Pathophysiology of the Neonatal Intestinal Mucosa of Swine

Tonisity Px

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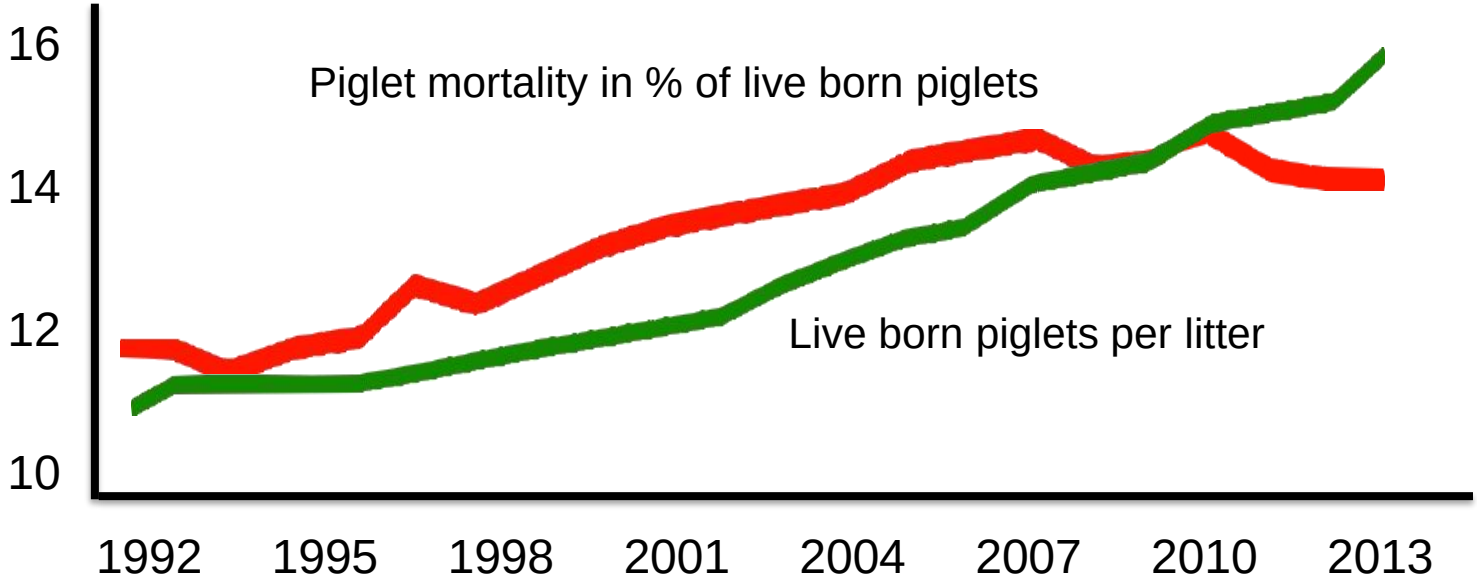
Problems;

Emerging and Re-emerging Diseases

Evolution of Litter Size (Total Number of Pigs Born) and of Piglet Mortality (% of Live Born Piglets) in Denmark from 1992 to 2013

Data from a representative number of commercial herds



DanAvl, 2014

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European average pre-weaning mortality is estimated at 13.3% (AHDB, 2016)

This means that about 40 million of live-born piglets die per year

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Philippines Swine performance

Parameters	2014			2016			2015
	Low	High	Avg	Low	High	Avg	Danish Avg
Litter size born alive	8.3	12.1	10.1	8.6	11.9	10.1	15.9
Preweaning mortality, %	2.1	18.4	9.0	1.6	22.4	10.6	13.4
Weaned / litter	7.7	10.7	9.2	7.1	11.0	9.0	13.8
Farrowing rate, %	67.1	90.5	80.1	55.5	89.5	80.1	
Farrowing index	1.9	2.5	2.2	1.8	2.4	2.2	2.3
Non productive days	3.8	39.2	16.7	1.9	55.3	17.9	13.0
ADG, kg	0.334	0.699	0.552	0.458	0.643	0.567	
WPSY	17.0	26.2	20.3	12.9	25.8	19.7	31.4
PPSY	17.0	26.2	20.3	12.5	21.1	17.4	
Avg weight sold, kg	23.4	116.9	86.8	75.9	106.2	92.4	
Avg. age sold, days	69.9	199.7	154.4	142.4	186.6	163.2	
Avg. price sold, Peso/kg	101	121	111	95	130	103	
USD @50:1	2.01	2.41	2.22	1.91	2.60	2.06	

PH data from The swine production performance monitoring project (SPPMP) by PSIRDFI & PCAARRD – DOST
Danish data from Jessen. SEGES 2015 requoted from Jens Jorgensen, 2017. Avg performance of 340,000 sows / year from 459 Danish sow units

Miranda Smit, University of Alberta, Saskatchewan Pork Industry Symposium 2012
https://www.saskpork.com/html/pork-symposium/sask-pork-proceedings/index.cfm

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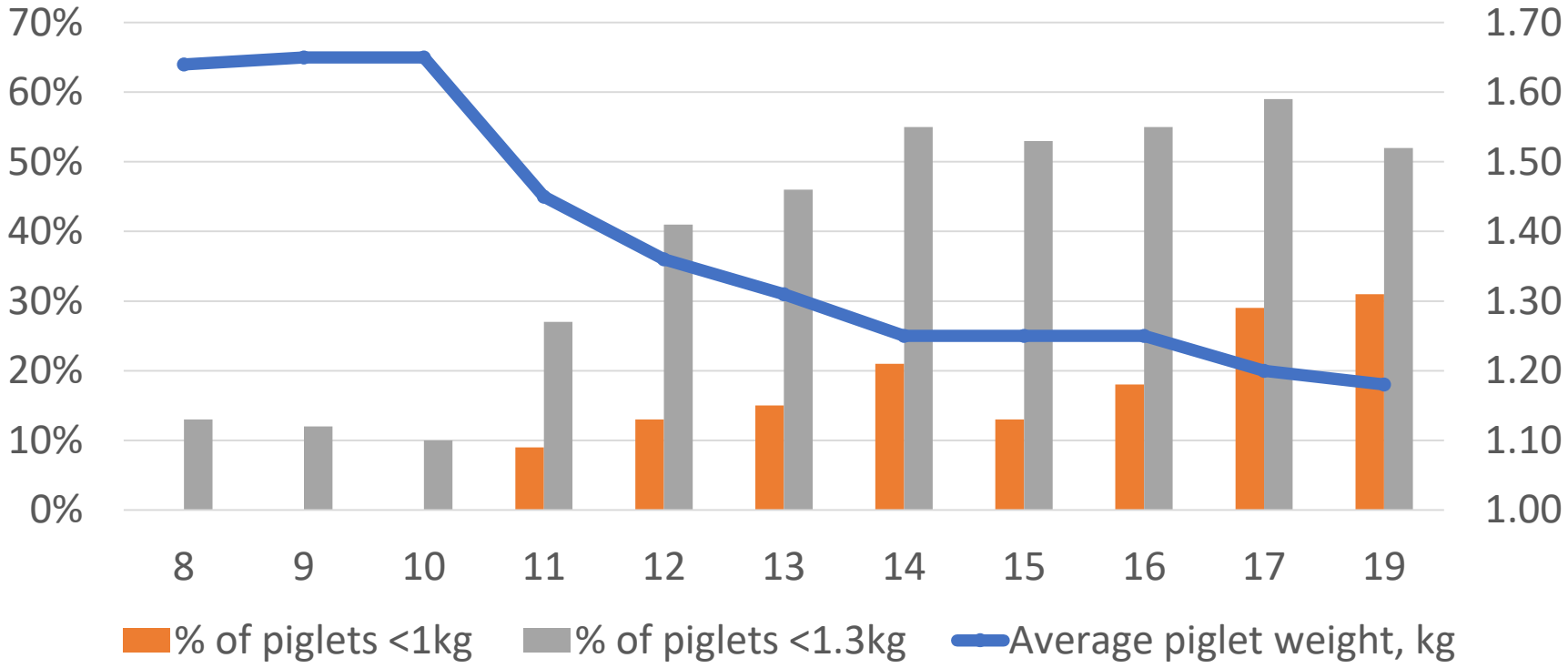
Increase in litter size is associated with a higher proportion of small piglets



1050 pigs from a single batch born during one week in a farrow-to-finish farm followed through the production cycle up to slaughterhouse

Calderón Díaz et al., 2016

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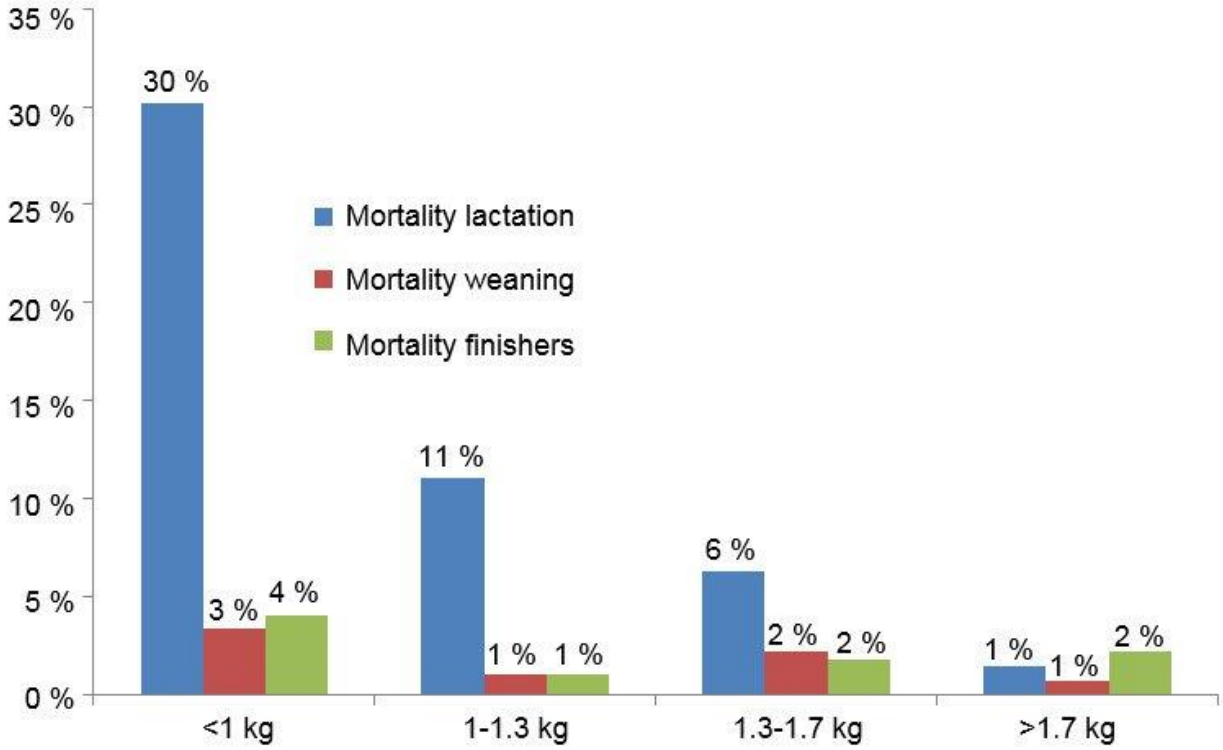
Reduced birth weight is associated with increased pre-weaning mortality



1050 pigs from a single batch born during one week in a farrow-to-finish farm followed through the production cycle up to slaughterhouse

Calderón Díaz et al., 2016

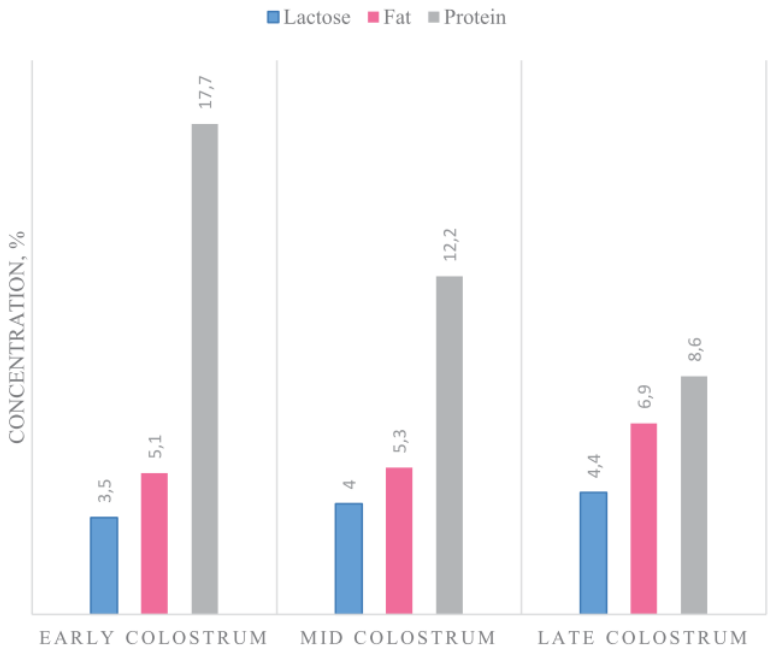
Importance of Colostrum

- Piglets are born with little immune protection and it can take time for them to build their own active immunity.
- Sufficient colostrum intake in the first 24 hours post-birth is essential for pig performance.
- Colostrum provides energy and proteins essential for the piglets to start suckling and to grow.
- Also enriched with maternal antibodies providing passive immunity.

