Dietary strategies to reduce the use of antibiotics

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Content webinar

Coen Smits

Animal nutrition strategies with focus on swine and poultry

1. Dietary measures in general
2. Enteric stimulation
3. Microbiota management
4. Support mucosal barrier function
5. Immune modulation

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Practical experiences within programs to reduce and minimize use antibiotics

1. Our nutritional programme
2. Field cases

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Animal nutrition strategies and options to reduce the use of antimicrobials in animal production

FAO Animal Production and Health Paper No. 184. Rome, FAO

- ✓ To highlight **dietary opportunities** to contribute to **disease resistance and resilience** in swine, poultry and ruminants
- ✓ To emphasise that **'prophylactic nutrition'** is one of the pillars in strategies to reduce use, or maintain low use, of antibiotics

Prof. Dr. Defa Li

- China Agricultural University

Prof. Dr. John Patience

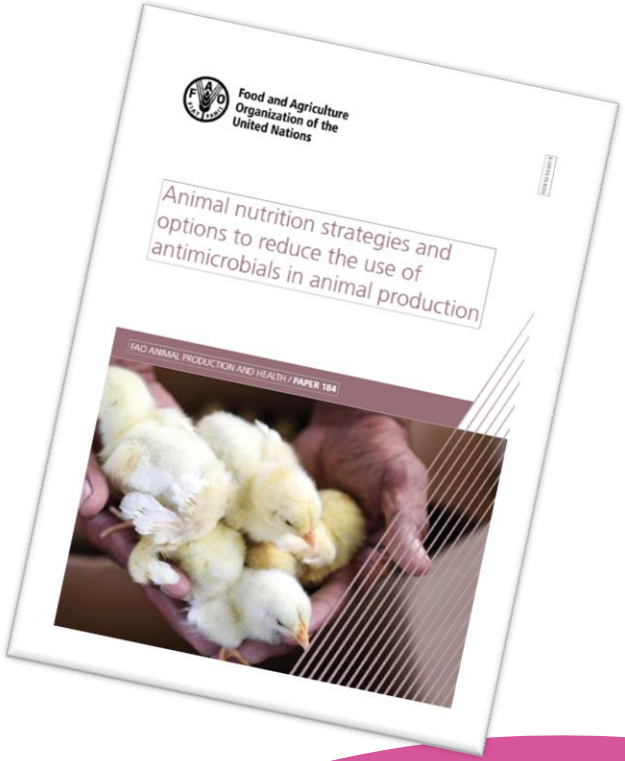
- Iowa State University

Prof. Dr. Ir. Leo den Hartog

- Wageningen University & Research

Dr. Ir. Coen Smits

- Trouw Nutrition Research & Development

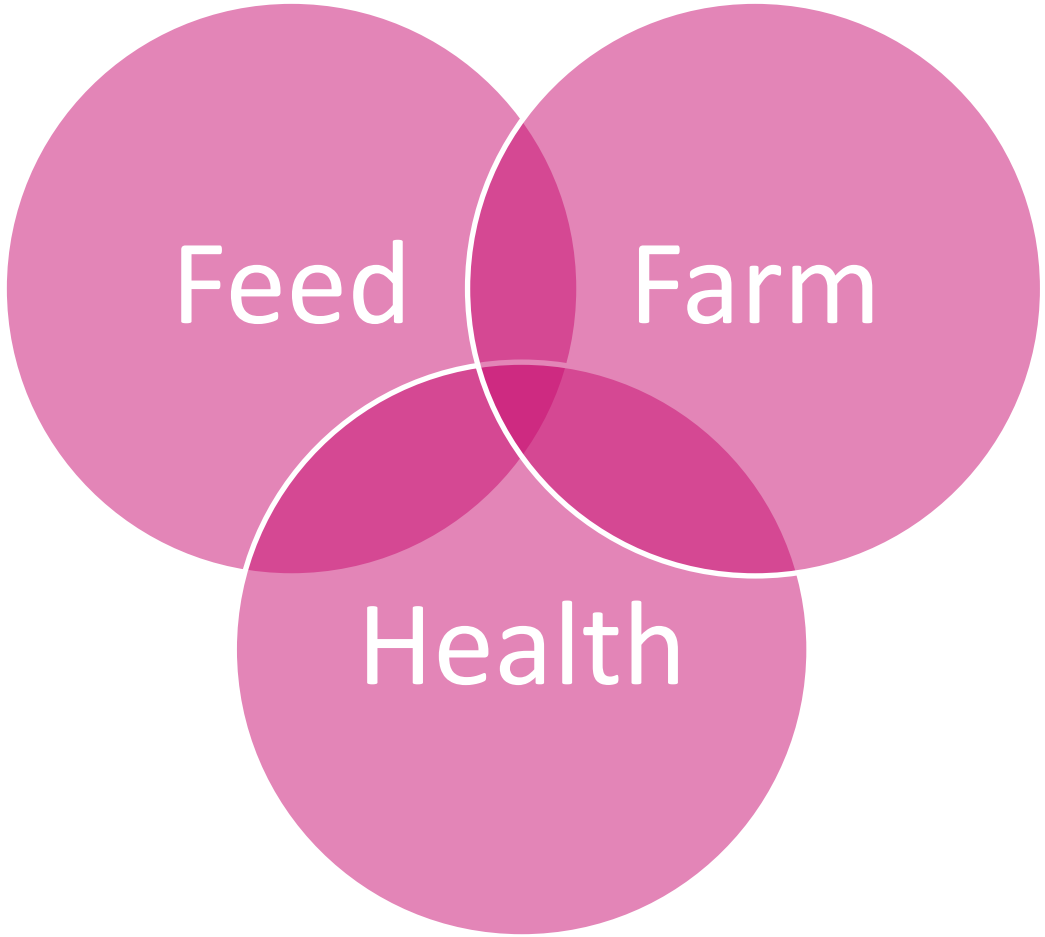


Safeguarding the efficacy of antibiotics for humans and animals

Lowering the risk of antimicrobial resistance by lowering the use of antibiotics

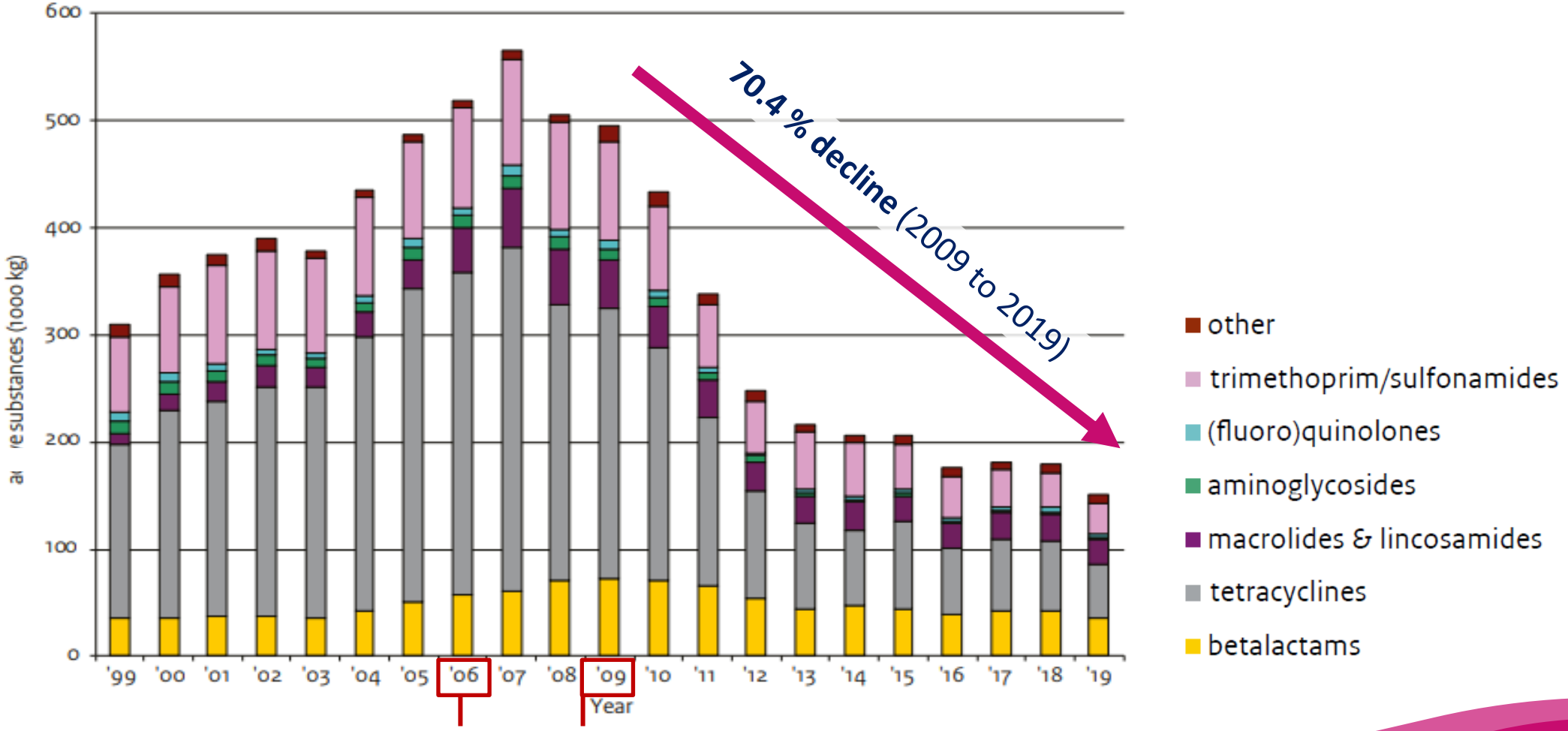
Facing the challenge. Together.

A multidisciplinary approach is required to reduce the use of antibiotics



70.4 % decline in antibiotic sales in the Netherlands (2009-2017)

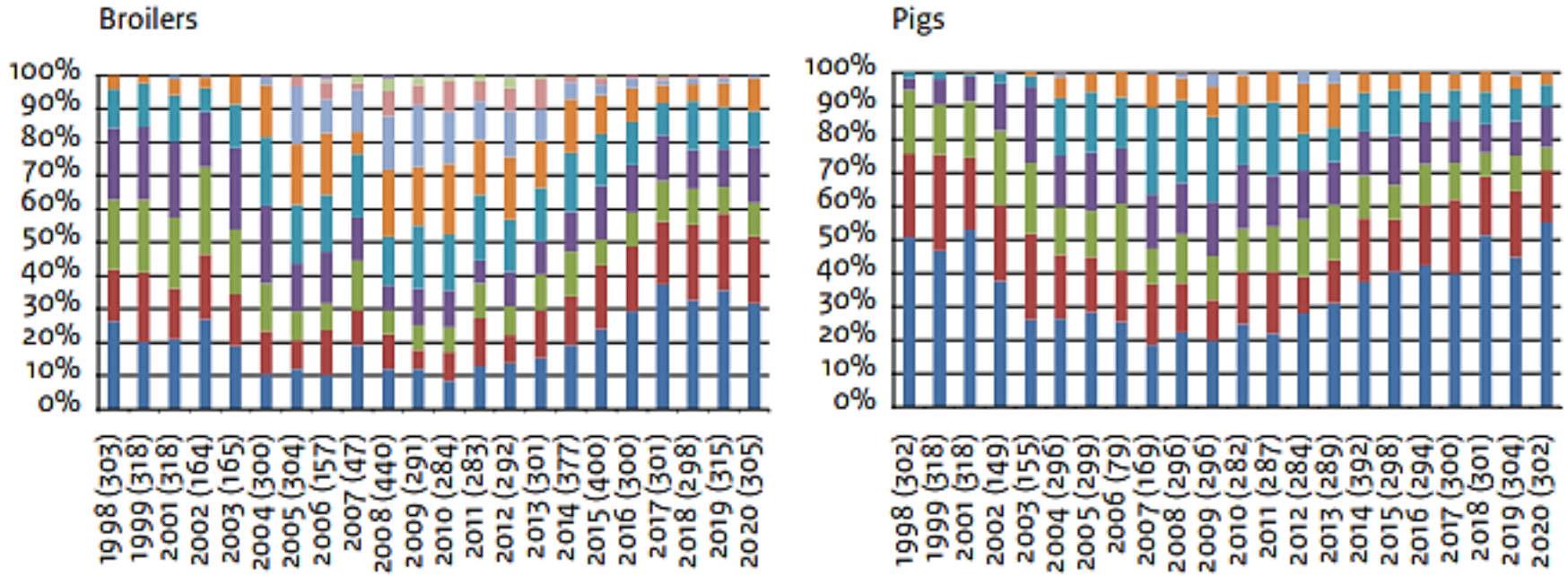
A ban on Antimicrobial Growth Promoters (AGPs) doesn't automatically reduce antibiotic use; ambitious targets in combination with multi-stakeholder commitment is pivotal



Maran, 2020

Antibiotic resistance is reversible

Reducing the use of antibiotics pays off: multi-resistance of E.coli decreases in NL



Resistance (%) to 0 - 9 antimicrobial classes among E. coli strains from broilers and pigs. 1998 – 2020 in the NL

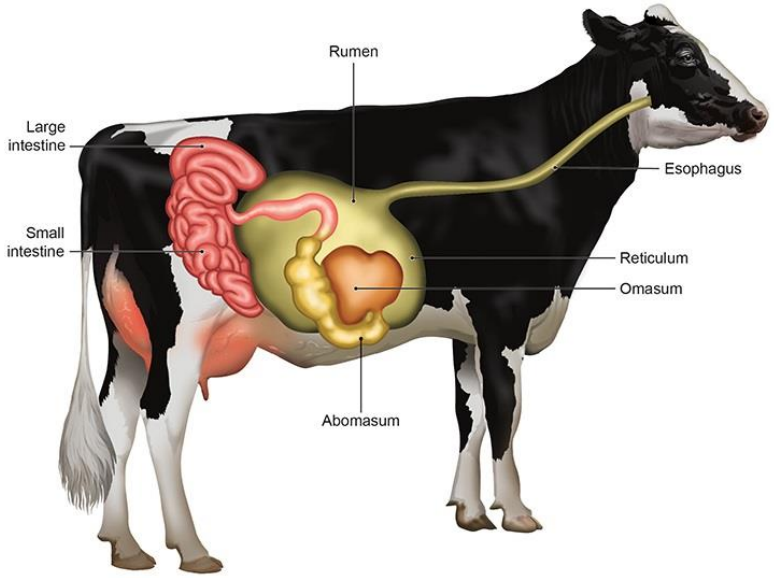
Maran, 2021

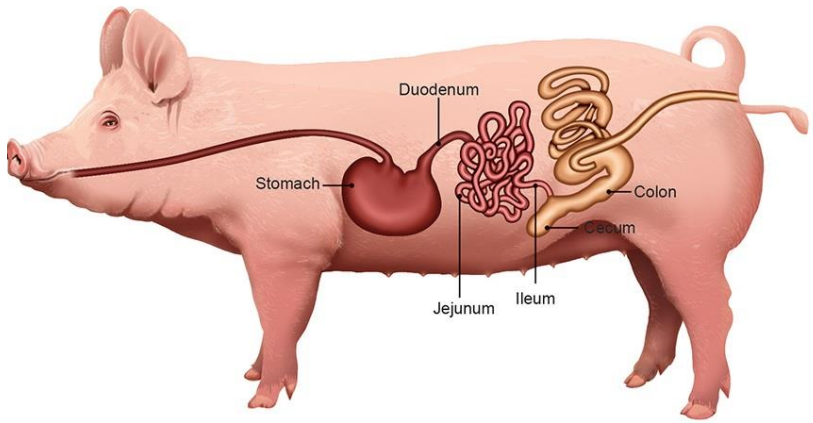
Dietary strategies to reduce use antibiotics

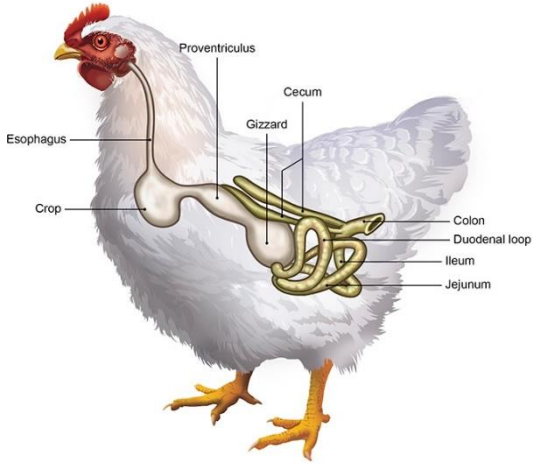
Focus on swine and broiler chickens

The animal has a great system to control the microbiota in the GIT

Acidifying digesta, anti- and pro-microbial secretions, mucosal barrier, immune defense





