas, unfortunately, scientific evidence may be sparse. For this reason, management practices seem to be the most effective (when compared to nutritional changes and immune status) in controlling PWD.

Immune status improvements (with the exception of antibiotic use, which will be discussed below) were very effective in controlling PWD when this is caused by some strains of pathogenic *E. coli*. These practices, especially piglet vaccination against *E. coli*, presented as highly specific and efficacious solutions for well-diagnosed problems. PWD and mortality are reduced by the implementation of these measures, while the growth rate may also improve. These measures were more costly when compared to other practices, especially considering the diagnostic approaches needed to inform veterinary advice before changes are implemented.

It seemed somewhat counterproductive to include antibiotic use as a practice to control PWD once ZnO was introduced and used to prevent or reduce the use of antibiotics. Besides, the use of antibiotics to control diarrhoea, especially under the new prescription rules, is only to be applied after a careful diagnostic approach and only in batches with the identified problem (Munoz Madero, 2019). More worryingly, the use of antibiotics per se does not solve the root cause of diarrhoea but rather just offers a quick fix for one batch of pigs. Nevertheless, there are times in which the health and welfare of pigs are severely impacted, and antibiotics are still necessary, hence the inclusion of this practice in this report. Despite the threat of antimicrobial resistance, antibiotics may still be efficacious as a treatment against pathogenic *E. coli*, provided that an antibiotic susceptibility test (AST) was performed to choose the best antibiotic and its concentration and that veterinary advice is followed. In addition to the considerations laid out above about this practice, its costs may also be significant.

All in all, one of the most important messages is that in all cases, though especially in the case of management practices, it is likely that the application of more than one practice at once has a synergistic effect. This means that implementing a range of measures tailored to the problems of each farm is probably the best solution to control PWD.

Cost considerations were listed for all practices, and we hope that these may help farmers when deliberating the implementation of one or more practices. The high feed costs and the aggravating losses verified in the UK pig sector over the last year leave a tight or non-existing margin for farm structural changes or for any increased costs. However, changes which have the potential to stabilise the farm in terms of disease and improve efficiency may present very good returns. This may be a good time to perform an internal audit to systematically assess all farm operations to identify areas and processes which can be improved. After this, a list of the most cost-effective actions could be prepared and its implementation studied. Following this chain of thoughts, we believe the industry would benefit from decision support tools to assist in identifying on-farm risk factors for PWD, planning the implementation of practices tailored to each farm, and assisting with monitoring its implementation and results over time.

# 13 Closing remarks

This REAs work aimed to identify practices to reduce or control PWD in pigs without using ZnO at therapeutic levels. Here, we looked at three main groups of practices: nutritional changes, management practices, and immune status improvement to produce an overall picture of the evidence landscape.

Despite all identified interventions, there is no single intervention that scores as highly on repeatability or reliability as the use of ZnO at therapeutic levels to control PWD. This should highlight the need for a multi-factorial approach tailored to each farm, where all parties (farmers, vets, nutritionists, advisors, etc.) are involved.

# 14 References

References are divided into the sections "Systematic searches" and "Manual searches".

# Systematic searches

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# 15 Appendices

# 15.1 Evidence for Farming Initiative (EFI) Draft - Evidence Standards

# 15.1.1 Effectiveness

**Appendix 1**. Scoring/rating for effectiveness used for the impact summaries in this report.

	Evidence founds to above a manafive offerst. The belower of evidence (including the			
-ve	Evidence tends to show a negative effect. The balance of evidence (including the			
	pooled effect size where available) suggests that the practice has a negative effect,			
meaning the practice made things worse. This takes into consideration the				
	studies showing positive and negative effects, and the levels of involvement (number and			
	size of participating entities) in those studies.			
0	No effect. The balance of evidence (including the pooled effect size where available)			
	suggests that the practice has no effect overall.			
+/-	Evidence tends to show a mixed effect. Studies show a mixture of effects and the			
	criteria for 'tends to negative effect' or 'tends to positive effect' are not met.			
+	Evidence tends to show positive effect. The balance of evidence (including the pooled			
	effect size where available) suggests that the practice has a positive effect. This takes			
	into consideration the number of studies showing positive and negative effects, and the			
	levels of involvement in those studies.			
++	Evidence shows consistently positive effect. The evidence (including the pooled effect			
	size where available) consistently suggests that the practice has a positive effect. This			
	takes into consideration the number of studies showing positive and negative effects, and			
	the levels of involvement in those studies.			

### 15.1.2 Cost

Appendix 2. Scoring/rating for cost used for the impact summaries in this report.

£	No new equipment or time constraints over and above existing business as usual (BAU		
	running costs.		
££	May need some additional time for training or experiential learning to establish new		
	practice, but once implemented this rapidly transitions into BAU running costs.		
£££	As above, plus new equipment and capital costs for machinery and implements on farm.		
££££	Major investment in new infrastructure on farm and/or loss of land utility/land use change		
	that is greater than the normal rotation(s).		

## 15.1.3 Speed of Change

**Appendix 3**: Scoring/rating for speed of change used for the impact summaries in this report.

Fast	Effective immediately, change within 0-3 months.	
Moderate	Effective within 12 months.	
Slow	Effective in longer than 12 months.	

# 15.1.4 Strength of Evidence

Appendix 4. Scoring/rating for strength of evidence used for the impact summaries in this report

	Very high	High	Moderate	Low	Very low
	••••	••••○	•••00	••000	•0000
Quality of literature	An extensive body of	A developing body of	Studies of the highest	Studies using quasi-	High quality
	high-quality evidence	high-quality evidence	quality (randomised	experimental methods	observational
	reviews.	reviews.	control trial equivalent)	OR at least one	studies.
			OR at least one high-	moderate-quality	
			quality evidence	evidence review.	
			review.		
Relevance of context	As level 4, but with	Includes evidence	Evidence generated in	Evidence generated in	Evidence generated
	excellent contextual	generated in farming	farming and growing	research centre farming	through laboratory
	and Implementation	and growing	businesses with the	and growing facilities.	research.
	insight drawn from	businesses with	practice applied by		
	high-quality studies and	farmers and growers	professional		
	on-farm practice.	testing the practice.	researchers.		
Overall	We can draw very	We can draw strong	We can draw some	We believe that the	The body of evidence
	strong conclusions	conclusions about	conclusions about	practice may/may not	displays very significant
	about impact and be	impact and be confident	impact and have	have the effect	shortcomings.
	highly confident that the			anticipated. The body	
	practice does/does not	does/does not have the	that the practice	of evidence displays	There are multiple
	have the effect	effect anticipated.	does/does not have the	significant	reasons to think that
	anticipated.		effect anticipated.	shortcomings.	contextual differences
		The body of evidence is			may unpredictably and
	The body of evidence is	diverse and credible,	The design of the	There are reasons to	substantially affect
	very diverse and highly	with the findings	research allows	think that contextual	practice outcomes.
	credible, with the	convincing and stable.	contextual factors to be	differences may	
	findings convincing and		controlled for.	substantially affect	
	stable.			practice outcomes.	

# 15.2 Nutritional changes

# Advisory note

- 1) As this section addresses changes made to pig diets, it is essential that any feed formulation must involve the farmer, the vet, and the nutritionist. Neither farmers nor vets have the skills to design or alter modern diets; and nutritionists need to be aware of management practices on the farm.
- 2) Feeding regimes (i.e., the use of creep feed) should be considered alongside nutritional changes. However, due to their connection with management, those practices involving feeding regimes are explored in the management practices section 15.3.6 Feeding Regimes.
- 3) Commercial feed companies have been trialling many products and generating a lot of trial data on the use of diets and feed additives as alternatives to the use of ZnO to control PWD in pigs. However, most of these data are commercially sensitive and have not been published for that reason.

# Considerations on the calculation of returns of investments

Given the commercial sensitivities and specificities associated with feed prices, it was not practical to estimate returns of investments (ROIs) for most practices. However, where possible, a list of feed cost considerations was prepared for each practice. As general advice, we recommend farmers to ask the following questions before adopting nutritional changes:

- Is the PWD seen in my farm related to nutritional factors?
- What is the list of priorities to address regarding my diets? Or what should you address first? Feed formulation, ingredients, feed form, quantities fed, etc.
- Is the quality of the diets, including feed form (i.e., pellets or mash), satisfactory?
- How does the new diet compare with the current one price, pig performance, scours?
- Can you trial the new diet in a few batches before feeding it to all pigs on a regular basis?
- How reliable is the supplier of your feed and how stable are the prices of new feed ingredients tested?
- Have you discussed diet formulation and ingredients with your nutritionist and your vet?
- Are you sure the feed additive you want to include is compatible with the diet formulation, ingredients and form you currently have on farm?
- How much training/resources do you need to adopt this new practice?
- Are my staff aware of required changes in feed management?
- Has your pig flow and management been adapted to the new diets and feed regime?

Additional information on factors to consider when adding feed additives to your diets could be found via the link:

https://ahdb.org.uk/knowledge-library/additives-as-an-alternative-to-zinc-oxide-in-pig-diets This AHDB webpage also presents a practical: "Additive case study – testing what works on farm". If diets are **home-milled**, there are a few more considerations to take into account. Generally, more flexibility to choose cheaper feed ingredients and to formulate new diets, but the mill in farm is likely to be the limiting factor in terms of adding extra ingredients. Pig nutritionist should be consulted when new ingredients are being tested and included in diets. A few questions to consider before formulating weaner diets include:

- What assurances do I have about the quality of this feed ingredient?
- Is my mill capable of producing this diet?
- Are you sure the new feed ingredients are compatible and palatable?
- If you are using by-products, and especially if you feed liquid diets, what is the microbiological stability of your new diet? Do you need to consider extra cleaning and disinfection of the feed pipes?

Apart from these generic questions, **the AHDB rearing costs calculator** (<u>https://ahdb.org.uk/Pig-production-costs-calculators</u>) can be consulted to input desired values (yellow) and the blue boxes will show the expected costs and performance with the practice that is being simulated. in this report an additional calculator which may be of use to predict return of investments and expected costs and performance has been developed.

#### 15.2.1 Reduce crude protein intake

#### Impact summary

Protein supplies amino acids which are the building blocks of muscles and are necessary for the repair of worn-out tissues in animals. Crude proteins levels in feed should be reduced or balanced to provide sufficient protein for growth but not in excess to cause detrimental effects to piglets. High protein diets (~230g/kg) can lead to high fermentation from residual undigestible proteins, and the generation of high levels of metabolites and pro-inflammatory cytokines, which can exert negative impact on the under-developed intestine of recently weaned pigs. As a result, nutrient digestibility, permeability, utilisation, bioavailability and energy status can be negatively affected. High crude protein level can also trigger the proliferation of pathogenic bacteria leading to increased incidence of diarrhoea in weaned pigs. Lowering crude proteins (~200g/kg) is preferable but should be well balanced with increased insoluble fibre and moderately fermentable carbohydrate sources to divert nitrogen from urine to faeces and provide a better substrate for microbial fermentation over proteins. As a result, healthy microbial community and faecal consistency would be maintained in the gut environment thus, preventing post-weaning diarrhoea.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	++
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	+
	Improved welfare	+
Cost		
		£
Speed of change		
		Fast
Strength of evidence		
	Quality of literature	Very high
	Relevance of context	Very high
	Overall	Very high

## **Narrative Summary**

# 1. What is the practice?

Reducing high protein levels from ~230 g/kg to below ~200g/kg in feeds of weaning piglets would provide sufficient protein source for tissue maintenance and repair to enhance growth but not in excess to provide substrate from residual undigestible proteins for bacterial fermentation. Enzymatic activity during fermentation generates metabolites and high pro-inflammatory cytokines, which affect nutrient digestibility and permeability, utilisation and bioavailability, energy status and proliferation of pathogenic bacteria. This can affect faecal consistencies and increase incidence of diarrhoea in weaning pigs. Lowering crude protein levels is beneficial to reduce the negative impact of fermentation but should be balanced with increased insoluble fibre and moderately fermentable carbohydrates to balance nutrition and enhance growth and performance.

### 2. How effective is it?

Reducing crude protein level in pig diets produces less protein residue for fermentation in pig guts to occur. As a result, harmful metabolites and pro-inflammatory cytokines which impact nutrient digestibility and permeability, nutrient utilisation, bioavailability, energy status and proliferation of diarrhoea causing bacteria are drastically reduced. Helpful in preventing post-weaning diarrhoea in pigs, and friendly to the environment and the pigs' welfare due to reduced nitrogen excretion in urine and odour.

#### 3. Where does it work?

Applicable to any scale of pig farming, whether indoors or out, and for all breeds. Also, good for any feed formulation, whether produced in-house or commercially sourced. Opting for low protein feeds is excellent but this feed must have a balanced amino acid content and should be supplemented with increased insoluble fibre and moderately fermentable carbohydrate sources to balance productivity and reduce proliferation of pathogenic bacteria which cause diarrhoea.

### 4. How much does it cost?

Less crude protein in a ration may reduce feeding costs, depending on whether the reduction in protein intake is supplemented with insoluble fibre, fermentable carbohydrate, amino acids, or lipids (fat) to make up the energy requirements of the pigs. This practice does not require additional equipment. It is not expected that the staff briefing before feeding the new diet will require too much time to affect the normal cost structure or a large investment in specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land.

