

**HIPRA**



# Gut health on nursery

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Introduction

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What can we do for you?

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Results

# What is Gut health?

Veterinary

"The absence of digestive pathologies that reduce the development of the animal in question"

Scientist

"More knowledge is needed to narrow the terms well"

Nutricionst

"State of the animal in which the digestive functions develop normally"

Farmer

"Let the piglets eat and fatten well"

# What is Gut Health?

"A steady state where the microbiome and intestinal tract exist in symbiotic balance and where animal welfare and performance are not limited by gut dysfunction"

*Pietro Celi*

Environment

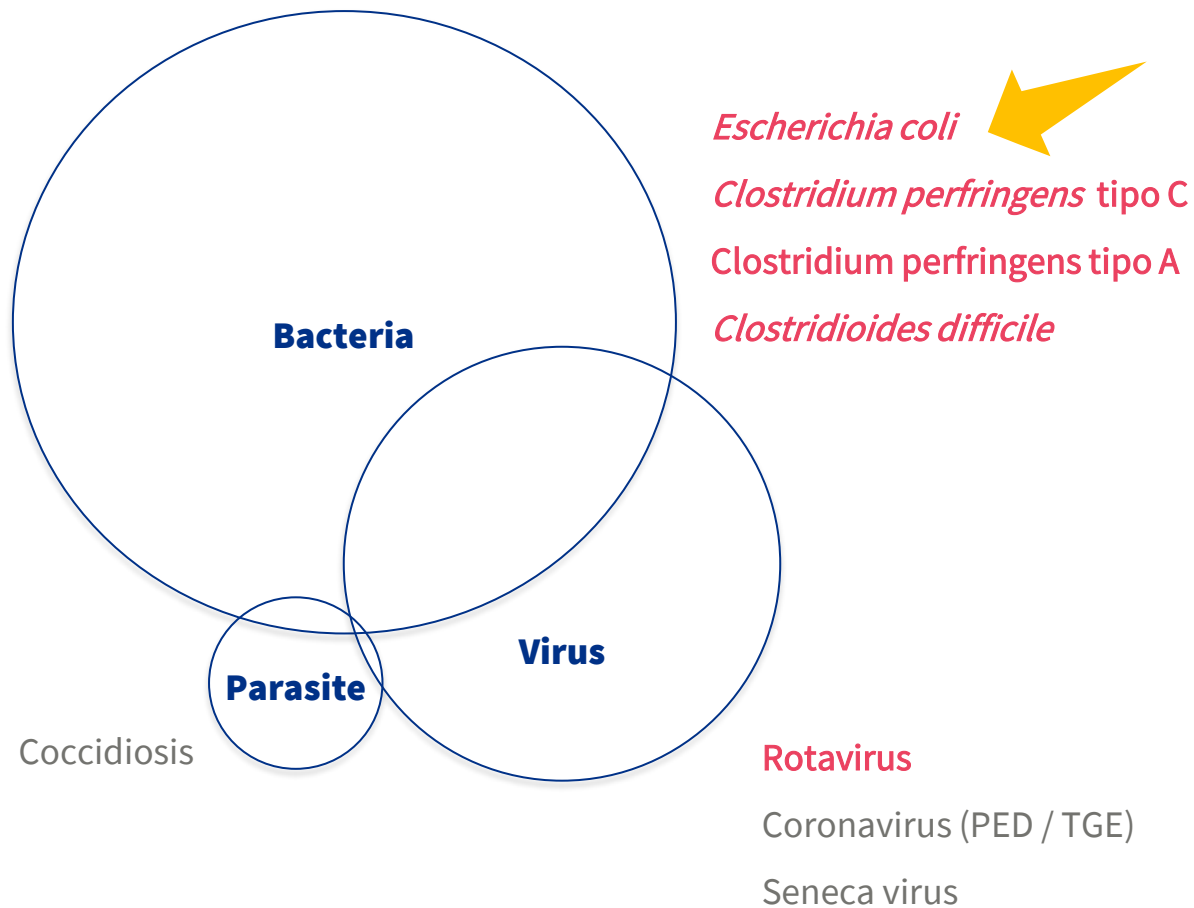


Microbiome

GUT

Host





## Enterotoxigenic E.coli (ETEC) and Verotoxigenic E.coli (VTEC)

- Worldwide problems, endemic manifestation or outbreaks
- Appearance: First days after weaning > introduction to fattening (rare)

### ETEC: Post-weaning diarrhoea

- Clinical signs:
  - **Low:** < 3% mortality + ↓ weight gain
  - **Severe:** > 25% mortality + ↓ ↓ weight gain

### VTEC: Oedema disease

- Signs:
  - **Clinical**
    - Sudden death
    - Eyelid oedema, incoordination, breathing problems, death
    - Mild subcutaneous oedema, pruritus and recovery
  - **Cronhical**
    - ↓ weight gain, neurological clinical signs, muscular atrophy
  - **Subclinical**
    - ↓ weight gain, secondary problems



# VTEC pathogenesis

1. Ingestion of VTEC

2. Small bowel colonization (receptors in jejunum & ileum)

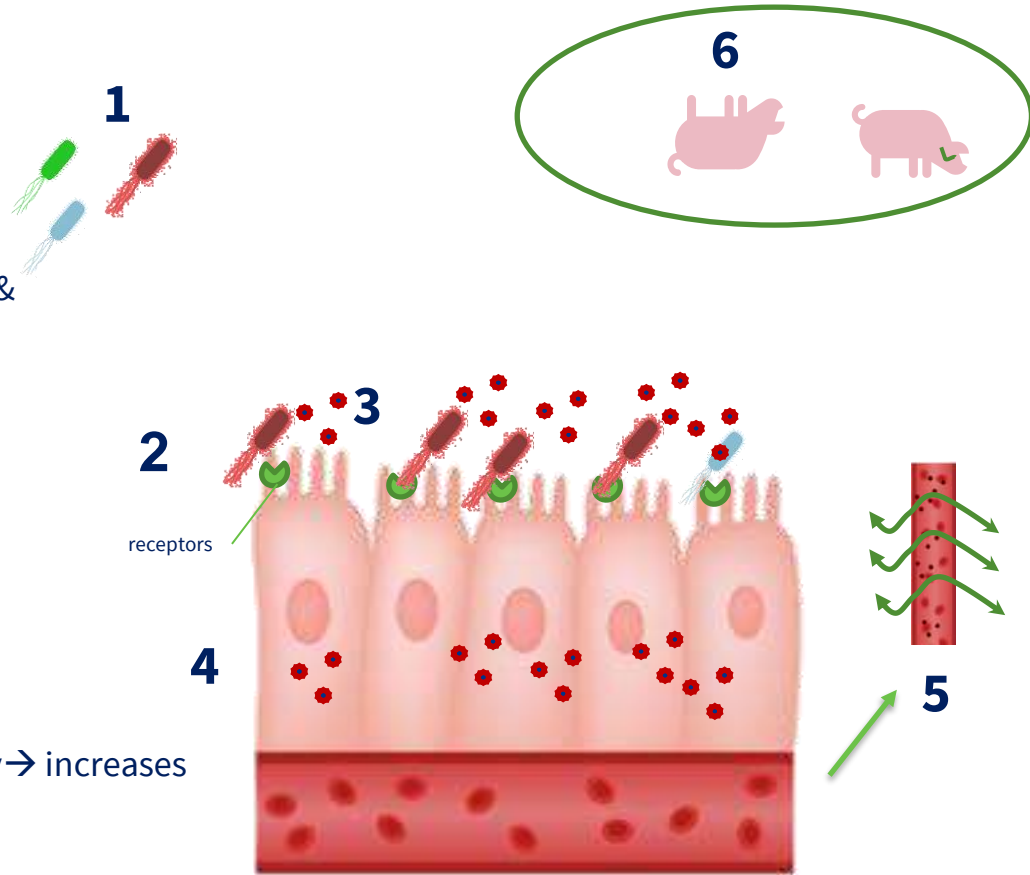
- **ETEC:F18** – depends on the age (+15 days) → 3 weeks ↑
  - Slow progression of the disease (5-7 días)
  - End of lactation and post-weaning

3. Verotoxin replication & production (Vt2e/Stx2e)

4. Transport of toxins into blood stream

5. Capillary involvement: degenerative angiopathy → increases vascular permeability and epithelial necrosis

6. Oedema, ataxia and death



## Pathogenesis ETEC and VTEC

### Mixed infections are common

ETEC + VTEC (or ETEC with VTEC in the same bacterium)

- ETEC + VTEC + other pathogens (*Clostridium*, *Salmonella*, *Lawsonia*, *Brachyspira*,...)