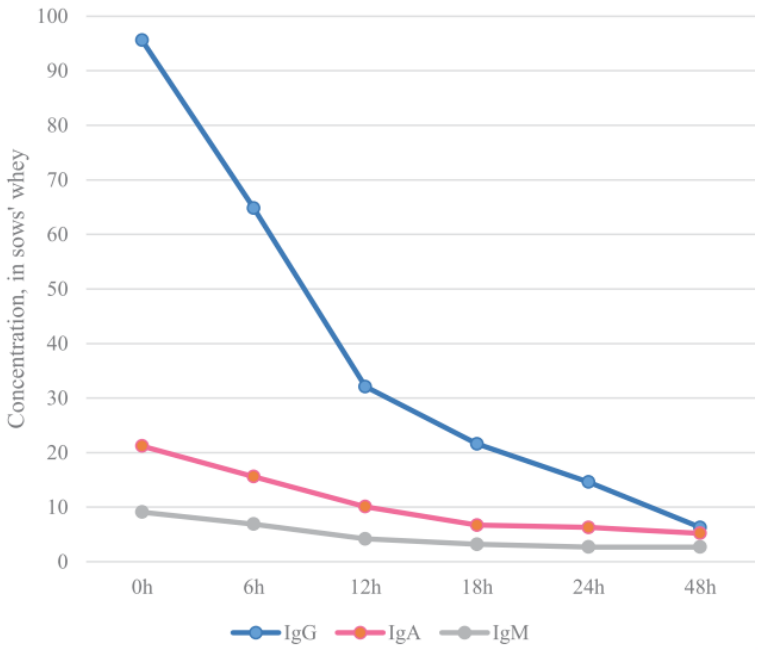
Tonisity Px

Importance of Colostrum

Average composition (%) of early (0h), mid (12h) and late (24h) colostrum



Concentrations of IgG, IgA and IgM in sows' whey during lactation



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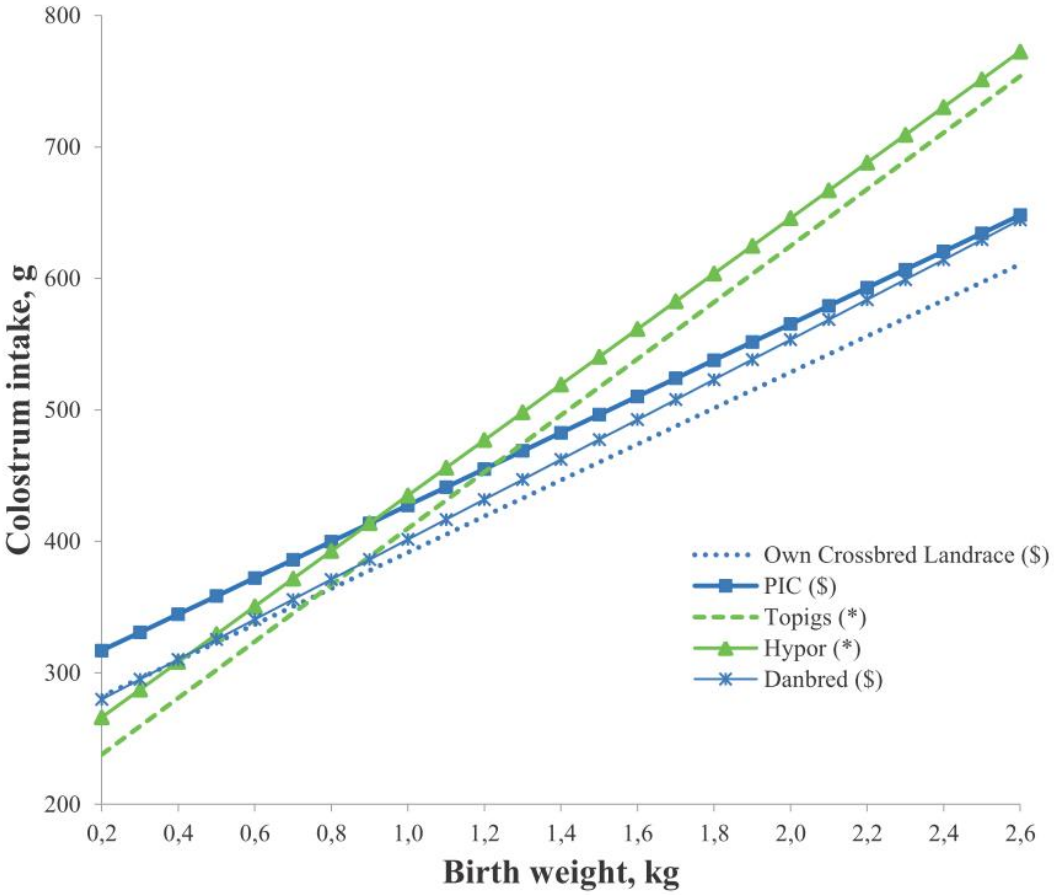
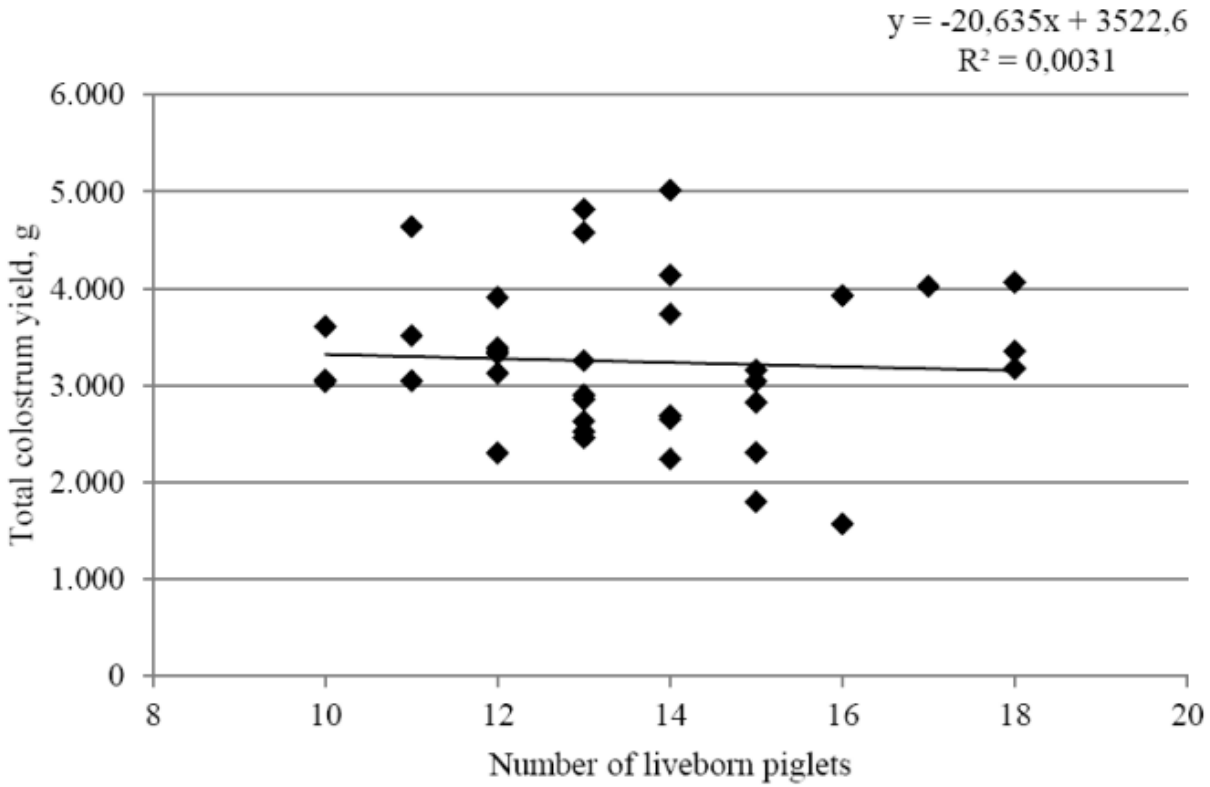
Ilse Declerck, Sows' colostrum yield and piglets' colostrum intake: a challenge in high-prolific pig production, Thesis, Ghent University, Belgium

Colostrum intake is related with birth weight



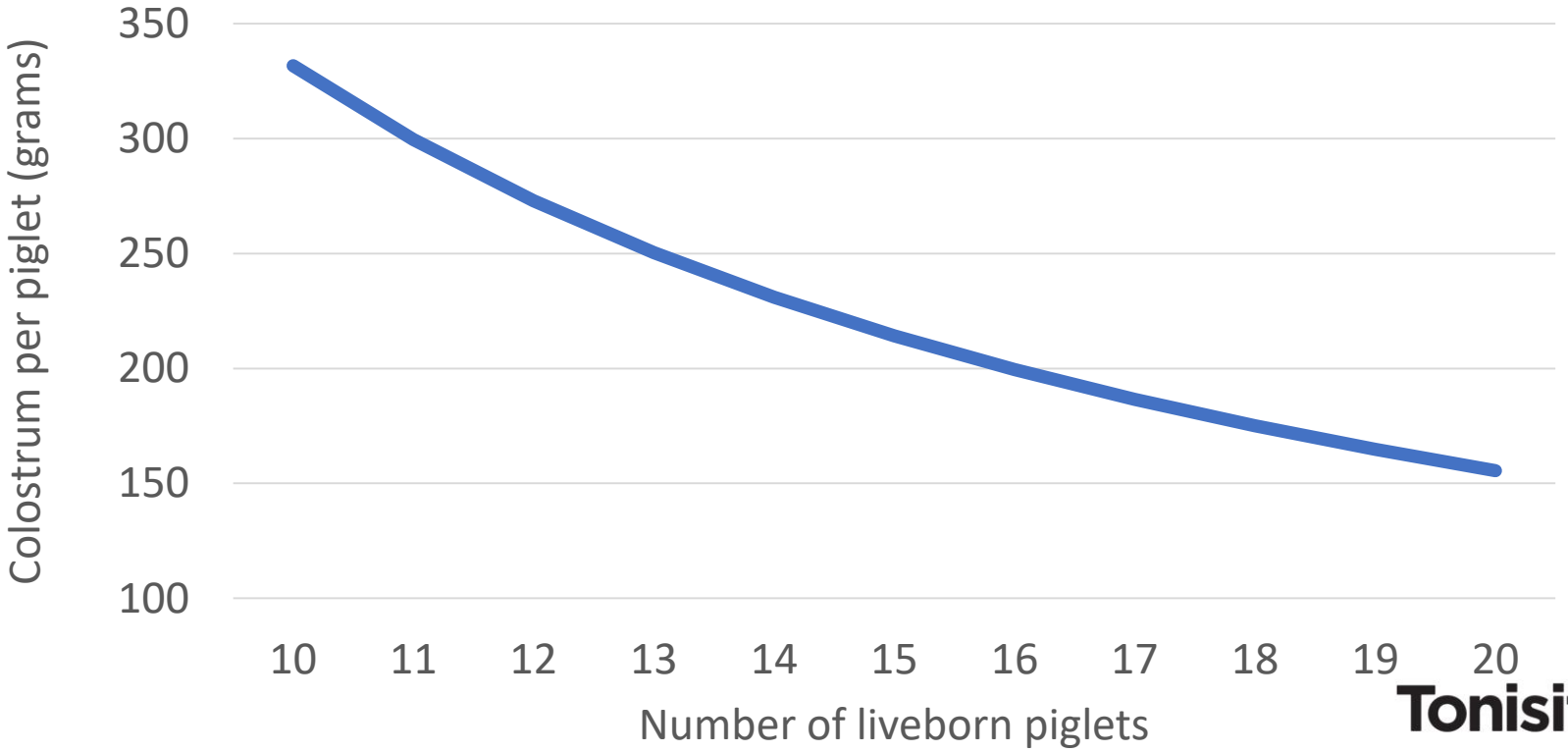
Ilse Declerck, Sows' colostrum yield and piglets' colostrum intake: a challenge in high-prolific pig production, Thesis, Ghent University, Belgium

Total colostrum yield is not associated with the number of live-born piglets



Ilse Declerck, Sows' colostrum yield and piglets' colostrum intake: a challenge in high-prolific pig production, Thesis, Ghent University, Belgium