If the farmer is home-milling, the farmer will need a new diet (proposed by a nutritionist) to make sure the energy requirements of the diet are met in the face of protein reduction. Home millers will also need to consider that this practice may slightly increase the complexity of production because the farmer needs to pay attention to the exact mix of protein with insoluble fibre and fermentable carbohydrate intake, or source his/her feed from a company that produces custommade feeds or already targets this segment of the market. Studies suggest that decreasing the crude protein contents is efficacious to reduce PWD, but it may reduce growth rate. This needs to be considered as potential cost (J. C. Kim et al., 2011; Lynegaard et al., 2021).

## 5. How can I do it well?

To harness the benefits of low crude proteins in weaner diets to maximally prevent diarrhoea and optimise productivity, feed should be supplemented with increased insoluble fibre, highly digestible proteins and moderately fermentable carbohydrate and sources of branched-chain amino acids. This would help reduce generation of protein fermentation metabolites, maintain a healthy microbial community in the gut environment thus preventing post-weaning diarrhoea. Alternatively, to maximise performance loss, pigs could be fed with reduced protein in the first two weeks post weaning when they are most susceptible to diarrhoea before implementing higher crude protein.

### 6. How strong is the evidence?

Feeding weaning pigs with low crude protein showed significant reduction in diarrhoea index, coliform shedding and thus reduced requirement of antibiotic treatments, faecal excretion of toxic substances such as plasma urea nitrogen, ammonia nitrogen and volatile fatty acids at least 5-14 days from the time of diet change. Also, within this timeframe, villus height and depth were significantly improved thus enhancing nutrient permeability, utilisation, and bioavailability in the jejunum. Put together, reducing crude protein level strongly decreases the incidence of diarrhoea in piglets.

### 7. Where can I find further information?

You can find extra information in these sources: <u>Sustainable systems for management of the</u> weaner pig through nutrition (NUTWEAN) | AHDB and in here:

https://www.pig333.com/articles/crude-protein-in-piglet-diets 3207/

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#### 15.2.2 Alternative protein sources

#### Impact summary

Although soyabean meals contain high limiting amino acids and have greater digestibility than those found in other protein sources, they contain antinutritional factors that could limit growth. Soyabean also contains phosphorus bound to phytic acid which has low digestibility unless it is supplemented with microbial phytase. Heavy reliance on soyabean meal has caused unnecessary competition in food, biofuel, and bioprocessing industries and rising cost of pig feeds. With many cultivars being genetically modified, concerned consumers who prefer non genetically modified or organic production shy away from this. Therefore, other protein sources such as faba beans, field peas, chickpeas, copra, rice, potato, whey/milk, pea, sunflower and are used as cheap and accessible alternatives. Other alternatives like, poultry meal, feather meal, blood meal and insect meal are not legal in the UK. In addition to their nitrogen-fixing ability, the plant sources are rich in calcium, fat, crude protein, amino acids, energy, minerals, carbohydrates, fibre and non-starch polysaccharides but also contain some antinutritional factors such as trypsin . Together, these alternative sources can help alleviate diarrhoea and improve performance of weaned pigs.

Effectiveness	
	· · · · · · · · · · · · · · · · · · ·
	+
Reducing post-weaning mortality	+
Enhancing growth rate	++
Other impacts	
Reduced costs -	++
Improved welfare	++
Cost	
	£
Speed of change	
F	ast
Strength of evidence	
Quality Mod	lerate
Relevance of context H	igh
Overall Mod	lerate

#### **Narrative Summary**

#### 1. What is the practice?

This practice entails the use of alternative plant and animal proteins as replacement sources of protein to reduce heavy reliance on soyabeans. Such alternatives are cheap and accessible and include sources such as faba beans, field peas, chickpeas, copra meal, rice, potato, whey/milk, pea, sunflower and palm kernel meal. Other alternatives like poultry meal, feather meal, blood meal and insect meal are not legal in the UK. The plant sources are rich in calcium, fat, crude protein, amino acids, energy, minerals, carbohydrates, fibre and non-starch polysaccharides. In addition to these nutritional advantages, legumes interact with rhizobia bacteria to fix nitrogen in the soil, which is beneficial to the environment. Some plant sources, however, have a few antinutritional factors such as trypsin.

#### 2. How effective is it?

Providing alternative protein sources in the diet can be seen as the elimination of a risk factor (soyabean antinutritional factors) for the development of PWD. Its effectiveness in controlling diarrhoea is low to medium - depending on how much post-weaning diarrhoea was directly caused by the consumption of soyabeans and its associated antinutritional factors.

#### 3. Where does it work?

Applicable to any scale of pig farming, whether indoors or out, and for all breeds. Since most farmers rely on commercially sourced formulated feeds the implementation of this practice will depend on the range of offers of your feed supplier. Implementing this practice in feed mills for large scale production of diets with alternative protein sources will depend on the protein sources available, their price, and quantity available. This practice may be unattractive due to requirements for extra equipment, labour and the need for specific production expertise.

#### 4. How much does it cost?

Substituting soyabeans with other sources of plant- or animal-based protein is not expected to increase production costs or only marginally if the alternative source is more expensive than soyabeans. This practice does not require additional equipment but may require additional training on the exact quantity of plant- or animal-based protein to add if the farmer is home milling his/her pigs' diets. In addition, supplementing soyabeans with other sources of protein is not expected to change the normal cost structure of the farm or require a large investment since there is no need for a specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land. This practice may slightly increase the complexity of production because the feed mills or home millers need to pay attention to the exact mix of soyabeans and the other source(s) of protein, or source feed from a company that produces custom-made feeds or already targets this segment of the market. This practice may be affected by the forces of international trade, which may have an impact on the UK price and on the stability of the supply chain in the UK and abroad. Some of the alternative sources of protein listed above can be produced in the UK and have an incipient market in the UK.

Note that some alternative protein sources can be cheaper, lowering the price of feed. If they do not impact on pig performance, this would equate to a positive ROI.

#### 5. How can I do it well?

If you are home-milling your diets and you are sourcing alternative protein sources, make sure your diet formulation is checked by a pig nutritionist. It is also advisable to consider any physical properties of the ingredients you are purchasing and its suitability for your mill.

If you are purchasing feed compound, your pig feed supplier should be able to advise you on the best products available and on the alternative protein sources used to produce them. Ensure regular emptying, cleaning and disinfection of farm silos, especially between different feed deliveries.

#### 6. How strong is the evidence?

This practice is effective based on the direct comparison between the inclusion of alternative protein sources (in general, without appointing any particular source) and the inclusion of soyabean meals in the diet. Evidence suggests that removing soyabean meals decreases the likelihood of PWD and this practice should be seen as complementary to others.

#### 7. Where can I find further information?

You can find further information about alternative protein sources by consulting your feed supplier and a pig nutritionist. If you are milling your own feed, contact your pig nutritionist for more information.

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#### 15.2.3 Dietary fibre

#### Impact summary

Supplementing pig feeds with dietary fibre helps to maintain healthy digesta and intestinal barrier function which can positively impact growth performance, digestibility of nutrients, and prevent diarrhoea in weaning piglets. Insoluble dietary fibres have prebiotic effects and can help elevate mucosal integrity by increasing villus length, reduce adhesion of pathogenic bacteria to epithelial cells and their retention in the gut thus, reducing the incidence of diarrhoea. Lowering colonisation of pathogenic bacteria has other concomitant effects, such as reducing competition for nutrients and space in the gut for good bacteria, which supports their proliferation hence, preventing diarrhoea in post-weaning pigs. Dietary fibres also increase bulk of diets which help to promote intestinal development, gut movement, alleviate constipation, promote intestinal health and function. Soluble dietary fibres provide energy in the form of volatile fatty acids, balances low protein diets and reduces protein fermentation metabolites. Excessively high fibre diets may have conflicting impact by reducing growth and productivity associated with weaning but balancing with protein has been shown to improve the health of weaners.

**Disclaimer:** It is important to acknowledge that most studies evaluated the effect of dietary fibre testing them on pigs on slats, not on straw systems. Pigs housed in straw will likely not benefit from increasing fibre intake. However, should a different type of fibre be provided in the diet, there may still be beneficial effects regarding the prevention of PWD.

Effectiveness		
	Reducing diarrhoea	+
	Reducing post-weaning mortality	+
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	+
	Improved welfare	+
Cost		
		£
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	High
	Overall	High
	• • • • • • • • • • • • • • • • • • • •	

# **Narrative Summary**

# 1. What is the practice?

This practice focuses on supplementing feed during post-weaning with different dietary fibre. The effect on preventing PWD depends on the properties of the fibre used. The prebiotic effect of insoluble fibres provides protection against diarrhoeal causing bacteria by reducing their ability to colonise the gut. Dietary fibres also promote intestinal health and function, ileal digestibility of nutrients, provides energy in the form of volatile fatty acids, balances low protein diets and reduces protein fermentation metabolites. Overall, the essence of the practice is to maintain healthy digesta, increase digestibility of nutrients thus, preventing diarrhoea and promoting growth and adaptation of weaning piglets.

# 2. How effective is it?

Activity depends on the properties of the dietary fibres used. For example, studies indicate that feeding pigs high insoluble fibre diets showed improved gut morphology and they are better protected against pathogenic bacteria than those fed with pectin-containing diets. These effects were observed within 9-15 days of treatments.

### 3. Where does it work?

Applicable to any scale of pig farming, whether indoors or out, and for all breeds. This practice is incorporated in feeds and works in the gut, intestine, jejunum, ileum, caecum, and colon. It has showed promise in different settings, whether outdoors or indoors. Several feeds with different fibre can be used or fibre supplements bought separately and added to feeds at required levels.

### 4. How much does it cost?

Providing supplementary fibre to piglets increases feeding costs. This practice does not require additional equipment but may require additional training on the exact quantity of supplementary fibre to add or on the different potential sources of the dietary fibre to utilise. In addition, supplying dietary fibre is not expected to change the normal cost structure of the farm or require a large investment since there is no need for a specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land. This practice may however increase the costs of production because it may need to be supplemented with alternative sources of protein. This practice may slightly increase the complexity of production because the feed mill or the home-miller needs to pay attention to the exact mix of protein with insoluble fibre and fermentable carbohydrate intake, or source his/her feed from a company that produces custom-made feeds or already targets this segment of the market. This practice may be affected by the forces of international trade, which may have an impact on the UK price and on the stability of the supply chain in the UK.

Note that the inclusion of dietary fibre (quantity and quality/type) may lower the price of feed. If this does not impact on pig performance, and reduces PWD and mortality, this would equate to a positive ROI.

## 5. How can I do it well?

If you are purchasing feed compound, your pig feed supplier should be able to advise you on the best products available and on the different types of fibre included. Ensure regular emptying, cleaning and disinfection of farm silos, especially between different feed deliveries.

If you are home-milling your diets, make sure your diet formulation is checked by a pig nutritionist. It is also advisable to consider any physical properties of the ingredients you are purchasing and its suitability for your mill. Different types of fibres will have different effects on the pigs' digestive system; insoluble fibres are recommended to prevent PWD.

### 6. How strong is the evidence?

The evidence available on this practice is high. Many academic publications discuss and test the benefits of dietary fibre inclusion in the management and control of PWD. Technical publications for nutritionists also denote the different aspects to be taken into account when including fibre in diets.

# 7. Where can I find further information?

You can find further information about dietary fibre by consulting your feed supplier and a pig nutritionist. If you are milling your own feed, contact your pig nutritionist for more information.

The following articles may be useful. A brief summary/explanation of its contents follows above each link.

This article explains different types of dietary fibres and what is effective in the control of PWD.

https://www.pig333.com/articles/the-impact-of-including-fiber-in-weaned-piglet-diets 18274/

Here you have a link to an Open Access scientific article. Item 3 of this article explains the effect of dietary fibre on growth performance and digestibility of nutrients of weaned piglets, on the gut health of weaned pigs, and on the incidence of post weaning nutritional diarrhoea.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6949732/

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## 15.2.4 Acidification of feed and water, including organic acids

#### Impact summary

Incorporation of organic and inorganic acids in feeds and water acts as a biosecurity step and can lower the gastric pH of the gut when consumed. The low gastric pH has antimicrobial effects by preventing the multiplication and colonisation of pathogenic bacteria responsible for diarrhoea. It also improves immune response, general digestibility of nutrient (such as protein) and mineral utilisation. These ensure feed efficiency, improved growth performance, overall gut health of weaned piglets and prevent post-weaning diarrhoea. However, several factors such as types of acid, dosage, feed formula and age of piglets play a considerable role in the outcome of activity.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	++
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	+
	Improved welfare	+
Coot		
Cost		00.000
		££-£££
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	High
	Overall	High

## 1. What is the practice?

This practice focuses on using organic and inorganic acids in feeds and water to lower the pH of the stomach. This decreases the proliferation of diarrhoeal pathogens and improves gut health, general nutrient digestibility and utilization, and immune response, thus, preventing diarrhoea and improving growth and performance.

#### 2. How effective is it?

The post-weaning stage is associated with stress and low hydrochloric acid and pancreatic enzymes production, and sudden changes in feed consistency and intake all of which affect pig growth. Lowering the gastric pH improves activity of enzymes on protein digestion and utilisation, improves immune system and reduces the multiplication and colonisation of pathogenic bacteria (*E. coli* and *Salmonella*). The addition of 1% citric acid can reduce stomach pH from 4.6 to 3.5 and 0.7% of fumaric acid from 4.6 to 4.2. Hydrochloric and phosphoric acids can reduce gastric pH but do not improve growth rate or feed conversion in pigs. Supplementing feeds with various doses (0.8-2.5%) of formic, fumaric, sorbic, citric, k-formate, lactic acid, propionic and benzoic acids showed significantly more daily weight gain and feed conversion in pigs than untreated groups.