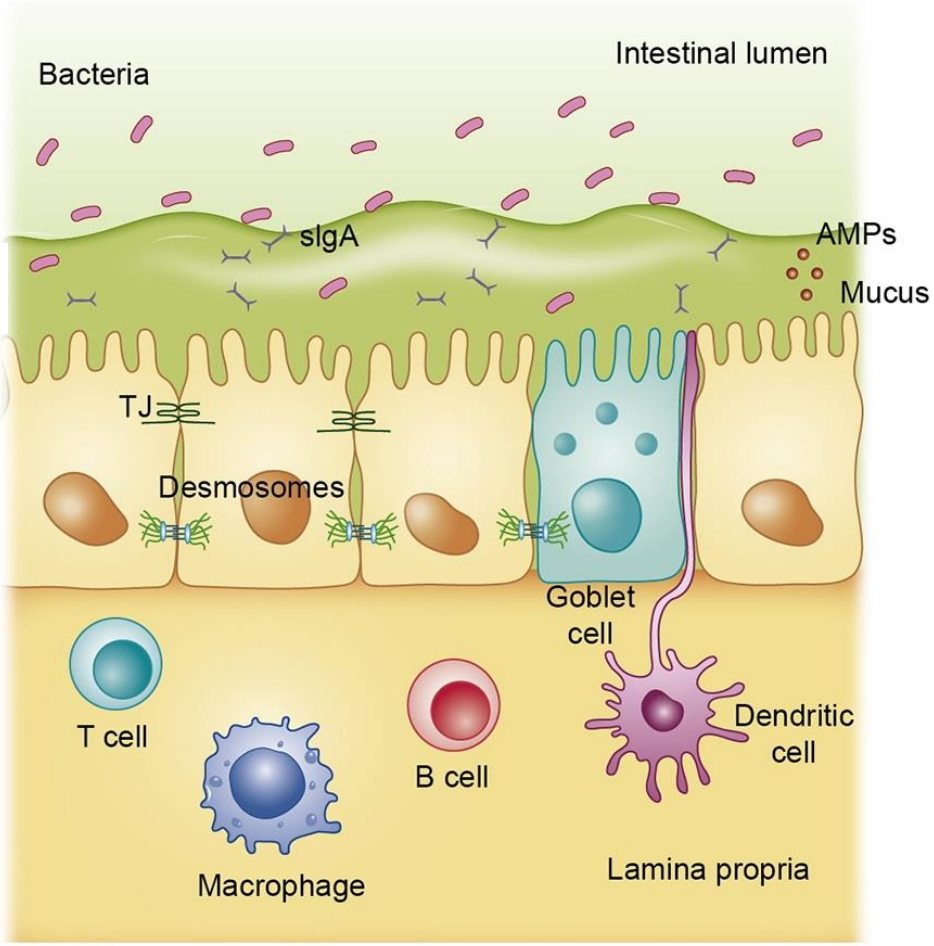


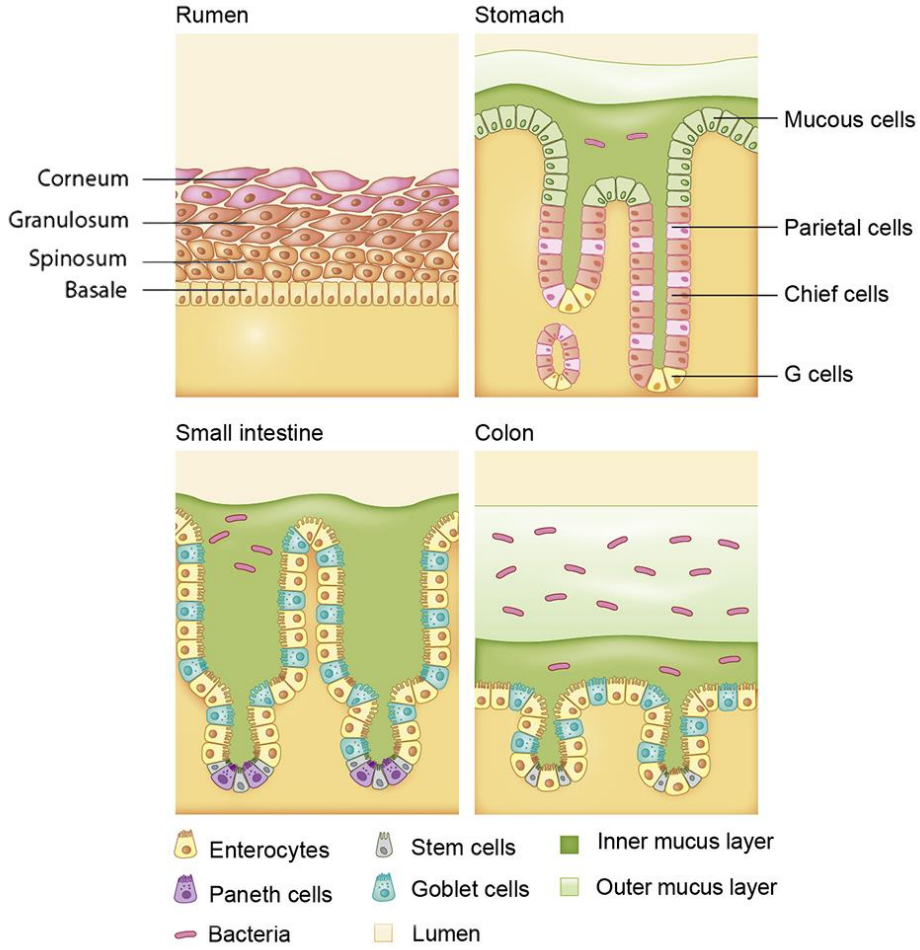
Regular feed intake leading to regular secretions and regular digesta flow is key

FAO report nr. 184, 2021

The mucosal barrier takes nutrients in, keeps microbes out

Barriers are differently organized in the various GIT sites

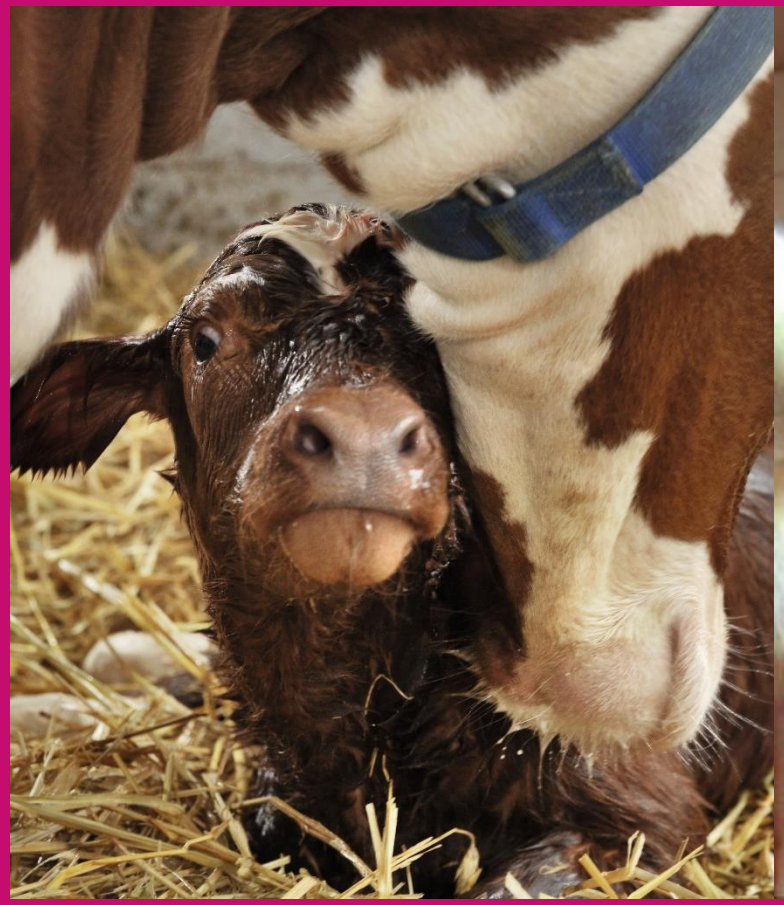




FAO report nr. 184, 2021

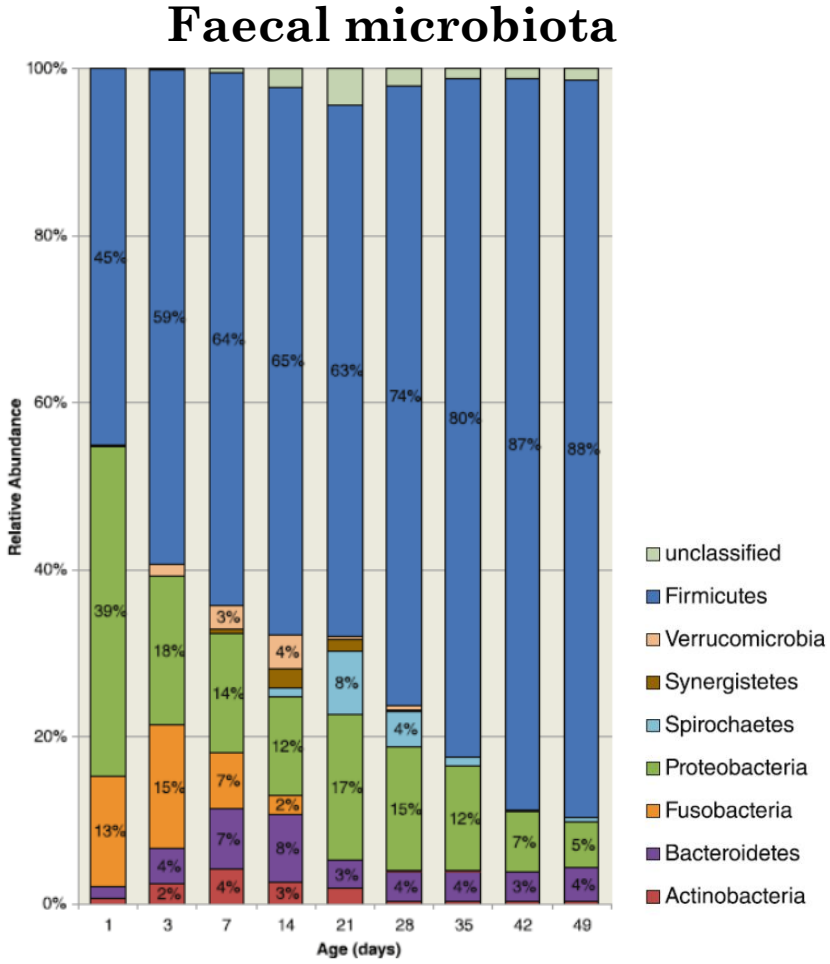
Animals are especially at-risk during transitions in early life

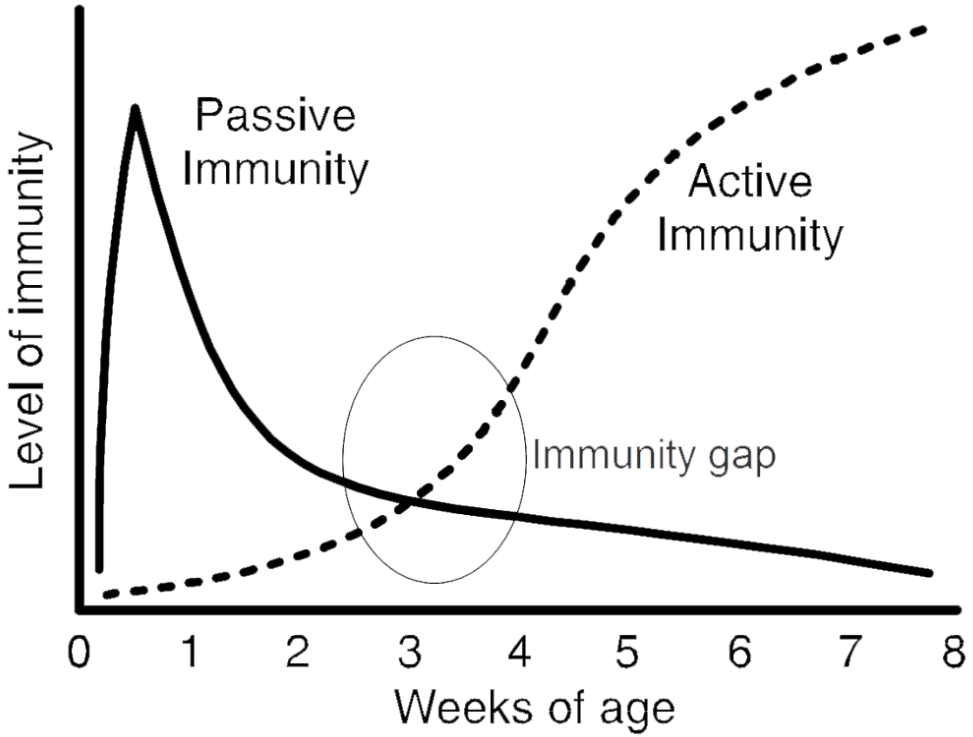
Birth or hatch, weaning, relocation



Early life microbiota development in pigs

Maturation of the intestinal microbiota overlaps with the immunity gap



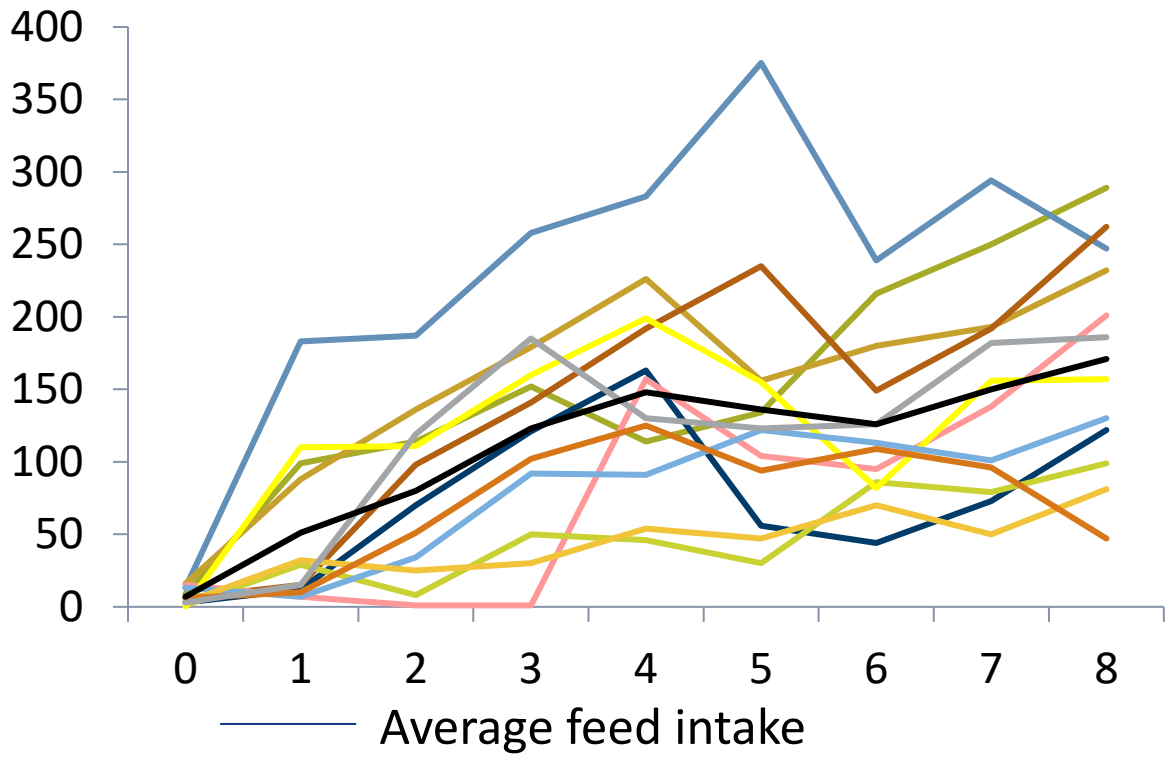


Slifierz, 2015

Weaning induces a 1st and 2nd dip in feed intake

…and possibly a 3d, 4th dip with (sub)clinical infections

Feed intake pattern (g/day) of individual piglets in one pen



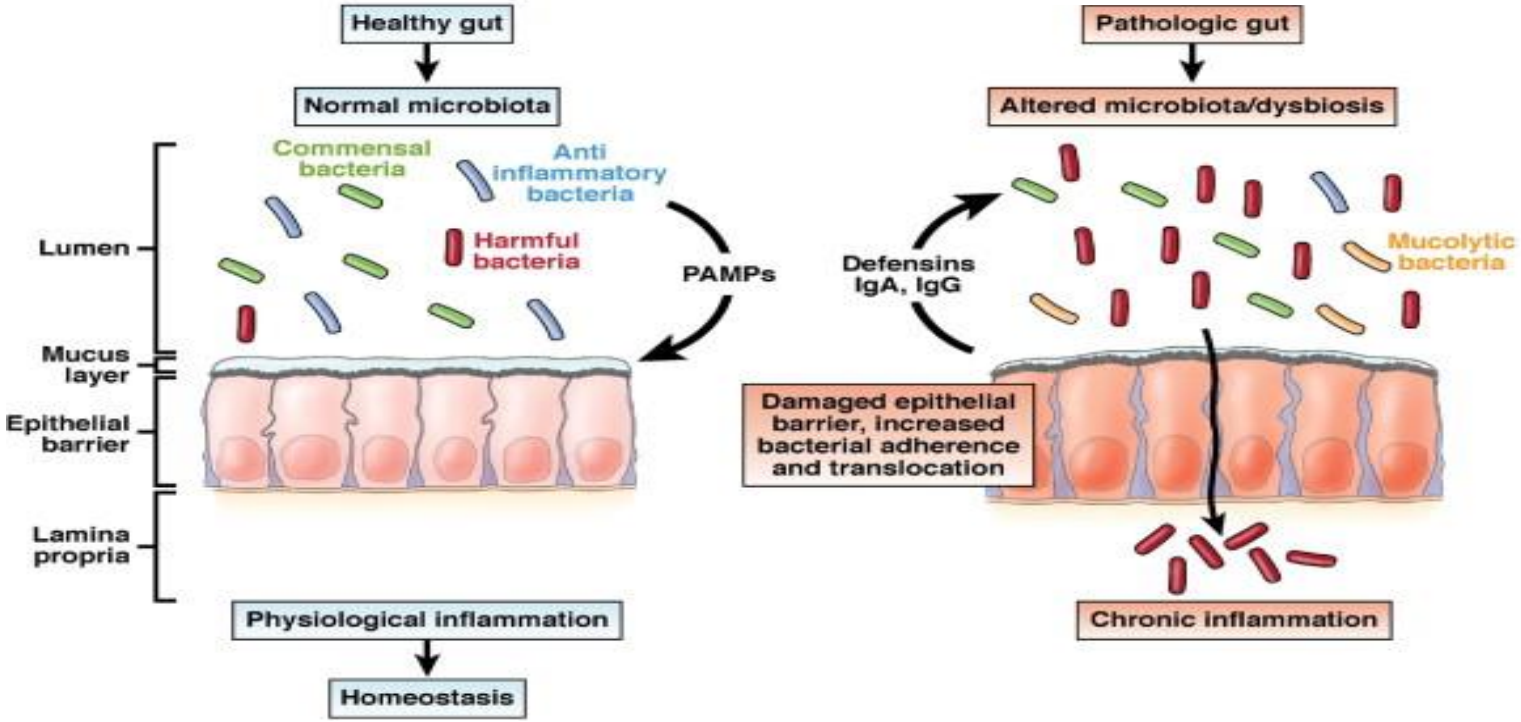
Trouw Nutrition R&D, unpublished

Critical transition moments may lead to an imbalance in microbiota and immunity

Especially young animals are sensitive to changes

Homeostasis

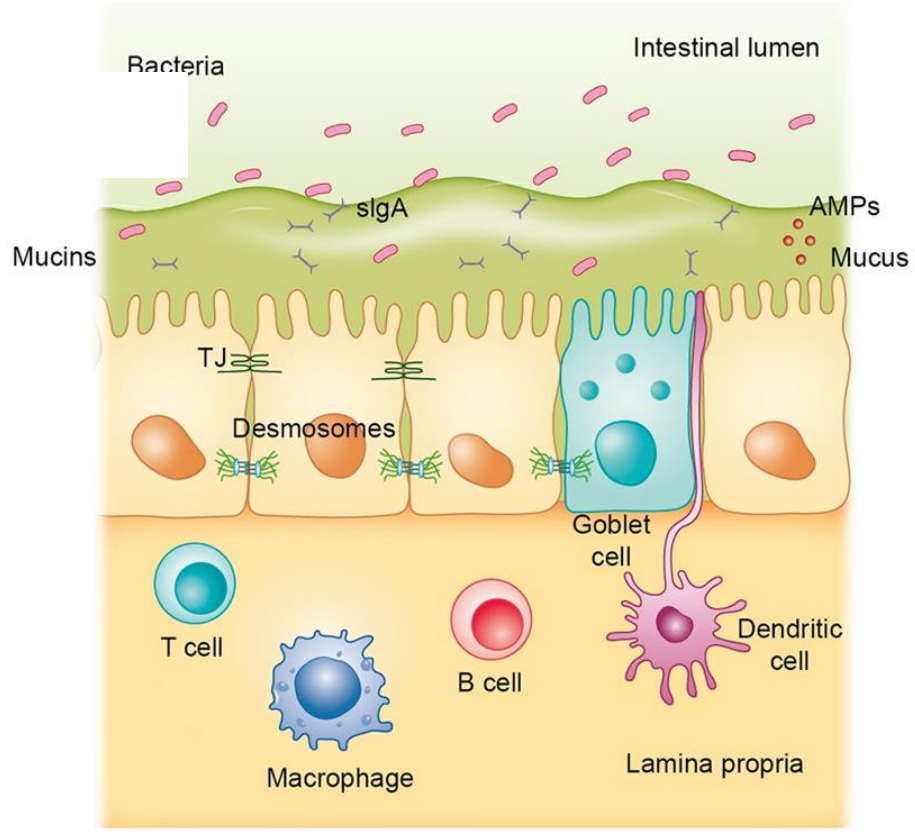
Dysbiosis



'Pathological Inflammation'