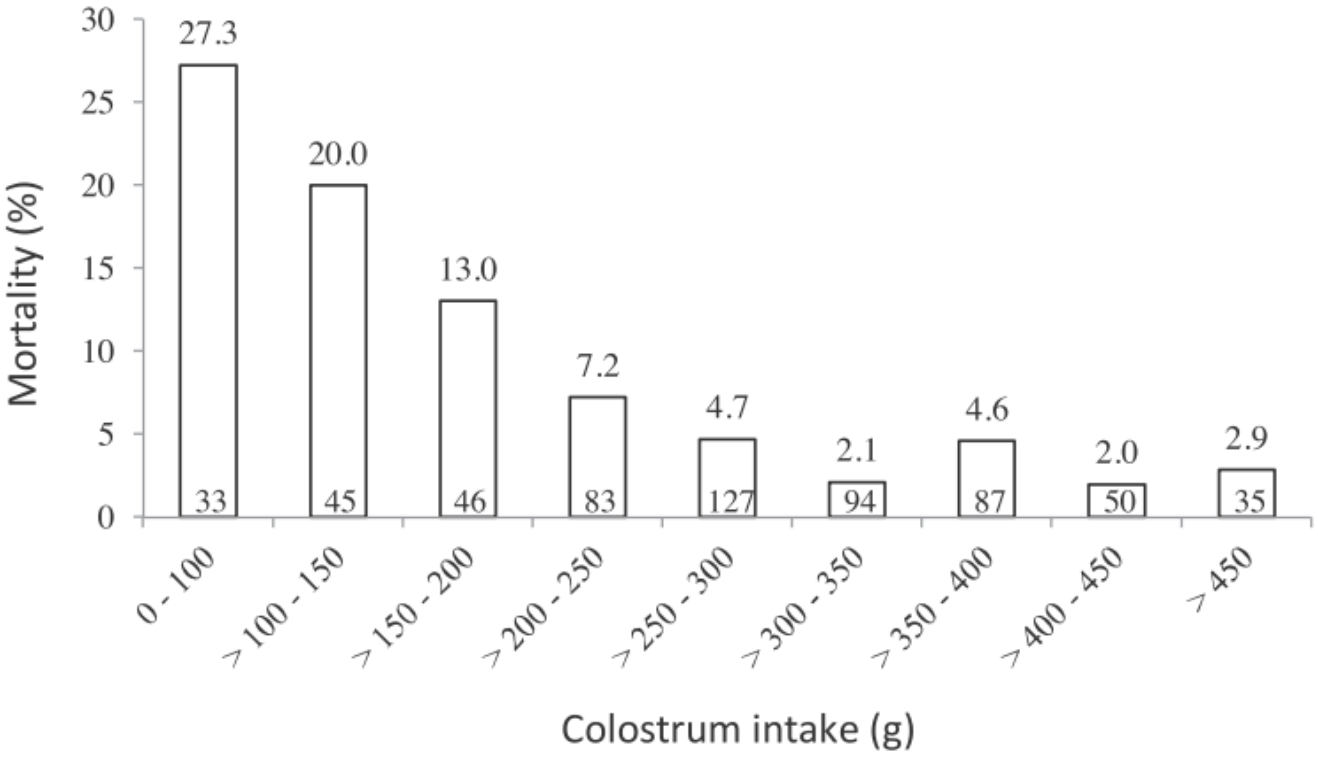
Quantity of colostrum available per piglet depending on litter size



Adapted from Ferrari et al., 2014

Mortality of piglets until 42 days of age according to colostrum intake

The numbers of piglets are shown within columns.



Ferrari et al., 2014

Development of intestinal mucosa

First Week of a Newborn Pig

- What happens in the first week of a piglet's life?
- What changes occur to the piglet's intestine?
- How can we modify or improve that?

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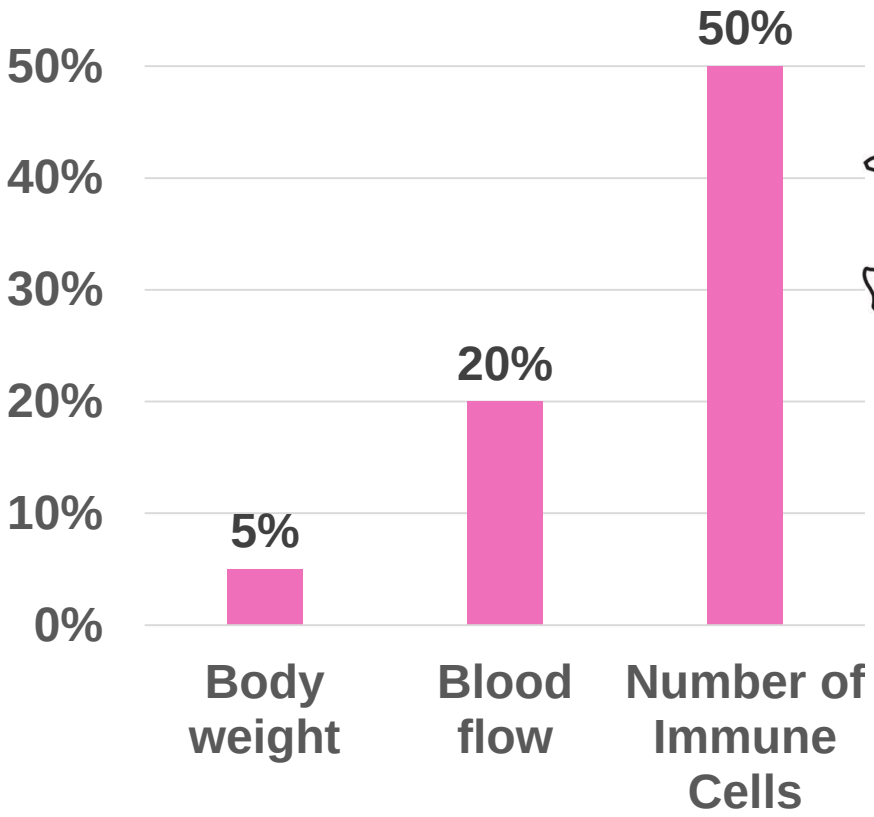
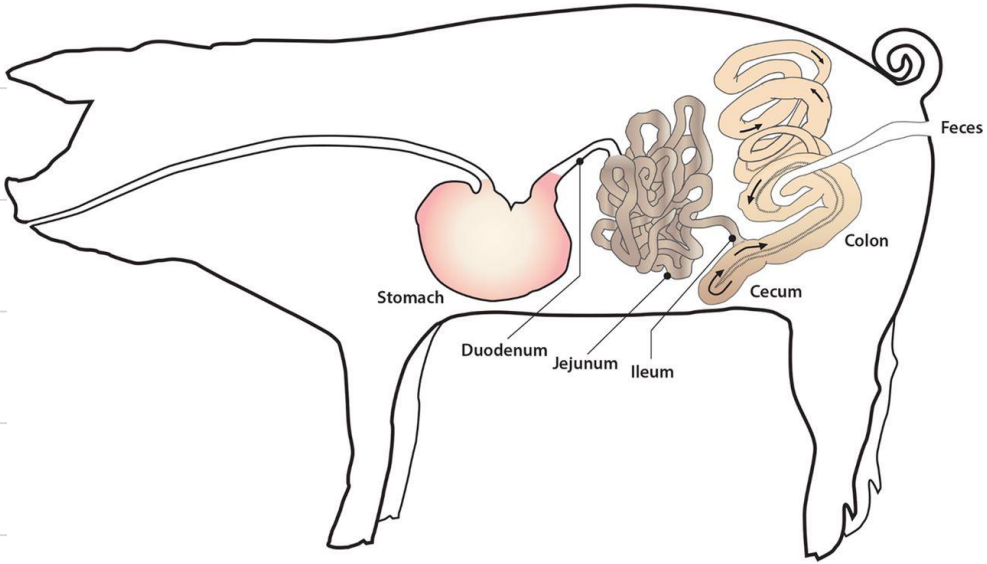
The Intestine represents…





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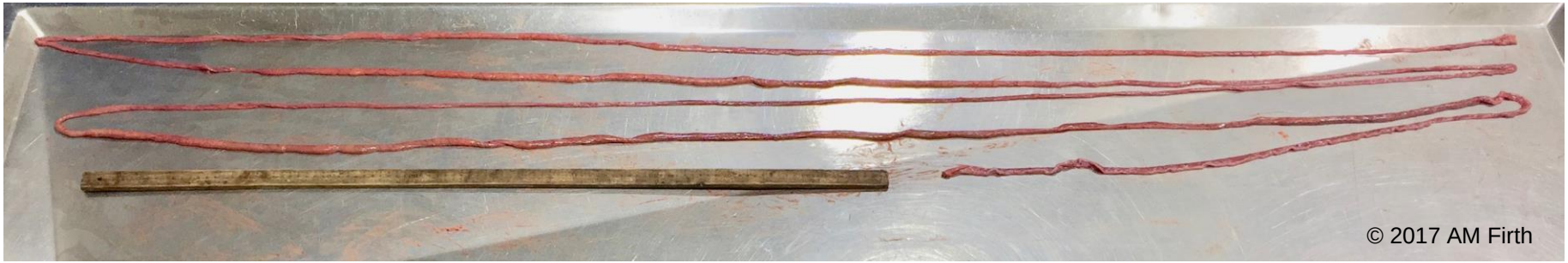
Devin B. Holman et al. mSystems 2017;2:e00004-17

Small Intestine

- At Birth: 4m long
- Number of cells doubles in 3 days
- Surface area doubles in 10 days
- By 3 weeks the length and surface area has increased 2-3 times.
- Good opportunity for **early intervention** and **support.**



Role of Enterocytes

- **Major Role**: Absorb lactose, amino acids and lipids from the colostrum and milk
- Enterocytes must have **Na** and **K** to absorb sugars and amino acids.

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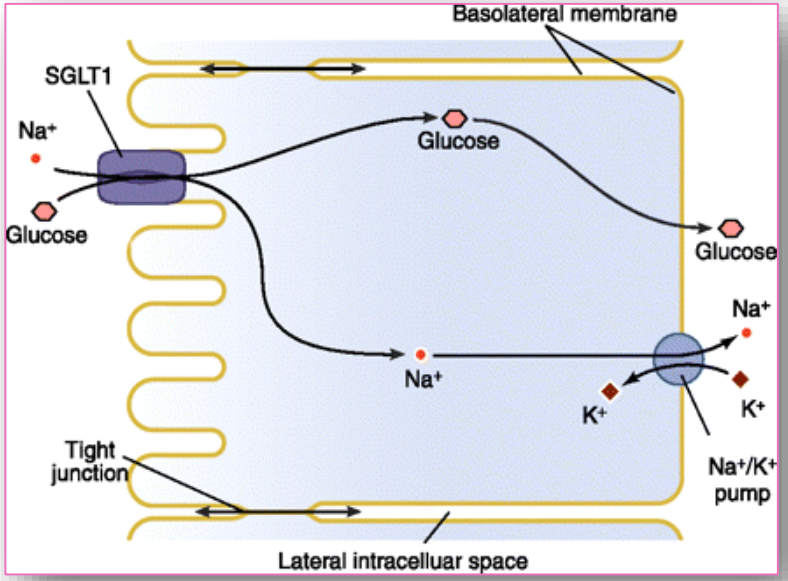
Role of Enterocytes

- There are about 150,000 gateways per enterocyte.
- These transport 4.5 billion Na molecules **per minute** per cell.



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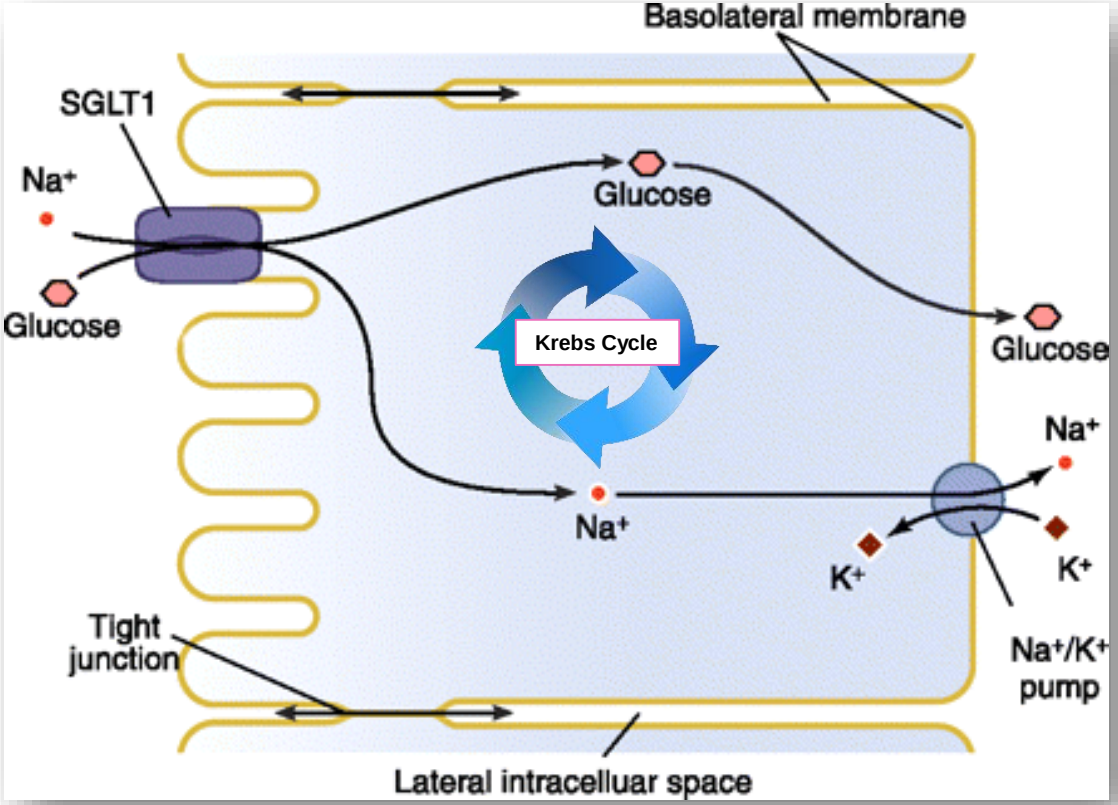
Enterocytes Need Energy Too!