#### 3. Where does it work?

This focuses on supplementation of feeds and water with weak organic and inorganic acids to lower the gastric pH, with an expected antimicrobial effect, and also increasing enzyme activity and source of energy. The effect and activity of this practice is largely dependent on the type of organic acid and hence care should be taken during selection of the appropriate acid to add.

#### 4. How much does it cost?

Incorporating organic and inorganic acids in feeds and water has some additional costs. Depending on the current layout and installed capacity of the farm, piglet drinkers should be bought and installed. These drinkers must be cleaned regularly to avoid the introduction of bacteria and viruses into the herd, or the creation of biofilms, which increases production costs and modifies the cost structure since new inputs and services are added to the pre-adoption cost structure. The farmer might also need to incur extension service costs or require more specialised training for the correct introduction of organic and inorganic acids in feeds and water. These costs can be phased out once the practice has been routinised. This practice may require the adaptation of the production unit to accommodate the introduction of drinkers and feeders containing acidified feeds or water, which could demand an investment in infrastructure. This practice may slightly increase the complexity of production because the farmer needs to introduce organic and inorganic acids in feeds and water in specific quantities or source his/her mix of acidified feed and/or water from a company that supplies these products. This practice may be affected by international trade forces, which may have an impact on the UK price and on the stability of the supply chain.

#### 5. How can I do it well?

It is essential to keep the water system clean to ensure efficacy, water flow rate, infrastructure and drainage, hardness and source of water, fungal bloom or biofilm and cleaning regimen. Prepare standard operating procedures (SOPs) and train staff on how to include acids in water and how to use the system. Make sure you follow your acids supplier's instructions for best results.

In the case of feed supplemented with acids, make sure the acids are not competing against the effect of other feed additives, such as probiotics.

#### 6. How strong is the evidence?

The evidence found in the literature supporting this practice is high. There is wide academic literature on the inclusion of acids in feed or water for the control of post-weaning diarrhoea, including randomized control trials to test the effect in real farm settings. The effect of the practice will depend on the type of acid used, and on the underlying issues behind the post weaning diarrhoea on farm.

#### 7. Where can I find further information?

You can find further information about acids in feed or in water by consulting your feed supplier and a pig nutritionist. If you are milling your own feed, contact your pig nutritionist for more information. For more information on water systems capable of delivering acids, please contact your veterinarian or your pig advisor.

This article presents a study on the use of organic acids and medium chain fatty acids (MCFA) as replacement for ZnO, with good results:

Zinc oxide alternatives for weaned pigs: organic acids and MCFAs | The Pig Site

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#### 15.2.5 Feed additives

There is very strict regulation around the use of feed additives in the EU and in the UK. Feed additives cannot be commercialised unless they have been authorised following a careful scientific evaluation carried out by EFSA/FSA where it needs to be proven the additive has no harmful effects on human and animal health, or on the environment (EFSA, n.d., access year: 2022).

However, as Modina et al. (2019) notes, "the efficiency of each additive depends on the diet itself, the state of health, and the age of the animals". Hence varying types of feed additives at different concentrations having varying results depending on the context of each farm. Correct application according to manufacturer's instructions is key to success.

#### 15.2.5.1 Probiotics

#### Impact summary

Probiotics are live microbial supplements containing optimal doses of good or friendly bacteria and they can be added to pig feed. They exert health benefits by colonising the gut, improving intestinal microbial balance and suppressing the growth of pathogenic bacteria. They also stimulate the immune system and produce antagonistic substances against pathogens and toxins thus reducing incidence of diarrhoea and mortality in post-weaning piglets. The overall intestinal health is also improved with probiotic usage leading to general health, better growth rate, feed efficiency and productivity. Probiotics also have antioxidative activity by alleviating stress, can produce some vitamins, and enzymes which can aid nutrient fermentation, digestion and uptake.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	++
	Enhancing growth rate	++
	Other impacts	
	Reduced costs	+
	Improved welfare	+
Cost		
		£-££
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	High
	Overall	High
Speed of change	Improved welfare Quality Context	+ £-££ Fast High High

# 1. What is the practice?

The practice involves supplementing feeds with optimal doses of good bacteria (probiotics) to colonise the gut and reduce the proliferation of pathogenic bacteria therein thus, preventing diarrhoea in pigs. The general mechanism of action of probiotics is called competitive exclusion and it involves the addition of (non-pathogenic) bacteria to the gut to reduce colonisation or decrease populations of pathogenic bacteria. The practice also improves intestinal health and growth performance of piglets. Optimal bacterial doses of good bacteria in the gut improves microbial (enriching against bad bacteria), chemical (enhancing mucosal layer with increased goblet cells and antimicrobial peptides), immunological (triggers intestinal immune response) and mechanical (flagella, pili, surface layer proteins, capsular polysaccharide prevent binding of pathogens to epithelial cells) barriers, thus improving gut health and preventing diarrhoea.

## 2. How effective is it?

Probiotics have proven results in controlling PWD, especially by improving gut microbiota and acting as competitive exclusion for pathogenic bacteria. However, the effectiveness of this practice will depend on the underlying causes of PWD, on the probiotic strain/product used, and on how well this practice is implemented (i.e., are pigs being treated with antibiotics when receiving probiotics in feed? Is the inclusion rate in-feed correct?).

#### 3. Where does it work?

Supplemented in feeds and applicable to indoors and outdoor systems. Applicable to any scale of pig farming, whether indoors or out, and for all breeds. This practice is incorporated in feeds and works in the gut. It has showed promise in different settings, whether outdoors or indoors.

## 4. How much does it cost?

Supplying probiotics to piglets increases feeding costs. This practice does not require additional equipment but may require additional training on the exact quantity of probiotics to supplement or on different sources of probiotics to utilise. Adding probiotics to the piglets' diet is not expected to change the normal cost structure of the farm or require a large investment since there is no need for a specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land. This practice is not expected to increase the complexity of production because probiotics are usually routinely added as a dressing or mixed with the daily ration, without adding any major complexity to the provision of the daily diet. This practice may be affected by international trade forces, which may have an impact on the UK price and on the stability of the supply chain.

To simulate the cost impacts of using probiotics in feed, you are referred to the AHDB calculator for rearing piglets. You need to take into account the costs associated with implementing this practice and which were mentioned above.

- Step 1. Input your current production data
- Step 2. Explore these changes
- Step 3. Look at the differences between the scenarios tested

In the AHDB calculator (see link <u>here</u> and in 14.2 **Nutritional changes**), you can manually insert your production parameters (your current weaning weight, your post-weaning mortality) and what would be the expected changes in these parameters should you feed probiotics to your pigs. This would allow you to have an overview of production figures and production costs (including net margin per pig) when adopting this practice.

## 5. How can I do it well?

Ensure antibiotics are not administered to feed in the days before and after the administration of probiotics in feed. Make sure feed storage does not impact on the viability of the probiotics.

If you are purchasing feed compound, your pig feed supplier should be able to advise you on the best products available and on the different types of probiotics included.

## 6. How strong is the evidence?

Many academic papers describe the benefits of probiotics in controlling PWD. Various concentrations of single and multi-species probiotics consistently showed reduced pathogenic bacteria, regulating pro-inflammatory cytokines and improved immune response in guts of pigs within 20 days of treatment compared to the control untreated groups.

## 7. Where can I find further information?

You can find more information about probiotics products by consulting your veterinarian, a pig nutritionist or a feed specialist. Your feed supplier will be able to advise on the best product to use and the available options in the market that can be integrated in the feed you are purchasing.

This article discussed the benefits of the inclusion of probiotics and prebiotics in pig feed.

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The paper below follows as an example of the scientific studies on the use of probiotics to prevent PWD caused by *E. coli*.

Probiotic supplementation protects weaned pigs against enterotoxigenic *Escherichia coli* K88 challenge and improves performance similar to antibiotics - PubMed (nih.gov) (Pan et al., 2017)

"These studies evaluated the effects of probiotics (PB) as a potential substitute for antibiotics (AB) on diarrhea in relation to immune responses and intestinal health in weaned pigs challenged with enterotoxigenic (ETEC) K88 (Exp. 1) and the effects of PB on performance and nutrient digestibility in weaned pigs (Exp. 2)."

"Collectively, PB supplementation protected the pigs against ETEC K88 infection by enhancing immune responses and attenuating intestinal damage and improved the performance and nutrient digestibility of weaned pigs. Therefore, PB could be a potential effective alternative to AB for ameliorating diarrhea and improving performance in weaned pigs."

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#### Impact summary

Prebiotics are selectively fermented components of feed which are indigestible by pigs but could help maintain gut microbial balance to add benefit to health. Examples include seaweed extract, inulin, pectin, unrefined wheat and barley, raw oats etc. Prebiotics exert selective pressure for certain good bacteria such as bifidobacteria and lactic acid bacteria which colonise the gut, utilising space and nutrient, and reducing pH to prevent outgrowth of pathogenic bacteria and fermentation of protein. Non-starch polysaccharide by-products of soyabean meal hydrolysis interfere with pathogenic bacteria attachment, and beneficial in fluid retention during diarrhoeal infection and improve immunity against pathogenic bacteria. Ideally, prebiotics are resistant to stomach acids, bile salts, enzymes, easily fermentable by intestinal microbiota and absorbed.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	++
	Enhancing growth rate	++
	Other impacts	
	Reduced costs	+
	Improved welfare	+
Cost		
		£
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	High
	Overall	High

## 1. What is the practice?

Several prebiotics are available in the market and can be incorporated into pig feeds at desired concentration at different age of the piglets. Prebiotics are known for their ability to modulate gut microbiota and support growth of good bacteria which has been shown to improve the overall gut health, performance and immune system. Example of pre-biotics include inulin and oligosaccharides.

## 2. How effective is it?

The evidence suggests that prebiotics are effective in controlling post-weaning bacteria. Prebiotics have been shown to significatively reduce the adhesion and shedding of enterotoxigenic *E. coli*, and to selectively stimulate the outgrowth of good bacteria such as bifidobacterial and lactobacillus as well, consequently mitigating diarrhoea. For example, incorporating 100 or 200 mg/kg of chito-oligosaccharide or 6.0 g/kg of isomalto-oligosaccharides improved growth performance, digestibility of dietary nutrients, decreased the incidence of diarrhoea, and improved small intestine morphology in weaning pigs. However, incorporating 0.1% of chicory, mannan oligosaccharides, or 0.02% of chitosan to diets for weaning pigs had no effect on growth performance or on immunity (Y. Liu et al., 2018). However, the effectiveness of this practice will depend on the underlying causes of PWD, on the prebiotic product being used and the interactions it may have with the feed ingredients used in the diet, and on how well this practice is implemented.

## 3. Where does it work?

Supplemented in feeds, works in the pig gut. These are applicable to pigs indoors and outdoors.

## 4. How much does it cost?

Supplying prebiotics to piglets increases feeding costs. This practice does not require additional equipment but may require additional training on the exact quantity of prebiotics to supplement or on different sources of prebiotics to utilise. In addition, adding prebiotics to the piglets' diet is not expected to change the normal cost structure of the farm or require a large investment since there is no need for a specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land. This practice is not expected to increase the complexity of production because probiotics are usually routinely mixed with the daily ration, without adding any major complexity to the provision of the daily diet. This practice may be affected by international trade forces, which may have an impact on the UK price and on the stability of the supply chain. Seaweed can be produced in the UK and there is an incipient market for this product in the UK.

A return of investment (ROI) was estimated for this practice. To estimate this measure, we made the following assumptions.

• First, we considered a commercially available prebiotic as an example. This product has a feed inclusion rate of 1.8-2.6 kg/tn. The computation was done only for administration for 10 days after weaning.

- Second, ZnO is mainly used in the feed at a dosage of 100 mg per kg body weight per day for 14 consecutive days, which equates to 2500 ppm zinc in feed. This amounts to (roughly) using 0.0105 kg of ZnO per piglet per production cycle.
- Third, we assume that all other production practices and feed proportions are maintained as usual.
- Fourth, performance is expected to increase with the inclusion of prebiotics (Pan et al., 2017). This effect depends on other practices.

We introduced these values, including performance assumptions and feed prices, in our calculator to estimate a ROI for this practice. This estimation is shown in **Table 7**. Thus, introducing prebiotics to a piglet's diet and stopping the use of ZnO, **under the parameters of this exercise**, was expected to **increase** net profits by 17.44% per pig (when compared to the use of ZnO), if there is a 5% increase in piglet weight at the end of the rearing stage (from 40 kg to 42kg).

**Table 7.** Return of investment estimation for the use of a commercial prebiotic in piglets to control post-weaning diarrhoea. This table corresponds to an extract of a calculator built in this project.

Concepts		Prebiotics	
Percentage change in piglet weight with new practice vs old practice	0%	1%	5%
Liveweight (LW) of the piglet with old practice (kg)	40	40	40
Liveweight (LW) of the piglet with new practice (kg)	40	40.4	42
Price of zinc oxide (£/kg)	12	12	12
Recommended use of zinc oxide for the whole treatment period (kg/treatment)	0.0105	0.0105	0.0105
Price of creep with ZnO (£/kg)	0.4	0.4	0.4
Price of link with ZnO (£/kg)	0.36	0.36	0.36
Price of creep without ZnO (£/kg)	0.39	0.39	0.39
Price of link without ZnO (£/kg)	0.35	0.35	0.35
Quantity of creep (kg/treatment period)	3	3	3
Quantity of link (kg/treatment period)	6	6	6
Prebiotic compound price (£/kg)	5.89	5.89	5.89
Quantity of prebiotics (kg) provided to a piglet during treatment period	1.8	1.8	1.8
Total costs per kg (£/kg) (including feeding costs associated with treatment period)	7.5	7.5	7.5
Gross margin per piglet with old practice (£/piglet)	-20	-20	-20
Gross margin per piglet with new practice (£/piglet)	-30.51	-27.71	-16.51

Concepts		Prebiotics	
ROI (%)	-52.56	-38.6	17.44

The figures displayed in **Table 7** are a product of a ROI estimation exercise made with the assumptions made above.