Principles of dietary measures in prophylactic nutrition

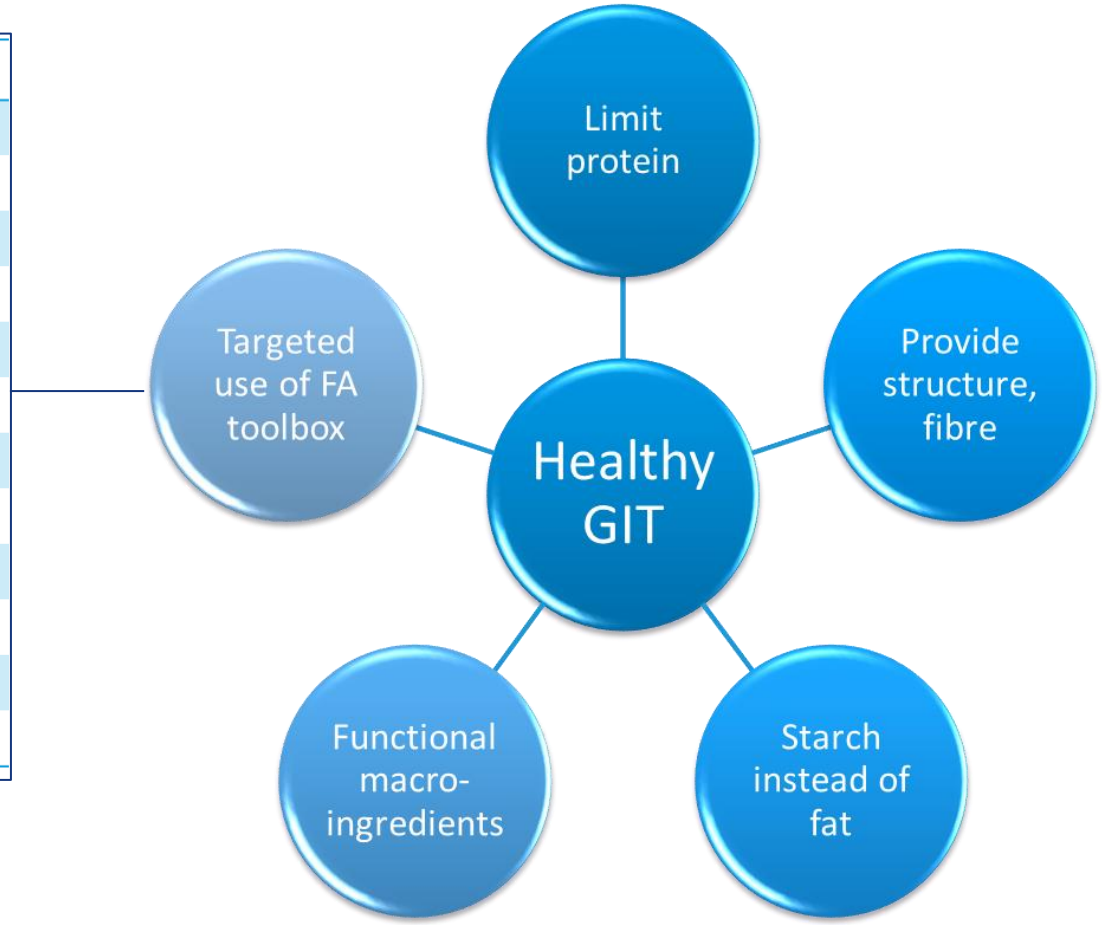
- ✓ Enteral stimulation
- ✓ Microbiota management
  - ✓ Pathogen specific approaches
- ✓ Support mucosal barrier function
- ✓ Immune modulation



Nutritionist has great toolbox for prophylactic nutrition

With a functional value beyond nutritional value

Feed additive tools
Organic acids
Medium chain fatty acids
Short chain fatty acids
Plant extracts, essential oils
Prebiotic sugars, polysaccharides
Yeast derived specialties
Probiotics
Enzymes
Clay minerals
Copper
Zinc Oxide
Others

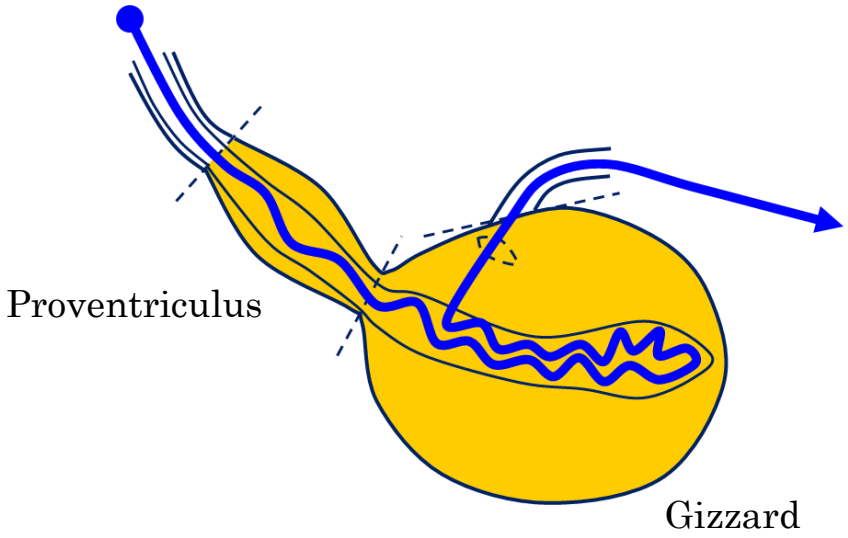


Prophylactic = ‘Intended to prevent disease’

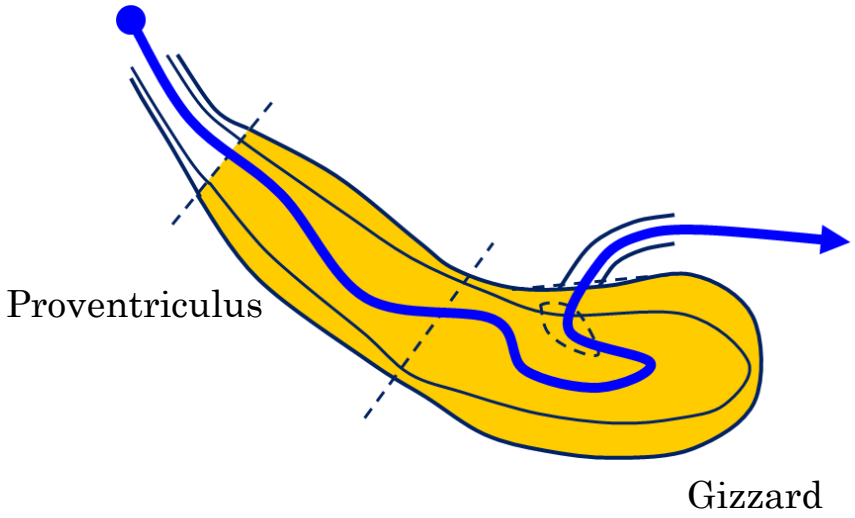
Enteral Stimulation

Fibre and structure promote appropriate functioning of the GIT

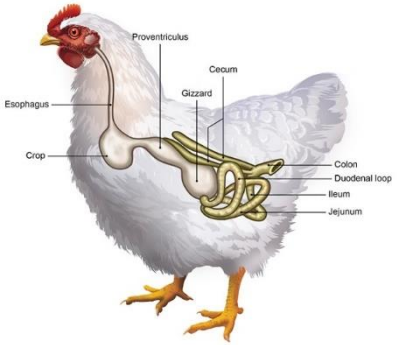
Example: Fibre, structure stimulates functioning proventriculus and gizzard



Normal situation



Lack of fibre, structure



Effect wheat bran on *E.coli* F4 excretion piglets after challenge

Piglets weaned at 17d, challenged with *E.coli* F4 at d9 experiment

	Negative control	Positive control (+ antibiotics)	NC + 4% Fine wheat bran	NC + 4% Coarse wheat bran
E. coli F4*	4.7^{x}	4.7^{xy}	2.2^{xy}	0.7^{y}
E. coli population*	6.3x	6.3xy	4.9y	4.1y

*Measured in the **ileum** 16d post challenge

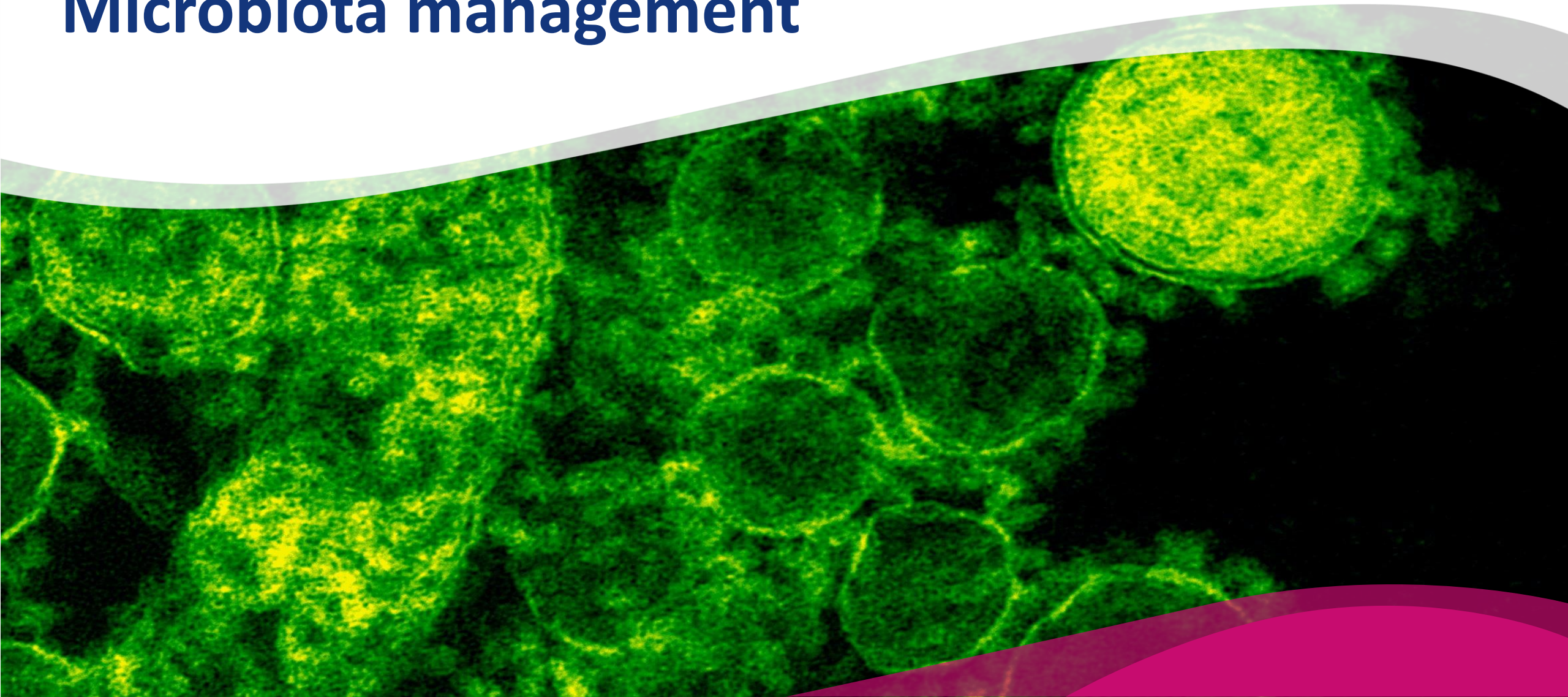
Molist et al., 2010

Lack of enteral stimulation, blood flow to GIT in peri-parturient sows

Factor in the development of Post-partum Dysgalactia Syndrome (PDS)

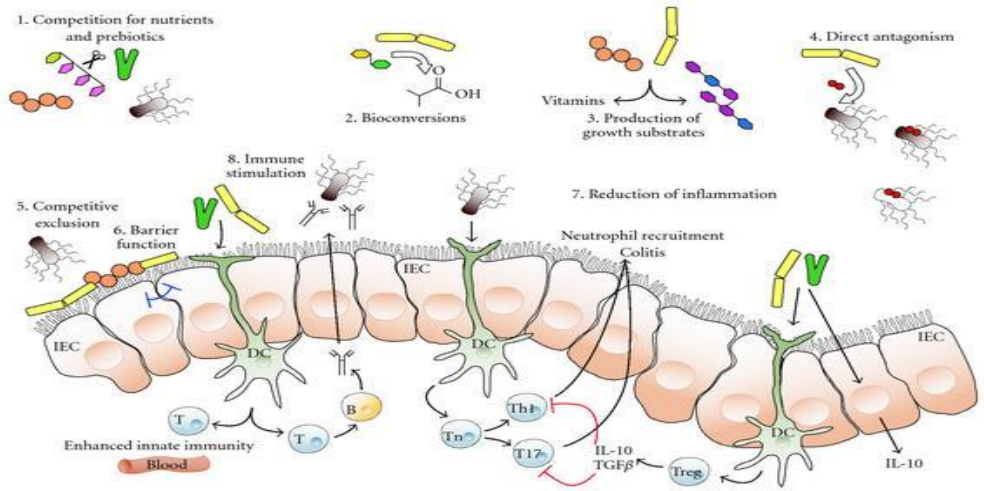
Maintain relative high feeding level with high dietary fibre level will contribute to prevention

Microbiota management



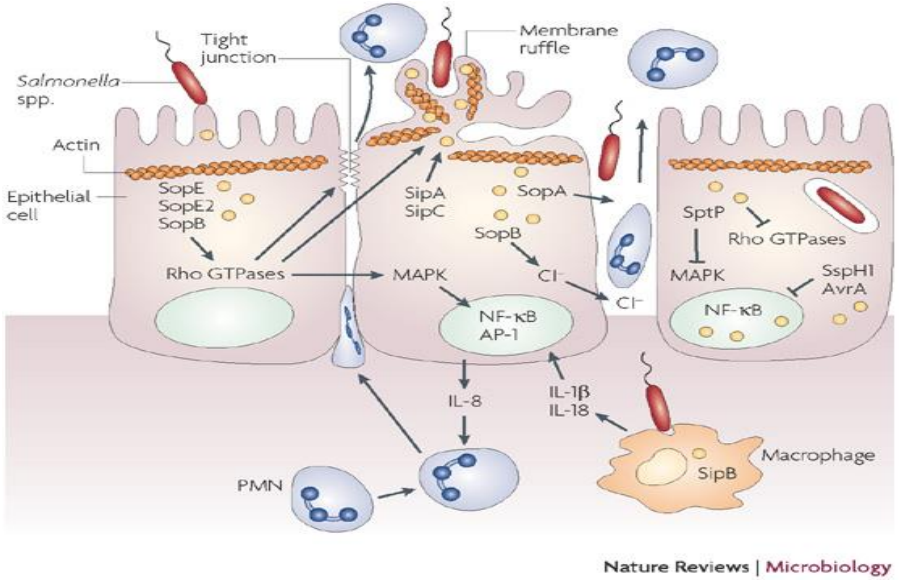
Generic and pathogen specific approaches are possible

General nutrition and health knowledge



Stabilization microbiota
Strengthen gut barrier function
Immune response

Knowledge pathogenesis infections

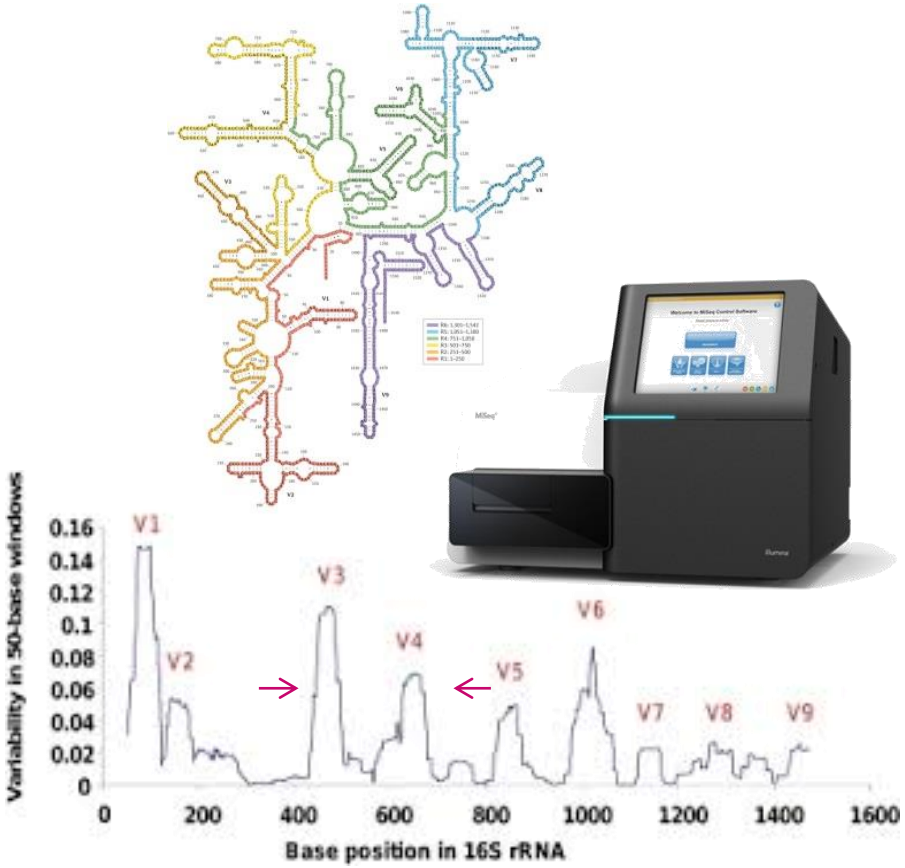


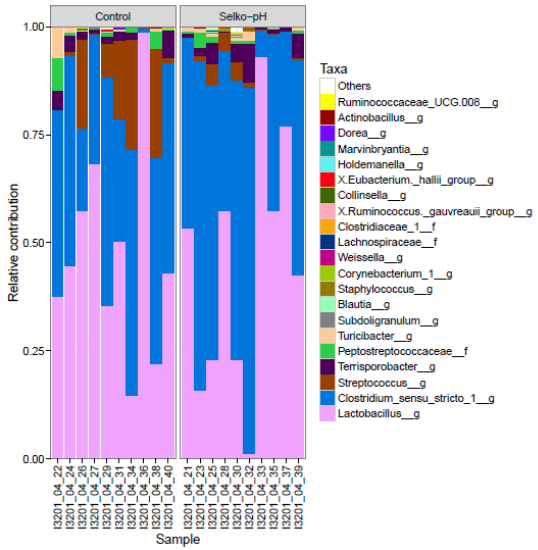
Harage, 2008

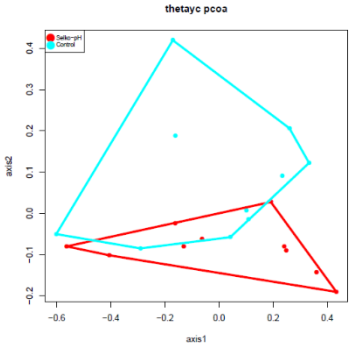
Pathogen specific approaches

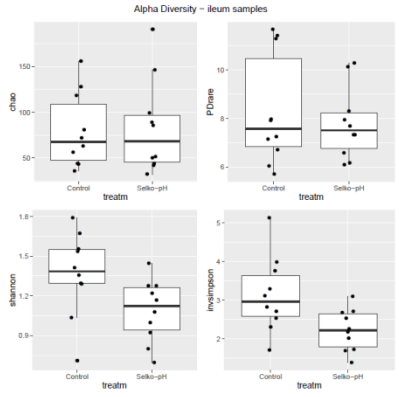
Microbial profiling using 16S rRNA sequencing is nowadays common