**Increased  
pathogenesis**

### Swine Enteric Colibacillosis in Spain: Pathogenic Potential of *mcr-1* ST10 and ST131 *E. coli* Isolates

Epidemiological study of 499 *E. coli* isolated from outbreaks of enteric colibacillosis with diarrhea in Spain

	Samples	%
ETEC	277	57,5 %
aEPEC	156	32,4 %
VTEC/ETEC	33	6,8 %
VTEC	15	3,2 %



**Risk factors**

## ED and PWD Risk Factors

Disease	Aetiology	Risk factors	
	<i>E. coli</i> patotipo	Host	Environment
Oedema Disease	VTEC/STEC:F18	<ul style="list-style-type: none"> <li>▸ Some resistant piglets lack F18 (ED + PWD) or F4 (PWD) receptor</li> <li>▸ Stress</li> <li>▸ Loss of calostrat antibodies</li> </ul>	<ul style="list-style-type: none"> <li>▸ Transport</li> <li>▸ Mixing of animals</li> <li>▸ Dietary changes</li> <li>▸ Low level of milk or other animal products</li> </ul>
Post-weaning diarrhoea	ETEC:F4, F18, ETEC:AIDA, EPEC, different pathotypes <i>E. coli</i>	<ul style="list-style-type: none"> <li>▸ Early weaning</li> <li>▸ High growth animals (ED)</li> </ul>	<ul style="list-style-type: none"> <li>▸ Some ingredients (ex: soy)</li> <li>▸ Presence of other infections such as PRRSv, rotavirus, Salmonella</li> </ul>

## ZnO ban in 2022

Intestinal balance should be more precise

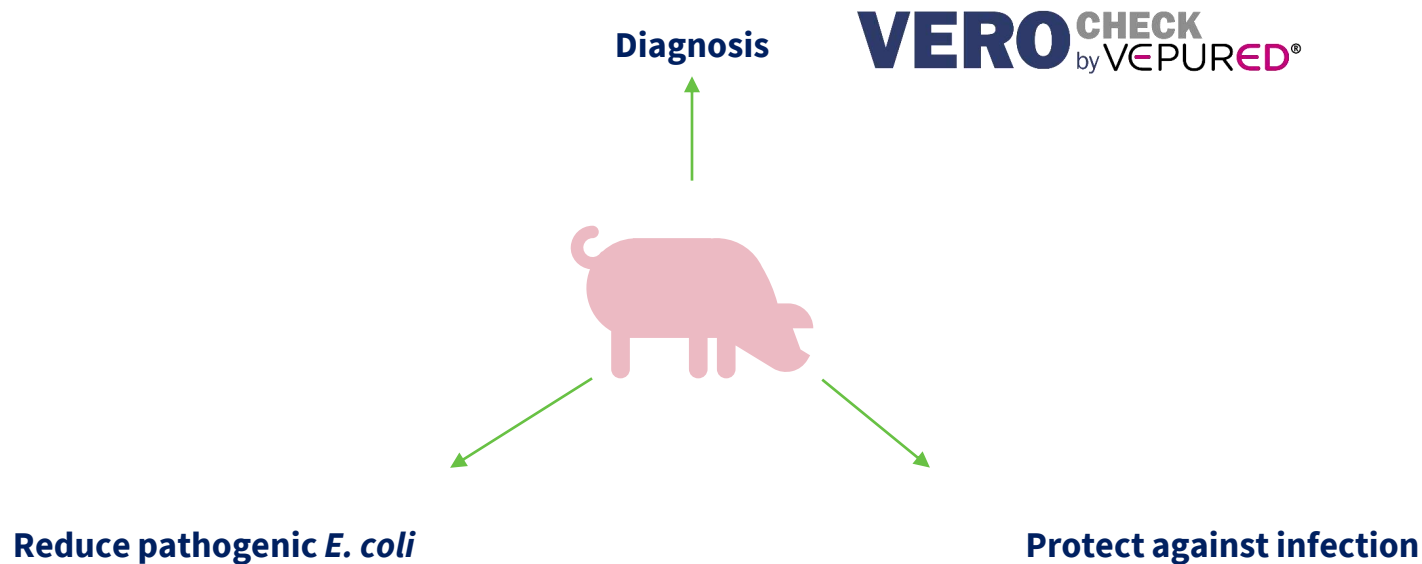
Table 1- Zinc oxide: 2 different uses - 2 different situations.

	ZnO as a feed additive	ZnO as a veterinary medicinal product (VMP)
EU agency	European Food Safety Authority (EFSA)	European Medicines Agency (EMA)
Legislation	Regulation (EC) No 1831/2003 on additives for use in animal nutrition	Directive 2001/82/EC on veterinary medicinal products + Regulation (EC) No 726/2004
Levels	Max. total 150ppm of zinc (from ZnO and other sources)	Normal dosage ca. 2500ppm
Ban?	No! There is no indication that ZnO will be banned as a feed additive.	Yes! Marketing authorisations for ZnO-based VMPs will be withdrawn the across EU by June 2022.