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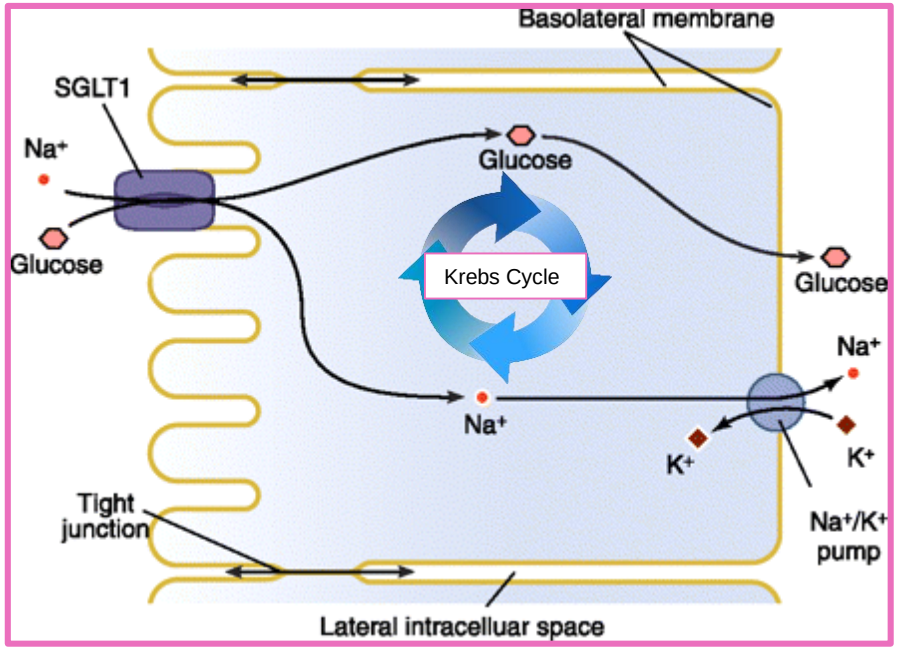
Tonisity Px: The First Isotonic Protein Solution

- Supplies Na, K, Cl, amino acids and Glucose
- Provides Fuel for the Enterocytes



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Physiologic Goals

- Feed **<u>the enterocytes</u>**
- Maintain mucosal integrity
- Support immune function
- Optimize hydration status

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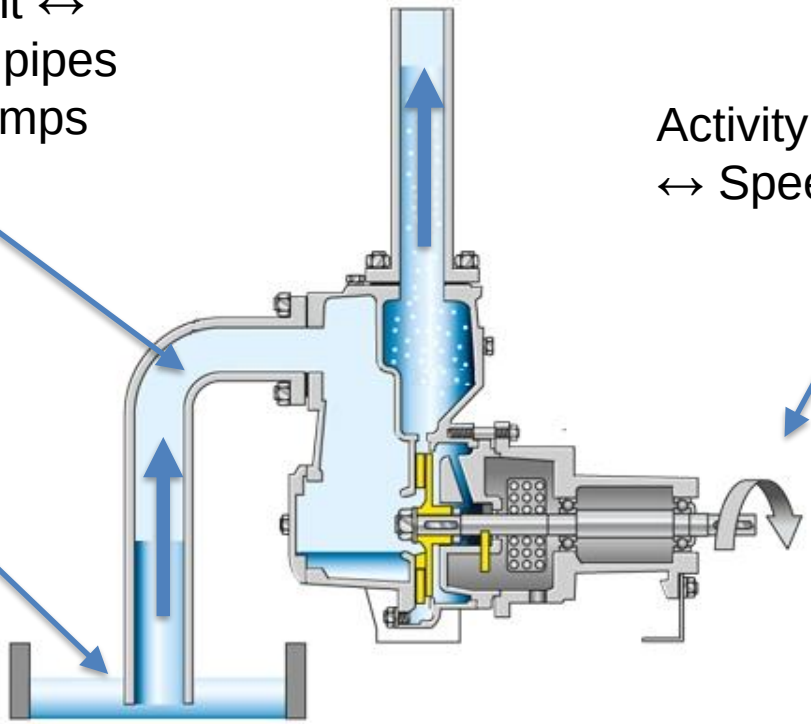
Enterocytes = pumps for nutrients

BLOOD FLOW

Villi development ↔
Diameter of the pipes
& Number of pumps

Activity of enterocytes
↔ Speed of the pump

Digestibility of milk
or feed ↔ Viscosity
of the liquid



SMALL INTESTINE

Tonisity Px

Enterocytes = pumps for nutrients

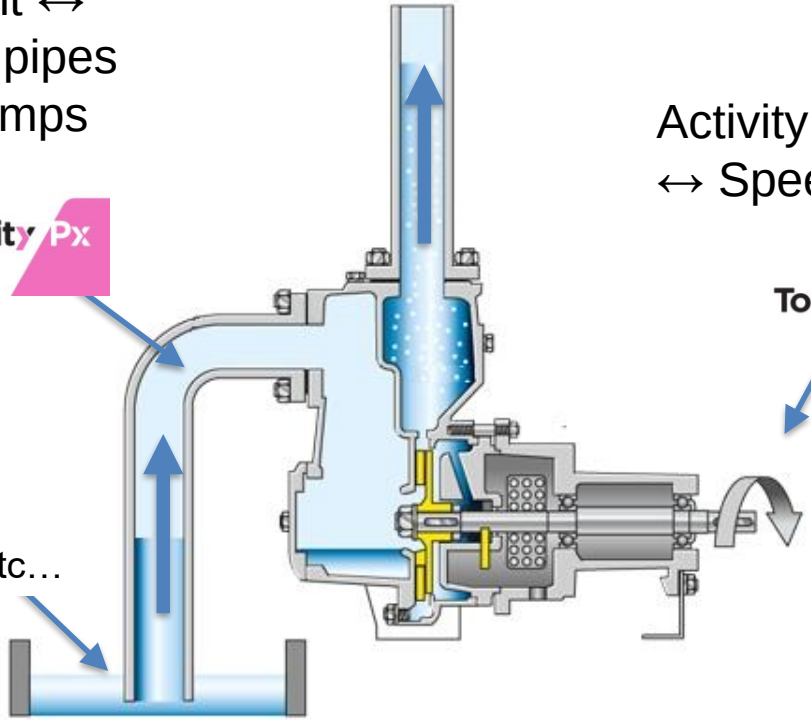
BLOOD FLOW

Villi development ↔
Diameter of the pipes
& Number of pumps

Activity of enterocytes
↔ Speed of the pump

Digestibility of milk
or feed ↔ Viscosity
of the liquid

Enzymes, acidifiers, etc…



SMALL INTESTINE

Isotonic protein drink;
Effect on Intestinal Morphology

Study: Effect of Px on Intestinal Morphology Pre-Weaning

- **Aim of Trial 16-004**
  - Determine whether Px in the first week of life had an impact on intestinal morphology

- **Materials & Methods of Pre-Weaning Study**
  - 12 sows and their litters (134 piglets)
  - Px 500 mL/litter/day on Days 2-8
  - Weaned at Day 21
  - Histopathology taken at Day 9 and Day 21

Tonisity Px

Day 2 - 8

Tonisity Px is the only product on the market that pigs will drink from a pan on Day 2 of life.

Dosage: **500 mL / litter / day**

MIXING INSTRUCTIONS

Px Powder + Water = Px Solution

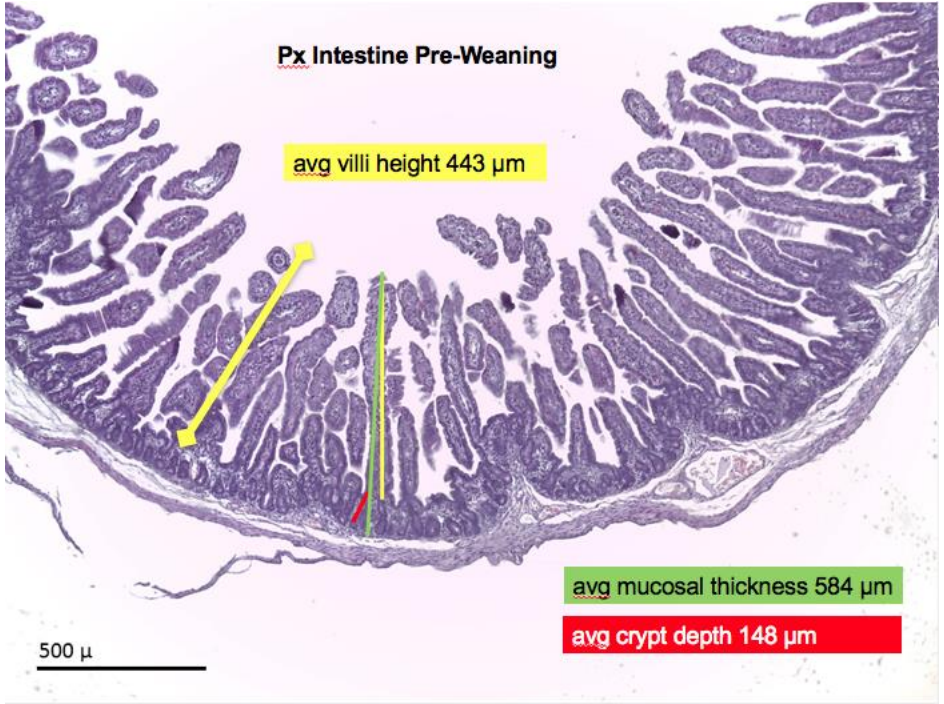
Use enclosed Tonisity International scoop to measure 2 level scoops per 10 L of water.

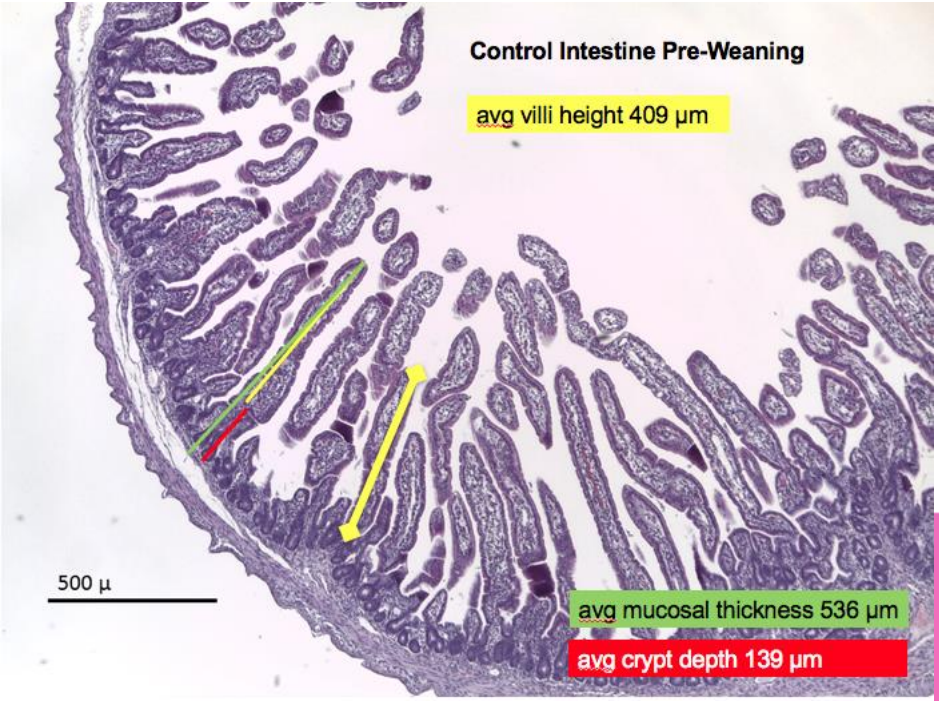
Photos: PorcMag

Tonisity Px

Histopathology Pre-Weaning

- Px villi larger by 8%
- Control





Study: Effect of Px on Intestinal Morphology of Piglets in Post Weaning Phase

- **Aim of Trial 16-003-2**
  - Part of a study that compared gruel made with Px vs. gruel made with water vs. dry creep feed.