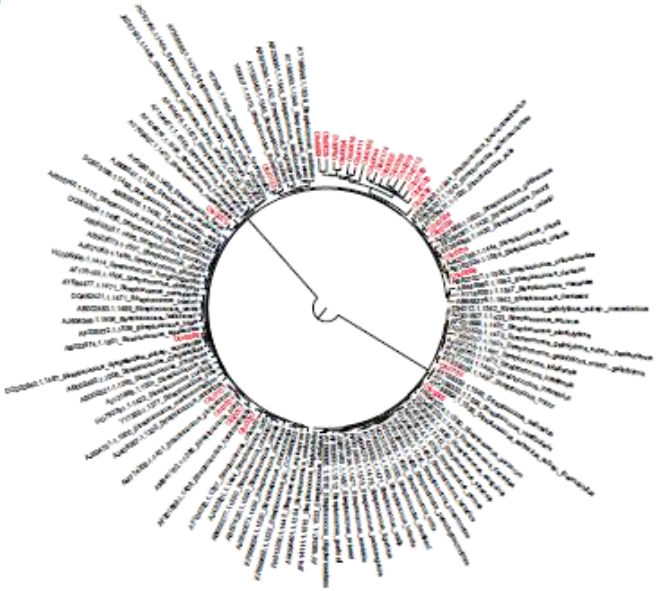
Leapfrog technology in 2010 when we started using this







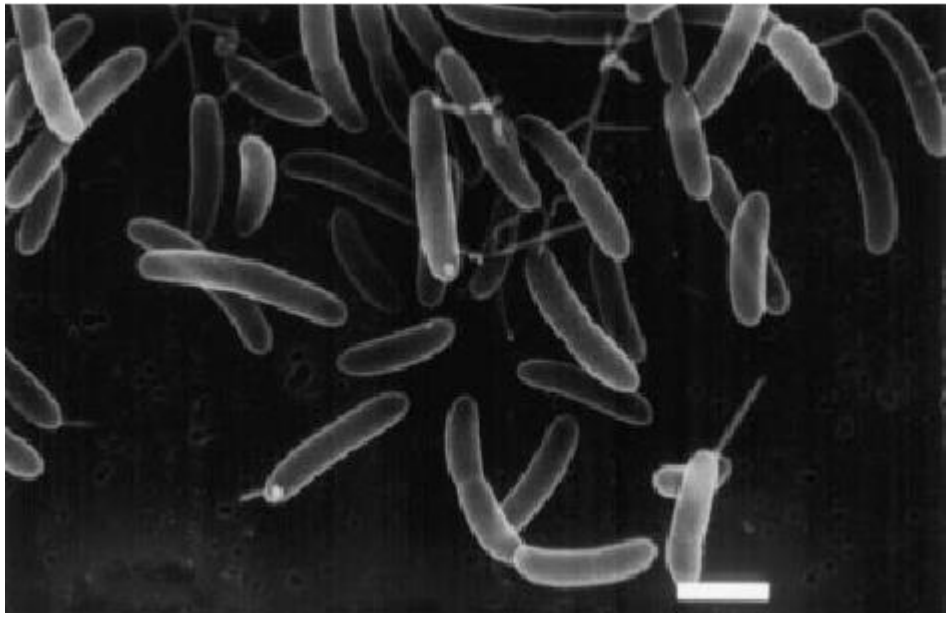




Mature microbiota of ‘healthy gut’ has high diversity in fibrolytic, butyrogenic bacteria

Potential beneficial bacteria (genus) in caecum, colon irt performance & health
Bifidobacterium
*Faecalibacterium**
*Roseburia**
*Ruminococcus**

*Members Clostridium clusters XIVa



Roseburia intestinalis

In the **small intestine** the activity and composition of ***Lactobacillus spp.*** may play an important role

Specific bacteria have been associated with health benefits

Example : *Faecalibacterium prausnitzii*

Microbiota changes in piglets weaned at different ages

Abundance of *Faecalibacterium prausnitzii*

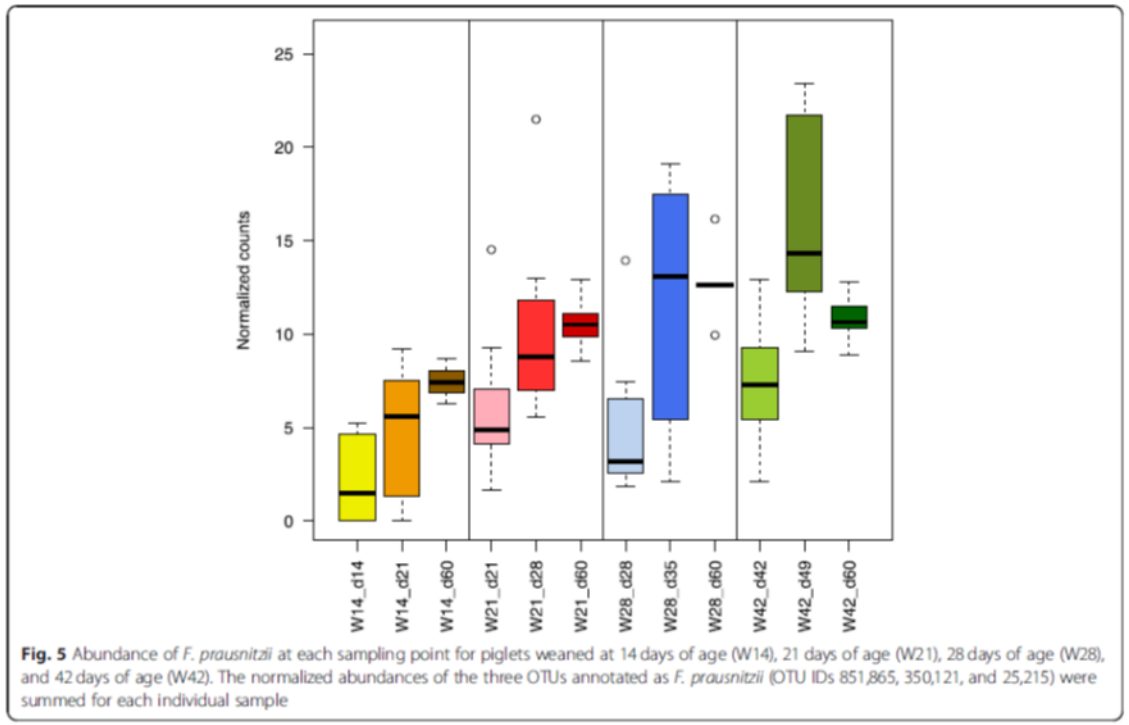


Fig. 5 Abundance of *F. prausnitzii* at each sampling point for piglets weaned at 14 days of age (W14), 21 days of age (W21), 28 days of age (W28), and 42 days of age (W42). The normalized abundances of the three OTUs annotated as *F. prausnitzii* (OTU IDs 851,865, 350,121, and 25,215) were summed for each individual sample

Massaci et al., 2020

REVIEW

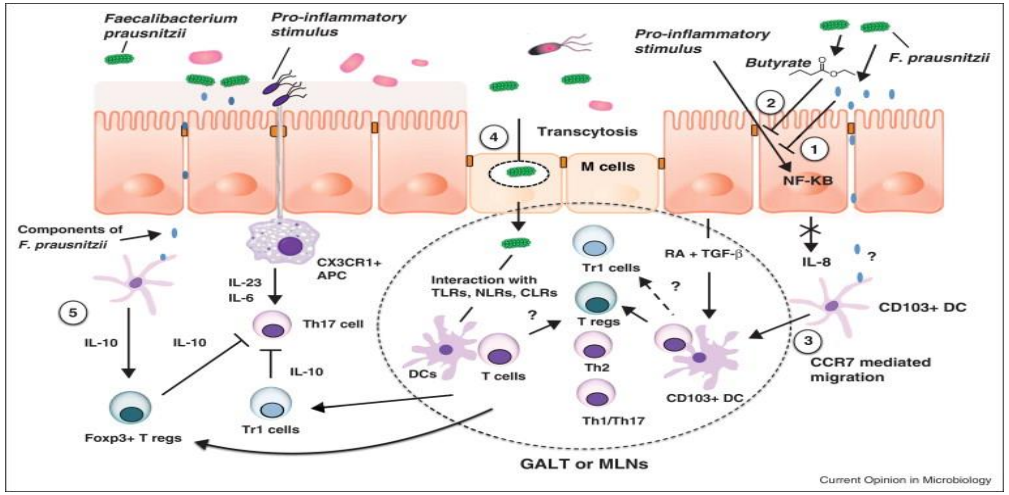
Gut Microbes 5:2, 146–151; March/April 2014; © 2014 Landes Bioscience

Ecology and metabolism of the beneficial intestinal commensal bacterium *Faecalibacterium prausnitzii*

Sylvie Miquel[1,2], Rebeca Martín[1,2], Chantal Bridonneau[1,2], Véronique Robert[1,2], Harry Sokol[1,2,3,4], Luis G Bermúdez-Humarán[1,2], Muriel Thomas[1,2], and Philippe Langella[1,2,*]

[1]INRA; Commensal and Probiotics-Host Interactions Laboratory; UMR 1319 Micalis; Jouy-en-Josas, France; [2]AgroParisTech; UMR1319 Micalis; Jouy-en-Josas, France; [3]ERL INSERM U 1057/UMR7203; Faculté de Médecine Saint-Antoine; Université Pierre et Marie Curie (UPMC); Paris, France; [4]Service de Gastroenterologie; Hôpital Saint-Antoine; Assistance Publique-Hôpitaux de Paris (APHP); Paris, France

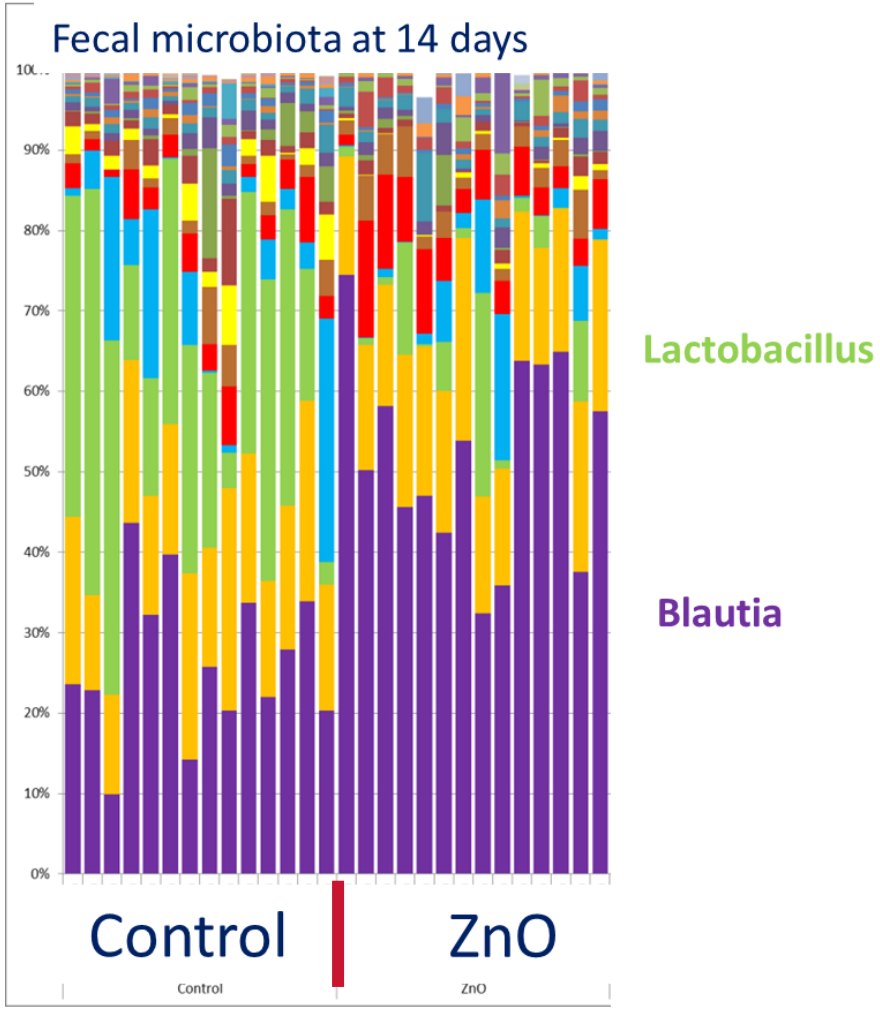
Keywords: metabolism, ecophysiology, nutrition, medicine



Miquel et al., 2013, 2014

Very high impact of ZnO in microbiota composition

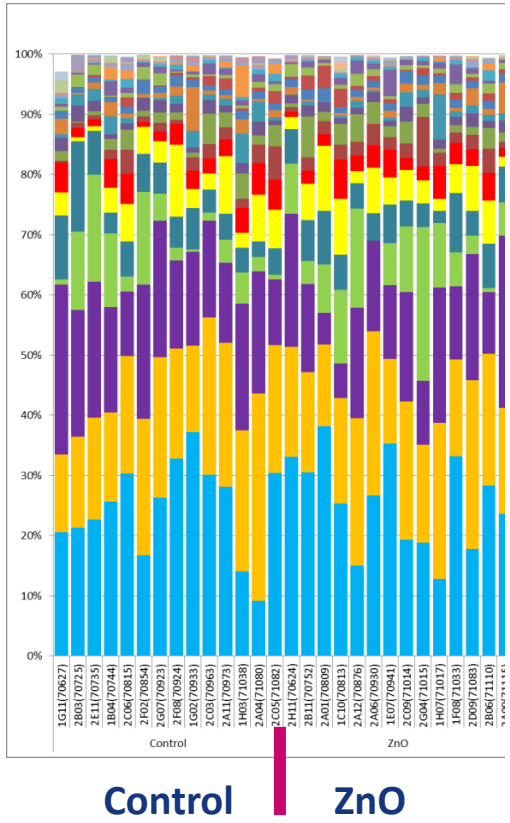
Significant reduction in abundance of *Lactobacillus* and increase in *Blautia*



Lactobacillus

Blautia

No differences observed after 14 days removal of ZnO

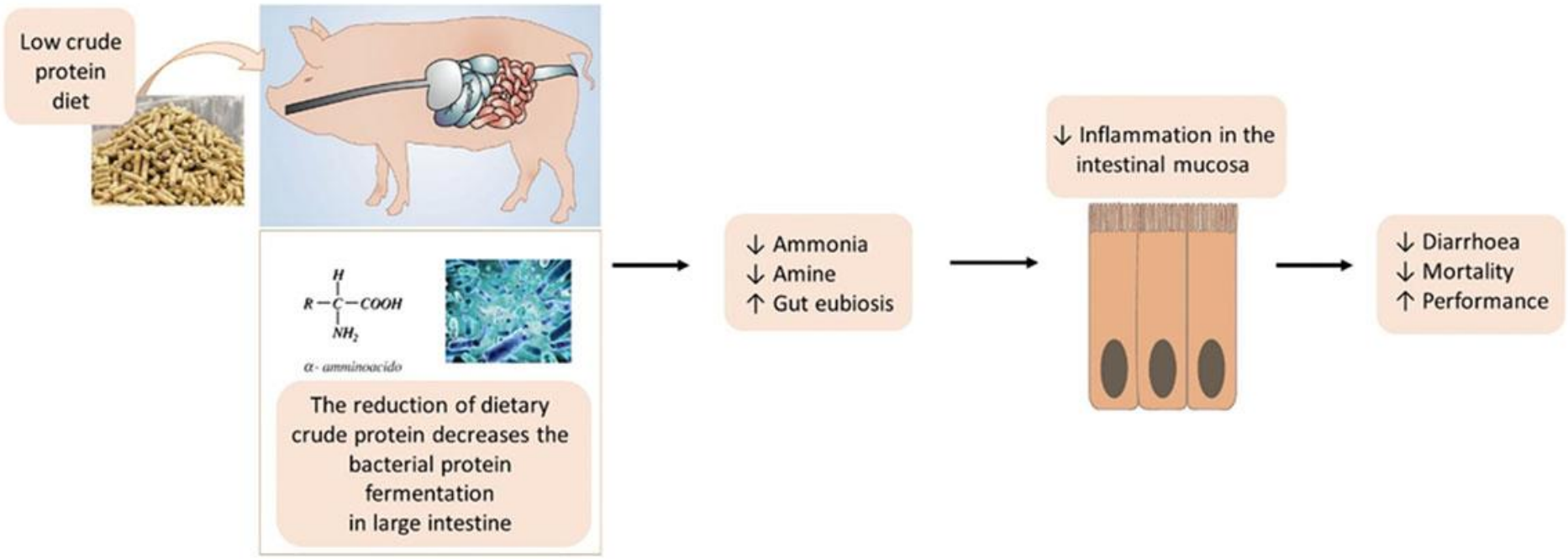


Some species in genera *Clostridium* and *Ruminococcus* have been reclassified as *Blautia*

Trouw Nutrition R&D, unpublished

Low protein diets contribute to prevention of diarrhea in piglets

….and prevention of wet litter in broiler chickens



Less favorable environment and substrate for proteolytic bacteria

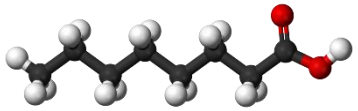
Note: Take care of covering amino acid requirements for optimal performance

Luise et al., 2021

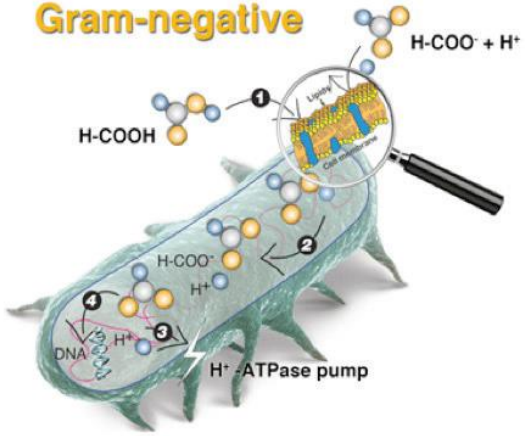
Organic acids and Medium Chain Fatty Acids