To better appreciate these figures and to simulate other scenarios (price changes, different growth rates, etc) please refer to the calculator prepared during this project.

## 5. How can I do it well?

Ensure staff training on how to include this product in the pigs' diet, especially if top dressing is used. Consult your nutritionist to ensure there are no interactions between the product and the ingredients included in the diet. Make sure feed storage does not impact on the viability of the prebiotics.

## 6. How strong is the evidence?

The evidence found in the literature is high. Research studies available document the trialling of different prebiotics in pigs and their effect on growth performance, gut function and morphology. For example, a study by Yang et al. (2012) in which the authors tested feeding weaning piglets with chito-oligosaccharides at 400 and 600 mg/kg showed greater proliferation of commensal bifidobacterial and *lactobacillus* in the caecum and improved growth performance within seven days post treatment. The corresponding proliferation of the two commensals correlated directly to the concentration of the prebiotic such that pigs treated 600 mg/kg did significantly better than those in the 400 mg/kg group. In addition to the commensal growth, a corresponding significant reduction of pathogenic strains such as *Staphylococcus aureus* was observed albeit no significant utilisation in addition to the observed increased colonisation of bifidobacteria as seen in chito-oligosaccharide supplementation above (Herfel et al., 2013).

https://www.researchgate.net/publication/234105899\_Stabilized\_rice\_bran\_improves\_weaning\_pig\_performance\_via\_a\_prebiotic\_mechanism.

## 7. Where can I find further information?

You can find more information about prebiotics products by consulting your veterinarian, a pig nutritionist or a feed specialist. Your feed supplier will be able to advise on the best product to use and what the options available in the market that can be integrated in the feed you are purchasing.

This article discussed the benefits of the inclusion of probiotics and prebiotics in pig feed.

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#### 15.2.5.3 Synbiotics

#### Impact summary

Synbiotics are combinations of both probiotics and prebiotic approaches used to achieve complementary or synergistic effects to improve microbial balance in the gut to prevent colonisation of pathogenic bacteria. Once colonisation of the pathogens is prevented diarrhoea would be mitigated. The complementary synbiotic consists of probiotic and a prebiotic selected independently to confer benefits to the host. The synergistic synbiotic comprised of prebiotic chosen specifically for the selected probiotics to enhance effects in the gut. An example is a combination of raw potato starch and a probiotic which was shown to increase microbial diversity and reduced diarrhoea in the gut of weaned pigs challenged with pathogenic enterotoxigenic *E. coli* (ETEC). Synbiotics can enhance growth performance by reducing immune response and oxidative stress in the jejunum.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	++
	Enhancing growth rate	++
	Other impacts	
	Reduced costs	+
	Improved welfare	+
Cost		
		£-££
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	High
	Overall	High

Because this practice consists in administering a mix of pro- and prebiotics, please follow the advice given in the respective sections above.

## 1. What is the practice?

A synbiotic is 'a mixture comprising live microorganisms and substrate(s) selectively utilised by host microorganisms that confers a health benefit on the host' (Swanson *et al*, 2020). Likewise, this practice consists in administering a combination of prebiotic and probiotic products in pig feeds with the aim of improving the gut microbiota and selectively promoting the growth of good bacteria, and consequently inhibiting the growth of pathogenic bacteria.

## 2. How effective is it?

There is high evidence of the effectiveness of synbiotics, which are a combination of two other tested and proven feed additives. For example, high-moisture fermented maize supplemented with *Lactobacillus acidophilus* showed improved body weight gain and reduced faecal shedding of coliforms within three weeks of starting the treatment but reduced the bacterial diversity and richness in the gut (Liao & Nyachoti, 2017). The effectiveness of this practice will depend on the underlying causes of PWD, on the probiotic strains/ and prebiotics used, and on how well this practice is implemented (i.e., are pigs being treated with antibiotics when receiving probiotics in feed? Is the inclusion rate of these products in-feed correct?).

## 3. Where does it work?

Supplemented in feeds and applicable to indoors and outdoor systems. Applicable to any scale of pig farming, whether indoors or out, and for all breeds. This practice is incorporated in feeds and works in the gut. It has showed promise in different settings, whether outdoors or indoors.

# 4. How much does it cost?

Supplying synbiotics to piglets increases feeding costs. This practice does not require additional equipment but may require additional training on the exact quantity of prebiotics and probiotics to supplement or on different sources of synbiotics in the UK. In addition, adding synbiotics to the piglets' diet is not expected to change the normal cost structure of the farm or require a large investment since there is no need for a specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land. This practice may slightly increase the complexity of production because the farmer needs to introduce a precise mix of prebiotics and probiotics in the daily ration or procure a pre-made mix from a company that supplies it. This practice may be affected by international trade forces, which may have an impact on the UK price and on the stability of the supply chain.

## 5. How can I do it well?

As the effect of synbiotics depends on the concomitant administration of different substances, it is essential to observe what products are administered simultaneously. Probiotics and prebiotics, included within synbiotic products, may also require additional precautions, like avoiding antibiotic

treatments before and after administration. Diet formulation may need to be adapted to ensure maximum efficacy of the synbiotic product. For example, administering dietary fibres with a mechanical effect in the gut will not take advantage or potentiate the synbiotic effect of probiotics or prebiotics administered (Wang et al, 2012).

## 6. How strong is the evidence?

Positive results were observed within three weeks of commencing treatment. The evidence found in the literature is robust and it is further supported by the strength of the evidence for probiotics and prebiotics separately.

## 7. Where can I find further information?

You can find more information about synbiotic products by consulting your veterinarian, a pig nutritionist or a feed specialist. Your feed supplier will be able to advise on the best product to use and the options available in the market that can be integrated in the feed you are purchasing.

The first article below discussed the benefits of the inclusion of probiotics and prebiotics in pig feed, whereas the second article is an example of a scientific study on the symbiotic effect between enzymes and probiotics when fighting *E. coli* infections in challenged pigs: <u>Prebiotics</u> and probiotics boost pig growth and health | The Pig Site

Frontiers | Synbiotic Effects of Enzyme and Probiotics on Intestinal Health and Growth of Newly Weaned Pigs Challenged With Enterotoxigenic F18+*Escherichia coli* (frontiersin.org) : In this paper, "synbiotics enhanced growth performance by reducing diarrhea, immune response, and oxidative stress in the jejunum".

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#### 15.2.5.4 Amino acids

## Impact summary

Amino acids (AAs) are the structural units ("building blocks") of protein. The key idea behind the use of AAs to prevent PWD is to allow the reduction of protein without the loss of performance. The availability of industrial AAs and the increased knowledge of AA requirements shed light on how to formulate diets based on essential amino acids, respecting the ideal protein profile and disregarding protein levels. AAs can be costly and their inclusion profile in diets must be checked by a pig nutritionist.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	+
	Enhancing growth rate	++
	Other impacts	
	Reduced costs	+
	Improved welfare	+
Cost		
		£-££
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	Moderate
	Overall	Moderate

## Narrative summaries

## 1. What is the practice?

This practice consists in changing the amino-acid (AA) profile administered in pig feed, allowing the reduction of protein content. When attempting the reduction of protein levels in feed, it is crucial to ensure the pig receives all the AAs it needs and that a certain balance between the amino acids is maintained. In order to give the weaned pigs what they need, the concept of ideal protein, defined as the AA profile that maximizes nitrogen retention (i.e., muscle) and covers the pigs' physiological and growth needs, is applied when formulating diets (Cristobal et al., 2019).

## 2. How effective is it?

This practice is effective in reducing diarrhoea indirectly – it works by allowing the reduction of protein in diet while still maximizing growth and building the ideal amino acid profile needed to boost the immune system.

#### 3. Where does it work?

This practice works in both indoor and outdoor farms as it corresponds to the administration/inclusion of amino acids in pig feed.

## 4. How much does it cost?

Supplying amino acids to the piglets' diet does not necessarily increase feeding costs as it will depend on the levels of added synthetic amino acids present before the level of crude protein is reduced. This practice does not require additional equipment but may require additional training on the exact quantity of amino acids to add and the correct introduction of amino acids to the piglets' diet (i.e., that the introduction of the amino acids does not enter in conflict with other practices employed, like the reduction of protein contents in the diets). In addition, supplying amino acids to the piglets' diet is not expected to change the normal cost structure of the farm or require a large investment since there is no need for a specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land. This practice may slightly increase the complexity of production because the farmer/ feed mill needs to pay attention to the exact mix of amino acids to add to the feed or source his/her feed from a company that produces custom-made feeds or already targets this segment of the market. This practice may be affected by the forces of international trade, which may have an impact on the UK price and on the stability of the supply chain in the UK and abroad.

## 5. How can I do it well?

If you are buying compound feed, especially creep and link feed (also called as pre-starter and starter), it is unlikely that you need to observe any particular care with this practice. However, if you use pre-mixes, make sure all amino acid inclusions meet dietary requirements. Discuss the inclusion of amino acids with your pig nutritionist and your vet.

Storage of feeds and pre-mixes must be adequate.

# 6. How strong is the evidence?

There is wide evidence in the literature (including scientific research and farm trials) about the benefits of amino-acids profiling in diet. A correct amino acid balance is one of key approaches for weaning without compromising performance, especially when feeding low crude protein diets. This practice works by allowing protein contents to be reduced in diet and by potentially boosting pigs' immune system.

## 7. Where can I find further information?

You can find more information about amino acids by consulting your veterinarian, a pig nutritionist. Your nutritionist will be able to advise on the best, most balanced and adequate AA profile to use and on the options available in the market that can be included in the diet formulation.

Additional references: <u>The Importance of Dietary Protein and Amino Acids after Weaning - Articles</u> - pig333, pig to pork community

Isoleucine: A missing link in the pivotal role of amino acids in safe weaning - Pig Progress

Use of low dosage amino acid blends to prevent stress-related piglet diarrhea (nih.gov)

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#### 15.2.5.5 Enzymes

#### Impact summary

Enzymes can be derived from plants and animals, but also from microorganisms. They help in gut fermentation and have been proven to improve digestibility and utilisation of nutrients and nutritional value of feeds thus, positively impacting growth performance in weaned piglets with comparable results to antibiotics as seen in multi-enzyme preparations. The effect of enzymes is related to the facilitation of the digestion. Given the variety of enzymes available, dosages, and presentation, not to mention their interaction with feed ingredients, it is difficult to assert their effectiveness and costs. Examples of enzymes are phytases, xylanases and beta-glucanases, proteases, and  $\beta$ -mannanase.

Effectiveness		
	Reducing diarrhoea	+/-
	Reducing post-weaning mortality	+/-
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	+
	Improved welfare	+
Cost		
		£-££
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	Moderate
	Overall	Moderate

#### Narrative summaries

## 1. What is the practice?

This practice consists of administering enzymes (e.g., phytase) to pig diets in order to facilitate digestion. Enzymes can be beneficial especially in the weaning phase, when their guts are not yet fully developed. Enzymes in feed increase the rate at which animals can digest and absorb nutrients. This translates into faster growth with fewer nutritional requirements and less waste. For example, phytase, which aids in phosphorus absorption, is particularly important in reducing phosphorus pollution (APEC, 2021).

## 3. How effective is it?

Given the variety of enzymes available, dosages, and presentation, not to mention their interaction with feed ingredients, it is difficult to assert their effectiveness, especially their effectiveness in decreasing PWD. The underlying causes of PWD need to be understood before prescribing enzymes to tackle the problem.

In a study designed to test the effect of  $\beta$ -mannanase feed supplementation on post-weaning pig performance, Vangroenweghe et al. (2021) concluded that the use of an heat-tolerant  $\beta$ -mannanase allowed the use of reduced levels of expensive protein in diets fed post-weaning, and a reduced net energy requirement in one of the post-weaning diets without adverse effects on intestinal health or overall performance. "In fact, the occurrence of PWD and number of individual treatments during the post-weaning period were significantly reduced on the  $\beta$ -mannanase supplemented diets", concluded the authors.

## 4. Where does it work?

This practice works by adding enzymes to pig feed. It is applicable to any scale of pig farming, whether indoors or out, and for all breeds. Since most farmers rely on commercially sourced formulated feeds the implementation of this practice will depend on the range of offers of your feed supplier.

## 4. How much does it cost?

Supplying enzymes to the piglets' diet does not always increase feeding costs. For example, phytase enzymes reduce diet costs as inorganic phosphate sources can be reduced. If matrix values are taken for other enzyme activities as opposed to being "added on top" then costs can be reduced. This practice does not require additional equipment but may require additional training on the exact quantity of enzymes to add. In addition, supplying enzymes to the piglets' diet is not expected to change the normal cost structure of the farm or require a large investment since there is no need for a specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land. This practice may slightly increase the complexity of production because the farmer needs to pay careful attention to the exact quantity of enzymes to add to the diet of each piglet, or source his/her feed from a company that produces custom-made feeds or already targets this segment of the market. This practice may be affected by the forces of international trade, which may have an impact on the UK price and on the stability of the supply chain in the UK and abroad.