- **Materials & Methods of Pre-Weaning Study**
  - 52 sows and their litters (608 piglets)
  - Px 500 mL/litter/day on Days 2-8
  - Pre-weaning and post-weaning gruel
  - Weaned on d19
  - Histopath at d24 and d28

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Px: A Taste Pigs Crave

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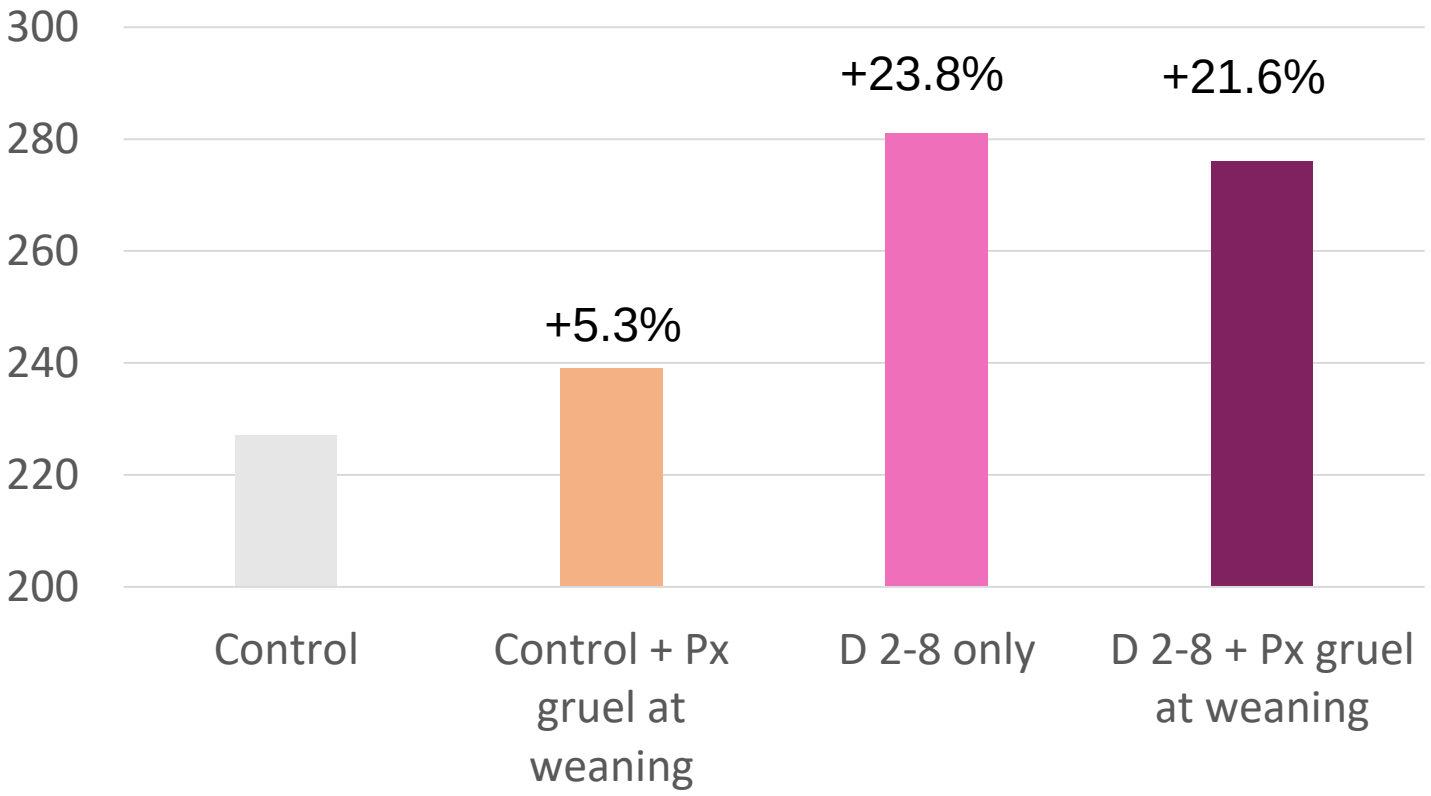
Effect of Tonisity Px on villi height (µm)



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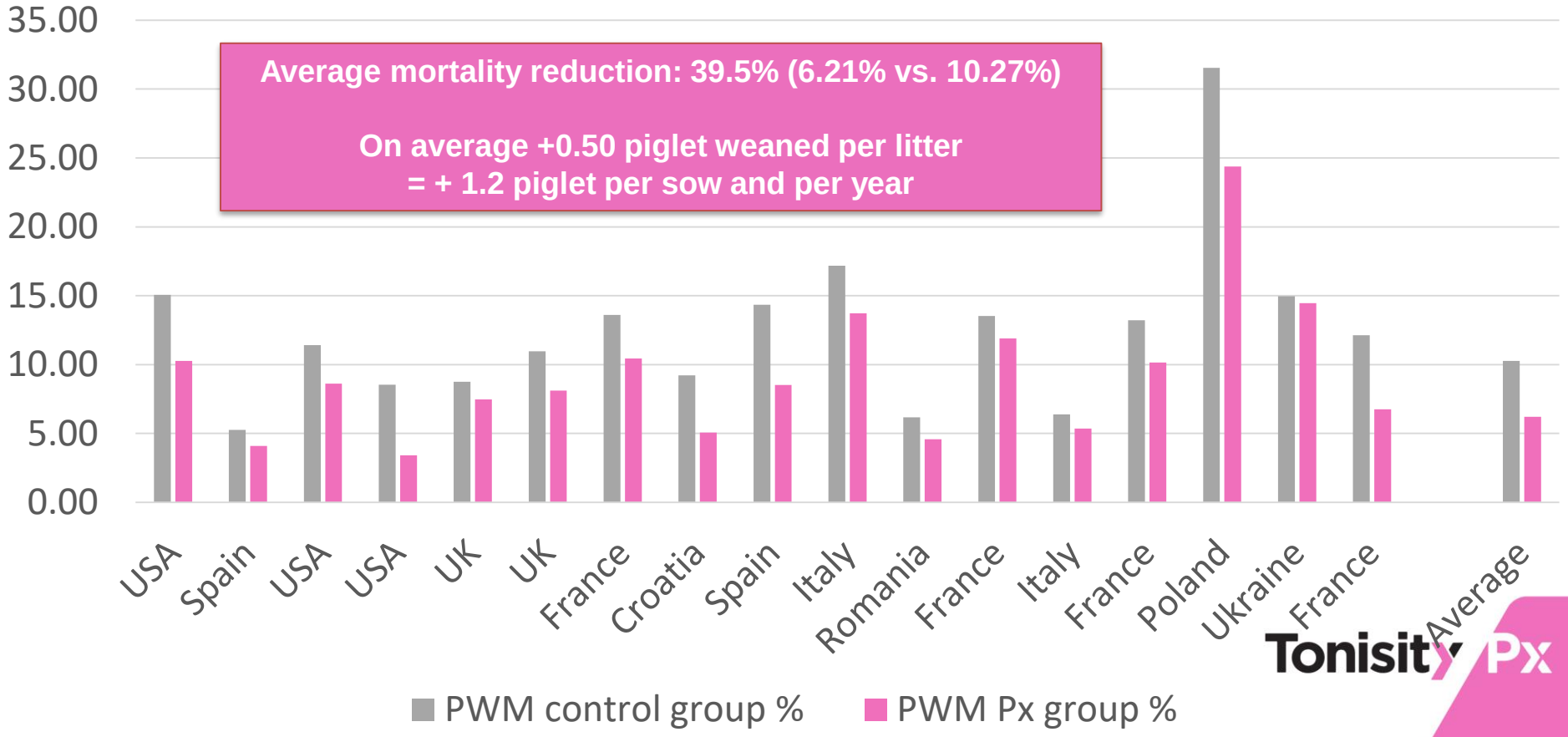
Tonisity Px:
Effect on Pre-Weaning Mortality

Meta-Analysis of Pre-Weaning Mortality

Country	Weaning age in days	Total litters in trial	Piglets/litter control	Piglets/litter Tonisity Px	PWM control %	PWM Tonisity Px %	% difference
USA	19	72	12.88	12.97	15.06	10.28	-31.8%
Spain	21	214	12.43	12.78	5.26	4.10	-22.2%
USA	21	86	11.00	11.07	11.42	8.61	-24.6%
USA	17	876	10.30	10.00	8.54	3.42	-60.0%
UK	28	73	12.05	11.89	8.74	7.48	-14.5%
UK	28	85	12.38	13.49	10.96	8.10	-26.1%
France	26	47	14.23	15.56	13.61	10.44	-23.3%
Croatia	28	36	12.02	12.03	9.22	5.07	-45.0%
Spain	21	70	13.30	13.32	14.35	8.52	-40.6%
Italy	21	23	11.64	12.75	17.19	13.73	-20.1%
Romania	28	79	13.35	13.44	6.18	4.58	-25.9%
France	28	47	13.77	13.44	13.53	11.90	-12.0%
Italy	20	80	11.75	12.15	6.38	5.35	-16.2%
France	23	26	16.21	16.42	13.22	10.15	-23.2%
Poland	27	76	16.26	15.42	31.55	24.38	-22.7%
Ukraine	28	41	17.10	17.30	14.97	14.45	-3.5%
France	21	42	14.42	14.00	12.14	6.75	-44.4%
Average	**20.8**	**1973**	**11.94**	**11.73**	**10.27**	**6.21**	**-39.5%**

Comparison of Mortality Between Tonisity Px and Control
1973 litters = 23,348 piglets in 17 trials



Average mortality reduction: 39.5% (6.21% vs. 10.27%)

On average +0.50 piglet weaned per litter
= + 1.2 piglet per sow and per year

Tonisity Px

Trial PRO-17-016A (Spain)

Effect Of Px On Mortality Depending on Birth Weight

Protocol

- Production farm in Spain (Danbred genetic)
- 37 sows (Tonisity Px group) + 33 sows (control group)
- Tonisity Px from day 2 to day 8 of life (500 ml per litter and per day) and again for the last 3 days before weaning at 21 days of age (500 ml per litter and per day).
- Piglets followed in nursery until 42 days of age
- All piglets were monitored individually during the trial

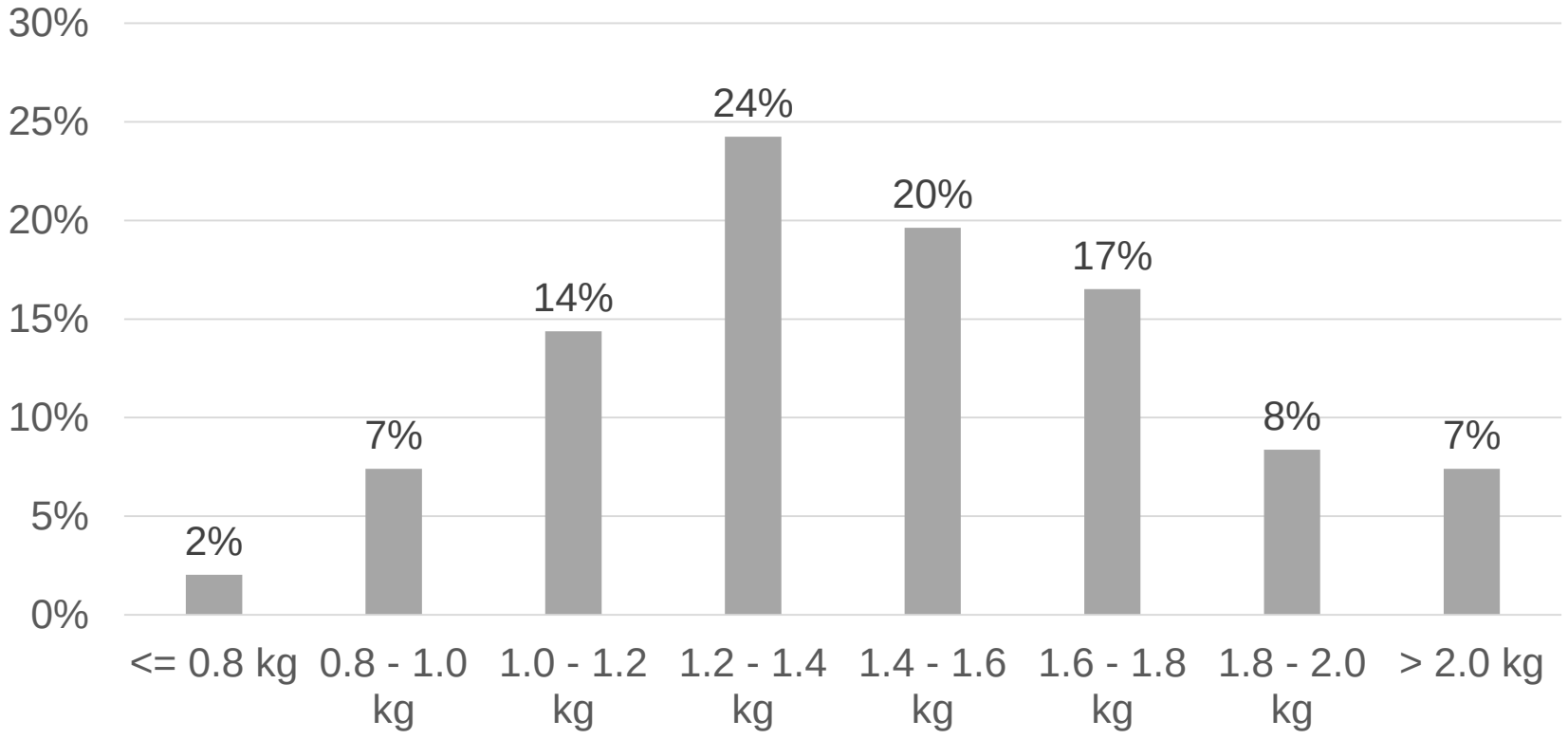
Tonisity Px

Results

	Control	Tonisity Px	Difference
Number of piglets per litter			
At D2	13.30	13.32	+ 0.16%
At weaning	11.39	12.19	+ 6.98%
Mortality D2 to weaning	14.35%	8.52%	- 40.64%
Average weight per piglet			
At D2	1.46	1.47	+ 0.71%
At weaning	5.69	5.55	- 2.44%
At 42 days of age	9.69	9.42	- 2.75%
Total weight per litter			
At D2	19.41	19.58	+ 0.87%
At weaning	64.83	67.66	+ 4.37%
At 42 days of age	100.70	109.50	+ 8.74%