Option to create synergistic blends for microbiota management

Organic acid	MW	pKa1	pKa2	pKa3	Solubility
Formic	**46**	**3.75**			***
Acetic	60	4.76			***
Propionic	74	4.88			***
Butyric	88	4.82			***
Lactic	90	3.83			**
Sorbic	122	4.76			*
Fumaric	116	3.02	4.38		*
Citric	192	3.13	4.76	6.40	**



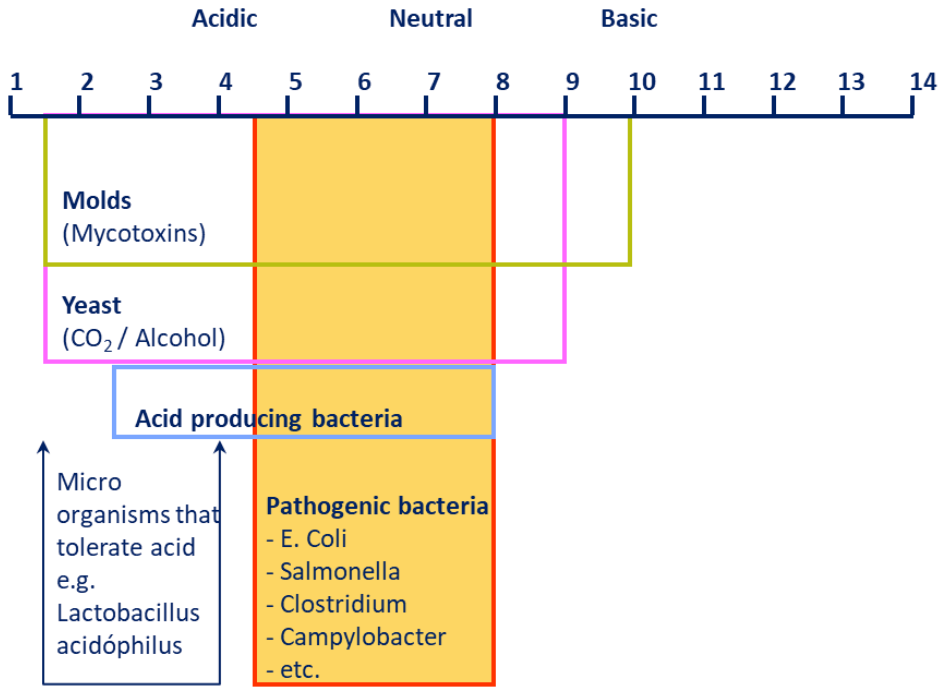
MCFA	
C6	Caproic acid
C8	Caprylic acid
C10	Capric acid
C12	Lauric acid



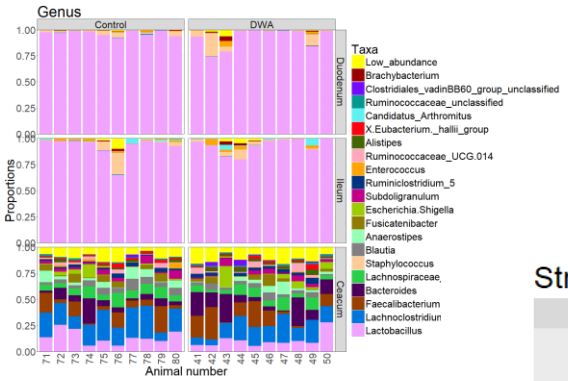
Fefana, 2014

Drinking water quality and safety

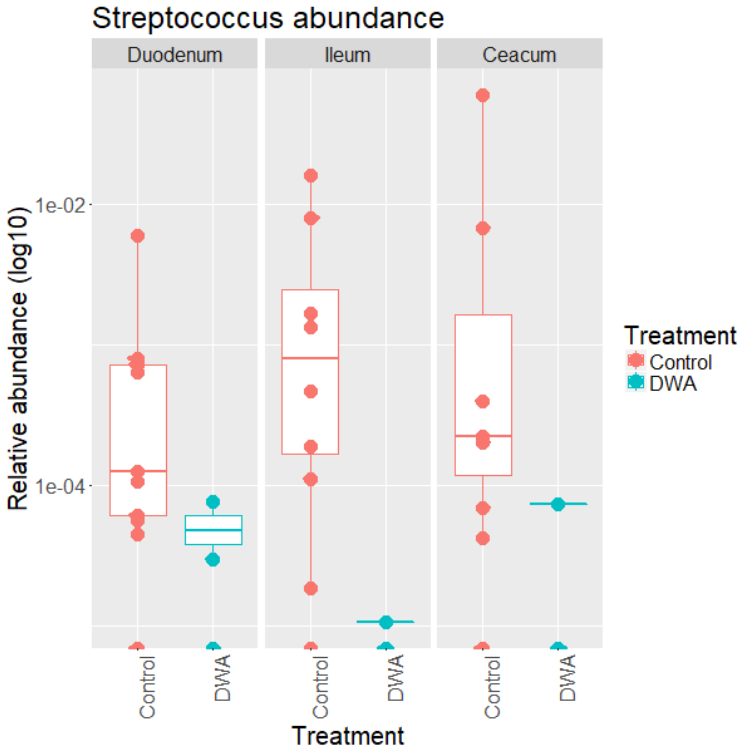
Acidifying water is option to assure microbial quality water

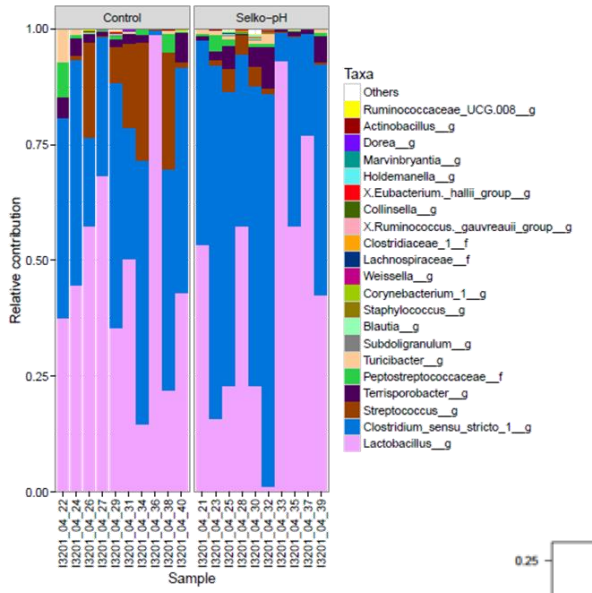


Drinking water acidifier showed less *Streptococcus spp* in the small intestinal tract in broiler chickens and piglets

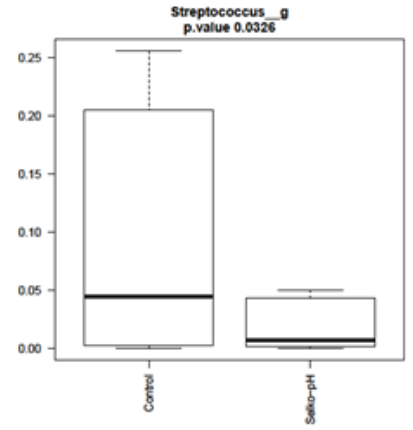


Broiler chickens





Piglets



Roubos et al., 2017

Drinking water acidifier reduced number Salmonella positive pigs in field study

Herd number (Samples/ treatment)	**Control % Positive**	**Water Acidifier* % Positive**	**Significance**
A (119)	**21.8%**	**8.4%**	$p<0.10$
B (140)	**27.1%**	**20.7%**	$p<0.10$
C (240)	**56.3%**	**12.5%**	$p<0.001$

Positive = cut-off OD%>10

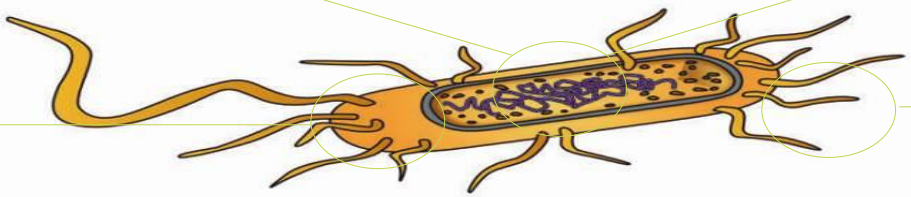
* Applied 25 to 115 kg, dose range 0.15 – 0.20%, water acidifier

Van der Wolf et al. 2001

Attacking Salmonella from different angles and supporting host defense

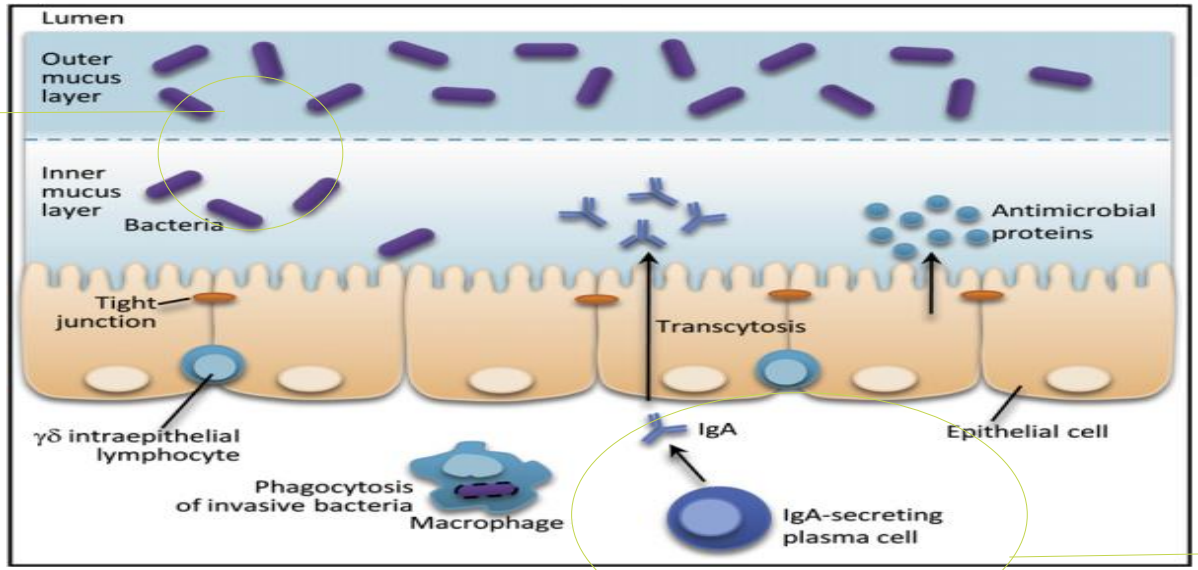
Metabolism ↓

Virulence ↓



Membrane function ↓

Adhesion ↓

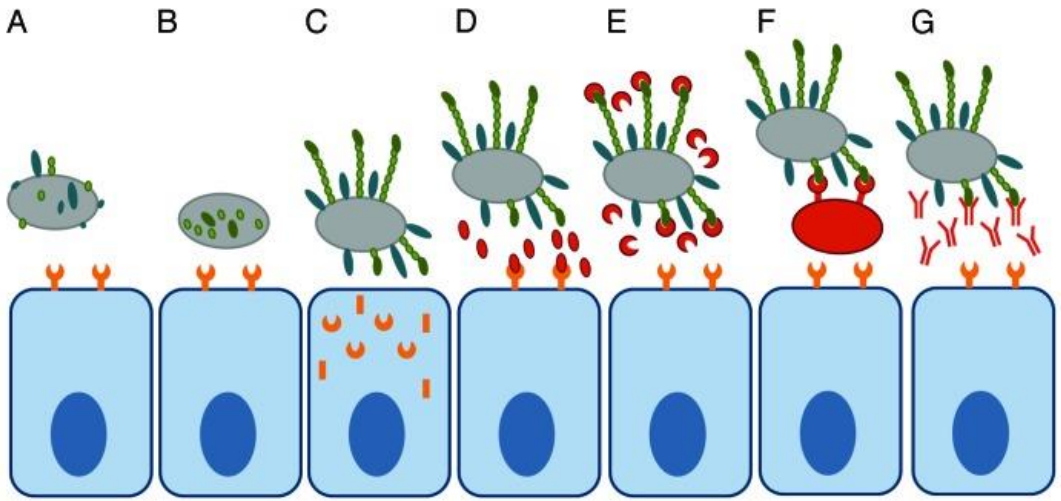


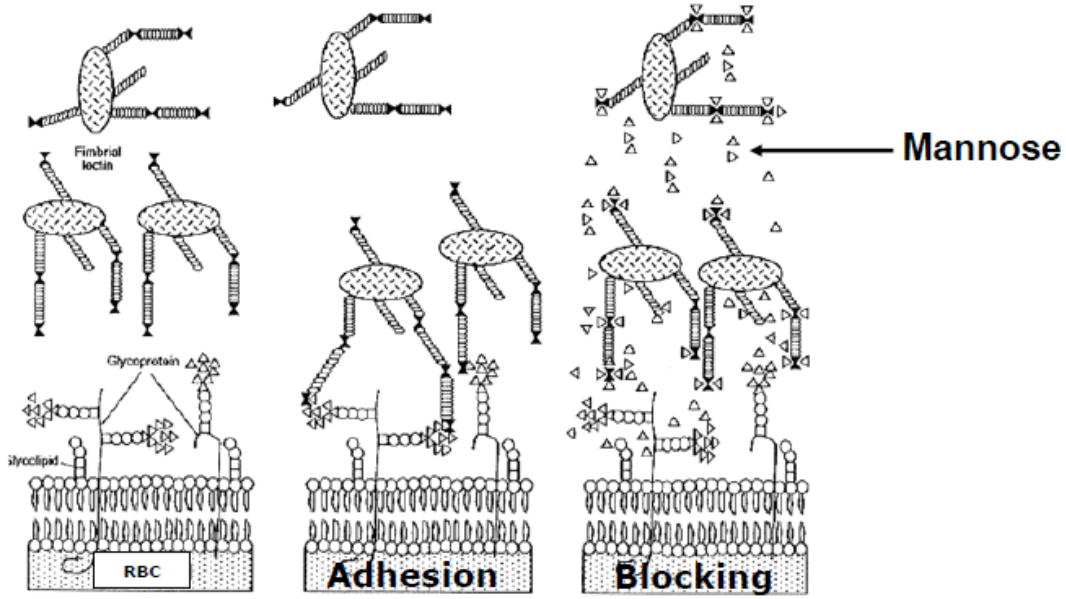
Beneficial bacteria ↑

Mucus secretion ↑

IgA secretion ↑

Prebiotic mono-, oligo- and polysaccharides may selectively promote beneficial microbes and/or inhibit pathogens.





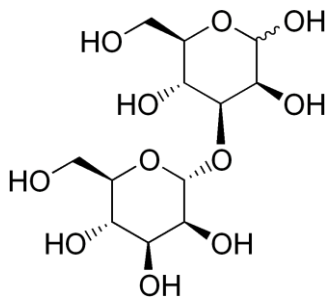
Strategies for anti-adhesion therapy:
Specific non-digestible oligosaccharides

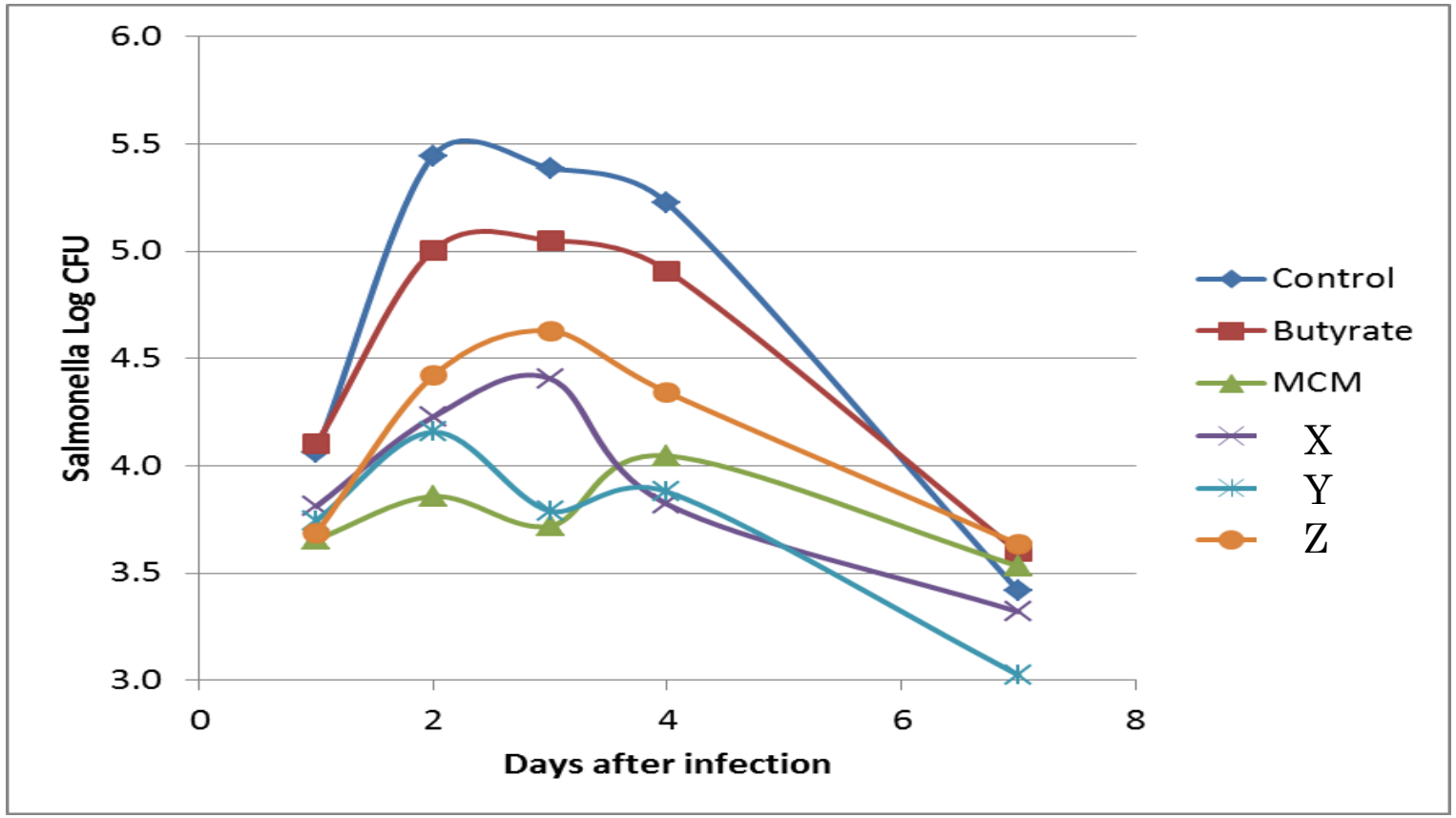
Krachler and Orth, 2013

Mannobiose reduced shedding of *Salmonella Typhimurium* in challenged piglets

Plant derived mannobiose: non-digestible, soluble disaccharide

Mannobiose (in MCM)