# 5. How can I do it well?

The most important direction when using enzymes is to follow the manufacturer's rules when adding enzymes to pig feed. This will prevent some of the most common issues that can compromise the effect of enzymes. This is particularly relevant for farmers home-milling their pig diets and using enzymes as supplements. Enzymes need to be added in accurate amounts, and likewise uniformly mixed throughout the feed compound. Any feed processing or treatments (like pelleting or heat treatments) might damage the enzymes and render them ineffective. It is necessary to ensure that the enzymes chosen are capable of enduring such treatments (APEC, 2021).

# 6. How strong is the evidence?

There is high quality evidence of the effects of enzymes in pig production. However, this evidence shows that context (farm setting, pig diet, disease in question, but also what enzyme, quantity, etc) is crucial for the determination of an enzyme's effectiveness. Many articles focused on the effect of enzymes in pig performance, especially in later stages of the pig production cycle, and did not target post-weaned pigs. This is why the overall strength of the evidence was classed as moderate.

# 7. Where can I find further information?

There are many websites with information available on enzymes, on the different types available and on its effects. In this website, you find an insightful comment on the benefits and uses of enzymes in animal feed: <u>Enzymes In Animal Feed | Importance And Future Use (infinitabiotech.com)</u>.

In another useful website, the authors examine the benefits of feeding enzymes to weaned pigs and debate on how enzyme supplementation improves digestion and feed efficiency. The article also revises research that shows the beneficial aspects with respect to prebiotic formation and potential modes of action within pig guts. <u>Enzyme Supplementation in pig diets - Engormix</u>

Finally, the article below presents a "review of the use of enzymes in pig nutrition" stating that implementation and profitability depends on the diets used and opening the door for the use of cheaper feed ingredients which, with the help of enzymes, may be more easily digested.

## Review of the use of enzymes in pig nutrition - Articles - pig333, pig to pork community

Consult your veterinarian or your pig nutritionist for more information on how to use enzymes, and which to use to control PWD in pigs.

## References

 Vangroenweghe, F., Poulsen, K. & Thas, O. Supplementation of a β-mannanase enzyme reduces post-weaning diarrhea and antibiotic use in piglets on an alternative diet with additional soybean meal. *Porc Health Manag* 7, 8 (2021). https://doi.org/10.1186/s40813-021-00191-5

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#### 15.2.5.6 Essential oils and Plant extracts

#### Impact summary

Natural or refined essential oils and extracts derived from medicinal plants have powerful antimicrobial, antioxidant and anti-inflammatory properties. Essential oils used in pig industry include carvocrol, thymol, citral, eugenol, thyme, tea tree, lemongrass, nutmeg, cinnamon, basil, oregano and hay leaf. Treatment with essential oils and plant extracts can reduce pathogen colonisation in caecum, colon and rectum and have been shown to downregulate expression of bacterial virulence factors such as toxins, adhesion to enterocytes, motility and quorum sensing. The extracts also improve intestinal morphology, enzyme activity and feed digestibility. Decrease in intestinal oxidative stress has been recorded with treatment with essential oil blends. The properties of these plant extracts and oils can improve gut health, mitigate against diarrhoea and positively impact growth performance in weaner pigs. Activity of the essential oils and plant extract can be affected by plant species, composition, harvesting season, extraction method and stability.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	+
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	+
	Improved welfare	+
Cost		
		£
Speed of change		
		Fast
Strength of evidence		
	Quality	Low
	Context	Moderate
	Overall	Low

#### 1. What is the practice?

This practice consists in adding essential oils or plant extracts to pig diets. Natural or refined essential oils and extracts derived from medicinal plants have powerful antimicrobial, antioxidant and anti-inflammatory properties. Treatment with essential oils and plant extracts can reduce pathogen colonisation in caecum, colon and rectum and have been shown to downregulate expression of bacterial virulence factors such as toxins, adhesion to enterocytes, motility and quorum sensing.

#### 2. How effective is it?

The effectiveness of these substances is widely variable, depending on the oil or plant extract in question. It seems that when carefully included in feed, it has good effects on reducing PWD by improving gut-health generally through antimicrobial or anti-inflammatory effects.

#### 3. Where does it work?

Applicable to any scale of pig farming, whether indoors or out, and for all breeds. Since most farmers rely on commercially sourced formulated feeds the implementation of this practice will depend on the range of offers of your feed supplier. Implementing this practice on feed mills for large scale production of diets will depend on the oils and plant extracts commercially available and their price.

There are some papers describing how dietary plant extracts alleviate diarrhoea and alter the immune response of weaned pigs experimentally infected with a pathogenic *E. coli* (Liu et al., 2013; Bontempo et al., 2014).

## 4. How much does it cost?

Adding essential oils and extracts of medicinal plants to piglets' diet increases feeding costs. This practice does not require additional equipment but may require additional training on the exact quantity of essential oils and extracts of medicinal plants to supplement or on different sources of essential oils and extracts of medicinal plants in the UK. In addition, adding essential oils and extracts of medicinal plants in the UK. In addition, adding essential oils and extracts of the piglets' diet is not expected to change the normal cost structure of the farm or require a large investment since there is no need for a specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land. This practice may slightly increase the complexity of production because the farmer needs to introduce a precise mix of essential oils and extracts of medicinal plants in the daily ration or procure a pre-made mix from a company that supplies it. This practice may be affected by international trade forces, which may have an impact on the UK price and on the stability of the supply chain.

#### 5. How can I do it well?

Follow the manufacturer's instructions when adding essential oils or plant extracts to pig feed. This is particularly relevant for farmers home-milling their pig diets. Essential oils and plant extracts need to be added in accurate amounts, and likewise uniformly mixed throughout the feed compound. It is necessary to ensure that the chosen products are capable of enduring such feed processing, like heat treatments or pelleting.

Ensure the quantities necessary for effectiveness do not lower the quality of the feed. For example, if large quantities of essential oils are added, the pelleting is likely to be compromised.

#### 6. How strong is the evidence?

The evidence found covers a wide range of products from which there is varying information. Even academic papers describing the effects of essential oils and plant extracts will denote how hard it is to reproduce experiments and replicate results. Hence, the evidence available on this practice was considered low.

#### 8. Where can I find further information?

Consult your veterinarian or your pig nutritionist for more information on how to use essential oils and plant extracts, and which to use to control PWD in pigs.

This article discusses the use of essential oils as an alternative to the use of in-feed antibiotics in pig production.

Potential use of essential oils as an alternative to feed grade antibiotics in pork production - Pork (msu.edu)

This website discusses the use of plant extracts as good management to combat PWD and presents one commercial produce (PigletPlus®) which may be used for that.

Plant extracts and good management to fight post-weaning diarrhea | PlusVet Animal Health

#### References

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# 15.3 Management practices

While good management practices help to mitigate the challenges impacting on commercially reared pigs at weaning, they require continual review to reflect the emergence of new challenges as patterns of disease evolve (Evans, 2001). The underlying principles of a well-planned pig flow, close attention to detail and skilled stockpersons highlighted by Evans are echoed in the AHDB's advice on "Establishing the weaned pig." This emphasises the importance of managing the weaned pigs' environment and paying close attention to the behaviours being exhibited. In seeking to better understand the effects of housing and/or social change on weaned pigs, Colson et al. (2012) found that moving and mixing pigs at weaning are not only stressful but additive. Accordingly, pro-active management practices benefit from a holistic or systemic approach and close attention to the observation of behaviours and recording of indicators.

Aside from implementing better management practices, it is important to assess what are the current practices on farm and whether *what the farmer thinks is happening is really happening*. For example, is cleaning and disinfection done properly? Is all-in all-out being practiced *de facto* (e.g., without mixing older pigs with younger ones)?

## Disclaimer regarding the strength of evidence for management practices

Strength of evidence for most management practices was lacking in the literature identified according to the defined search terms of this review. This is mostly because the management practices listed can be implemented through varied measures and are largely overlapping.

For example, "stress reduction" as a practice encompasses changes in different areas – such as nutrition, environment, feeding and management practices. Indeed, delayed weaning, early exposure and adaptation to new (highly palatable) feeds, keeping pigs in their original litters when weaning, offering good and enriched environments (temperature, air quality, clean), and separating different age groups will all contribute to a reduction of the stress levels, less "enteric" stress when digesting new feed, and less social stress when moving to a new environment.

For this reason, management practices are rarely implemented as a single measure, but rather as a group of measures or interventions which will inevitably **encompass a synergistic effect**. It is difficult to find scientific studies documenting measure A or B due to the overlap of these measures and to the many combinations of measures to be tested.

This disclaimer serves to alert the reader about the apparent low strength of evidence of management practices. This is because there is lack of scientific literature on the subject. Empirically, there is sound evidence of the effectiveness of most management practices.

## 15.3.1 Stress Reduction

#### Impact summary

Mitigating the stress associated with the weaning process has potential to reduce diarrhoea and post-weaning mortality; and to help newly weaned pigs become established. The cost of implementing stress reduction management practices is variable and this reflects the range of measures and the different contexts in which they may be applied. For example, on the one hand, maintaining litter groups may require wider change of prevailing routines and infrastructure, including capital expenditure. While on the other hand, attending to the post-weaning environment to ensure a comfortable and even temperature, freedom from draughts and appropriately matched groups and stocking rates may be more readily implemented.

Reducing diarrhoea       +         Reducing post-weaning mortality       +         Enhancing growth rate       +         Other impacts       +         Reduced costs       +/-         Improved welfare       ++         Cost       £-£££
Enhancing growth rate       +         Other impacts       -         Reduced costs       +/-         Improved welfare       ++
Other impacts       Reduced costs       Improved welfare       ++
Reduced costs     +/-       Improved welfare     ++       Cost
Reduced costs     +/-       Improved welfare     ++       Cost
Improved welfare ++ Cost
Cost
£-£££
Speed of change
Fast to
Moderate
Strength of evidence
Quality Low
Context High
Overall Moderate

# 1. What is the practice?

Stress Reduction: newly weaned pigs are not only making the transition from drinking milk to eating a solid diet, while adjusting to the absence of maternal care; but also experiencing the challenge of mixing with other pigs and exposure to an unfamiliar environment. Mitigating these cumulative social and environmental challenges may help to reduce the stress associated with weaning and reduce susceptibility to PWD.

In practice, social stress reduction management strategies include:

- Keeping pigs in their original litters at weaning, to minimise the circulation of disease between litters; or
- Familiarising batches of piglets through a multi-suckling environment to minimise the disruption that accompanies the mixing of groups.

Strategies to mitigate the stress of exposure to a new environment focus on managing the environmental conditions and monitoring for behavioural indications of stress. Maintaining a comfortable and consistent temperature; preventing draughts; stocking at an appropriate rate to avoid over-crowding; and ensuring ease of access to fresh, clean water and an appetising diet are all advised. Potential indications of stress include excessive noise. More specifically, chilling may prompt piglets to lie in huddles and to dung in the lying area; and emerging vices may reflect discomfort due to draughts, over-stocking or insufficient access to food and water.

## 2. How effective is it?

Considering the different strategies that may be employed to reduce stress and the employment of a holistic (preferred) approach to reduce stress, this practice is considered to be very effective. The scale of effectiveness will depend on what practice was implemented and on the overall management practices on the farm (age at weaning, cleaning and disinfection), as well as on the pig's health status.

## 3. Where does it work?

This practice works by acting in different areas of management, health, and welfare of pigs and sows. The objective is to mitigate social and environmental challenges in a combined effort to reduce the exposure and susceptibility to PWD. Likewise, this practice works in the farrowing house and in the nursery, mostly. Particular care should be exerted in the days before weaning, especially when vaccination is performed and if pigs are inter-mingled or sorted by sizes before mixing at weaning.

## 4. How much does it cost?

Stress reduction activities may encompass a diverse range of actions within the farm. Including, for example, the provision of litter-specific pens and the introduction of environmental enrichment. Cost analysis is dependent on the specific practice(s) employed. However, in general, stress reduction practices may require an investment in implements or infrastructure. These costs are usually transitory and do not require a repeat expense every production cycle. Hence, stress

reduction practices are associated with additional capital costs. Also, stress reduction practices may slightly increase the complexity, and costs, of production – for example, to allow time for observation of piglet behaviours in the post-weaning period. All these requirements increase the complexity in which the farm must be designed and provisioned.

We do not provide a computation of a ROI for this practice because it is composed of a series of structural changes that are farm specific. Some units may need to change the layout of the pens or introduce a new flooring. Hence, there will be a ROI per required change. Overall, the cost of implementation of these measures is going to improve the health and welfare of the pigs, but the ROIs may only be seen after a medium-to-long term period.

## 5. How can I do it well?

This practice can best be implemented by following good management practices and good sense. A careful examination of the most stressful hazards for pigs around weaning is necessary in each farm. After listing these, record any mitigation strategies or management changes that can be implemented to minimize stress. For example, vaccination is a very stressful event for pigs. How feasible is it to vaccinate pigs one or two weeks before weaning?

## 6. How strong is the evidence?

Although the quality of the evidence was classified as "low", there is strong empirical evidence supporting this practice, hence the contrast with "high" contextual strength of evidence. There are a number of papers relating welfare friendly/stress free environments with healthier pigs.