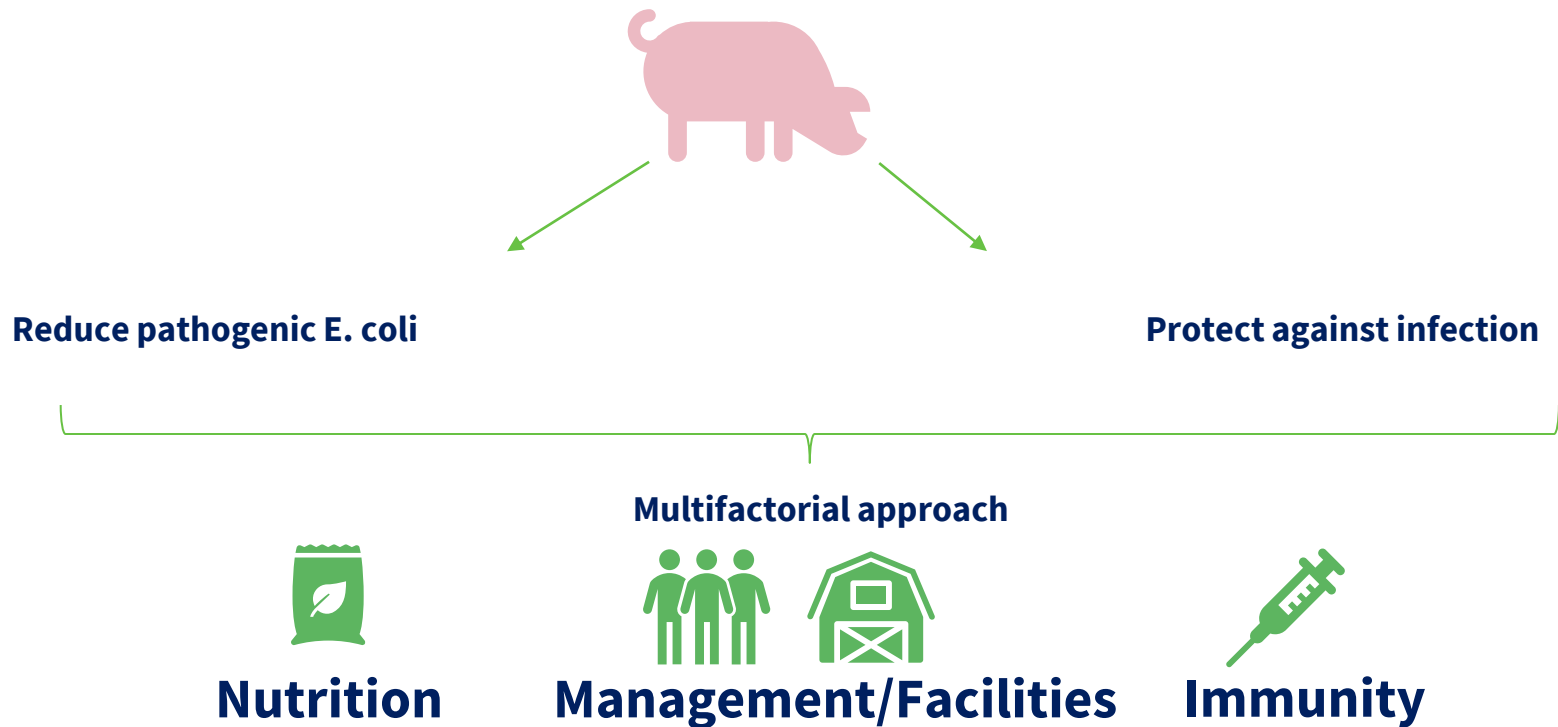
## Control strategies



# Control strategies

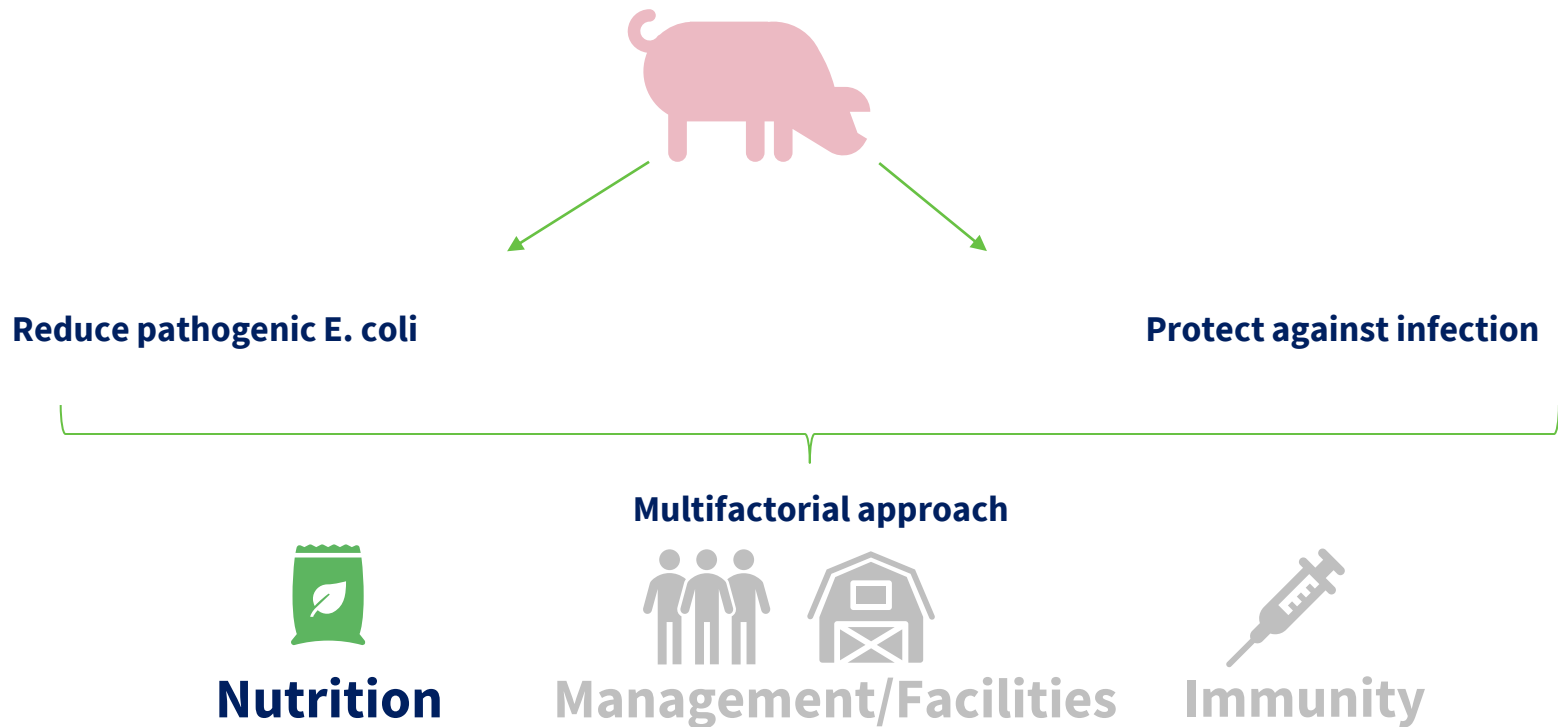


# Control strategies





# Control strategies



## Nutrition vs. ETEC and VTEC

### Reduction of pathogenic *E.coli* and increase of resistance

#### Water

- Additives: Organic and inorganic

#### Ingredients (diet)

- Highly digestive
- Milk proteins
- Protein reduction (<18%)
- Intake restriction
- Fiber increase
- Flour vs pellets
- Calcium reduction 10% (buffer capacity)

#### Additives

- Organic and inorganic acids
- Essential oils
- ZnO boosted
- Antimicrobial peptides
- Hydrolyzed plasma
- Beta-glucans
- Probiotics
- Prebiotics
- Oligosaccharides
- Enzymes

# Nutrition against ETEC and VTEC

## Redution of protein (<18% / <180g/kg)

### Effects

- Reduction of proteolytic bacteria

### How?

- Use highly digestible proteins: plasma, lactic proteins
- Complement with syntetic amino acids following the ideal AA profile

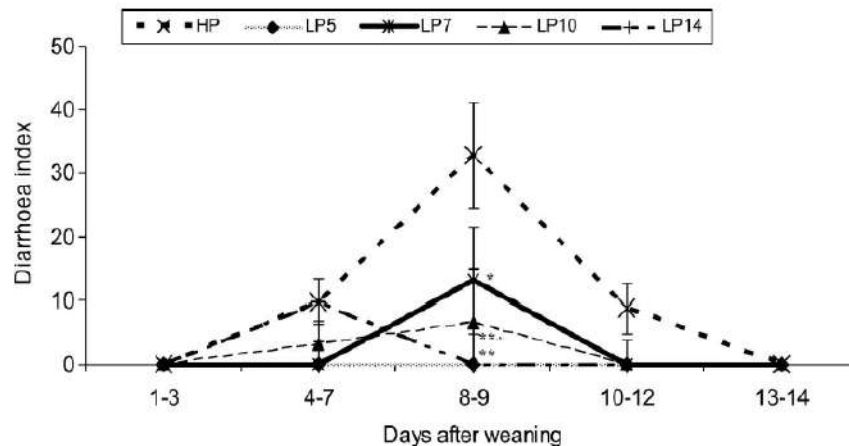
**HP** = high protein (24,3%)

**LP5** = low protein (17,3%) fed for 5 d after weaning

**LP7** = low protein (17,3%) fed for 7 d after weaning

**LP10** = low protein (17,3%) fed for 10 d after weaning

**LP14** = low protein (17,3%) fed for 14 d after weaning





## Article

# Protein Content in the Diet Influences Growth and Diarrhea in Weaning Piglets

Rosa Marchetti <sup>1,\*</sup>, Valerio Faeti <sup>1,\*</sup>, Maurizio Gallo <sup>2</sup>, Massimo Pindo <sup>3</sup>, Davide Bochicchio <sup>1</sup>, Luca Buttazzoni <sup>4</sup> and Giacinto Della Casa <sup>1</sup>

2023

**Table 2.** Growth phases based on piglet body weight and overall crude protein percentage in the diet, depending on growth phase and protein level.

Growth Phase	Protein Level (% CP)	
	High	Low
From the start of weaning to 15 kg (Period I and II)	18.5	16.5
From 15 kg to the end of the experiment (Period III)	16.5	14.5

**Table 6.** Influence of dietary protein level on the diarrhea score summations. The percentages of the scores are shown in parentheses with respect to the total score, referring both to the protein level in the period and to the whole period.

Growth period	Diarrhea Score Summations <sup>1</sup>			Significance of the Difference
	Protein Level		Total in the Period	
	High	Low		
Period I	91 (85.0)	16 (15.0)	107 (45.7)	p < 0.01 NS
Period II	5 (83.3)	1 (16.7)	6 (2.6)	
Total (Period I + Period II)	96 (85.0)	17 (15.0)	113 (48.3)	
Period III	51 (59.7)	59 (41.3)	110 (51.7)	
Total score	167 (71.4)	67 (28.6)	234	

<sup>1</sup> Scores were calculated as reported in Table 4. NS: not significant.

**Table 5.** Average value of selected growth parameters during the experiment and significance of the difference between high-protein and low-protein diets (n = 6 per treatment).

Growth Parameter	Protein Level		Significance of the Difference
	High	Low	
Initial body weight (kg)	7.80	7.77	NS
From weaning to change of housing			
Period I <sup>1</sup>	17.2	15.6	NS
Period II <sup>2</sup>	29.8	28.0	NS
Period I + Period II	23.5	21.8	NS
Average daily gain (g)			
Period I	377	313	p < 0.01
Period II	599	593	NS
Period I + Period II	479	440	p < 0.05
Average daily feed intake (g)			
Period I	585	536	NS
Period II	1181	1138	NS
Period I + Period II	857	810	NS
Feed conversion ratio (-/-)			
Period I	1.55	1.72	p < 0.01
Period II	1.97	1.92	NS
Period I + Period II	1.79	1.84	p < 0.05
From change of housing to the end of post-weaning (period III) <sup>3</sup>			
Average daily gain (g)	439	437	NS
Average daily feed intake (g)	952	952	NS
Feed conversion ratio (-/-)	2.11	2.18	NS
Final body weight (kg)	40.7	38.5	NS

<sup>1</sup> Period I: From the start of the experiment until the change of diet; <sup>2</sup> Period II: From the change of diet until the change of housing; Period I + Period II: From the start of the experiment until the change of housing; <sup>3</sup> Period III: From the change of housing until the end of the experiment.

# Nutrition against ETEC and VTEC

## Probiotics

Live micro-organism  
that when  
administered in  
adequate amounts  
confer benefits to the  
host (FAO/WHO 2001)

A lot of research on  
reducing ETEC, VTEC  
and other  
pathogens

## Benefits?



Barba-Vidal *et al.* 2018

Table 1 Pig in vivo scientific works evaluating the use of probiotics against digestive bacterial pathogens (*Escherichia coli* and *Salmonella* sp.)

References	Probiotic	Pathogen	Animals	
	Strain, dose per pig and dosing method	Strain and dose per pig	Days old: weaning → Inoculation	Benefits Main results
De Cupere <i>et al.</i> (1992)	(a) <i>Bacillus cereus</i> var. <i>Toyo</i> ( $1 \times 10^8$ cfu/g) (b) <i>Lactobacillus</i> spp. ( $7.5 \times 10^7$ cfu/g) (c) <i>Streptococcus faecium</i> ( $5.6 \times 10^8$ cfu/g) Included in feed	<i>Escherichia coli</i> O141 K85 ( $10^8$ cfu)	28 → 30	No No improvements on clinical symptoms or mortality. No improvements on fecal <i>E. coli</i> shedding
Shu <i>et al.</i> (2001)	<i>Bifidobacterium lactis</i> HN019 ( $10^8$ cfu/day) Oral administration	<i>E. coli</i> sp.	21 → natural acquisition	Yes Reduced diarrhea scores and fecal shedding of <i>E. coli</i> . Improved animal performance. Increased T-cell differentiation and pathogen-specific antibody titers
Bhandari <i>et al.</i> (2008)	<i>Bacillus subtilis</i> ( $6 \times 10^8$ cfu/kg) Included in feed	<i>E. coli</i> K88 ( $4 \times 10^{10}$ cfu)	17 → 24	Yes Reduced diarrhea scores and mortality. Modulated microbial diversity.
Lessard <i>et al.</i> (2009)	(a) <i>Pediococcus acidilactici</i> (b) <i>Saccharomyces cerevisiae</i> (c) <i>P. acidilactici</i> + <i>S. cerevisiae</i> Lactation ( $10^9$ cfu). Oral administration Weaning ( $10^8$ cfu/kg). Included in feed	<i>E. coli</i> O149: F4 K88 ( $10^9$ cfu)	21 → 49 + 50 + 51	Yes Before challenge: (a) increased T-cell differentiation. After challenge: (a, b, c) Reduced bacterial translocation. (b) Increased ileal immunoglobulins
Zhang <i>et al.</i> (2010)	<i>Lactobacillus rhamnosus</i> GG ( $10^{11}$ cfu/day) Oral administration	ETEC 149: K91, K88ac ( $10^{10}$ cfu)	18 → 26	Yes Reduced diarrhea scores and fecal coliform shedding. Modulated microbial diversity, increased jejunal immunoglobulins. Modulated systemic inflammatory cytokines
Bhandari <i>et al.</i> (2010)	<i>E. coli</i> ( $4.5 \times 10^{12}$ cfu) Included in feed (daily mix) <sup>1</sup>	<i>E. coli</i> K88 ( $1.2 \times 10^{11}$ cfu)	21 → 27	Yes Reduced ETEC in ileum. Improved animal performance
Wang <i>et al.</i> (2009)	<i>Lactobacillus fermentum</i> IS007 ( $2 \times 10^9$ cfu) Oral administration	<i>E. coli</i> K88ac ( $2 \times 10^8$ cfu)	21 → 21	Yes Increased T-cell differentiation and ileum cytokine expression
Konstantinov <i>et al.</i> (2008)	<i>Lactobacillus sobrius</i> DSM 19698 ( $10^{10}$ cfu) Included in feed (daily mix) <sup>1</sup>	ETEC K88 O149 F4 ( $1.5 \times 10^{10}$ cfu)	21 → 28	Yes Reduced levels of ETEC in the ileum, improved performance and increased diarrhea
Krause <i>et al.</i> (2010)	<i>E. coli</i> ( $1.5 \times 10^{11}$ cfu) Included in feed (daily mix) <sup>1</sup>	<i>E. coli</i> K88 ( $1.4 \times 10^{10}$ cfu)	17 → 24	Yes Increased animal performance and microbial diversity. Reduced diarrhea scores (in presence of raw potato starch)
Daudelin <i>et al.</i> (2011)	(a) <i>Pediococcus acidilactici</i> MA18/5 M (b) <i>S. cerevisiae</i> SB-CINCM 1-1079 (c) <i>P. acidilactici</i> + <i>S. cerevisiae</i> Sows: gestation ( $3 \times 10^9$ cfu) + lactation ( $6 \times 10^9$ cfu). Included in feed (daily mix) <sup>1</sup> Piglets: lactation ( $1 \times 10^9$ cfu). Oral administration	ETEC O149 F4 ( $5 \times 10^9$ cfu)	21 → 28	Yes (a, b) Reduced ETEC attachment to intestinal mucosa. (a, c) Induced ileum cytokine expression
Trevi <i>et al.</i> (2011)	Weaning: $2 \times 10^9$ cfu/kg. Included in feed <i>L. rhamnosus</i> GG ( $6 \times 10^9$ cfu) Included in feed (daily mix) <sup>1</sup>	ETEC F4 ( $1.5 \times 10^{10}$ cfu)	21 → 28	No Reduced animal performance. Increased diarrhea scores. Reduced serum immunoglobulins. Tended to a worse histomorphology