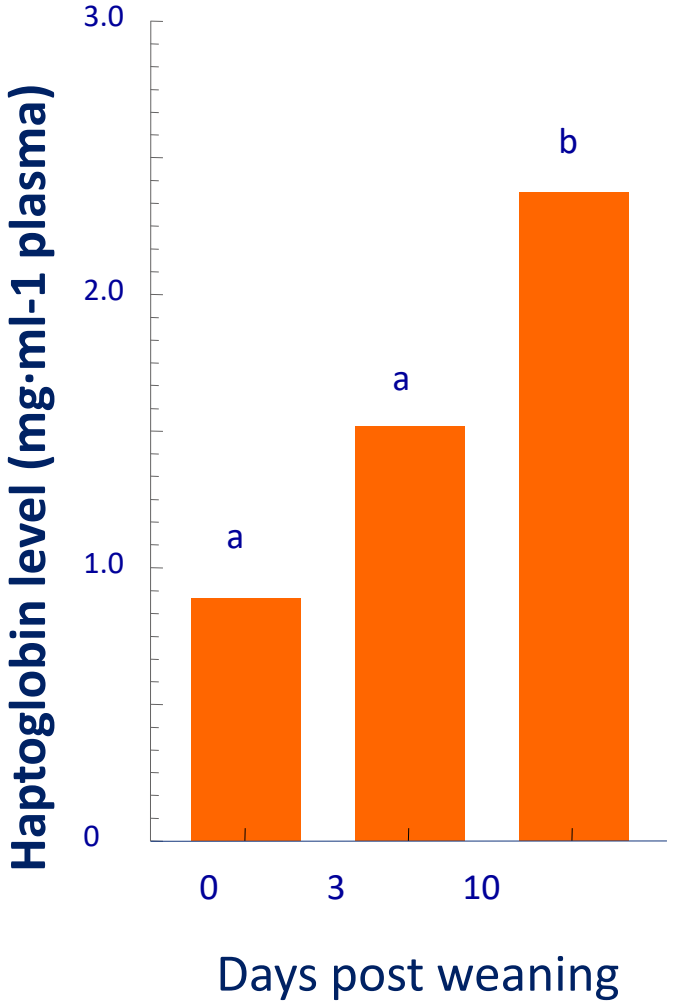
Anti-adherence properties have also been reported of cell-wall MOS of yeast derived products

Trouw Nutrition R&D, unpublished

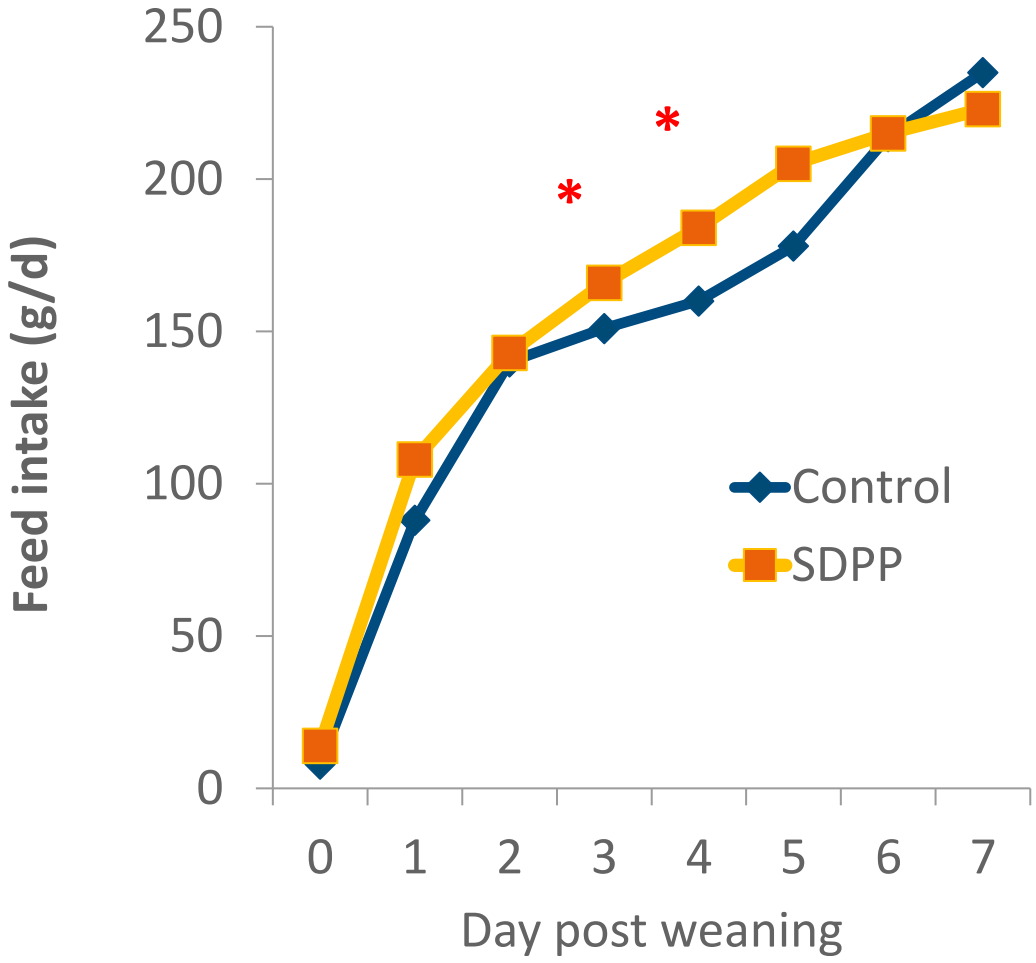
Support mucosal barrier & immune modulation

Spray dried blood plasma reduces the impact of the 2nd feed intake dip

Example of functional macro-ingredient



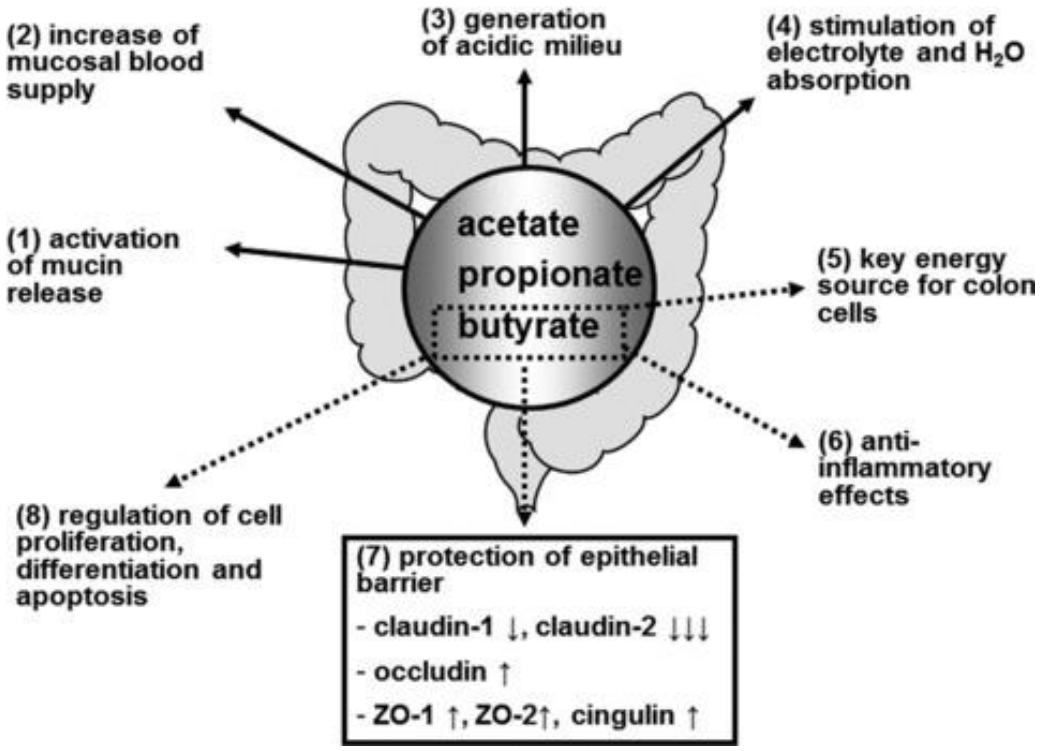
Spreeuwenberg et al. 2003



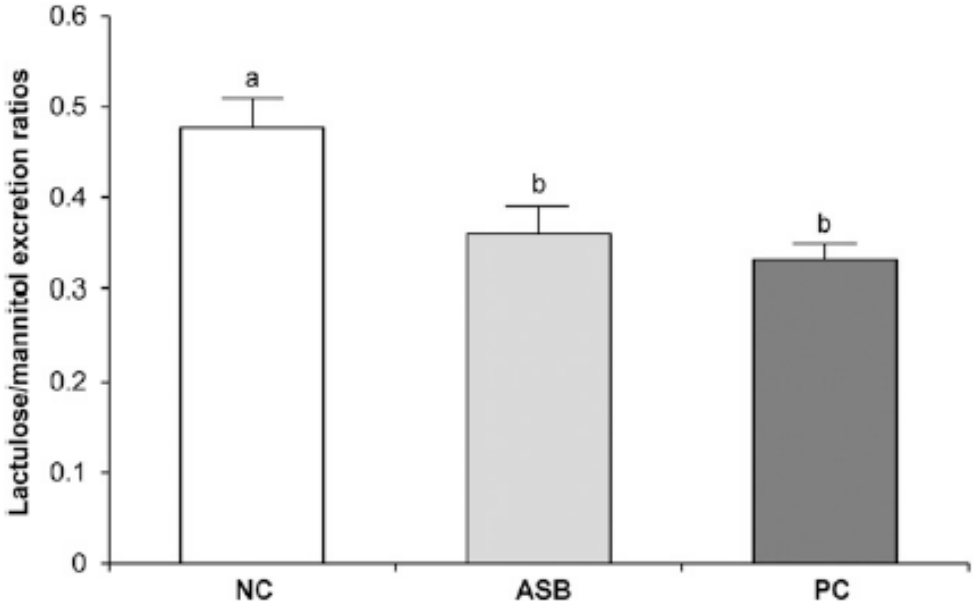
Trouw Nutrition, unpublished

Butyrate is a special short-chain fatty acid

Various beneficial effects on mucosal barrier function



Reduced gut permeability in weaned piglets fed 0.1% coated sodium butyrate



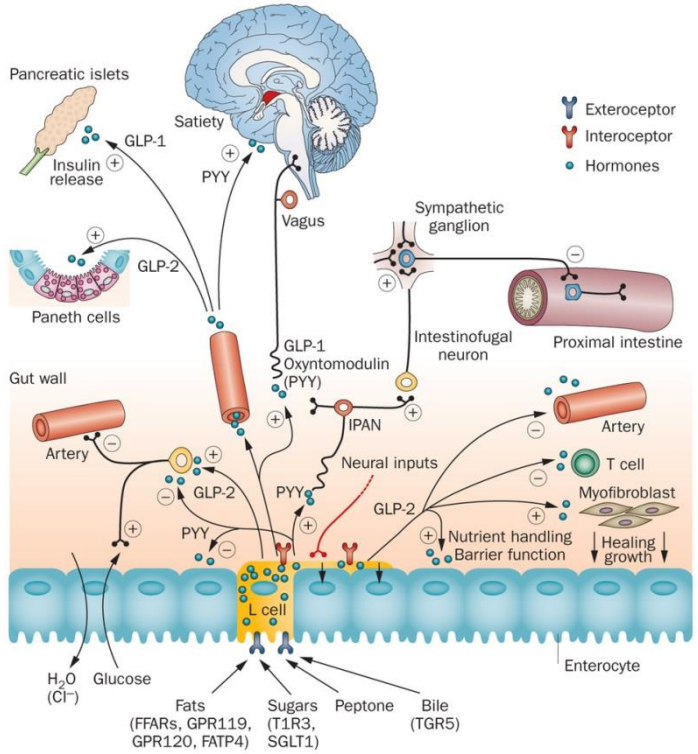
Huang et al., 2015

Sensing and modulation of the neuro-endocrine system

Important mode-of-action of phytochemicals

Bioactive	Origin
Capsaicin	Pepper
Carnosic acid	Rosemary
Carvacrol	Oregano
Cinnemaldehyde	Cinnamon
Eugenol	Clove
Thymol	Thyme
And > 3000 other candidates	

Gut sensing



Furness et al. 2013

Phytochemicals reduced diarrhea in *E.coli* F18 challenged piglets

Effects may be mediated via anti-inflammatory effects

	Treatment[2]								
	Sham				*E. coli*				
Item	CON	CAP	GAR	TUR	CON	CAP	GAR	TUR	SEM
Diarrhea score[5]									
d 0 to 2	1.96[a]	1.17[b]	1.21[b]	1.29[b]	1.93	1.67	1.35	1.36	0.36
d 3 to 5	2.06[a]	1.35[b]	1.46[b]	1.67[b]	3.43[a]	2.50[b]	2.13[b]	2.00[b]	0.31
d 6 to 8	1.44	1.18	1.17	1.21	2.86	2.58	2.83	2.90	0.52
d 9 to 11	1.09	1.04	1.08	1.00	3.51[a]	2.13[b]	1.21[c]	1.15[c]	0.26
Pig days[6]	64	64	64	64	53	64	64	53	
Frequency[7]	20	4	7	9	40	26	17	16	—

No significant effect on performance or excretion haemolytic E.coli

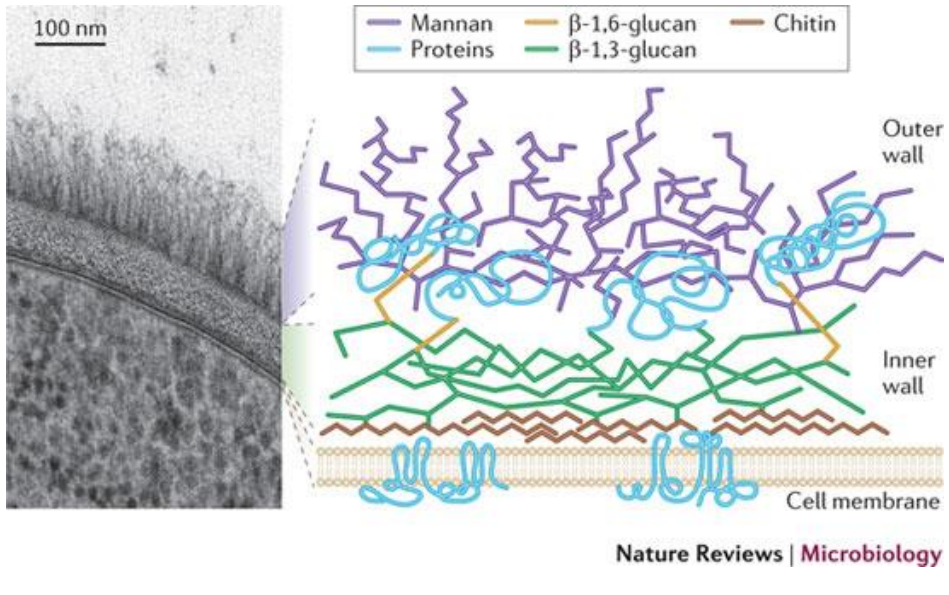
Significant effect of CAP, GAR, TUR on inflammation markers TGF-β and haptoglobin

Liu et al., 2014

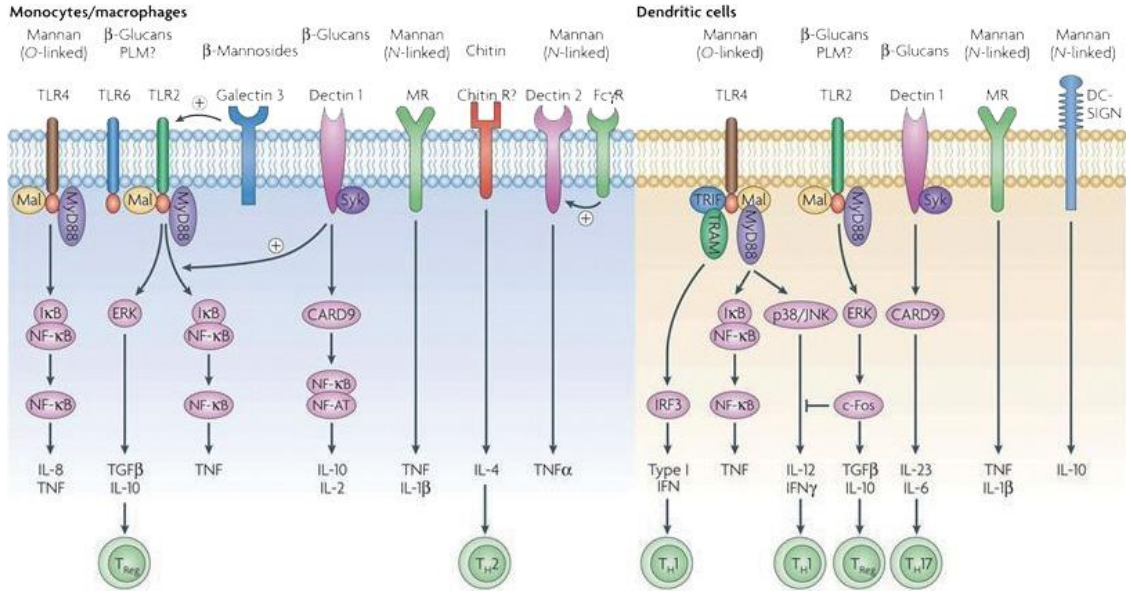
Fungal cell walls contain a wide range of immune-modulatory compounds

β-Glucans, Mannan and Chitin

Yeast cell wall structure



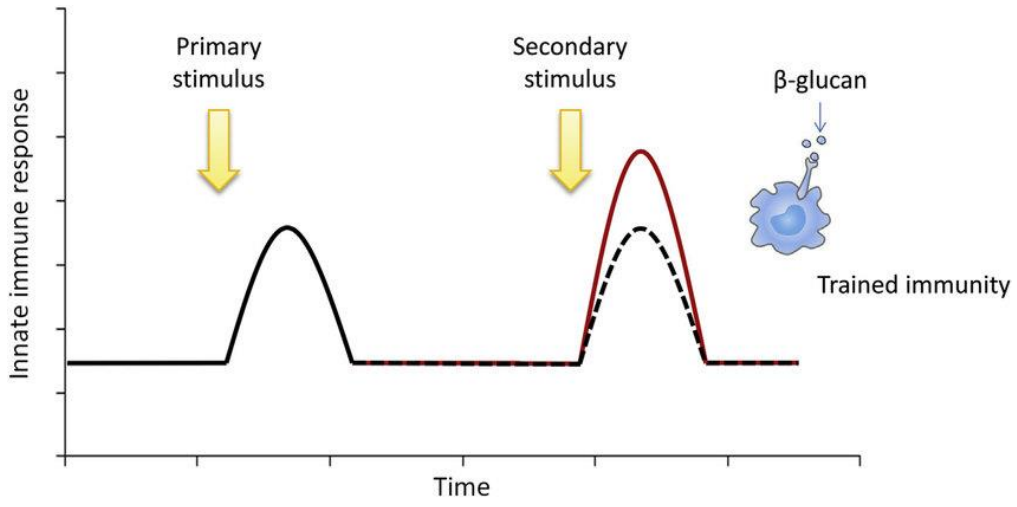
Immune-modulatory compounds in fungal cell walls