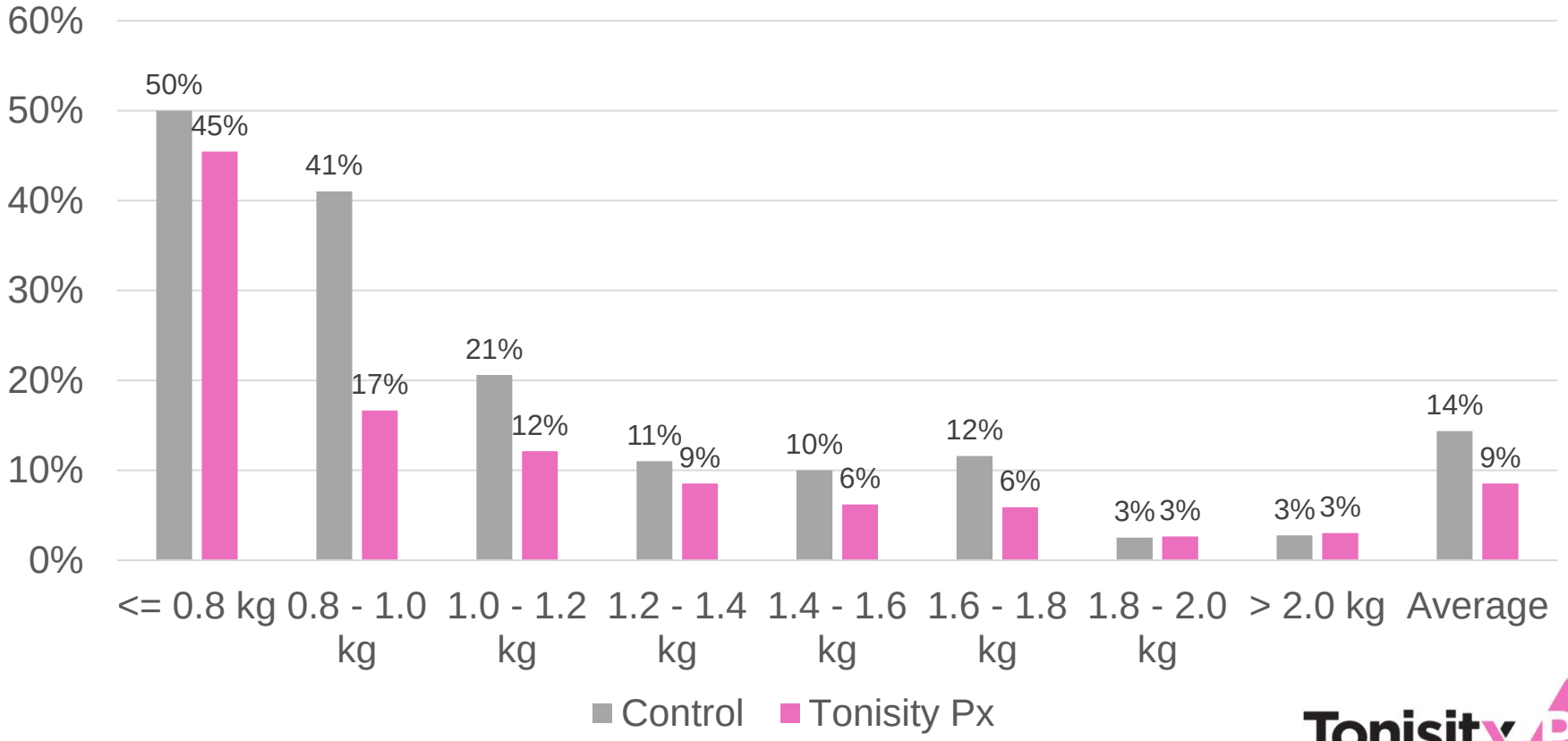
Tonisity Px

% of piglets per class of birth weight



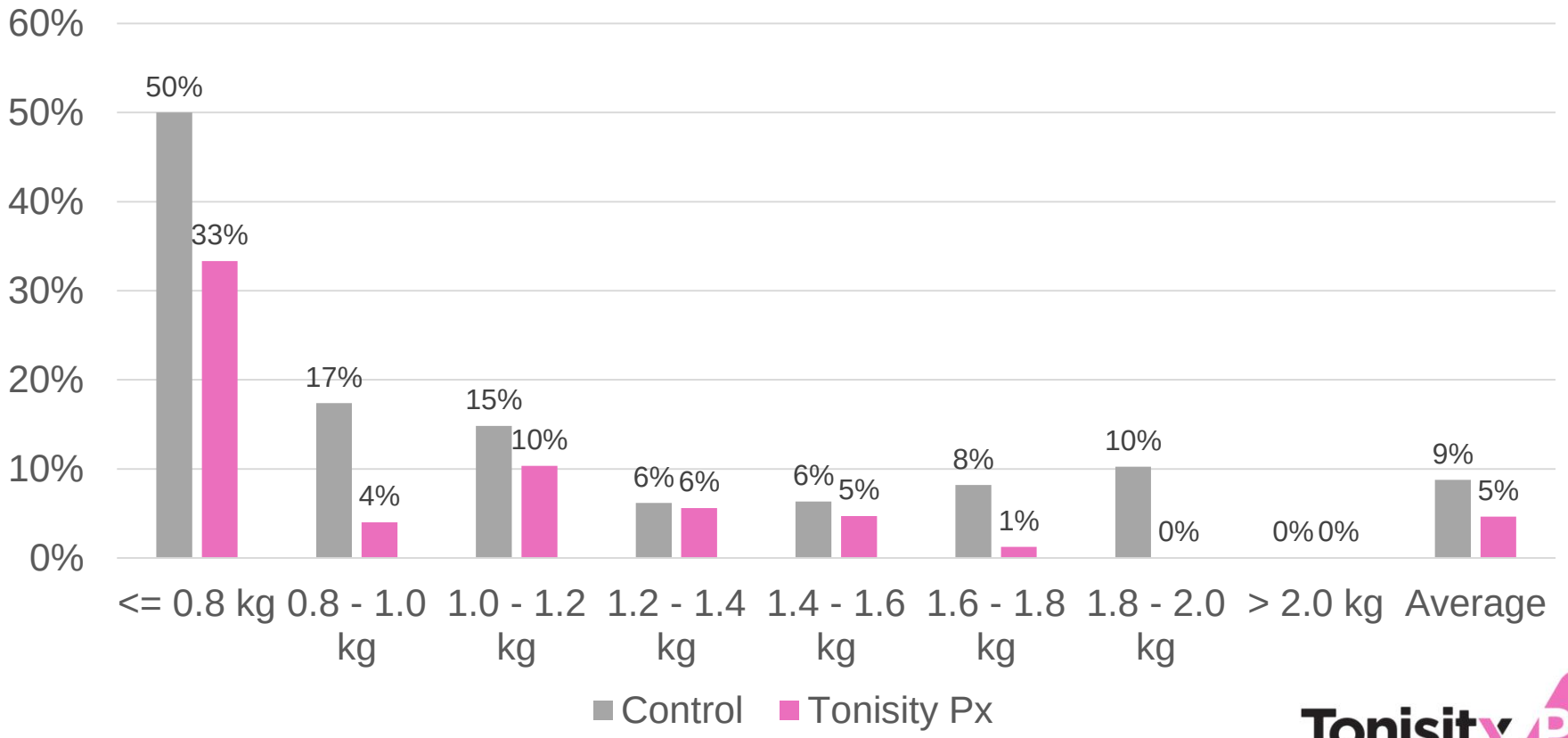
Tonisity Px

Mortality depending on birth weight: Day 2 to Weaning



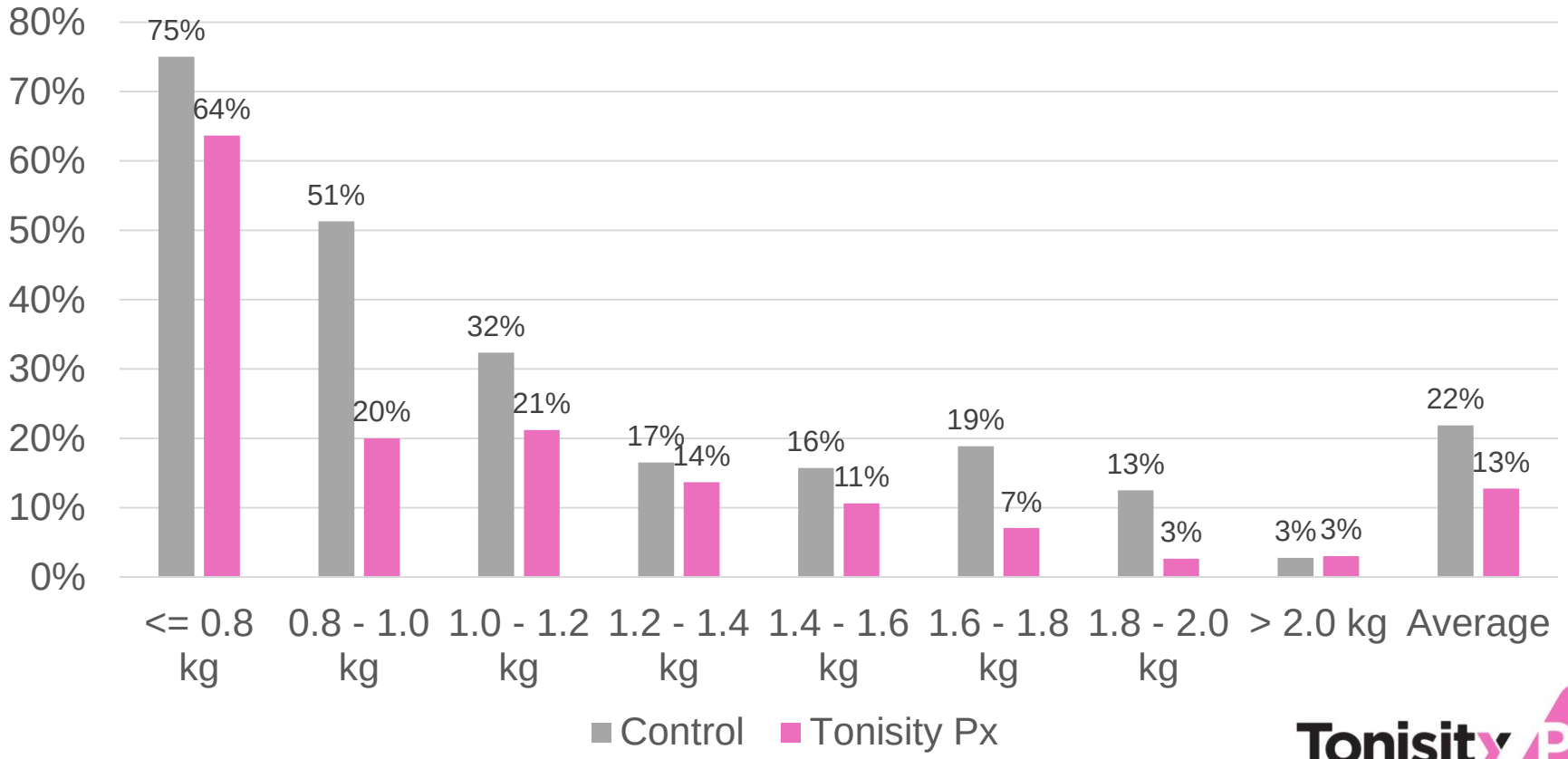
Tonisity Px

Mortality depending on birth weight: Day 21 to Day 42



Tonisity Px

Mortality depending on birth weight: Day 2 to Day 42



Tonisity Px

Trial T20 (USA)

Effect Of Px On Piglets With Scours

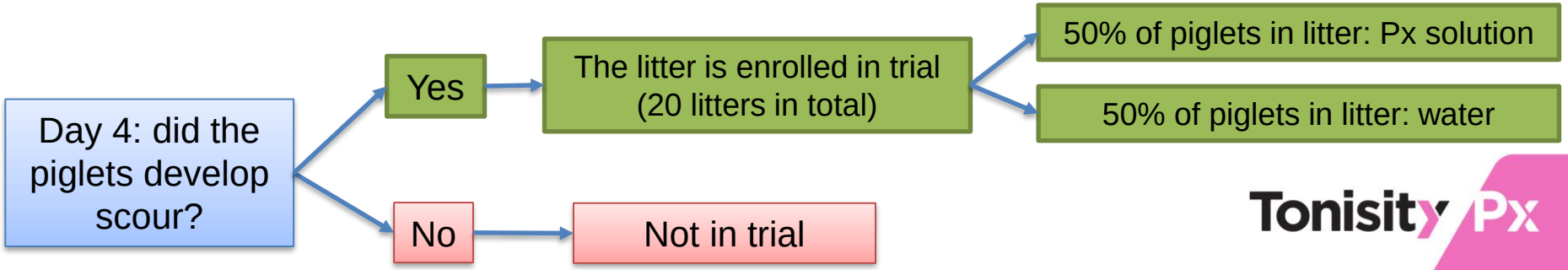
Aim of the Trial

- Evaluate the effect of Px given to suckling piglets with scours (history of E. coli and rotavirus in the farm)
  - Comparison with a control group