## 7. Where can I find further information?

The general farming press (e.g., Farmers Weekly) and the specialist sector press (e.g. Pig World) provide articles and discussion about minimising stress. There is discussion about minimising stress at weaning on the websites of the various Animal Health companies (see for example: <u>Minimising piglet stress at weaning | Zoetis UK</u>; and <u>Six Keys to Promoting Nursery Pig Health |</u> <u>Swine Health (swineresource.com)</u>) with an interest in pig health and in the newsletters of specialist pig veterinary practices. On-line community groups, including for example <u>Reducing</u> <u>weaning stress: is pre-weaning socialisation a good strategy? - Articles - pig333, pig to pork community</u> also provide discussion and information.

## 15.3.2 Housing and pen layout

#### Impact summary

The general management of housing and pen layout overlaps with various other practices, including stress reduction, feeding regimes and water quality. Underlying housing and pen layout practices include allowing for evenly-sized groups; handling piglets quietly and gently; ensuring a draft-free and warm environment to prevent chilling; and working on an all-in/all-out basis to allow accommodation to be cleaned, disinfected and dried between batches. These measures all contribute to reductions in diarrhoea and mortality and an improved growth rate. Similarly, steps to smooth the transition between pre and post-weaning housing, such as establishing a solid diet pre-weaning and carrying this over to the post-weaning environment may also be of value; likewise, adopting the same feeders and drinkers helps to ensure consistency.

Effectiveness		
	Reducing diarrhoea	+
	Reducing post-weaning mortality	+
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	0
	Improved welfare	+
Cost		
		£-££
Speed of change		
		Moderate
Strength of evidence		
	Quality	Low
	Context	Low
	Overall	Low

## 1. What is the practice?

Managing housing and pen layout may help to ensure a smooth transition between the pre and post weaning environment. While age and condition of housing, and floor type (slats or straw) will influence available options, there are underlying practices that apply more widely. Including, a well-planned pig flow, close attention to detail and skilled stockpersons. Adaptability is also required in order to respond to new challenges as patterns of disease change.

Reflecting the interactions between various management practices, e.g., feeding and housing, studies have shown that embedding feeding habits and establishing a solid diet in the preweaning environment may help pigs adjust more readily to a new, post-weaning environment.

Low or variable temperatures and drafts increase the susceptibility of newly weaned pigs to PWD. Chilling, in particular, is a risk to newly weaned pigs as it may result in the blood supply being diverted away from the gut and towards the vital organs. A target temperature of 28 - 30°C, or 25°C in a straw system, is advised immediately post-weaning and while it may be reduced over time, reductions should be incremental and carefully monitored.

While depopulation has proven effective in tackling pathogens like *Mycoplasma hyopneumoniae* or PRRS, unless the problem is caused by a specific pathogen then it is not indicated in response to PWD. An all-in-all-out approach is, however, advised to allow accommodation to be effectively cleaned, disinfected and dried between batches of pigs.

## 2. How effective is it?

Considering different housing and pen layouts can be an effective practice to reduce PWD. For example, a pen layout where pigs are kept with sows for a longer period of time, or a pen layout where pigs from adjacent farrowing crates mingle weeks before weaning may be an effective socialization strategy for pigs to reduce stress and prevent disease. The scale of effectiveness will depend on the underlying issues behind the PWD on each farm and on the overall management practices on the farm, as well as on the pig's health status.

## 3. Where does it work?

This practice works by changing the housing and pen layout in the farrowing house and nursery (weaned pig's accommodation). Similar to the stress reduction practice, the objective is to mitigate social and environmental challenges in a combined effort to reduce the exposure and susceptibility to PWD.

## 4. How much does it cost?

Pen/housing design is one of the practices of stress reduction mentioned above. This practice is expected to require additional capital costs for infrastructure if the current layout of the farm does not have a well-planned pig flow or adequate flooring, or a good ventilation or heating systems. This practice may increase the complexity in which the farm must be designed and provisioned.

We do not provide a computation of return of investment (ROI) for this practice because it is composed of a series of structural changes that are farm specific. Overall, the cost of implementation of these measures is going to improve the health and welfare of the pigs, but the ROIs may only be seen after a medium-to-long term period.

## 5. How can I do it well?

This practice can be best implemented by gathering the staff involved in the daily management of the farm, the manager, and the veterinarian to discuss housing and pen layout changes and their impacts on management and pig flow. Careful planning and execution are key for the success of this intervention. What are the best/most cost-effective changes that can be done on the farm to increase the overall pig performance while easing the weaning process for piglets?

## 6. How strong is the evidence?

Although the quality, context, and overall strength of the evidence was classified as "low", there is empirical evidence supporting this practice.

## 7. Where can I find further information?

The AHDB's Knowledge Library includes information about considerations of pig housing and useful onward links (<u>Pig buildings and housing | AHDB</u>). For producers in England and Wales, Defra's interactive Farm Business Survey (<u>FBS Farm Business Benchmarking</u> (<u>farmbusinesssurvey.co.uk</u>)) provides a resource for comparing a range of management and performance measures across like enterprises.

## 15.3.3 Water Quality

#### Impact summary

Managing water quality and ensuring a clean and fresh supply is vital not only in the prevention of diarrhoea and reduction of post-weaning mortality but also in maintaining appetite and consistent feed intake. Routine measures include attention to hygiene, for example day-to-day cleaning and thorough disinfection of water troughs and drinkers between batches; capital spending may be required where the underlying infrastructure, for example pumps and pipes, requires maintenance or renewal.

Please see section 15.2.4 Acidification of feed and water, including organic acids for more details on water acidification.

#### **Disclaimer:**

All farmers subscribing to the Red Tractor assurance scheme are required to provide adequate access to a supply of fresh, clean drinking water. The scheme specifies requirements in terms of number of water access points and flow rates, but also in terms of water quality. For example, "if using non-mains water, the water is independently tested annually as close to the source as possible for total viable count (TVC) and coliform levels." (Red Tractor, n.d., access year: 2022).

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	++
	Enhancing growth rate	++
	Other impacts	
	Reduced costs	0
	Improved welfare	+
_		
Cost		
		£-££
Speed of change		
		Moderate
Strength of evidence		
	Quality	Low
	Context	Low
	Overall	Low

# 1. What is the practice?

Provision of fresh, clean drinking water that is readily accessible and free from microbiological and physical-chemical contamination is vital in the prevention of bacterial and viral infections. Water intake is also essential in encouraging feed intake. Monitoring and maintaining the infrastructure of pumps and pipes to ensure that the water is available at the right temperature, flow rate and pressure will all help to encourage uptake. Providing a consistent delivery mechanism (nipple/bowl/trough) between the farrowing and weaning accommodation will help to ensure familiarity and encourage drinking. Routine cleaning is essential to prevent the build-up of debris with more intensive cleaning of the water system forming an integral part of the wider cleaning of housing between batches.

## 2. How effective is it?

The scientific and empirical evidence gathered suggests this practice is effective in preventing viral and bacterial infections – both by impeding exposure to pathogens which may be transmissible through water, and by promoting hydration in pigs, which is essential for general health of the pigs.

## 3. Where does it work?

This practice works in all areas of the farm irrespective of the pigs being kept indoors or outdoors where there are water pipes or water stored, including water utilized for cleaning and disinfection procedures on farm.

## 4. How much does it cost?

Provisioning of quality of water is expected to require capital costs for infrastructure and implements. This practice requires equipment to clean and service the pipes that provide the water and the drinkers that supply the water to the pigs. This practice is expected to change the cost structure of the farm since it requires the introduction of new inputs and services to the production cycle. This practice is also expected to increase the complexity of production because the farm must be designed to provide a clean and bacteria-free water to the piglets. This practice is also expected to require extension service support that tests the water if the farm does not have the equipment to do so. Some units may need to adopt the whole structure of the practice, introducing drinkers and hiring cleaning services or contracting workers to do this job.

We do not provide a computation of a return of investment (ROI) for this practice because it is composed of a series of tasks that are farm specific and can include multiple steps covering water access and water quality.

## 5. How can I do it well?

Additional costs will be incurred where there is scope for improvement to existing practice. For example, implementing good cleaning and disinfection practices, including that of water bowls, implementing cleaning protocols for drinkers, water pipes and water tanks, and regularly testing the physical and microbiological properties of the water provided to pigs. Testing water bowls and

nipples (water flow, pressure) on each pen of the farm is also extremely important – what is the point of having good water if pigs can't access it? A standard operating procedure (SOP) regarding testing water bowls and nipples weekly, when cleaning and disinfecting pens, should be done. A protocol for microbiological testing of water in water tanks and in the water bowls should be designed and executed with a defined frequency. Finally, provide a minimum of two drinkers per pen, with a recommended one drinker per 10 to 15 pigs. Additional measures, for example testing, may be required for farms with a private water supply.

## 6. How strong is the evidence?

Although the quality, context, and overall strength of the evidence was classified as "low", there is empirical evidence supporting this practice.

## 7. Where can I find further information?

If you subscribe to a quality assurance scheme, make sure you comply with their requirements in terms of water supply and water quality. Consult their standards and recommendations. For example, Red Tractor's certified standards for Feed and Water can be found here:

#### Feed And Water - Pigs (PG) - Red Tractor Assurance

For additional information, please see the AHDB's Knowledge Library for information (<u>Water</u> <u>usage on pig farms | AHDB</u>).

- Water: the forgotten nutrient for pigs | Agriculture and Food
- Water quality: the winning formula for pig production | The Pig Site
- Red Tractor. Feed and Water, v5.1. Retrieved from <u>https://redtractorassurance.org.uk/standards/feed-and-water-10/#</u>

#### 15.3.4 Hygiene and Biosecurity

#### Impact summary

Observing good hygiene and biosecurity management practices reduces diarrhoea and postweaning mortality and contributes to an enhanced growth rate. For example, an all-in-all-out approach to weaner accommodation is advised to allow for cleaning and disinfection between batches. While avoiding shared airspace between newly weaned pigs and older animals is preferable to prevent any transfer of disease. Costs are variable depending on the context of each unit, but the strength of evidence is high regarding overall effectiveness.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	++
	Enhancing growth rate	++
	Other impacts	
	Reduced costs	+
	Improved welfare	+
		· .
Cost		
		£-£££
Speed of change		
		Moderate
Strength of evidence		
	Quality	High
	Context	Moderate
	Overall	Moderate

# 1. What is the practice?

Hygiene and biosecurity measures work together to prevent infection. Effective hygiene management reduces the pressure of infection and exposure to bacteria, virus and parasites that may cause diarrhoea. Biosecurity management helps to prevent these pathogens from entering the farm or farm compartment, and from spreading between different buildings/barns, breaking the disease transmission cycle. In clean and disinfected accommodation, where neither the same air space nor environment is shared with older pigs, newly weaned pigs will be less challenged and have less outbreaks of PWD. Mortality is reduced due to less diarrhoea and other diseases. An all-in-all-out approach to weaner accommodation is advised to allow thorough cleaning and disinfection between batches. This process should allow for: i) removal of organic matter; ii) soaking with a mix of cold water and detergent; iii) washing, preferably with hot water and under pressure; iv) drying; v) disinfecting, with an approved product used at the recommended strength and applied at low pressure; and vi) drying.

## 2. How effective is it?

Considering different hygiene and biosecurity measures which can be implemented this can be considered an effective practice to reduce PWD. If the problem causing PWD on farm is directly linked with pathogens, the elimination of these agents from the environment will directly decrease or prevent exposure to it, leading to a reduction of PWD. Hygiene measures between compartments (which can be considered as "internal biosecurity measures") are likely to break the transmission cycle between older animals and younger animals. Using only clothing and footing specific to each barn is an effective way of preventing the spread of disease on farm. Other measures such as control of pests will prevent the spread of disease. The scale of effectiveness will depend on the underlying issues behind the PWD.

## 3. Where does it work?

This practice works in farm compartments where pigs are housed before and after weaning, mostly. However, any farm area where materials used for handling pigs around this age is stored may be included in hygiene and biosecurity practices. The objective of these practices is to clean and disinfect areas contaminated with pathogens causative of disease, particularly pathogenic *E. coli* so that pigs' exposure to it is minimized. External biosecurity measures in place will prevent the introduction of disease from external sources.

## 4. How much does it cost?

Introducing hygiene and biosecurity measures may increase production costs, depending on which biosecurity measures are in place in a pig unit. This practice may require additional equipment and training on how to operate under hygiene conditions and following biosecurity protocols. The farmer may need to invest in modifying his/her unit to introduce cleaning points for workers and implements. The farmer may also need to introduce a new expense to cover disinfectants and new PPE for workers. These changes are expected to change the cost structure of the farm or require a large investment in specialised training. This practice is expected to require additional costs for machinery or implements for the farm, or major investment in

infrastructure or land. This practice substantially increases the complexity of production because the farmer needs to introduce a biosecurity protocol and cleaning procedures to be adhered by workers, which complicates production substantially. This practice may be affected by international pathogens that may affect local biosecurity measures within the UK, which may have an impact on the production costs in the UK price.

We do not provide a computation of a ROI for this practice because this practice is composed of a series of structural changes that are farm specific. The introduction of better cleaning and disinfection protocols, or biosecurity measures is likely to have a ROI especially if the farm has a poor health status.

## 5. How can I do it well?

To ensure hygiene and biosecurity measures are done properly, it is necessary to create and implement a protocol detailing all steps to be done on a weekly basis. A checklist to be used weekly may be a useful tool to adopt. It is necessary to ensure staff know what to do and how to do it, likewise, training is another step crucial for the good implementation of these practices. Develop a biosecurity plan with your veterinarian, tailored to your farm. Set goals which are realistic and achievable. Review your biosecurity plan annually – you may use commercially available assessment protocols which will help you benchmark your farm practices against your peers.