Netea et al. 2008

Fungal cell walls can be applied to improve immune competence

Training the innate immune system in early life is an interesting direction



Netea et al., 2016

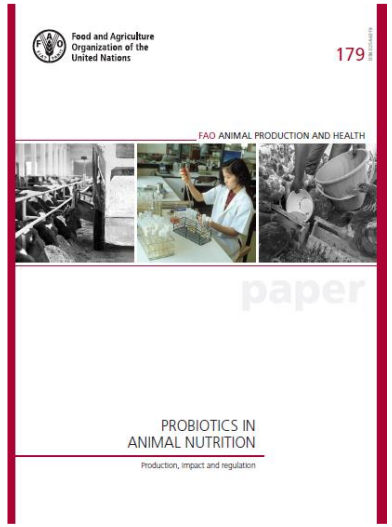
<u>Preweaning</u> adminstration ß1-3,1-6 glucan improved response piglets to *E.coli* challenge post-weaning

PW	Control	Glucan	*p*-value
BW day 7*	8.0	8.4	0.04
BW day 21	14.4	15.0	0.12
FE	0.68	0.71	0.23
Diarrhoea	39	36	0.07
Behavior	2.7	1.5	0.12
Skin	9.6	7.2	0.06

* Post-infection

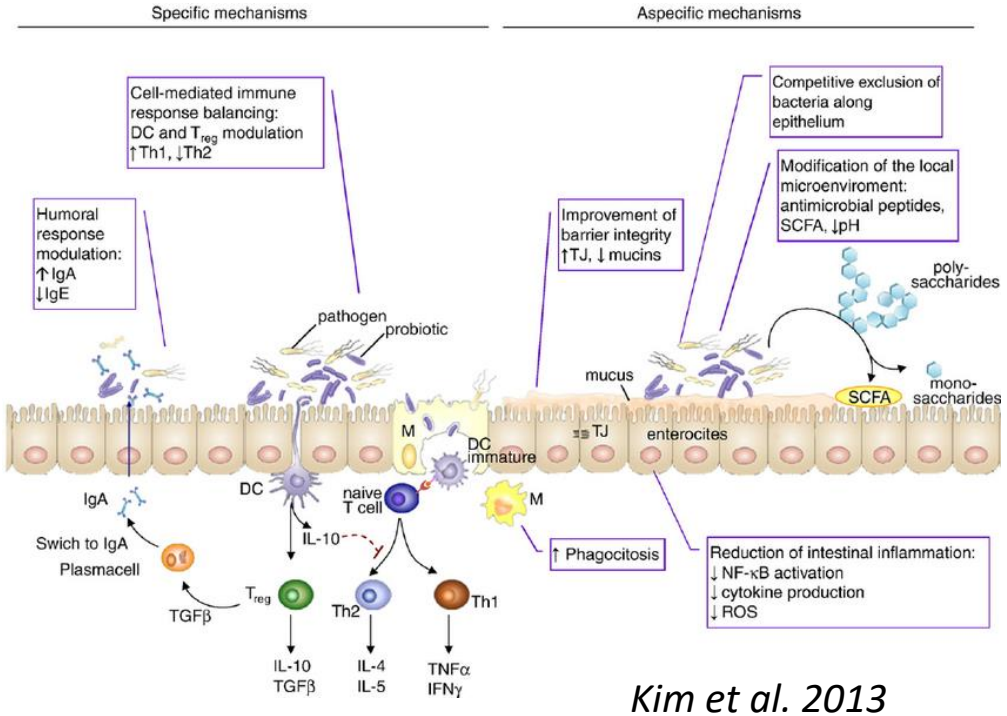
Trouw Nutrition R&D, unpublished

Microbiota and immune-modulatory effects of probiotics may contribute in early life to steer the microbiota balance and immune competence into the desired direction



Probiotic
Bacillus spp.
Enterococcus faecium
Lactobacillus spp.
Pediococcus spp.
Saccharomyces cerevisiae
Others

Bajagai et al., 2016; FAO report 179

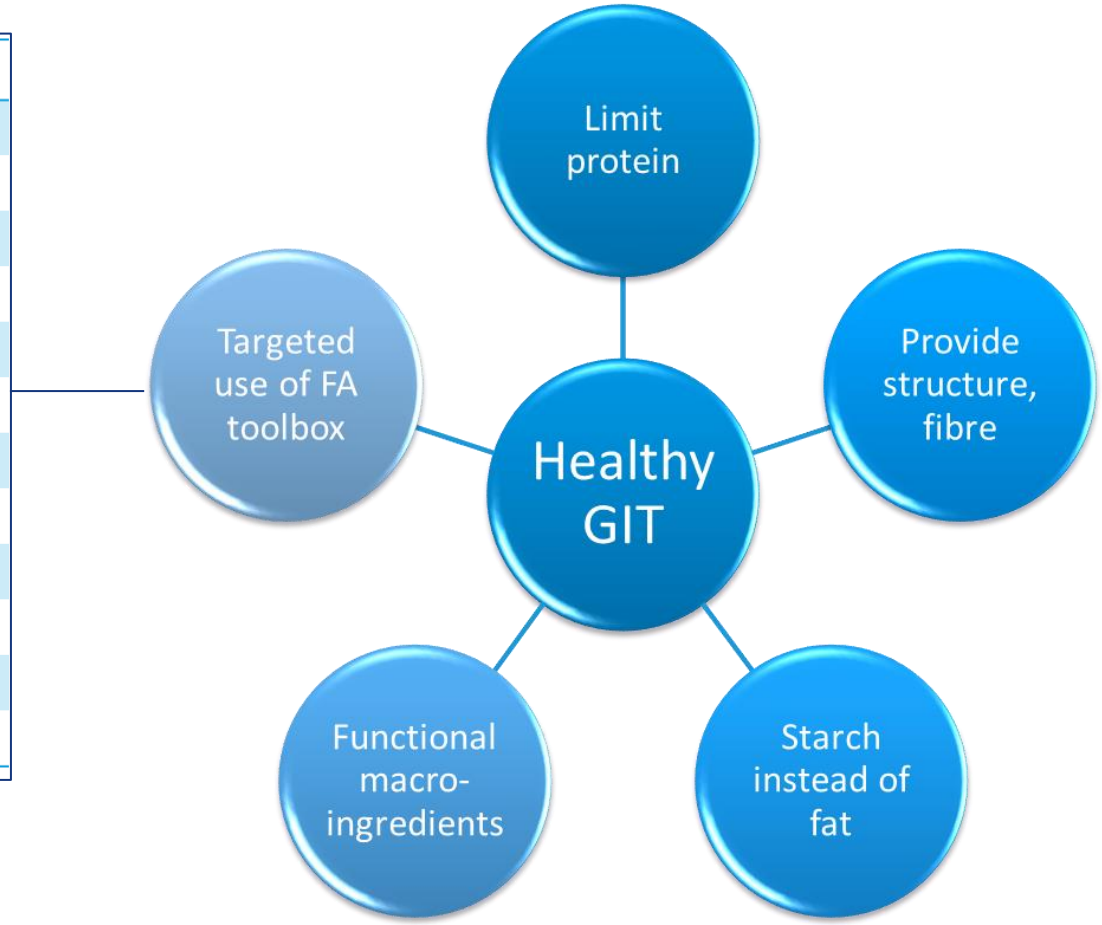


Kim et al. 2013

Nutritionist has great toolbox for prophylactic nutrition

With a functional value beyond nutritional value

Feed additive tools
Organic acids
Medium chain fatty acids
Short chain fatty acids
Plant extracts, essential oils
Prebiotic sugars, polysaccharides
Yeast derived specialties
Probiotics
Enzymes
Clay minerals
Copper
Zinc Oxide
Others



Prophylactic = ‘Intended to prevent disease’

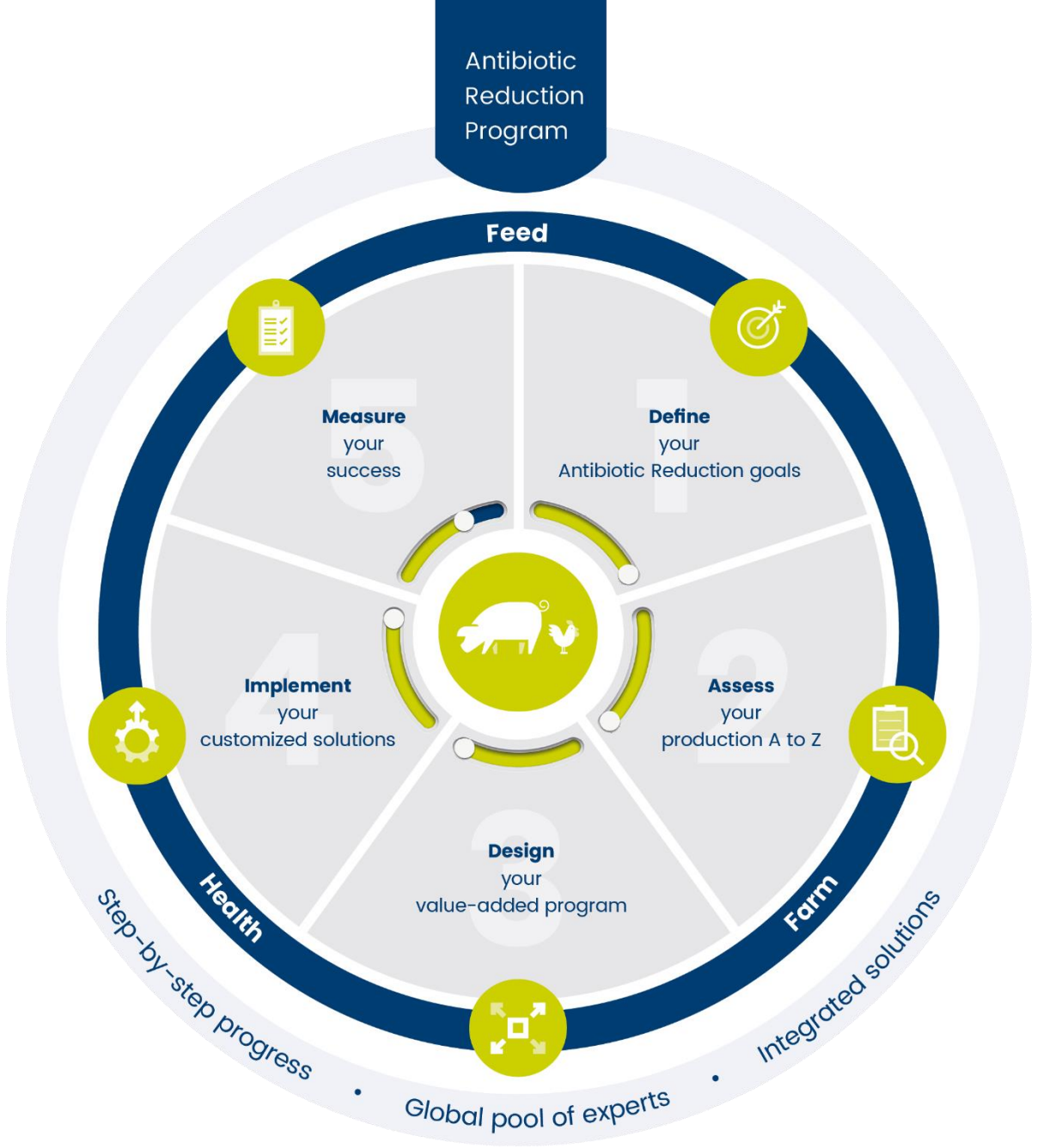
Regulatory framework to facilitate progress in adopting solutions for sustainability challenges, including AMR

Regulatory recognition for prophylactic nutrition!

Prophylactic = 'Intended to prevent disease'

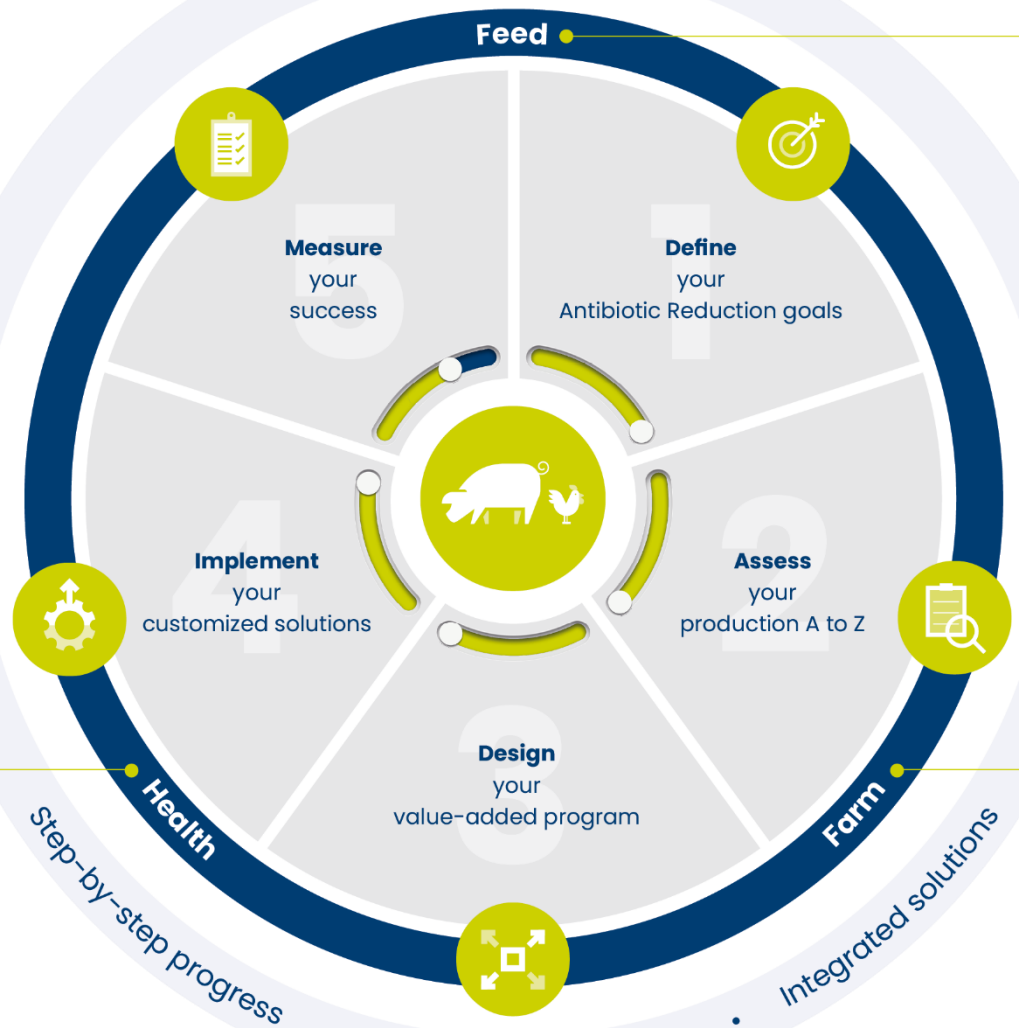
Multidisciplinary strategies to reduce the need for antibiotics in poultry and swine, practical experiences from Spain

Barbara Brutsaert, DVM



Small switches.
Big change.

Antibiotic Reduction Program



Feed Management

- Microbiological quality of raw materials and feed
- Optimize Nutritional strategies
- Optimize Feed form and physical properties

Health Management

- Animal Health Monitoring
- Responsible Antibiotic use and targeted vaccination strategies
- Strategic use of Feed and Water additives

Farm Management

- Biosecurity
- Farm Conditions
- Animal Management

Across the full value chain

Feed Management

- Microbiological quality of raw materials and feed
- Optimize Nutritional strategies
  - **Max protein** levels and use of protein sources with relative high rate of digestion
  - **Min starch, max fat** level
- Optimize Feed form and physical properties
  - Assuring sufficient structure, **'functional' fibre** in the feed

Farm Management

- Biosecurity
- Farm Conditions
- Animal Management

Health Management

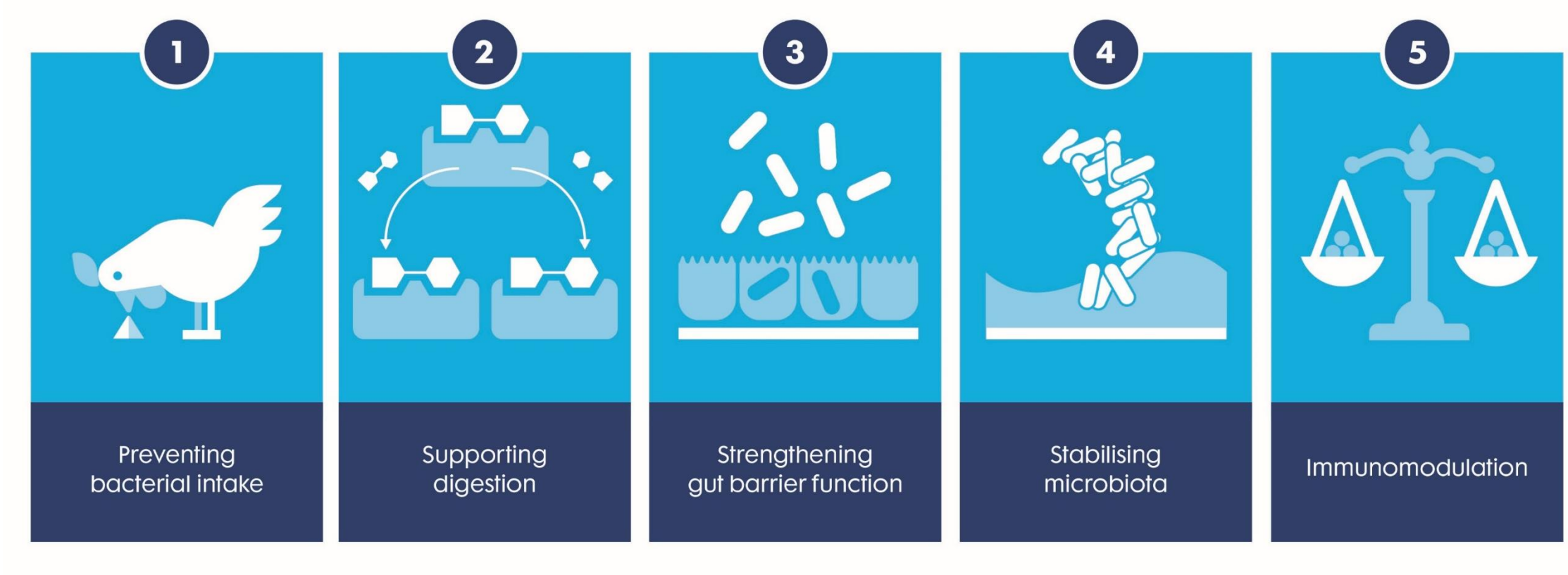
- Animal Health Monitoring
- Responsible Antibiotic use and targeted vaccination strategies
- Strategic use of Feed and Water additives
  - **Organic** acid blends in feed and/or water
  - Blend of controlled **release MCFAs, butyrates and phytochemicals**

In specific functional diets:

- **Prebiotic fibres** with anti-adherence properties
- **Probiotics**

Our 5 pillars, to secure animal health and performance

from animal disease resistance and resilience perspective



Practical experience at a broiler integration, focus on main attention points

Feed Management

- Feed quality
  - nutritional
  - feed safety

Farm Management

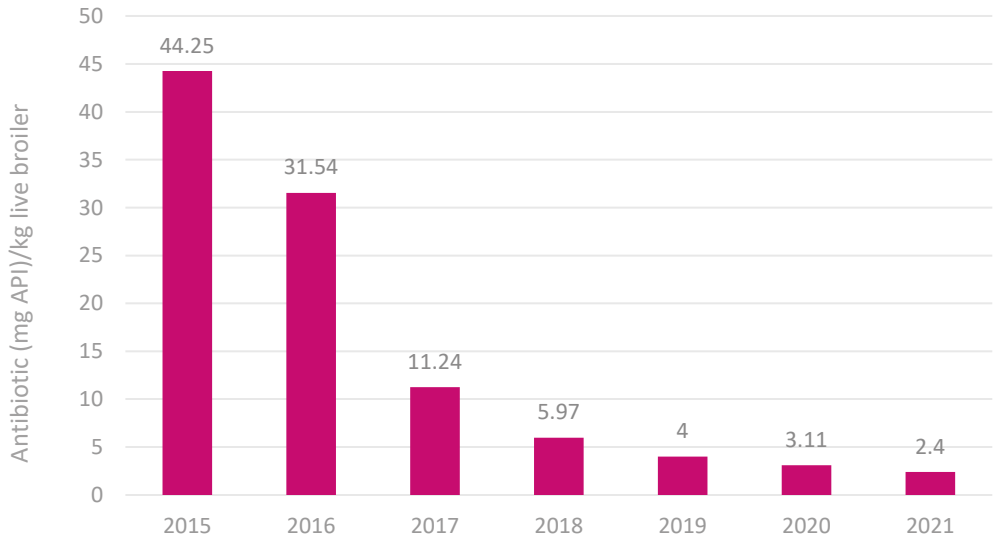
- Biosecurity
- Housing and climate
- Animal management
  - DOC quality
- Drinking water quality

Health Management

- Animal health monitoring across the entire value chain
- Narrow spectrum antibiotics
- Strategic use of feed and water additives

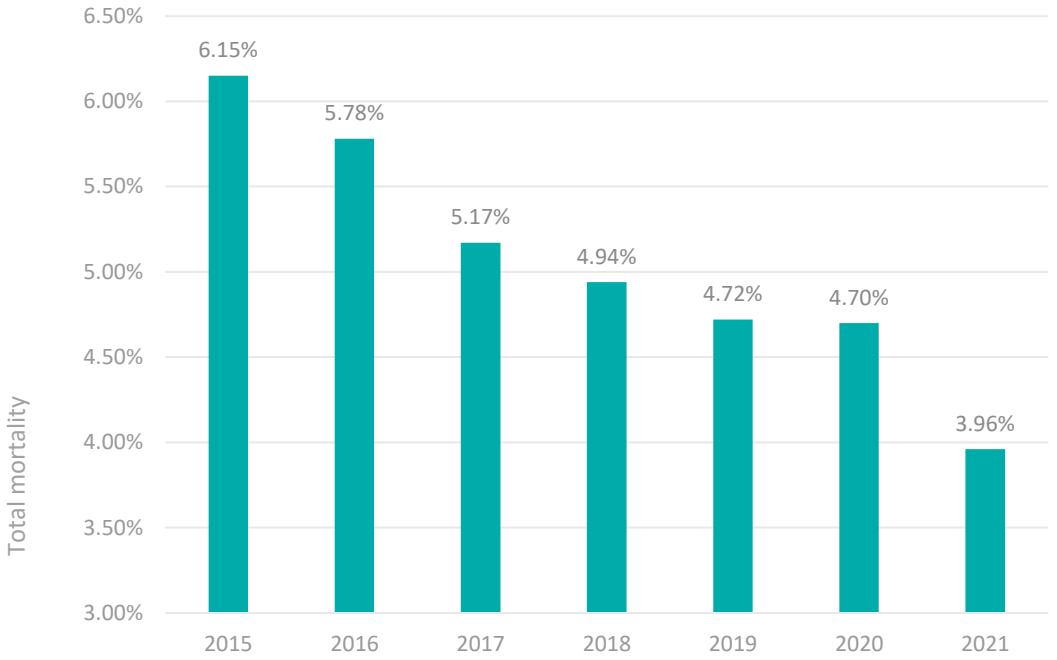
…results in successful antibiotic reduction

-95% of antibiotics in 6 years

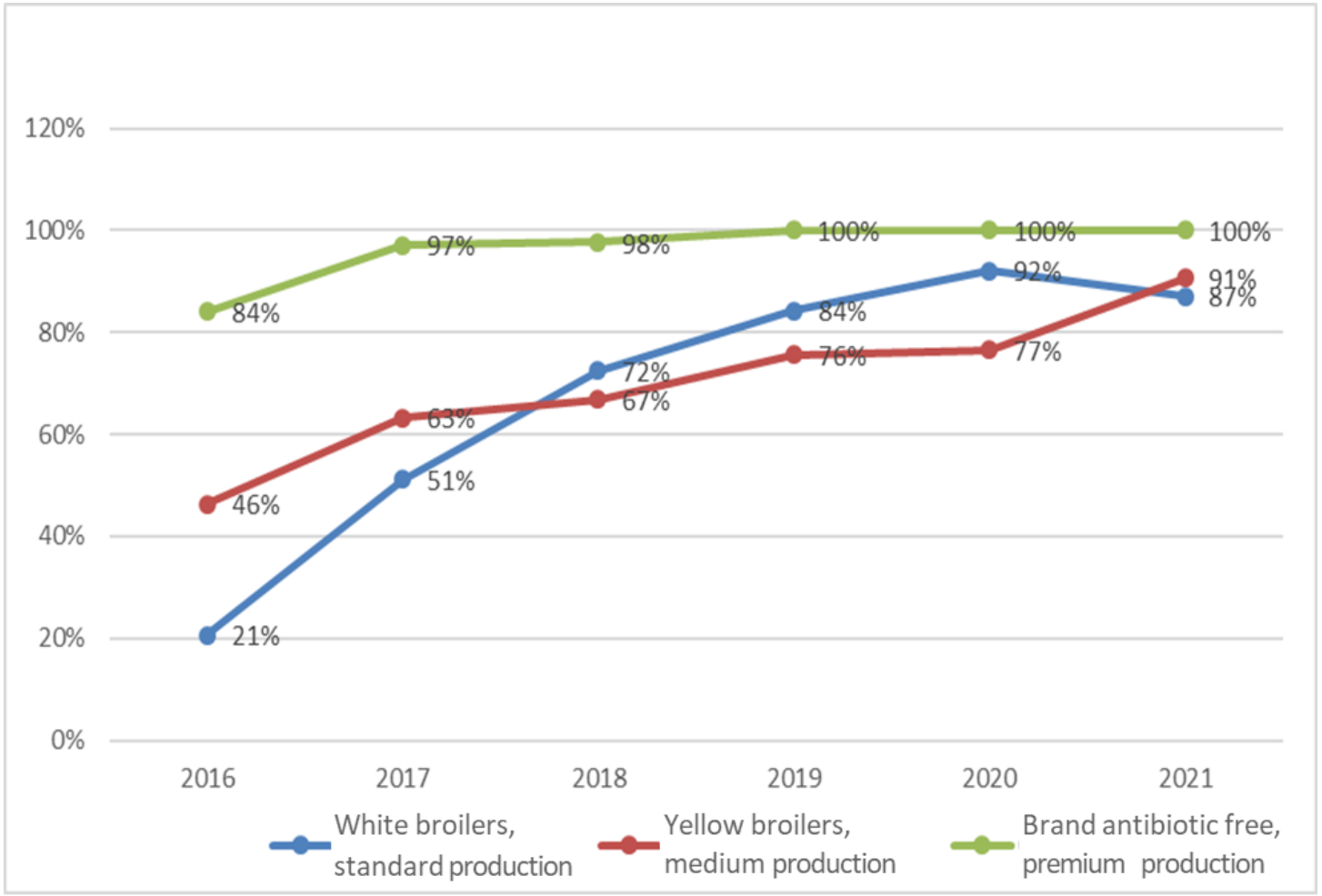


Spain

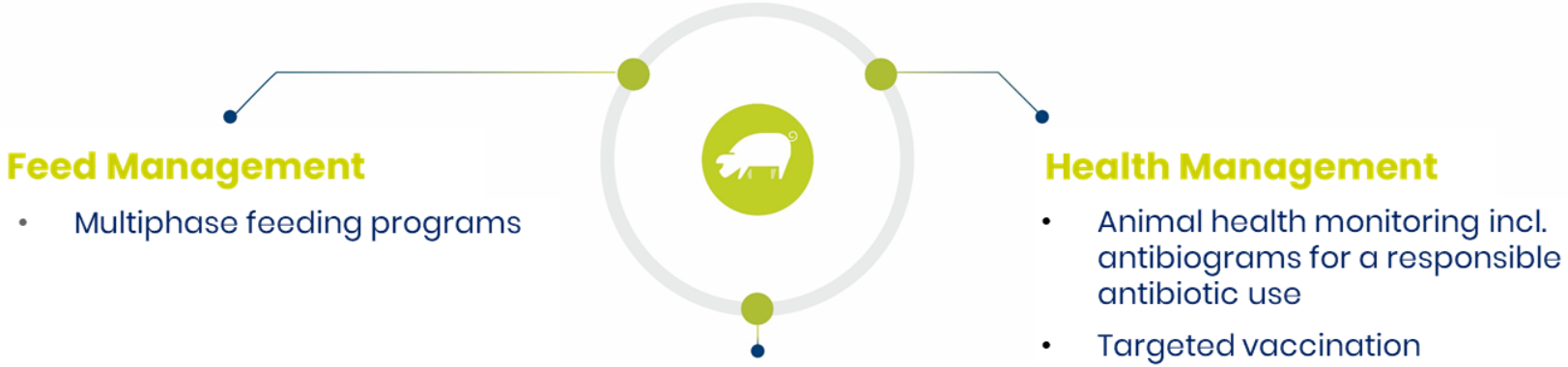
with 36% lower mortality



Up to 100% of broilers antibiotic free



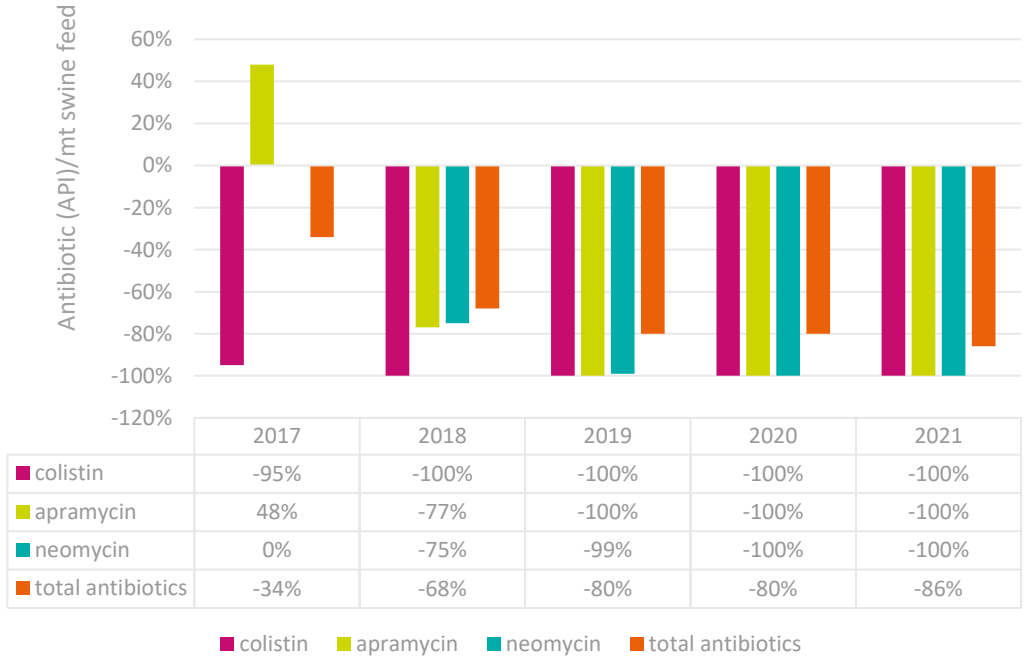
Practical experience at a swine feed mill, focus on main attention points



…results in successful antibiotic reduction

-86% antibiotics in 5 years

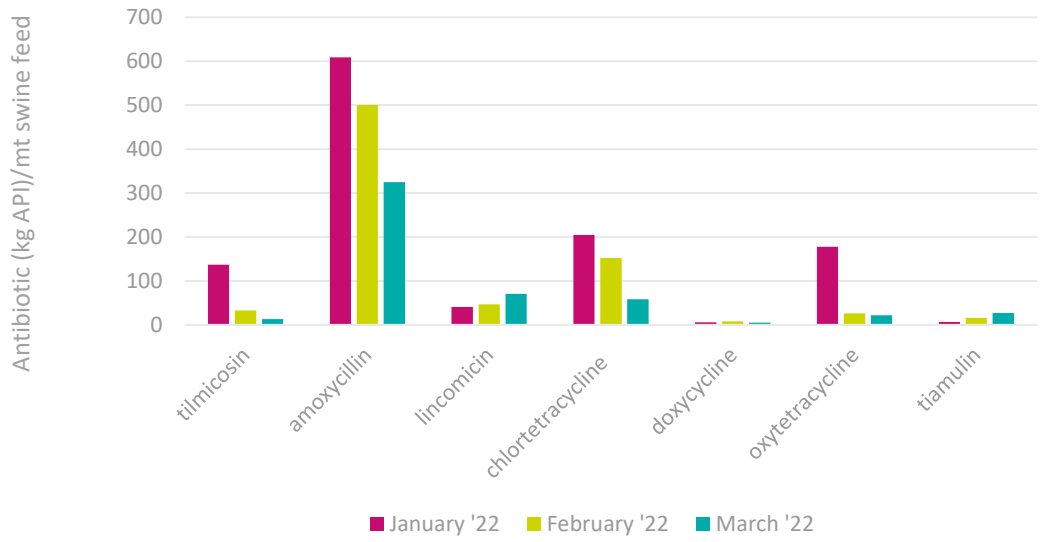
-100% for CIA's colistin, apramycin, neomycin



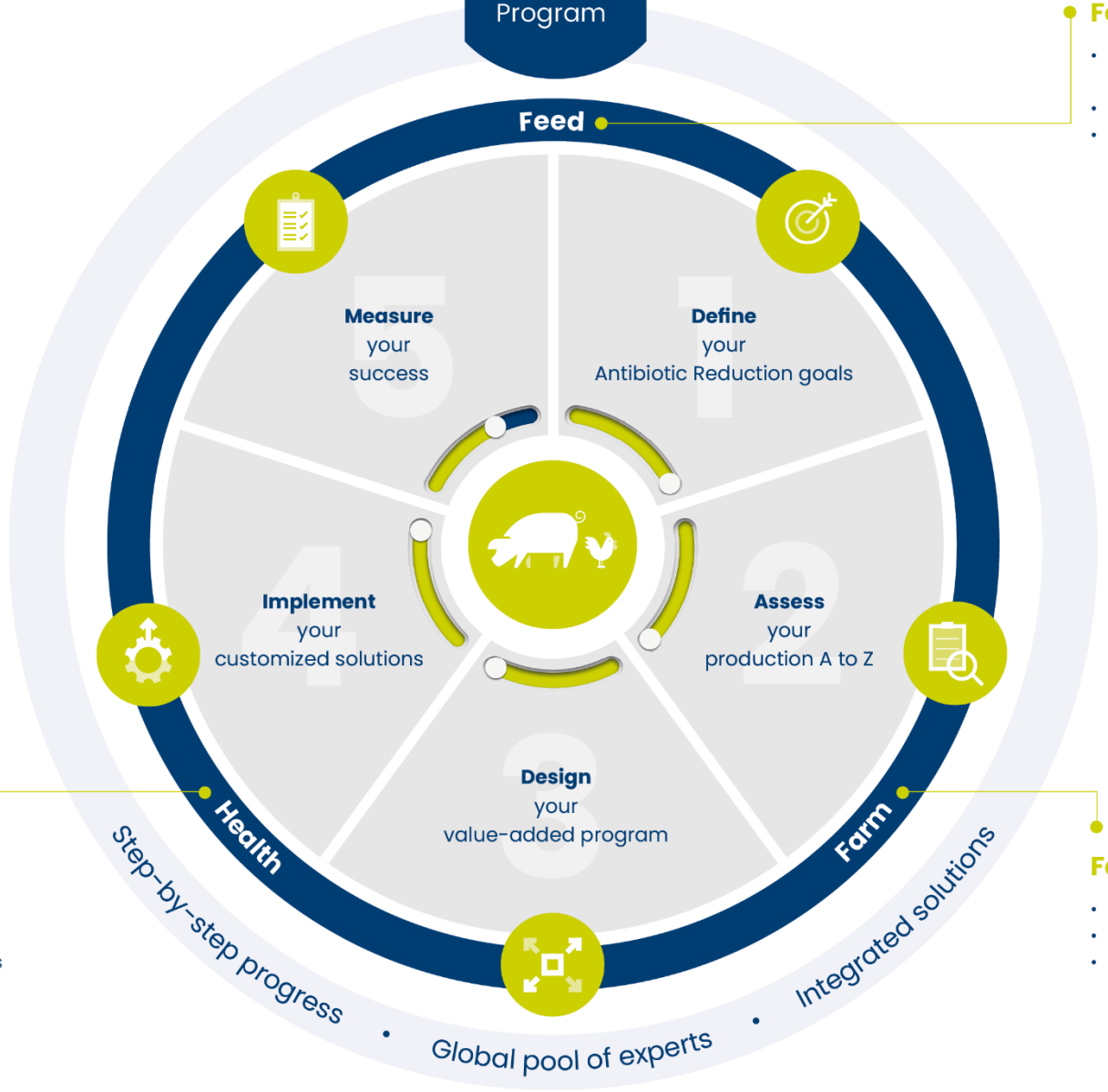
	2017	2018	2019	2020	2021
colistin	-95%	-100%	-100%	-100%	-100%
apramycin	48%	-77%	-100%	-100%	-100%
neomycin	0%	-75%	-99%	-100%	-100%
total antibiotics	-34%	-68%	-80%	-80%	-86%

Spain

while continuing to reduce every day



Antibiotic Reduction Program



Feed Management

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Health Management

- Animal Health Monitoring
- Responsible Antibiotic use and targeted vaccination strategies
- Strategic use of Feed and Water additives

Farm Management

- Biosecurity
- Farm Conditions
- Animal Management

Small steps. Big change.

To reduce significantly the need for antibiotics in your livestock business.

Final comments

- ✓ Nutrition can contribute significantly to prevention of dysbiosis and improve disease resistance and resilience.
- ✓ Nutrition is one of the pillars in strategies to reduce use of antibiotics
- ✓ Multidisciplinary approaches, including dietary measures, have already demonstrated in practice to be effective in reducing use of antibiotics

The presenters would like to thank the FAO for the opportunity to present in this webinar

Reference list

References used

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