Tonisity Px

Protocol

- 20 litters (268 piglets) in the trial, from d4 to d18 of life
- Litters were prospectively enrolled in the study when they developed scour between 2-4 days of age
- In each litter
  - half of the piglets were given 2 x 2 ml of Px solution per day
  - half were given 2 x 2 ml of water per day
- Parameters: mortality + fall behinds = removals



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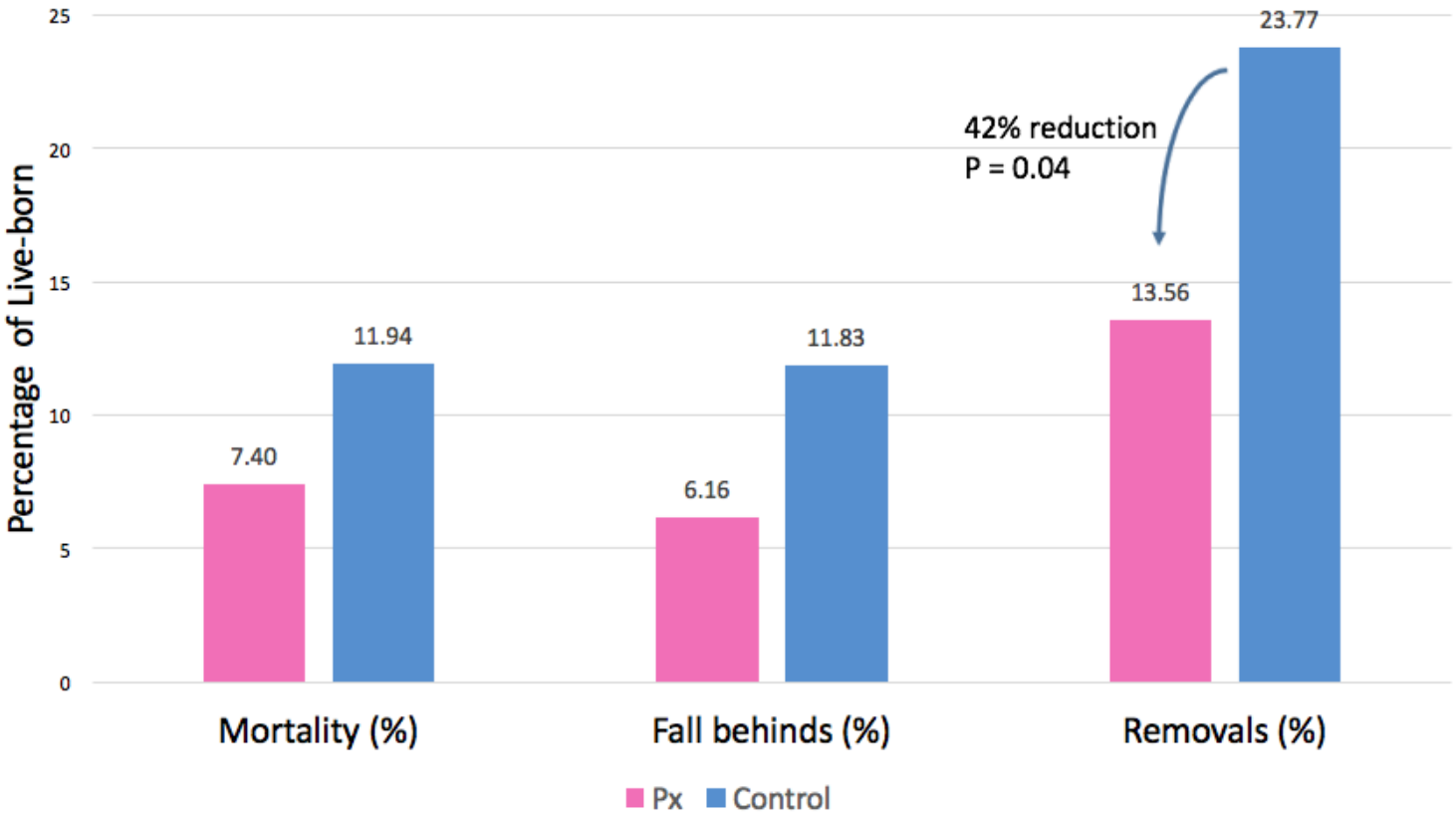
Results (T20)



Tonisity Px

Benefits of Tonisity Px in a Porcine Reproductive and Respiratory Syndrome Virus (PRRSV) Positive Farm

USA, June-August 2017

Usage of Tonisity Px in a PRRSV positive farm

PROTOCOL (farrowing house):

- 876 sows from a 14,000 sow farrowing-only farm were assigned to one of two groups, spread across 10 farrowing rooms.
- Pigs were weaned at an average age of 17 (range 14-20) days. This farm was recovering from a PRRSV outbreak at the time of this study.
- **From Day 2-8 of Age**, The Px litters received Px as a 3% solution, (500 mL per litter, per day) in an open pan. The Control group did not receive Px. Both groups had 24 hour access to the sow and clean, fresh water throughout the study.
- **Pre-Weaning/ Pre-Transport**: On the 2 days immediately pre-weaning, 3% Px solution was again given to the Px litters at the rate of 500 mL / litter/ day.

Tonisity Px

Usage of Tonisity Px in a PRRSV positive farm

RESULTS (farrowing house):

FARROWING	Tonisity Px		Control		Difference
	Number	% Mortality	Number	% Mortality	
Number of litters	480		396		
Number of pigs born alive	5,036		4,341		16.0%
Avg pigs/litter	10.5		11.0		-4.3%
1st 24 h mortality	235	4.67%	264	6.08%	-11.0%
Number of pigs alive on Day 2 post-farrowing	4,801		4,077		17.8%
Number of pigs shipped	4,637		3,729		24.3%
Total PWM (birth to wean)	399	7.92%	612	14.10%	-34.8%
On-Test PWM (day 2 to wean)	164	3.42%	348	8.54%	-52.9%

Tonisity Px

Usage of Tonisity Px in a PRRSV positive farm

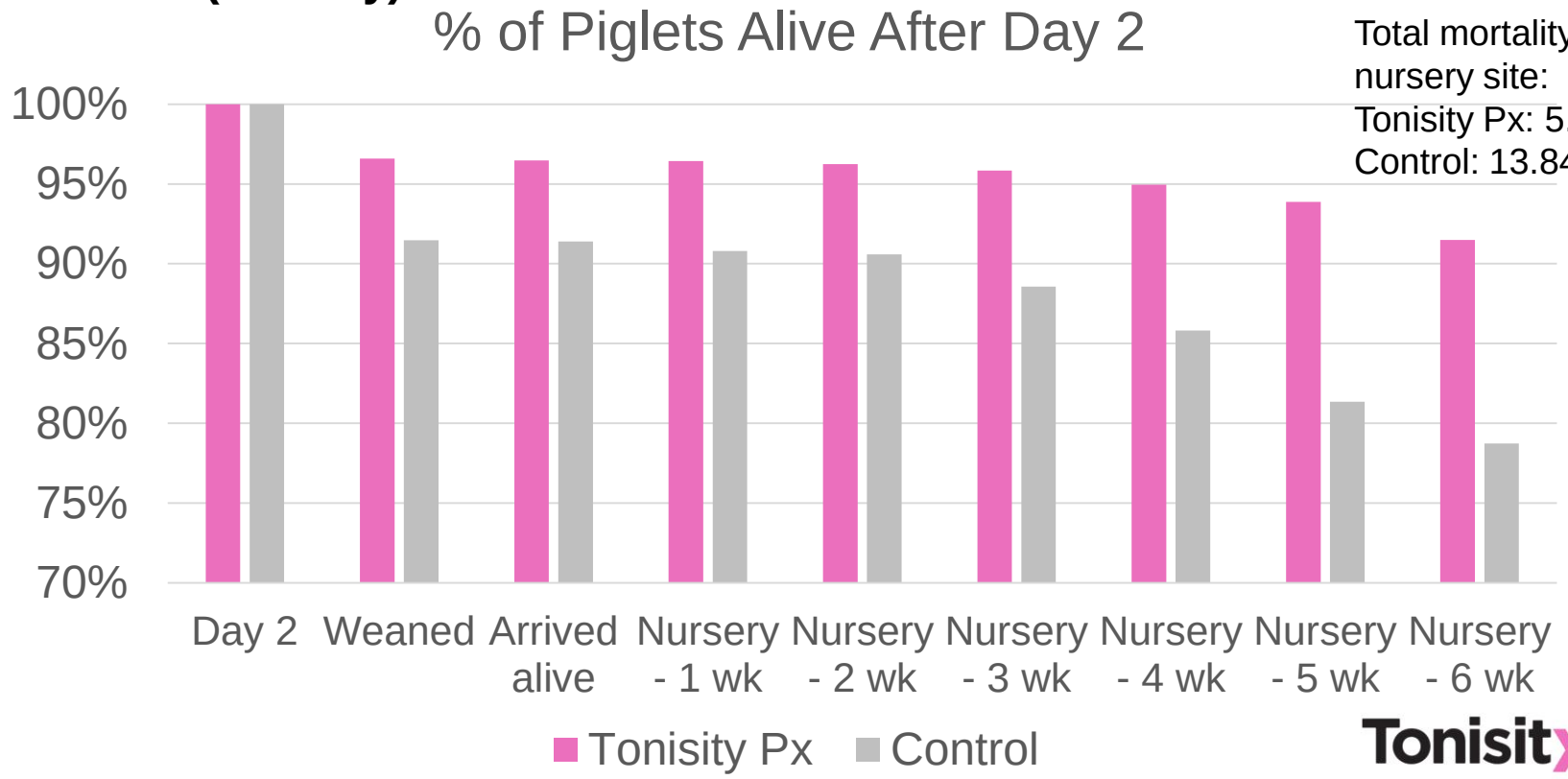
PROTOCOL (nursery):

- Control Group:
- Pigs received standard solution (energy, electrolytes, and acidification) in pans for the first 5 days. Fall-back pigs received same solution-gruel for the first 15 days. All pigs received the solution in their water lines.
- Px group:
- Nursery day 1 - All Px pigs (healthy + fall-behinds) received 3% Px solution, 75 ml/pig, 3 times per day (time of arrival, arrival + 1 h, and arrival + 4 h).
- Nursery day 2 - All Px pigs received 3% Px solution (75 ml/pig) twice, 4-6 hrs apart.
- Nursery day 3 - Px solution was discontinued for normal pigs. Fall-behinds were switched from Px solution to Px-gruel (200 grams per pig).
- Nursery day 4 and 5 – same as day 3, Px-gruel was given to fall-behind pigs only (200 grams per pig).
- All pigs had their usual food available ad lib.

Tonisity Px

Usage of Tonisity Px in a PRRSV positive farm

RESULTS (nursery):



Total mortality at nursery site:
Tonisity Px: 5.18%
Control: 13.84%

Tonisity Px

Usage of Tonisity Px in a PRRSV positive farm

EXTRA COSTS *		EXTRA INCOME		
Number of piglets at D2	4801	FARROWING: Expected losses based on control mortality (D2-weaning) @ 8.54%	410	piglets
Cost of Tonisity Px, USD/piglet	0.58	FARROWING: Actual losses with mortality (D2-weaning) @ 3.42%	164	piglets
Cost of extra labour USD/piglet	0.16	Value of 246 (= 410-164) pigs @ $29/head	7,134	USD
Total Cost, USD/piglet	0.74	NURSERY: Expected losses based on control mortality of 13.85%	641	piglets
		NURSERY: Actual losses with mortality of 5.18%	240	piglets
		Value of 401 (= 641-240) pigs @ $45/head	18,045	USD
Total Cost, USD	**3,573.50**	**Total Extra Income**	**25,179**	**USD**

ROI = $25,179 / $3,573.50 = 7.05

Tonisity Px

*The costs of supplying the standard electrolyte solution in control group are not calculated

Summary of European Trials

January – July 2017

Summary of European Commercial Trials January to June 2017

Farm location	Weaning age (days)	Number of litters		Piglets/litter on Day 2			Piglets/litter at weaning			Mortality Day 2 to weaning (%)		
		Control	Tonisity Px	Control	Tonisity Px	Difference (%)	Control	Tonisity Px	Difference (%)	Control	Tonisity Px	Difference (%)
France	26	31	16	14.23	15.56	9.40%	12.29	13.94	13.40%	13.61	10.44	-23.25%
Croatia	28	18	18	12.02	12.03	0.08%	10.94	11.44	4.57%	9.22	5.07	-45.01%
Italy	21	12	11	11.64	12.75	9.57%	9.64	11.00	14.15%	17.19	13.73	-20.14%
Romania	28	40	39	13.35	13.44	0.64%	12.53	12.82	2.36%	6.18	4.58	-25.88%
France	28	22	25	13.77	13.44	-2.42%	11.91	11.84	-0.58%	13.53	11.90	-12.02%
Italy	20	40	40	11.75	12.15	3.40%	11.00	11.50	4.55%	6.38	5.35	-16.19%
France	23	14	12	16.21	16.42	1.25%	14.07	14.75	4.82%	13.22	10.15	-23.18%
Poland	27	38	38	16.26	15.42	-5.17%	11.13	11.66	4.76%	31.55	24.38	-22.71%
Ukraine	28	20	21	17.10	17.30	1.17%	14.54	14.80	1.79%	14.97	14.45	-3.47%
France	21	24	18	14.42	14.00	-2.89%	12.67	13.06	3.07%	12.14	6.75	-44.43%
Average	**25.2**			**14.04**	**14.08**	**0.24%**	**12.01**	**12.49**	**3.94%**	**13.78**	**10.81**	**-21.55%**
Number of piglets	**6987**	**3637**	**3350**	**3637**	**3350**		**3111**	**2972**				