# Nutrition against ETEC and VTEC

## Probiotics

## Benefits?

### Conclusions:

- **Effects:** more articles describing beneficial effects with probiotics (>80%) compared to negative.
- **Against pathogens:**
  - In most of the cases, the effects are positive, although they are quite “dicreet”
  - **Potential risks: some probiotics in animals with intestinal damage can suffer translocation pressure.**
  - **High variability:** probiotics may have a positive effect in some trials and not in others. Differences in diets, dosages, genetics or management can influence

## TAKE-AWAY

Probiotics can help BUT...

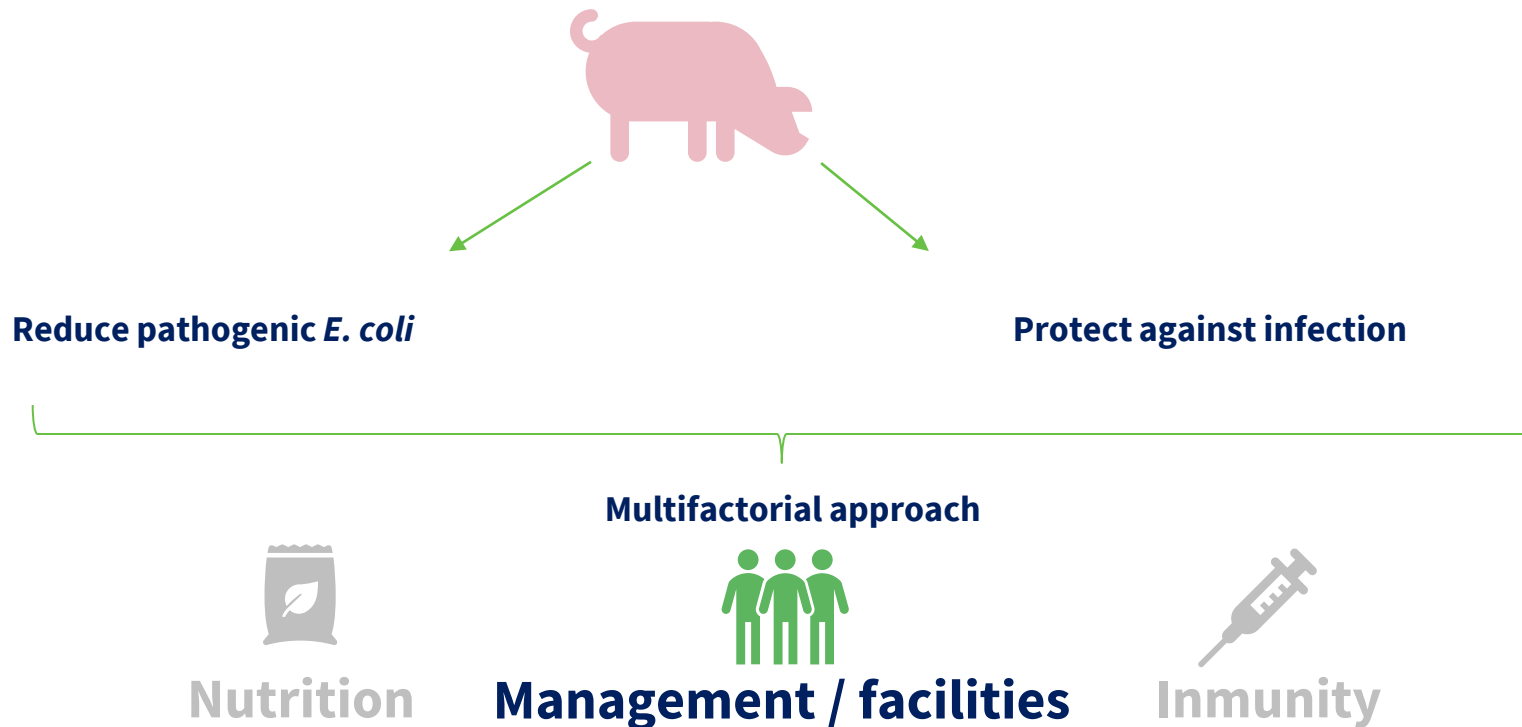
“Do not look to probiotics as a replacement for antibiotics, combine them with other nutritional solutions, management or vaccination strategies”

Table 1. Pig (in vivo) studies modulating the use of probiotics against digestive bacteria (coliforms, *Escherichia coli*, and *Salmonella* sp.)

References	Probiotic	Pathogen	Animals	
			Days old, weighing → inoculation	Results: main results
De Capua et al. (1992)	a) <i>Bifidobacterium</i> 10 <sup>10</sup> CFU/g b) <i>Lactobacillus</i> 10 <sup>10</sup> CFU/g c) <i>Streptococcus</i> 10 <sup>10</sup> CFU/g Inoculated in feed	<i>Escherichia coli</i> O157 K88 (10 <sup>10</sup> CFU)	28 → 35	No improvements on clinical symptoms, or mortality No improvements on feed <i>E. coli</i> shedding
Shu et al. (2001)	<i>Bifidobacterium</i> 10 <sup>10</sup> CFU/g Oral administration	<i>E. coli</i> sp.	21 → weaned apoptosis	Yes Reduced diarrhea scores and fecal shedding of <i>E. coli</i> Improved animal performance, increased feed efficiency and pathogen-specific antibody titer
Blanchard et al. (2008)	<i>Bifidobacterium</i> 10 <sup>10</sup> CFU/g Inoculated in feed	<i>E. coli</i> K88 (10 <sup>10</sup> CFU)	17 → 24	Yes Reduced diarrhea scores and mortality. Modulated intestinal diversity
Imouh et al. (2009)	a) <i>Probiococcus acididurans</i> b) <i>Probiococcus acididurans</i> c) <i>P. acididurans</i> + <i>S. cerevisiae</i> Lactation (10 <sup>10</sup> CFU), oral administration Weaning (10 <sup>10</sup> CFU), inoculated in feed Lactation (10 <sup>10</sup> CFU), inoculated in feed	<i>E. coli</i> O148: H4 K88 (10 <sup>10</sup> CFU)	21 → 49 & 56 → 57	Yes Reduced diarrhea scores and mortality. Modulated intestinal diversity. (a, b) Reduced diarrhea score. (c) Increased feed efficiency
Zhang et al. (2010)	<i>Lactobacillus</i> 10 <sup>10</sup> CFU/g Oral administration	ETEC 149: K91, K88a: 10 <sup>10</sup> CFU	18 → 26	Yes Reduced diarrhea scores and fecal shedding Modulated intestinal diversity, increased plasma immunoglobulins. Modulated systemic inflammatory responses
Blanchard et al. (2010)	<i>E. coli</i> B5 (10 <sup>10</sup> CFU) Inoculated in feed (daily mix)	<i>E. coli</i> K88 (1.2 × 10 <sup>10</sup> CFU)	21 → 27	Yes Reduced ETEC in feces. Improved animal performance and feed efficiency
Wang et al. (2009)	<i>Lactobacillus</i> 10 <sup>10</sup> CFU/g Oral administration	<i>E. coli</i> K88a (2 × 10 <sup>10</sup> CFU)	21 → 27	Yes Increased feed efficiency and fecal shedding reduction
Konopetsky et al. (2008)	<i>Lactobacillus</i> 10 <sup>10</sup> CFU/g Inoculated in feed (daily mix)	ETEC K88 (10 <sup>10</sup> CFU)	21 → 28	Yes Reduced levels of ETEC in the feces. Improved performance and increased diarrhea
Reuter et al. (2010)	<i>E. coli</i> B5 (10 <sup>10</sup> CFU) Inoculated in feed (daily mix)	<i>E. coli</i> K88 (1.4 × 10 <sup>10</sup> CFU)	17 → 24	Yes Increased animal performance and intestinal diversity. Reduced diarrhea scores (in presence of low protein diet)
Franklin et al. (2011)	a) <i>Probiococcus acididurans</i> 10 <sup>10</sup> CFU/g b) <i>S. cerevisiae</i> 10 <sup>10</sup> CFU/g c) <i>P. acididurans</i> + <i>S. cerevisiae</i> d) <i>P. acididurans</i> + <i>S. cerevisiae</i> e) <i>P. acididurans</i> + <i>S. cerevisiae</i> + <i>lactulose</i> f) <i>P. acididurans</i> + <i>S. cerevisiae</i> + <i>lactulose</i> + <i>inulin</i> g) <i>P. acididurans</i> + <i>S. cerevisiae</i> + <i>lactulose</i> + <i>inulin</i> + <i>xylooligosaccharide</i> h) <i>P. acididurans</i> + <i>S. cerevisiae</i> + <i>lactulose</i> + <i>inulin</i> + <i>xylooligosaccharide</i> + <i>inulin</i> Inoculated in feed (daily mix)	ETEC O149: H4 K88 (10 <sup>10</sup> CFU)	21 → 28	Yes In <i>S. cerevisiae</i> ETEC attachment to intestinal mucosa. (a) Reduced fecal shedding
Travis et al. (2011)	<i>Lactobacillus</i> 10 <sup>10</sup> CFU/g Inoculated in feed (daily mix)	ETEC 14 (1.5 × 10 <sup>10</sup> CFU)	21 → 28	No Reduced animal performance. Increased diarrhea scores. Reduced serum immunoglobulin. Limited to a severe immunosuppression