## 6. How strong is the evidence?

There is strong evidence in the literature on the effect of these practices on control of PWD. There is scientific literature on trials testing different hygiene procedures and biosecurity measures and the onset and clinical features of PWD, and there are technical publications targeting farmers with explanations on how to implement these practices for the benefit of pig's health before and after weaning. The strength of the evidence in context is moderate due to the variety of measures tested.

# 7. Where can I find further information?

The AHDB's Knowledge Library (<u>Biosecurity on pig farms | AHDB</u>) provides a range of information and onward links about all aspects of hygiene and biosecurity.

## 15.3.5 Delayed Weaning

#### Impact summary

The management of many commercial units is predicated on a 4-week weaning system. Delaying the weaning age beyond 4-weeks impacts on the wider business model. Nevertheless, delayed weaning is associated with potential health benefits for newly weaned pigs since their guts are more fully developed and their feeding habits are better established at the time of weaning. Implications for the health and welfare of the sow arising from an extended lactation also have to be considered. For example, delayed weaning would reduce the farrowing index, increase damage to sows teats from increasingly robust piglets, and potentially reduce fertility rates due to low body condition of sows. There are considerations too around the increased sow feeding costs, but these must be balanced against a reduced cost for early-weaning diets. Also, labour costs may be reduced since later-weaned pigs require less support.

Effectiveness		
	Reducing diarrhoea	+
	Reducing post-weaning mortality	+
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	0
	Improved welfare	+/++ <sup>a</sup>
Cost		
		£-££
Speed of change		
		Fast
Strength of evidence		
	Quality	Moderate
	Context	Low
	Overall	Low

<sup>a</sup> Because this practice can range from weaning at five weeks or weaning much later (i.e., 8-10 weeks), the impact on welfare can shift.

# 1. What is the practice?

In commercial herds, pigs are typically weaned at four weeks of age (28 days). While this fits with the wider routine of the unit, the gut of the weaned pig is still developing and susceptible to infection. Delaying weaning allows the growing pig time to develop a more mature gastrointestinal function and to have better established feeding and foraging behaviours. Some have argued that delaying weaning to 35 days may increase the gross margin per sow with the increased sow feeding costs more than offset by reduced costs of early weaning rations and reduced labour costs as the pigs are more independent at the time of weaning. Split-suckling systems offer a middle-way. In this system, sows are removed from their piglets for certain periods of time. They will come into heat allowing them to be serviced while still nursing their litter before weaning at a time beyond the typical 28-day period.

# 2. How effective is it?

Delayed weaning is an effective practice to combat PWD, especially if this is caused by nutritional challenges. Delayed weaning has the advantage of extending the period of transition and adaptation of the pig to solid feed, allowing the gut to mature. Though split-suckling systems are rare, they can provide an opportunity for the pigs to learn feeding behaviour and habits, while developing their guts and socializing with other pigs for much longer periods of time (several weeks). Such a system would largely overlap with other practices described such as stress reduction practice and feeding regime practices.

## 3. Where does it work?

This practice works by allowing more time for the piglet's gut to mature and learn how to process and digest feed before weaning. The adaptation of the gut to changes in feed would not be so abrupt and the risk of PWD is greatly minimized. The farm's farrowing house and nursery would need to accommodate sows and pre-weaning pigs for longer and adapted to house older/bigger weaned pigs.

Outdoor systems may have an advantage compared to indoor systems where space is more restricted and pig flow dictates the feasibility of certain farm operations.

# 4. How much does it cost?

Delaying weaning may slightly increase production costs. This practice does not require additional equipment but may require additional training on the exact days to wean a piglet. In addition, delaying weaning is expected to slightly change the normal cost structure of the farm because it requires changing the feed offered to piglets during pre-weaning, which extends the use of creep feed. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land, unless a farm does not count with the space to keep non-weaned piglets. In the latter case, the farmer needs to invest in infrastructure to modify the unit to accommodate a longer pre-weaning period. This practice may slightly increase the complexity of production because the farmer needs to know when to wean a litter and how to plan the next cycle of production.

We do not provide a computation of a return of investment (ROI) for this practice because there is no available information on how much PWD is decreased, how much performance improves, and how much mortality reduces with delayed weaning. Additional costs are related to the effect on sow production performance (fewer pigs produced per sow per year).

## 5. How can I do it well?

Careful planning and execution are key for the success of this intervention. This practice can be best implemented by gathering the staff involved in the daily management of the farm, the manager, and the veterinarian to discuss how weaning can be delayed in their farm and their impacts on production performance, management and pig flow.

## 6. How strong is the evidence?

Empirical evidence is very strong regarding this practice. However, this practice is not very popular because of the impact it might have on reproductive performance indicators on farm and the additional resources necessary to keep pigs for five or more weeks with their mothers before weaning. In most countries outside Europe, weaning is legal at 3 weeks of age (21 days) with many studies focusing on early weaning with the purpose of weaning pigs free from disease (before exposure).

## 7. Where can I find further information?

The AHDB's Knowledge Library provides resources on managing the weaned pig (<u>Weaning and</u> <u>small pig management | AHDB</u>). Pig Progress consider the pros and cons of moving from weaning at 4 weeks to 5 weeks (<u>Delayed weaning better for piglet welfare - Pig Progress</u>).

This article highlights key points to consider before transitioning to weaning at 5 weeks of age:

What to consider before a switch to five-week pig weaning - Farmers Weekly (fwi.co.uk).

## 15.3.6 Feeding Regimes

#### Impact summary

Feeding management goes hand-in-hand with water management as any restrictions in water intake will result in a reduced feed intake. Both feed and water management require close attention to hygiene of troughs and care to ensure ease of access. Managing the feeding regime begins pre-weaning and establishing feeding habits at this stage will be of benefit to the growing pig at weaning. For example, establishing creep feeds and continuing these for 24-48 hours post-weaning may help to encourage feeding. Good feeding management practices, including attention to stock rotation and storage, apply.

**Disclaimer:** This practice should always be considered in conjunction with other nutritional changes, especially those involving protein reduction and feed additives. Please refer to section 15.2 Nutritional changes.

Effectiveness		
	Reducing diarrhoea	+
	Reducing post-weaning mortality	+
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	0
	Improved welfare	+
Cost		
		£-££
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	High
	Overall	High

## 1. What is the practice?

Feed and water management are closely integrated with any reduction in water intake resulting in a reduction in feed consumption. Both require close attention to hygiene. In addition, feeding regimes for newly weaned pigs should avoid indigestible ingredients (for example, raw cereals) that may precipitate scours; ensure that feed is fresh and free from contamination by cleaning feeders and paying attention to stock rotation and storage; and seek to avoid gorging in the early stages by offering feed little and often rather than on an ad lib basis. Managing the feeding regime over the weaning period begins by training the suckling pig to start learning how to feed. Creep feeds are typically highly palatable and by continuing to offer these familiar rations for a minimum of 24 - 48 hours after weaning, post-weaning fasting may be minimised. Pigs should be encouraged to eat pre-weaning as this increase early post-wean feed intake and minimises stress and may help with PWD. Feeding regimes can promote the development of the gut and the earlier adaptation of enzymes to the digestion of weaner diets and help to reduce diarrhoea outbreaks. Mortality can be reduced indirectly, by preventing diarrhoea outbreaks. Creep and link feeds are known to promote growth, also by preventing lack of appetite and for proportionating a smoother transition from milk to solids

## 2. How effective is it?

This practice can be considered as training of the piglet's digestive system to digest solid feed (weaner pigs' diets). It is an effective way of promoting feed intake and feed acceptability, preventing fasting and growth check at weaning. Feeding regimes should be considered as a routine practice in the transition to weaning and as such are known to be effective in the prevention or minimization of PWD or scours caused by nutritional factors.

## 3. Where does it work?

This practice works in the farrowing house and in the nursery with piglets before and after weaning being exposed to different diets and feed forms to stimulate intake. It works by promoting gut maturation and adaptation to solid feed before weaning.

## 4. How much does it cost?

While implementing a targeted feeding regime may require investment in equipment, for example troughs and feeding infrastructure, it is more likely that investment in training to implement and monitor the approach is required. Creep and link diets which are an essential component of feed training are the most expensive and the highest quality diets that pigs eat throughout the course of their life. Changing diets or providing a third diet can increase the costs of production.

Some units may need to adopt change their feeding regimes entirely whereas others may only need to slightly modify these regimes.

We do not provide a computation of a return of investment (ROI) for this practice because we did not find relevant information on the literature consulted. Because pigs in intensive commercial settings are weaned at much earlier ages compared to what would happen in nature, feed training and the provision of highly palatable- high quality feeds should be considered good practice and a requirement before weaning, and not as a facultative intervention. Thus, ROI could be tested by comparing a normal farm providing around 3.5kg of creep feed per pig and 8kg of link per pig to the administration of a higher amount of creep and link feed per pig, or different types of creep/link feed and its effects on the gut adaptation of piglets.

## 5. How can I do it well?

This practice can be done well by discussing the feeding regime with your veterinarian, the pig nutritionist, and a feed specialist. The most adequate feed regime to your farm needs to take into account farm management in the farrowing house and the feed form to be supplied to pigs. Typically, a specified quantity (kg) of creep and link feed per pig is defined, with timing of administration (the week before weaning, or perhaps earlier) and number of diets to be defined. Presentation of the feed with sprinkled milk powder or other techniques to increase palatability can be another strategy to employ.

## 6. How strong is the evidence?

There is wide evidence in the literature about the effect of creep feeding and link diets on the development of the piglet's gut and its maturation. Empirical evidence confirms scientific findings.

## 7. Where can I find further information?

The AHDB's Knowledge Library (Feeding the weaned pig | AHDB) contains information specific to managing the diet at and around weaning. In addition, the Animal Feed companies that supply pig feeds and piglet diets offer information about diets and feeding (including, for example:

- Gut health in piglets Antibiotics and ZnO reduction | Lallemand Animal Nutrition;
- Diarrhea in Pigs | Alltech; Zinc-free feeding weaning piglets without zinc | AB Neo (abneo.com);
- Harbro Pig Feeds | Harbro Quality Livestock Nutrition | Harbro).

# 15.4 Immune status

#### 15.4.1 Colostrum management

#### Impact summary

Colostrum management reduces diarrhoea by conferring (passive) immunity to the piglets and reducing susceptibility to infectious agents causative of PWD. Pigs which had sufficient and timely access to colostrum are often healthier and present better growth rates compared to those which did not. To make the most of this practice, it is advisable to vaccinate pregnant sows a few weeks before farrowing. Costs associated with this practice are related to the logistics and labour required at farrowing.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	+
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	+
	Improved welfare	++
Cost		
		£
Speed of change		
		Fast
Strength of evidence		
	Quality	Moderate
	Context	Low
	Overall	Moderate

## 1. What is the practice?

This practice consists of providing access to colostrum to all new-born piglets. Colostrum is an essential source of energy, nutrients and immunity for the new-born piglet. It is secreted immediately after farrowing and after a few hours its composition changes to that of sow milk.

Managing access to colostrum using different techniques like split suckling, assisted suckling, cross fostering to homogenize litter size and ensure access to udder, and ensuring those are done in the first few hours after birth can boost the immune status of the piglets and enhance their chances of fighting-off pathogenic bacteria and viruses which may cause diarrhoea before and after weaning.

## 2. How effective is it?

This practice is effective in preventing PWD caused by pathogenic agents, especially *E. coli* in the first few weeks of life, provided that 1) the sows had circulating antibodies against the disease, 2) the piglets had access to colostrum in the first few hours after birth, and 3) the piglets ingested a sufficient amount. However, the effect of colostrum management in controlling PWD is debatable to the extent that the profile of maternally derived antibodies depends on the amount of colostrum ingested and its timing after birth, and it declines with age and exposure to pathogens.

## 3. Where does it work?

This practice works in the farrowing house, at birth. New-born piglets must have access to colostrum and ingest in sufficient quantity.

## 4. How much does it cost?

Managing colostrum is expected to increase marginally feeding costs or not at all. This practice does not require additional equipment but may require additional training on how to supply colostrum to piglets, and labour to provide assistance around farrowing. In addition, this practice is not expected to change the normal cost structure of the farm or require a large investment since there is no need for a specialised training. This practice is not expected to require additional capital costs for machinery or implements for the farm, or any major investment in infrastructure or land.

We do not provide a computation of a return of investment (ROI) for this practice because we did not find relevant information on the literature consulted. Colostrum management is primarily implemented for the benefit of new-born pigs and to prevent pre-weaning mortality. Though its effects are likely positive, we did not find scientific studies quantifying the effect of colostrum management on PWD, post-weaning mortality, and pig performance.

## 5. How can I do it well?

Manage sows in order to optimise colostrum production. Though not much is known on the factors affecting colostrum production, it has been noted that relaxed sows produce more colostrum. Likewise, reduce stress before, during and after farrowing and feed diets appropriate for

pregnancy and lactation. Many other factors can influence both colostrum production and consumption, e.g., sow parity, litter size and piglet vigour at birth. Make sure all piglets had access to colostrum (consider split suckling and assisted suckling) and ingested a sufficient amount (200-350g) within the first few hours after birth (ideally within 12h-24h after birth). Supervise farrowing and, for a better allocation of resources and a defined window of action, consider synchronising sow's reproductive cycles. Cross-fostering may be an effective practice to ensure all piglets have access to colostrum.