## Control strategies



# Management against ETEC and VTEC

## Reduction of pathogenic *E.coli* patogénicos and increase of resistance



### Water

- Quality control (regularly)

### Hygiene

- Washing, disinfection and drying
  - Pen
  - Feeders and drinkers
  - Others: farm boots? toys?
- Sanitary break (+4 days)
- Lactation (animales menos contaminados)

### Facilities and environment

- Walls and floors (avoid wind zones, humidity zones, etc.)
- Temperature
- Humidity
- Feeder and drinker space

### Management

- All in/All out
- Late weaning
- Transport
- Group size (preferable smaller groups)
- Density
- Stress
- Health control (vaccination)



# Management ETEC and VTEC

## Temperature

### Low temperature

**Reduces intestinal peristaltic activity and consequently increases bacterial colonization**

Low temperatures at weaning → more diarrhoea  
Diseases of Swine. Fairbrother & Nadeau 2019.

### T°C fluctuations

High fluctuation of T°C increases diarrhoea

<b>23.5 ± 3°C</b>	<b>23.5 ± 0,5°C</b>
<b>High DAW</b>	Low DAW



Research | [Open Access](#) | Published: 18 June 2008

## Risk factors for post-weaning diarrhoea on piglet producing farms in Finland

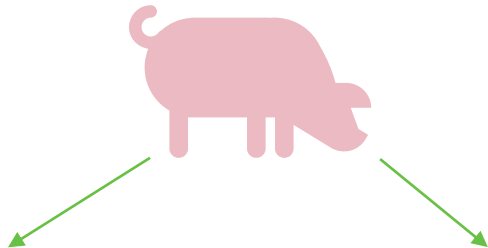
[Taina M Laine](#) , [Tapani Lyytikäinen](#), [Maija Yliaho](#) & [Marjukka Anttila](#)

*Acta Veterinaria Scandinavica* **50**, Article number: 21 (2008) | [Cite this article](#)

Variable	P-value
Temperature control: Automatic vs. Manual	0.03
Number of sows	0.02
Only 1 feeder	0.08

Automatic temperature control reduces risk of post-weaning diarrhea

# Strategies against ETEC and VTEC



Reduce pathogenic *E. coli*

Protect against infection

Multifactorial approach



Nutrition



Management/Facilities



Immunity



# Immunity against ETEC and VTEC

## Reduction of pathogenic *E.coli* and increase of resistance

### Vaccination

- Vaccination of sows (for neonatal diarrhoea. ex. F4(K88
- Oral vaccines *E.coli* non-virulent F4(K88) and F18 → Post-weaning diarrhea
- Toxoid vaccines against Vt2e (Stx2e) → Edema disease

•

### Oral antibodies

- Oral egg yolk powder with hens immunized against F4(K88) and F18

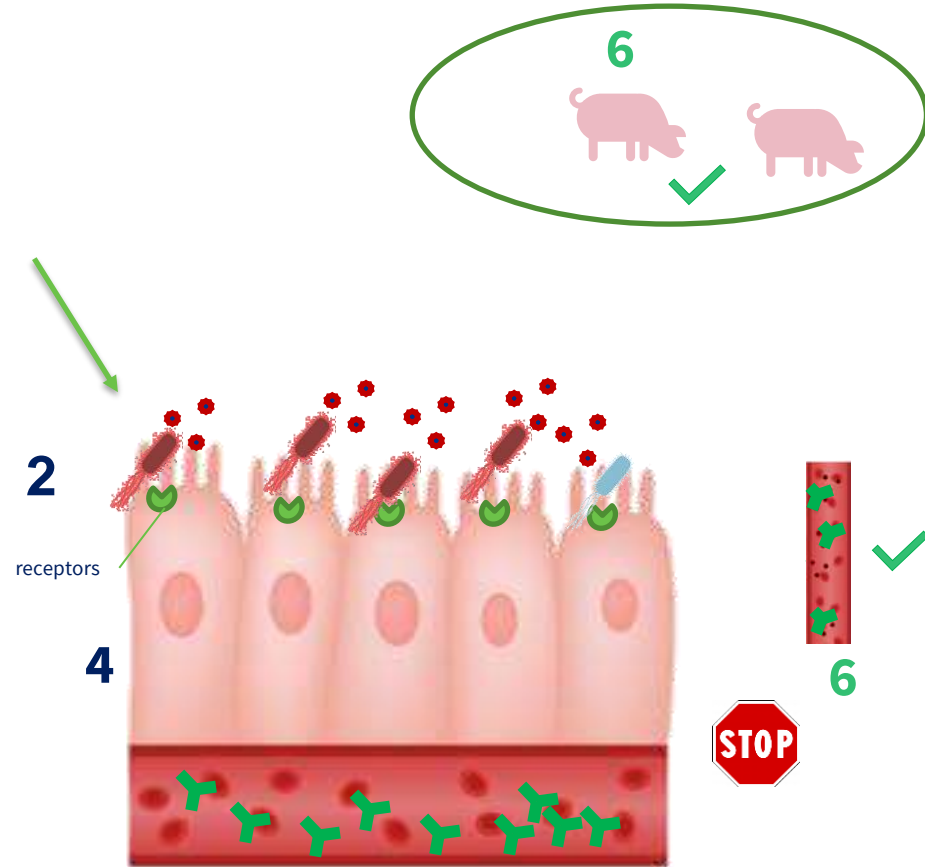
### Genetic selection

- Animals resistant to F4(K88) and F18

# Immunity against VTEC

## Vaccination to increase the resistance of the animals

1. Ingestion of VTEC
2. Small bowel colonization (receptors in jejunum & ileum)
  - **ETEC:F18** – depends on age (+10 days?/+20 days?)  $\times$  3 weeks.  $\uparrow$
  - - cause disease slowly (after 5-7 days)
  - - end-lactation and post-weaning
  -
3. Verotoxin production (Vt2e/Stx2e)
4. Transport of toxins into circulation
5. Antibodies neutralize the toxin
6. NO capillary damage
6. Healthy piglets, WITHOUT edema or ataxias



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Introduction

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What can we do for you?

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Results

# VEPURED®

1 ml / IM – One dose

From day 2 of life

Protection until slaughterhouse

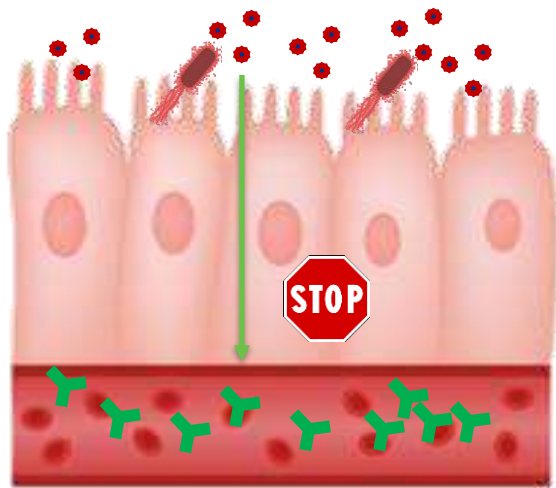
Prevention of mortality

Reduction of clinical signs

PURIFICATION



# Intestinal integrity



Maintaining intestinal integrity is key to avoiding possible primary or secondary processes that disrupt the intestinal balance

Post-weaning diarrhea  
*Streptococcus suis* problems  
Oedema problems

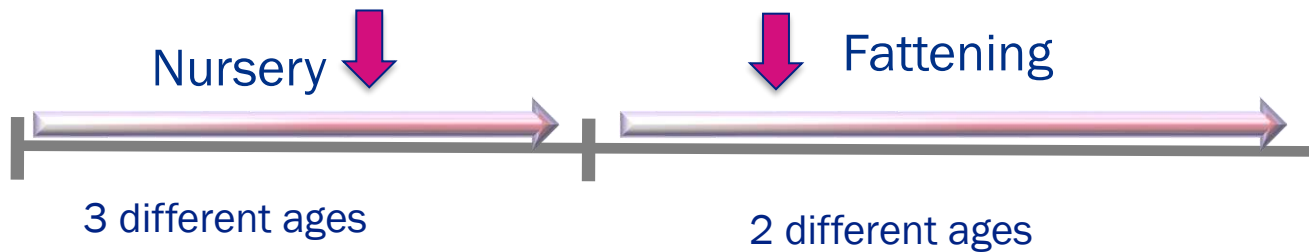
# VERO<sup>CHECK</sup> by VEPUR<sup>ED</sup>®



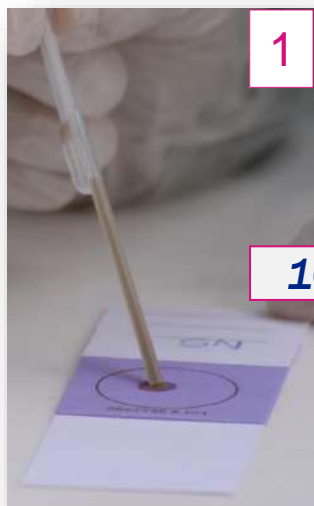


## Sampling moment

5 VEROCHECKS IN A PACK



# FTA INOCULATION



1

1<sup>st</sup>  
inoculation

10 seg.