Keep records with sow farrowing information, including farrowing time, visible to all staff. Design a split suckling protocol and train staff in how to do it.

## 6. How strong is the evidence?

The literature and the evidence available are adamant in stating that access to colostrum is the single most important requirement to predict the viability of piglets and the preparation of their immune system for the challenges to come in the first few weeks of like. However, most literature discusses the protective effect of colostrum in preventing infectious diseases pre-weaning, and their effects post-weaning are not clear.

## 7. Where can I find further information?

You can find more information on how to manage colostrum in the websites below. They contain practical tips for how to do this practice well, especially the AHDB reference (<u>Colostrum</u> management for pigs | AHDB).

How to increase the amount of colostrum available to newborn piglets - Articles - pig333, pig to pork community

#### References

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3. Farmer, C. (2021). A simple tool to increase the amount of colostrum available to newborn piglets. Retrieved from <u>https://www.pig333.com/articles/how-to-increase-the-amount-of-colostrum-available-to-newborn-piglets\_16649/</u>

#### 15.4.2 Vaccination for E. coli

#### Impact summary

There are vaccination schemes designed to prevent PWD and prevent severe clinical signs in pigs by vaccinating gilts and sows before farrowing. The objective is to maximise antibodies against pathogenic E. coli strains, especially those producing F4 and F18 factors. The choice of the vaccine to use and the vaccination programme to follow need to be decided following veterinary advice. Sow vaccines against *E. coli* confer good protective levels to new-born piglets via colostrum, but antibodies decline and are unlikely to confer protection at weaning. At the time of writing only one piglet vaccine is currently licenced to control PWD - Coliprotect® F4/F18 by Elanco. This oral vaccine contains live non-pathogenic *E. coli* strains expressing F4 and F18 factors. According to the manufacturer, it was designed for active immunisation of pigs from 3 weeks of age against ETEC expressing F4 and F18 in order to reduce the incidence of moderate to severe PWD caused by E. coli, and to reduce the faecal shedding of pathogenic ETEC bacteria from infected pigs. Immunity starts at 7 days after vaccination and lasts for 3 weeks, covering the critical post-weaning period. Vaccine costs, labour and logistics are factors to consider when deciding which vaccination strategy to follow, including whether to vaccinate sows, piglets, or both.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	++
	Enhancing growth rate	++
	Other impacts	
	Reduced costs	+
	Improved welfare	++
Cost		
		£-££
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	Very high
	Overall	High

## 1. What is the practice?

This practice consists in vaccinating pigs against *E. coli*. This will boost the pigs' immune system and "teach" it how to combat *E. coli* infections.

The only available commercial vaccine against pathogenic E. coli causing diarrhoea in piglets is an oral vaccine and contains live non-pathogenic *E. coli* strains expressing F4 and F18 factors. According to the manufacturer, it was designed for active immunisation of pigs from 3 weeks of age against ETEC expressing F4 and F18 in order to reduce the incidence of moderate to severe PWD caused by E. coli, and to reduce the faecal shedding of pathogenic ETEC bacteria from infected pigs. Immunity starts at 7 days after vaccination and lasts for 3 weeks, covering the critical post-weaning period.

Vaccinating sows and/or piglets against *E. coli* strains prevent the development of disease, and therefore reduces the incidence of PWD, and the severe outcomes of disease (reduces mortality).

## 2. How effective is it?

This practice is very effective provided that vaccination has been correctly done in pigs and that the PWD on farm is caused by *E. coli*. Though piglet vaccination is the only one licenced to prevent PWD, sow vaccination may also have positive effects by increasing the amount of maternally derived antibodies against *E. coli* in weaned pigs.

## 3. Where does it work?

This practice is to be implemented in the farrowing house, when the piglets are to be vaccinated, or in the dry sow house, should gestating sows be vaccinated against *E. coli* infections too.

## 4. How much does it cost?

Vaccinating piglets against *E. coli* does not affect feeding costs but increases production costs per piglet. This practice may require additional training or capital for infrastructure or new implements. This practice does not change the cost structure of the farm or makes production more complicated. Considering a price of  $\pounds$ 1/vaccine and one dose per piglet, a ROI can be estimated for this practice. To estimate this measure, we make the following assumptions.

- First, we consider the vaccine "Coliprotect®".
- Second, ZnO is mainly used in the feed at a dosage of 100 mg per kg body weight per day for 14 consecutive days, which equates to 2500 ppm zinc in feed. This amounts to (roughly) using 0.0105 kg of ZnO per piglet per production cycle.
- Third, we assume that all other production practices and feed proportions are maintained as usual.
- Fourth, we assumed that Coliprotect® does not affect pig performance as per the results obtained by a trial by Nadeau et al. (2017).
- Finally, using a vaccine does not affect feeding rations or other production costs.

With all these assumptions in place, we introduced these values to the calculator to estimate a ROI for this practice. This estimation is shown in **Table 8**. Thus, vaccinating a piglet against *E. coli*, **under the parameters of this exercise**, is expected **to reduce** net profits by 4.55% per pig.

**Table 8.** Return of investment (ROI) estimation for the use of a commercially available vaccine in piglets to control post-weaning diarrhoea. This table corresponds to an extract of a calculator build in this project.

Concepts	Vaccine
Percentage change in piglet weight with new practice vs old practice	
Liveweight (LW) of the piglet with old practice (kg)	
Liveweight (LW) of the piglet with new practice (kg)	40
Price of ZnO (£/kg)	12
Recommended use of ZnO for the whole treatment period (kg/treatment)	0.0105
Price of creep with ZnO (£/kg)	
Price of link with ZnO (£/kg)	0.36
Price of creep without ZnO (£/kg)	0.39
Price of link without ZnO(£/kg)	
Quantity of creep (kg/treatment period)	
Quantity of link (kg/treatment period)	
Price of vaccine (£/dose)	1
Quantity of vaccine (per dose) provided to a piglet during treatment period	
Total costs per kg (£/kg) (including feeding costs associated with treatment period)	
Gross margin per piglet with old practice (£/piglet)	
Gross margin per pig with new practice (£/piglet)	
ROI (%)	

The figures displayed in **Table 8** are a product of a ROI estimation exercise made with the assumptions made above.

To better appreciate these figures and to simulate other scenarios (price changes, different growth rates, etc) please refer to the calculator prepared during this project.

# 5. How can I do it well?

Choose the vaccines after a careful diagnostic approach has been performed and a positive diagnosis achieved. Make sure the vaccination programme is practicable on your farm and brief the staff involved.

Vaccination success depends on many factors. Vaccination storage and correct administration (technique) are essential. Only vaccinate healthy sows and pigs. Make sure staff knowledge about vaccination best practices is refreshed regularly.

Make sure to follow the vaccine manufacturer's directions and beware that vaccination timing may limit its effectiveness. Specifically, you need to allow sufficient time between vaccination and weaning so that pigs can develop an adequate immune response and be prepared to fight-off infections post-weaning.

If you are administering live vaccines to piglets, make sure antibiotics are not administered to the pigs in the days before and after the live vaccine was given.

## 6. How strong is the evidence?

The evidence available is high or very high. There are many studies testing the efficacy of piglet vaccines targeting pathogenic *E. coli* under commercial and research settings. Empirically, it is well known that vaccination to control PWD caused by pathogenic *E. coli* is effective.

## 7. Where can I find further information?

The best source of information regarding vaccination to prevent PWD is your veterinarian. Please consult your veterinarian to discuss vaccination protocols on farm. Further information may be found in the labels of the vaccine products purchased.

Some pharmaceutical companies offer diagnostic testing to identify the different pathogens and strains involved in PWD on farm. This article discusses the need to diagnose disease to better create a prevention programme.

• <u>Vaccination can help pig producers manage post-weaning diarrhoea (PWD) without zinc</u> <u>oxide | The Scottish Farmer</u>

Here is another interesting article mentioning vaccination against *E. coli*:

• Tackle post-weaning *E. coli* issues with aggressive cleaning, vaccination | The Pig Site

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## 15.4.3 Antibiotic usage for E. coli

#### Impact summary

In the past, antibiotic usage was the standard approach to treat PWD. However, with the threat of antibiotic resistance and the restrictions to their use, alternatives to antibiotic usage have been pursued. Antibiotics are typically administered in-feed or in water to affected batches. Historically, antibiotics that reach therapeutic concentrations in the small intestine such as amoxicillin and clavulanic acid, fluoroquinolones, cephalosporins, apramycin, ceftiofur, neomycin, or trimethoprim have been used. Antibiotics critically important to human medicine such as fluoroquinolones and cephalosporins of 3<sup>rd</sup> and 4<sup>th</sup> generation must be used as last resort and are under a moratorium in the UK, just like the use of colistin. Due to the diagnostic approach necessary before its prescription and the costs associated with its purchase and inclusion in feed, this practice can be costly. As antibiotic usage is increasingly controlled, this practice is only applicable as control measure.

#### Disclaimer

The use of antibiotics, especially under the new veterinary prescription rules, which are under consultation by the VMD in the UK, is only to be applied after a thorough diagnostic approach, including antibiotic sensitivity testing (AST) and only in batches with the identified problem.

Effectiveness		
	Reducing diarrhoea	++
	Reducing post-weaning mortality	++
	Enhancing growth rate	+
	Other impacts	
	Reduced costs	+
	Improved welfare	+
-		
Cost		
		££-£££
Speed of change		
		Fast
Strength of evidence		
	Quality	High
	Context	Very High
	Overall	High

## 1. What is the practice?

This practice consists in the administration of antibiotics in feed or water to treat batches of affected pigs with scours, or PWD. Individual sick pigs may also be treated parenterally (by injecting antibiotics).

## 2. How effective is it?

This practice is highly effective in treating the disease provided that its root cause has been identified as *E. coli* or other bacterial infections and the antibiotic chosen has proven efficacy against the field strain. Given the rise of antibiotic resistance (which is when bacteria acquire defence mechanisms against antibiotics), the efficacy of some antibiotics may be reduced. It is advisable to conduct an antibiotic susceptibility test (AST) to identify which antibiotic is most effective for each treatment. Your veterinarian will be able to advise you on this matter.

## 3. Where does it work?

For group treatments, this practice works in-feed or in water, where the antibiotic drug is administered, and the pigs ingest it. It acts in the gut by killing bacteria. For individual treatments, antibiotics are injected, being processed by the animal, and acting in the gut to kill bacteria. Historically, in-feed antibiotics were the go-to treatment when PWD caused by bacteria was diagnosed. However, the restrictions and the more prudent use of antibiotics mean that in-feed medication is not advisable. In addition, and perhaps more importantly, sick pigs typically go off-feed meaning that they will not be adequately medicated. In-water medication provides a more targeted treatment by allowing medication to single pens of piglets in a given building or barn. These systems, though more expensive, are now preferred.

## 4. How much does it cost?

Costs associated with the implementation of this practice can be high due to the diagnostic approach necessary to identify the problem, veterinary consultation, and the costs of the drugs. Other costs related to the administration of medication in water may need to be considered, like the installation of a system capable of delivering such treatments. Other indirect costs can be the labour required to administer these treatments and to keep records of antibiotic usage. Reporting antibiotic usage is required in most quality assurance schemes (i.e., Red Tractor) on a quarterly basis (electronic Medicines Book – eMB).

In addition, the eMB has a benchmarking tool which identifies "Persistently High Users" (PHUs) - producers who fall into the top 5% or 10% of antibiotic users for different holding types over a rolling 12-month period. PHUs are either warned about the high usage (10% cohort) or are required to install an antibiotic reduction plan in conjunction with their vet (5% cohort) (AHDB, 2022). If you use antibiotics to treat PWD, you need to consider the risk of becoming a PHU and the costs associated with it.

We do not provide a computation of a return of investment (ROI) for this practice because antibiotic treatment costs will largely vary according to the type of antibiotic administered, the route of administration (in-feed, in water, parenteral), and the number of animals to treat. As explained above, diagnostic procedures should also be counted as costs for antibiotic treatment as correct diagnostics is not only good practice, but also a legal requirement. ROI for this practice will depend on all of these factors and on the severity of the outbreak. Because antibiotics cannot be used for preventing PWD – only for treating it – there would be losses in terms of performance and mortality before treatment can be started. Thus, the ROI for this practice is likely to be negative.

#### 5. How can I do it well?

Ensure correct administration, dosage, and technique (if injecting animals). Ensure medicated feed is stored properly and inclusion rates are appropriate (if mixing on farm). Carefully read label and preparation guidelines for any water medication. Ensure delivery system is well installed and that drugs are delivered to the diseased group of animals.

#### 6. How strong is the evidence?

Given that historically antibiotics were used routinely when treating PWD, there is wide evidence of its effectiveness. There is broad literature on the efficacy of antibiotic treatments to control PWD, provided that a positive diagnostic has been reached.

#### 7. Where can I find further information?

The best source of information regarding antibiotic usage to treat PWD is your veterinarian. Please consult your veterinarian to discuss antibiotic treatments employed on farm. Further information may be found in the labels of the products purchased.

#### References

- 1. Fairbrother, J. M., & Nadeau, É. (2019). Colibacillosis. In Diseases of Swine (pp. 807-834)
- 2. Luppi, A. (2017). Swine enteric colibacillosis: Diagnosis, therapy and antimicrobial resistance. Porcine Health Management, 3. doi:10.1186/s40813-017-0063-4
- 3. AHDB. (2022). PHWC Antimicrobial Usage. Retrieved from https://ahdb.org.uk/knowledge-library/phwc-antimicrobial-usage