2

2<sup>nd</sup>  
inoculation



3

Dry for 1 hour at room  
temperature

1 hour

**CRITICAL!**



4

Put into the plastic  
bag with the silica  
gel

## RESULTS

	VT2e PCR-REAL TIME
6 Semanas 6S-1	POS ++ (Ct 33,5)
6 Semanas 6S-2	POS + (Ct 35,5)
9 Semanas 9S-1	NEG
9 Semanas 9S-2	NEG
9 Semanas 9S-3	POS + (Ct 38,1)

### COMENTARIO

Valores de referencia para VT2e (Ct): POS < 38,5

NEG: No se ha detectado DNA bacteriano

POS (+): Se ha detectado DNA bacteriano en baja cantidad

POS (++) : Se ha detectado DNA bacteriano en moderada cantidad

POS (+++) : Se ha detectado DNA bacteriano en alta cantidad

### DIAG. MOLECULAR

	VT2e PCR-REAL TIME
7 Semanas T2	POS ++ (Ct 33,7)
7 Semanas T2	POS ++ (Ct 34,6)
7 Semanas T2	POS + (Ct 35,5)
9 Semanas T1	POS +++ (Ct 29)
9 Semanas T1	POS +++ (Ct 27,6)
9 Semanas T1	POS +++ (Ct 29,7)

### COMENTARIO

Valores de referencia para VT2e (Ct): POS < 38,5

NEG: No se ha detectado DNA bacteriano

POS (+): Se ha detectado DNA bacteriano en baja cantidad

POS (++) : Se ha detectado DNA bacteriano en moderada cantidad

POS (+++) : Se ha detectado DNA bacteriano en alta cantidad

# Prevalence of Verotoxin in Europe



## European screening reveals risk of Oedema Disease with the reduction of ZnO

Anne Strunz<sup>1</sup>, Anni Andersen<sup>1</sup>, Lola Tolstrup<sup>1</sup>, Emilii Barba<sup>2</sup>

<sup>1</sup>HIPRA Nordic (Denmark)

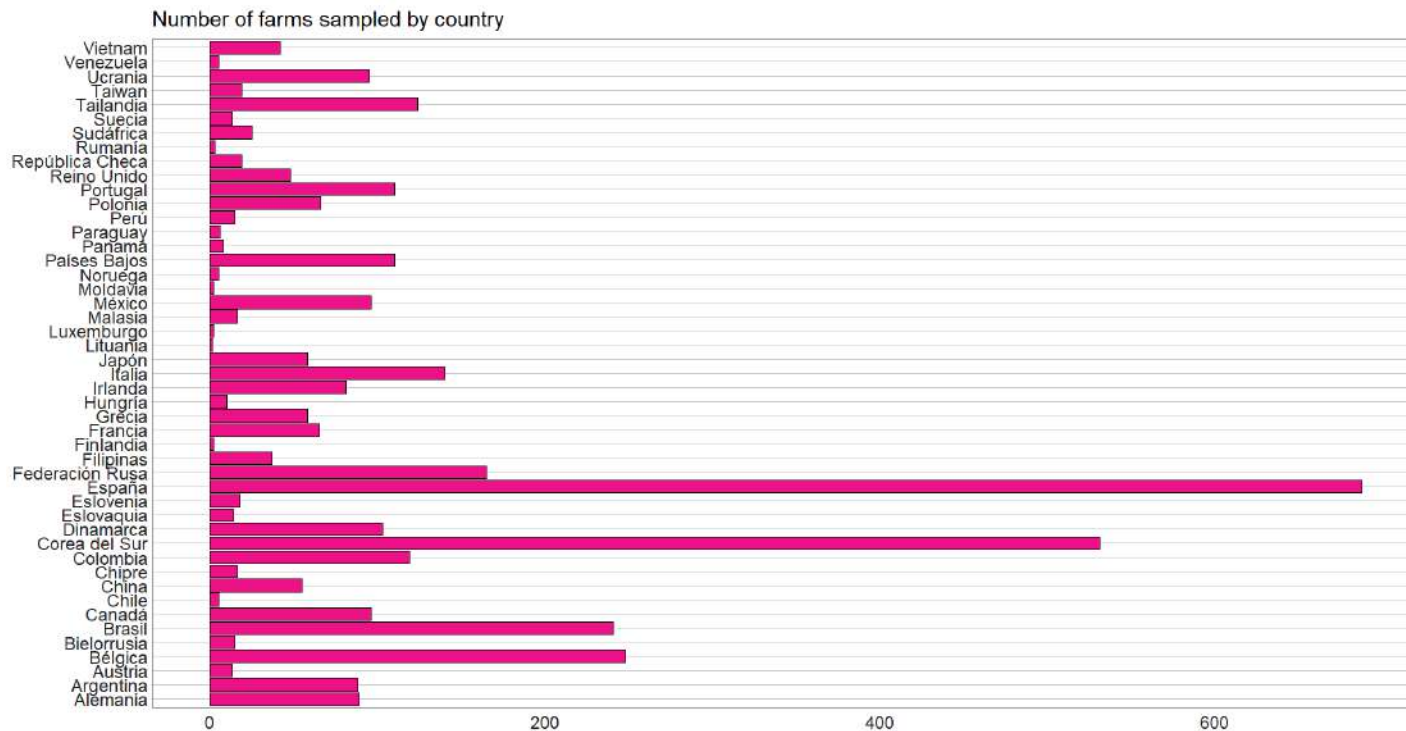
<sup>2</sup>HIPRA, Amer (Spain)

Corresponding author: [anne.strunz@hipra.com](mailto:anne.strunz@hipra.com)

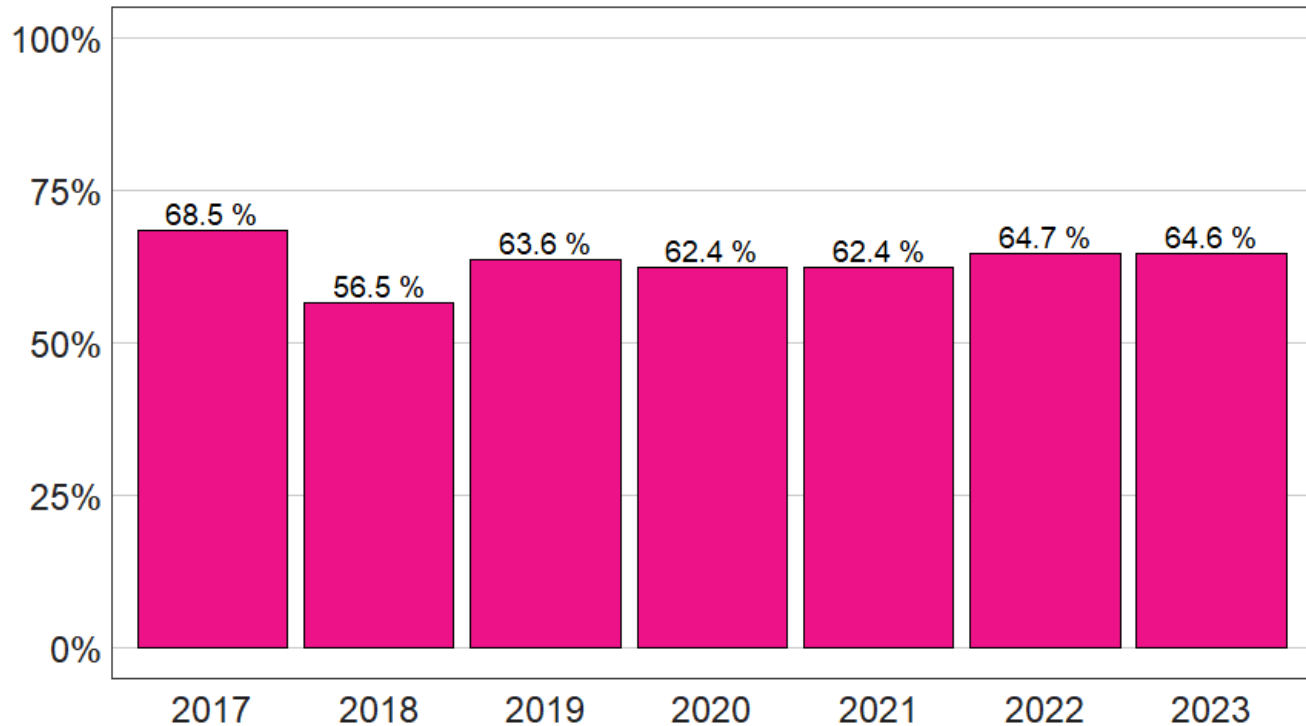
# MONITORING VEROCHECK PCRs



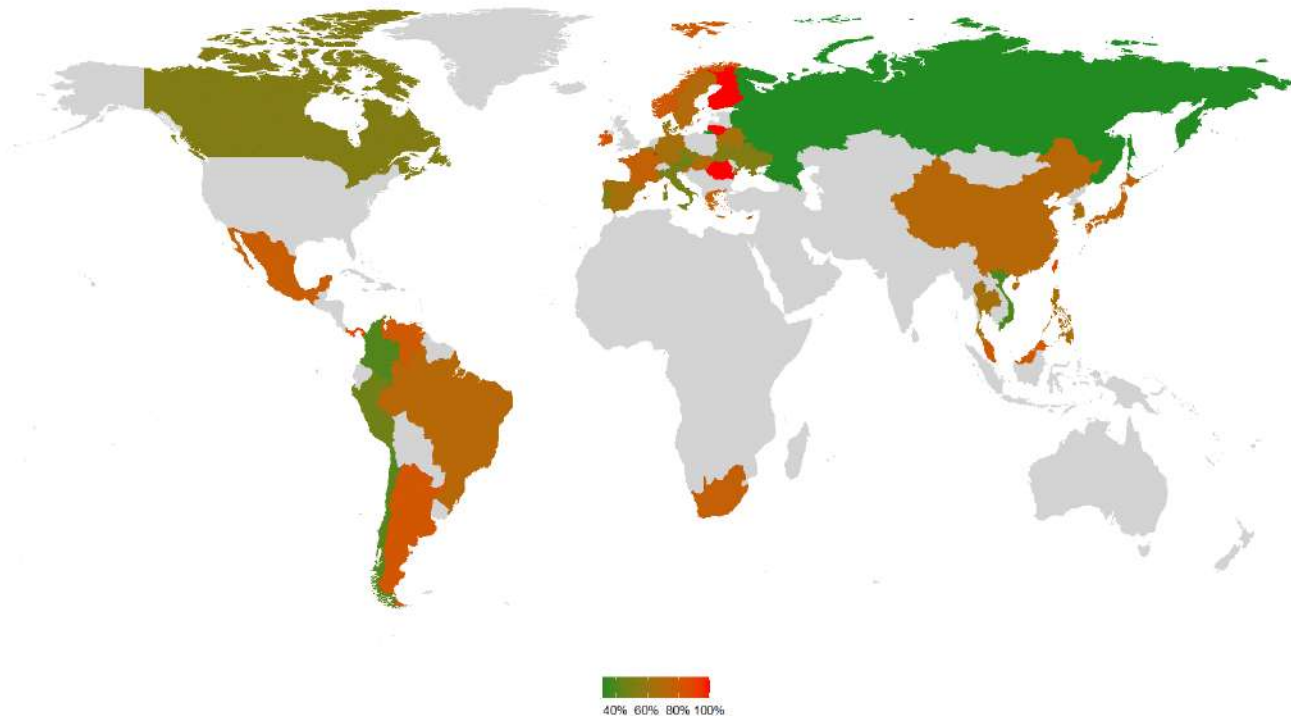
3 785 farms  
19 633 samples



## Percentage of Vtx positive farms over time



## % OF POSITIVE FARMS



1

Introduction

2

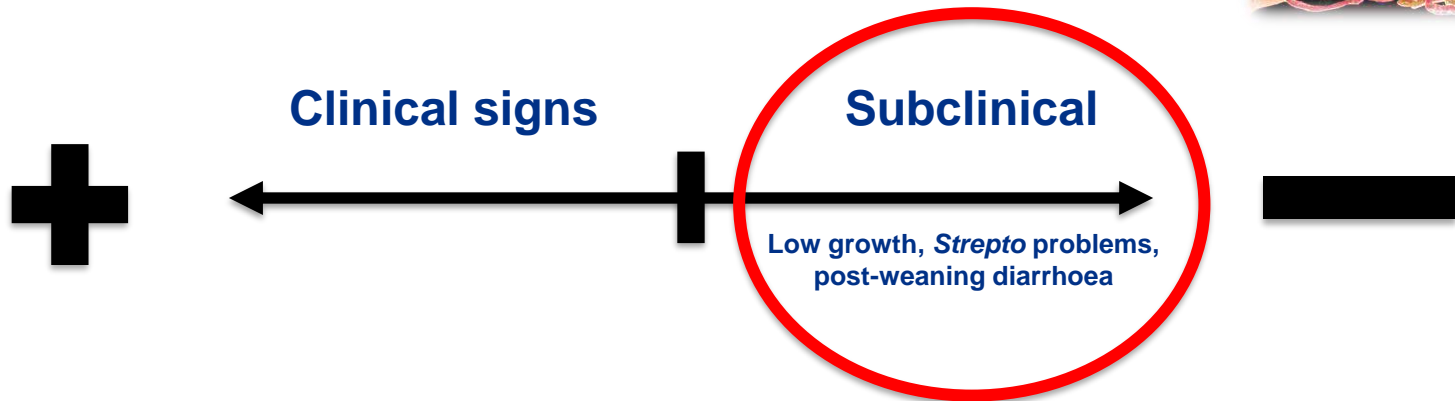
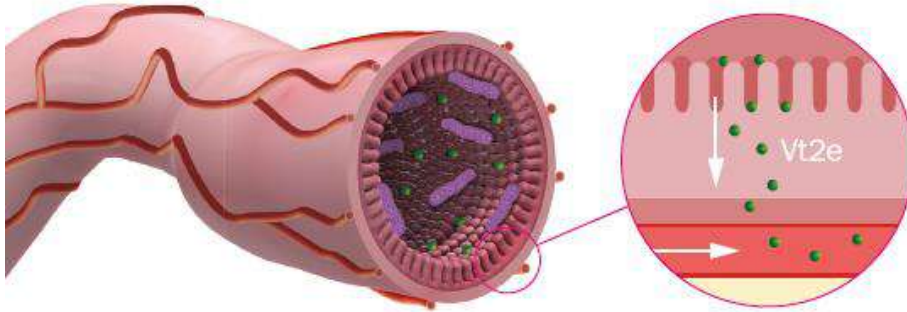
What can we do for you?

3

Results



# The verotoxin effect is dose-dependent





# Immunity against VTEC

## Vaccination to increase the resistance against VTEC

### Trial on 4 commercial farms with oedema problems

#### Mortality

Farm	Treatment	Number of pigs (n)	Number of pigs that died due to Edema Disease (%)
3	Placebo	120	7 (7)
	Vepured	121	0 (0)
4	Placebo	180	6 (3.3)
	Vepured	299	1 (0.3)
All	Placebo	643	26 (4.0)
	Vepured	764	2 (0.3)

( $P < .001$ )

\*Overall comparison p value for Generalized Linear mixed model with binary response and Farm as random effect. Results are statistically significant if the P value  $< .05$ .

#### Clinical signs

Table 5. Summary of animals showing Edema Disease Clinical Signs.

Farm	Treatment	Number of pigs (n)	Number of pigs with Edema Disease Clinical Signs (%)
1	Placebo	223	8 (3.6)
	Vepured	224	1 (0.4)
2	Placebo	120	7 (5.8)
	Vepured	120	0 (0)
3	Placebo	120	11 (9.2)
	Vepured	121	0 (0)
4	Placebo	180	16 (8.9)
	Vepured	299	4 (1.3)
All	Placebo	643	42 (6.5)
	Vepured	764	5 (0.6)

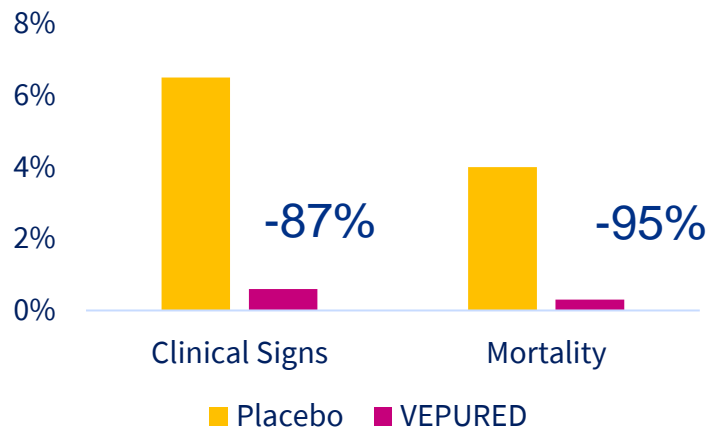
( $P < .001$ )

Overall comparison P value for Generalized Linear mixed model with binary response and Farm as random effect. Results are statistically significant if the P value  $< .05$ .

## A Multicenter, Randomized Field Trial on the Efficacy and Safety of VEPURED<sup>®</sup>, A New Vaccine Against Edema Disease in Pigs

Eva Perozo<sup>1</sup>, Joaquim Mallorquí<sup>1,\*</sup>, Ainhoa Puig, David Sabaté, Laura Ferrer-Soler, Ricard March

### VEPURED<sup>®</sup> vs PLACEBO





# Immunity against VTEC

## Vaccination to increase the resistance against VTEC

### Trial on 4 commercial farms with oedema problems

Wight increase

Table 6. Evolution of animal weights in farms with clinical Edema Disease (Mean  $\pm$  SD).

Farm	Treatment	d-1	d28	d42	d115	End of fattening
1	Placebo	2.26 $\pm$ 0.54	8.66 $\pm$ 1.52	13.98 $\pm$ 2.61	64.69 $\pm$ 11.2	101.44 $\pm$ 15.24
	Vepured	2.29 $\pm$ 0.58	8.62 $\pm$ 1.81	14.01 $\pm$ 3.15	66.69 $\pm$ 10.99	105.42 $\pm$ 13.76
2	Placebo	2.04 $\pm$ 0.45	8.87 $\pm$ 1.73	13.87 $\pm$ 2.66	62.90 $\pm$ 9.07	109.84 $\pm$ 11.12
	Vepured	2.05 $\pm$ 0.45	9.20 $\pm$ 1.78	14.25 $\pm$ 2.42	65.84 $\pm$ 7.92	113.27 $\pm$ 11.89
3	Placebo	1.82 $\pm$ 0.46	6.5 $\pm$ 1.35	14.61 $\pm$ 2.71	59.42 $\pm$ 9.55	97.67 $\pm$ 13.63
	Vepured	1.84 $\pm$ 0.5	7.23 $\pm$ 2.01	14.69 $\pm$ 3.27	62.47 $\pm$ 9.59	101.46 $\pm$ 12.96
4	Placebo	1.95 $\pm$ 0.37	7.05 $\pm$ 1.18	9.57 $\pm$ 2.01	57.22 $\pm$ 8.5	110.93 $\pm$ 13.77
	Vepured	1.98 $\pm$ 0.37	6.93 $\pm$ 1.16	10.47 $\pm$ 1.85	60.27 $\pm$ 9.17	115.45 $\pm$ 13.60
All	Placebo	2.01 $\pm$ 0.47	7.71 $\pm$ 1.69	12.67 $\pm$ 3.28	60.62 $\pm$ 9.96	105.54 $\pm$ 14.81
	Vepured	2.03 $\pm$ 0.49	7.77 $\pm$ 1.82	13.04 $\pm$ 3.21	63.5 $\pm$ 9.81	109.64 $\pm$ 14.35
P value*		0.584	0.799	0.009	< .001	< .001

SD: standard deviation.

\* P values for overall group comparison at fixed times using a Linear mixed model with farm as a random effect. Results are statistically significant if the P value < .05.

## A Multicenter, Randomized Field Trial on the Efficacy and Safety of VEPURED<sup>®</sup>, A New Vaccine Against Edema Disease in Pigs

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## VEPURED<sup>®</sup> vs PLACEBO

Weights end of fattening (kg)



# *Streptococcus suis*

It has been reported that coinfections with other pathogens can influence the severity of *Streptococcus suis* problems<sup>1</sup>

On a farm with *S.suis* problems and positive to Verotoxin:

VEPURED® VS



350 mg/kg amoxicillin  
in feed after weaning

## Antibiotic reduction in a farm with *Streptococcus Suis* diagnosis by vaccinating against VT2E

Annelies, M.<sup>1</sup>; De Jong, E.<sup>2</sup>; Claeyé, E.<sup>1</sup>; Barba-Vidal, E.<sup>2</sup>; García, G.<sup>2</sup>; Boix, O.<sup>2</sup>; Matthijs, W.<sup>3</sup>; Van Poucke, S.<sup>4</sup>

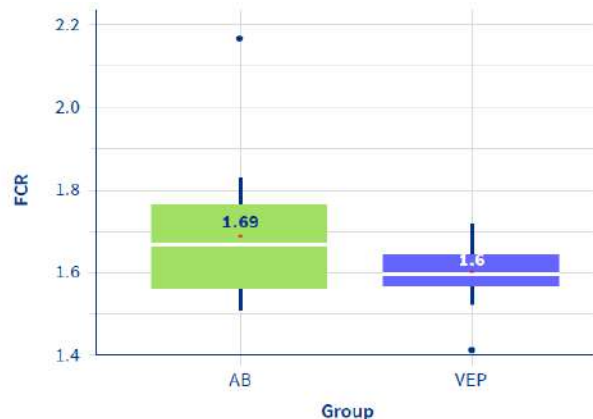
<sup>1</sup>Hipra Benelux

<sup>2</sup>HIPRA HQ, Amer (Spain)

<sup>3</sup>DSM Nutritional Products

<sup>4</sup>Synt

\*Corresponding author: gonzalo.garcia@hipra.com



The production cost per piglet at 36.6 kg was reduced by € 1.32 in the VEPURED® group

## Recombinant Verotoxin 2e (Vt2e) vaccine reduces the cost of medicine on a farm with subclinical swine Oedema Disease

Byun, J.<sup>1</sup>; An, K.<sup>1</sup>; Noh, H.<sup>1</sup>; Seo, S.<sup>1</sup>; Barba, E.<sup>2</sup>; García, G.<sup>2</sup>

<sup>1</sup> HIPRA Korea Inc.  
<sup>2</sup> HIPRA H.Q. Spain

# Subclinical disease

Farm from South Korea (850 sows)  
 VT2e rtPCR (Verocheck) → Positive  
 Without clinical signs or high mortality

VEPUR<sup>ED</sup>®

Before



Onset of immunity

After

March 2020

March 2021

June 2021

March 2022

### MOLECULAR DIAG.

	VT2e PCR-REAL TIME
6 Weeks	POS ++ (Ct 32,4)
7 Weeks	POS ++ (Ct 33,3)
9 Weeks	POS +++ (Ct 28,5)
10 Weeks	POS ++ (Ct 32)
11 Weeks	POS + (Ct 38,4)

## Recombinant Verotoxin 2e (Vt2e) vaccine reduces the cost of medicine on a farm with subclinical swine Oedema Disease

Byun, J.<sup>1</sup>; An, K.<sup>1</sup>; Noh, H.<sup>1</sup>; Seo, S.<sup>2</sup>; Barba, E.<sup>2</sup>; García, G.<sup>1</sup>

<sup>1</sup> HIPRA Korea Inc.

<sup>2</sup> HIPRA HQ Spain

# Subclinical disease

## Results

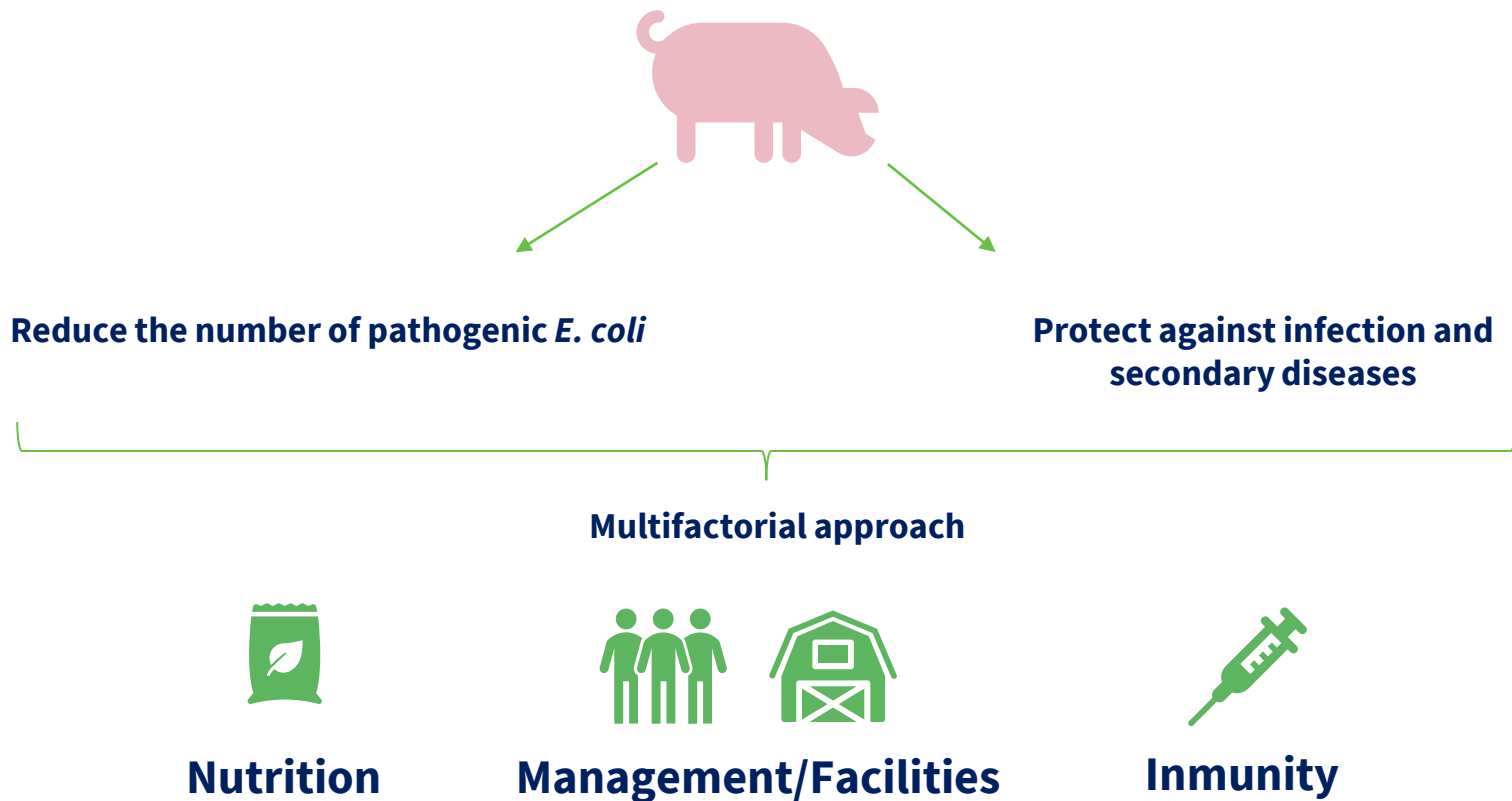


Fig 1. Monthly cost of all antibiotics and additives over time

Monthly expenses (Unit: millions KRW)	Prevaccination	VEPURED®	P-value
Antibiotics in feed	116	104	0.32
Injectable Antibiotic**	502	269	0.006
Additives	190	261	0.17
Additives & all antibiotics*	809	634	0.02
Total	1,556	1,532	0.21

Even on a farm without clinical signs of oedema, production costs were lower after vaccination, especially because of the reduction of injectable antibiotics

## Conclusions



# Conclusions

Reduce the number of pathogenic *E. coli*

Protect against infection



## Nutrition

Water

Ingredients

Additives



## Management/facilities

Hygiene

Facilities &  
environment

Management  
(calostration)

Temperature



## Immunity

Vaccines

Oral antibodies

Genetic selection



# HIPRA

Building Immunity  
for a Healthier World