Summary of European Commercial Trials
January to June 2017

Farm location	Weaning age (days)	Number of litters		Piglets/litter on Day 2		Average Piglet weight on Day 2 (kg)			Piglets/litter at weaning		Average Piglet weight at weaning (kg)			
		Control	Tonisity Px	Control	Tonisity Px	Control	Tonisity Px	Difference (%)	Control	Tonisity Px	Control	Tonisity Px	Difference	
													grams	%
Croatia	28	18	18	12.02	12.03	1.38	1.37	-0.13%	10.94	11.44	7.26	7.09	-164	-2.26%
Italy	21	12	11	11.64	12.75	1.42	1.40	-1.03%	9.64	11.00	5.73	5.81	81	1.41%
Romania	28	40	39	13.35	13.44	1.32	1.33	0.58%	12.53	12.82	7.18	7.93	757	10.55%
France	28	22	25	13.77	13.44	N.A.	N.A.	N.A.	11.91	11.84	8.24	8.80	561	6.81%
Italy	20	40	40	11.75	12.15	N.A.	N.A.	N.A.	11.00	11.50	5.32	5.48	160	3.01%
Poland	27	38	38	16.26	15.42	1.40	1.41	1.07%	11.13	11.66	6.41	6.81	400	6.24%
Ukraine	28	20	21	17.10	17.30	1.32	1.26	-4.55%	14.54	14.80	7.55	7.56	10	0.13%
Average	**25.7**			**13.80**	**13.81**	**1.36**	**1.36**	**-0.37%**	**11.73**	**12.17**	**6.71**	**7.07**	**360**	**5.37%**
Number of piglets	**5275**	**2623**	**2652**	**2623**	**2652**	**1850**	**1830**		**2229**	**2337**	**2229**	**2337**		

Commercial Trial France May 2017

Table 1: Live Weight (kg) of Pigs Post-Weaning

Age	Tonisity Px	Control	Difference	%
21 days	6.67	5.90	0.77	13.1%
28 days	7.39	6.46	0.93	14.4%
35 days	9.61	8.46	1.15	13.6%
42 days	12.89	11.64	1.25	10.7%
49 days	16.18	14.93	1.25	8.4%

Table 2: Weekly Feed Intake (kg) of Pigs Days 21 – 49

Period	Tonisity Px	Control	Difference	%
D21 - 28	0.89	0.67	0.22	32.8%
D28 - 35	2.53	2.24	0.29	12.9%
D35 - 42	4.05	3.90	0.15	3.8%
D42 - 49	5.31	5.27	0.04	0.8%

88 piglets as control and 176 piglets in Px group.

Piglets received Tonisity from D2-8 and around weaning. Weaning at D21.

Piglets were weighed once a week in nursery and feed intake was recorded.

Tonisity Px

Commercial Trial Ukraine April 2017

TABLE 4: LIVE WEIGHTS (KG) OF PIGS POST-WEANING

Age	Tonisity Px	Control	Difference	%
28 Days	7.56	7.55	0.01	0.13%
75 Days	33.12	31.53	1.59	5.04%

291 piglets as control and 311 piglets in Px group.

Piglets received Px from D2- 8 and around weaning.

Weaning at 28 days.

Tonisity Px

Tonisity Px - Directions for Use:

Feeding Rates Vary with Live Weight (LW) and Litter Sizes		
Stage	Time Frame	Quantity
Suckling	2-8 Days Old	500 mL / Litter / Day
Suckling-Weaning	2-3 Days Pre-Weaning	500 mL / Litter / Day
	1 Day Pre-Weaning to 2 Days Post-Weaning	Mix 1.5 L Px™ + 1 kg dry feed, then feed ~ 200g / Pig / Day
Transport	Weaned Pigs	1 L Px™ per 25 pigs, on arrival
	Slaughter Pigs	1 L Px™ per 100 kg LW, prior to transport

Mix 310g (2 level 155g scoops) of Tonisity Px™ (Px) with 10 litres of fresh water to make a 3% liquid Px™ solution. For best results, add Px™ powder to the water and stir until dissolved. Make fresh Px™ daily and use clean feeder pans for delivery.

Questions??

Tonisity Px

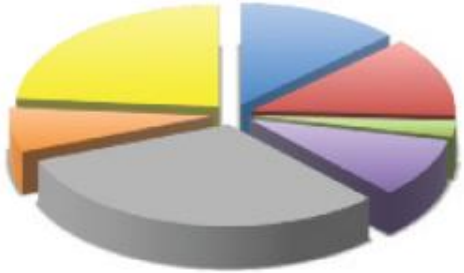
Additional slides

Causes of pre-weaning mortality day 0-4 and later found by autopsy of 1,364 dead suckling piglets collected over one week from 30 Danish farms

Day 0-4

Crushed	46.6%
Nutrition	19.5%
Weak born	18.5%
Enteritis	5.1%
septicaemia	2.6%
Malformation	1.7%
Other	5.2%

Day 5›



Crushed	13.0%
Nutrition	12.7%
Arthritis	2.7%
Enteritis	9.5%
septicaemia	31.3%
Hernia	7.1%
Other	23.7%

adapted from Frandsen & Haugegaard, SEGES, 2017

Tonisity Px

Growth performance data (kg) from high- (HW) and low- (LW) birthweight pigs

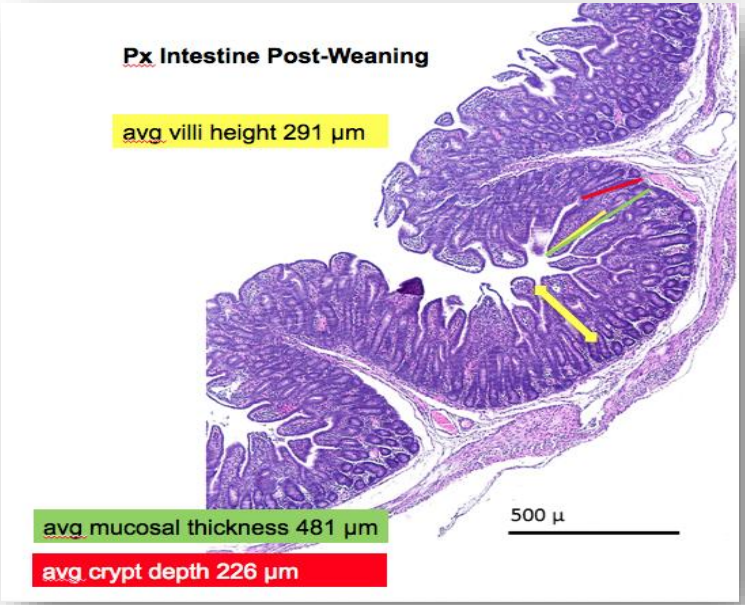
Parameter	Weight group		s.e.m.	*P*-value
	HW ($n = 112$)	LW ($n = 98$)		
Birthweight	1.93	1.09	0.019	–
Weaning weight	7.63[a]	4.97[b]	0.256	<0.01
Weight at 63 days	28.35[a]	21.75[b]	0.553	<0.01
Weight at 104 days	67.41[a]	57.56[b]	0.955	<0.01
Weight at 150 days	106.94[a]	99.19[b]	0.910	<0.01

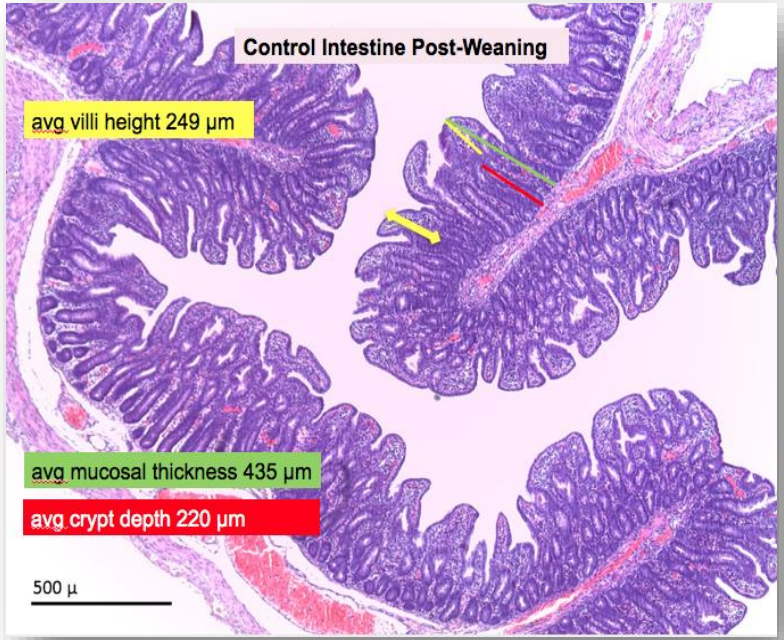
a,b: Within a row, least-square means without a common superscript differ significantly

Intra-uterine growth retardation affects birthweight and postnatal development in pigs, impairing muscle accretion, duodenal mucosa morphology and carcass traits. Alvarenga et al., 2012

Tonisity Px

Histopathology: Jejunum from Px Group Post - Weaning





Tonisity Px

Histopathology

	Villi height (µm)	Crypt depth (µm)	Villus height/ crypt depth ratio	Intestinal mucosal thickness (µm)
Day 2-8				
Px	443 [b]	148 [a]	3.6 [a]	584 [a]
Control	409 [a]	139 [a]	3.6 [a]	536 [a]
Difference	+ 8.3%	+ 6.5%	0%	+ 9.0%
P-value	<0.001	0.199	0.962	0.087
Day 2-8 + Gruel at Weaning				
Px	291 [d]	226 [c]	1.4 [d]	481 [d]
Control	249 [c]	220 [d]	1.2 [c]	435 [c]
Difference	+ 16.8%	+ 2.7%	+ 16.7%	+ 10.6%
P-value	0.003	0.512	0.018	0.033

Study 16-003: Effect of Px on Piglets At Weaning

52 litters, Px 500 mL/litter/day, Days 2-8
Px-Gruel or Water-Gruel or Dry Creep around weaning at D19

% of Pigs with positive ADG In The First Week Post-weaning by Feed Type (Number Of Piglets And %)

	Px-gruel	Water-gruel	Dry creep
ADG >0	$170^{a\ t}$ (86%)	139^{b} (77%)	$113^{ab\ t}$ (78%)

[a, b] Different superscripts in same row indicate statistical difference of P<0.05

[t] Superscript indicates tendency towards statistical difference between groups in the same row, P<0.10

Tonisity Px

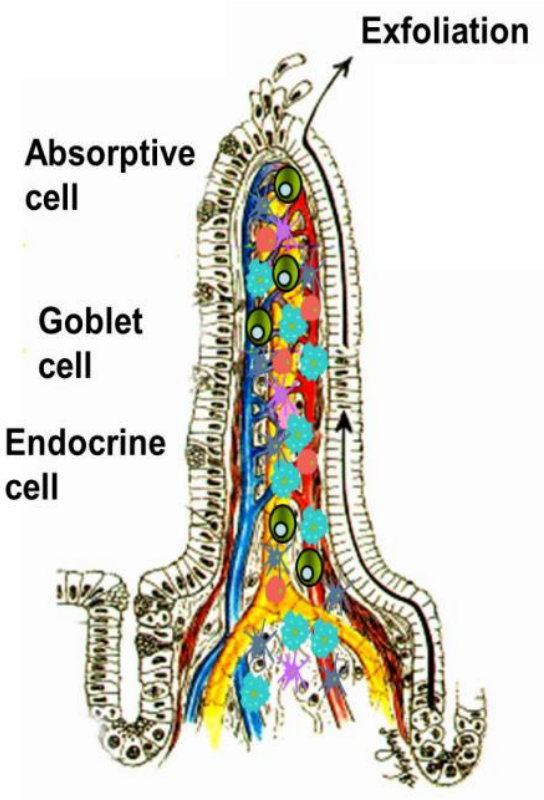
Study 16-003: Effect of Px on Piglets At Weaning

Pigs with Positive ADG In The First Week Post-weaning (by Feed Type and Weight Class) (Number Of Piglets And %)

Weight of piglets		Px-gruel	Water-gruel	Dry creep
Heavy (>5.8 kg)	ADG >0	26 (70%)	34 (69%)	29 (76%)
Medium	ADG >0	**88[a] (88%)**	74[ab] (81%)	51[b] (75%)
Light (<4.1 kg)	ADG >0	**56[a] (92%)**	31[b] (78%)	33[ab] (87%)

Tonisity Px

Why is it important?



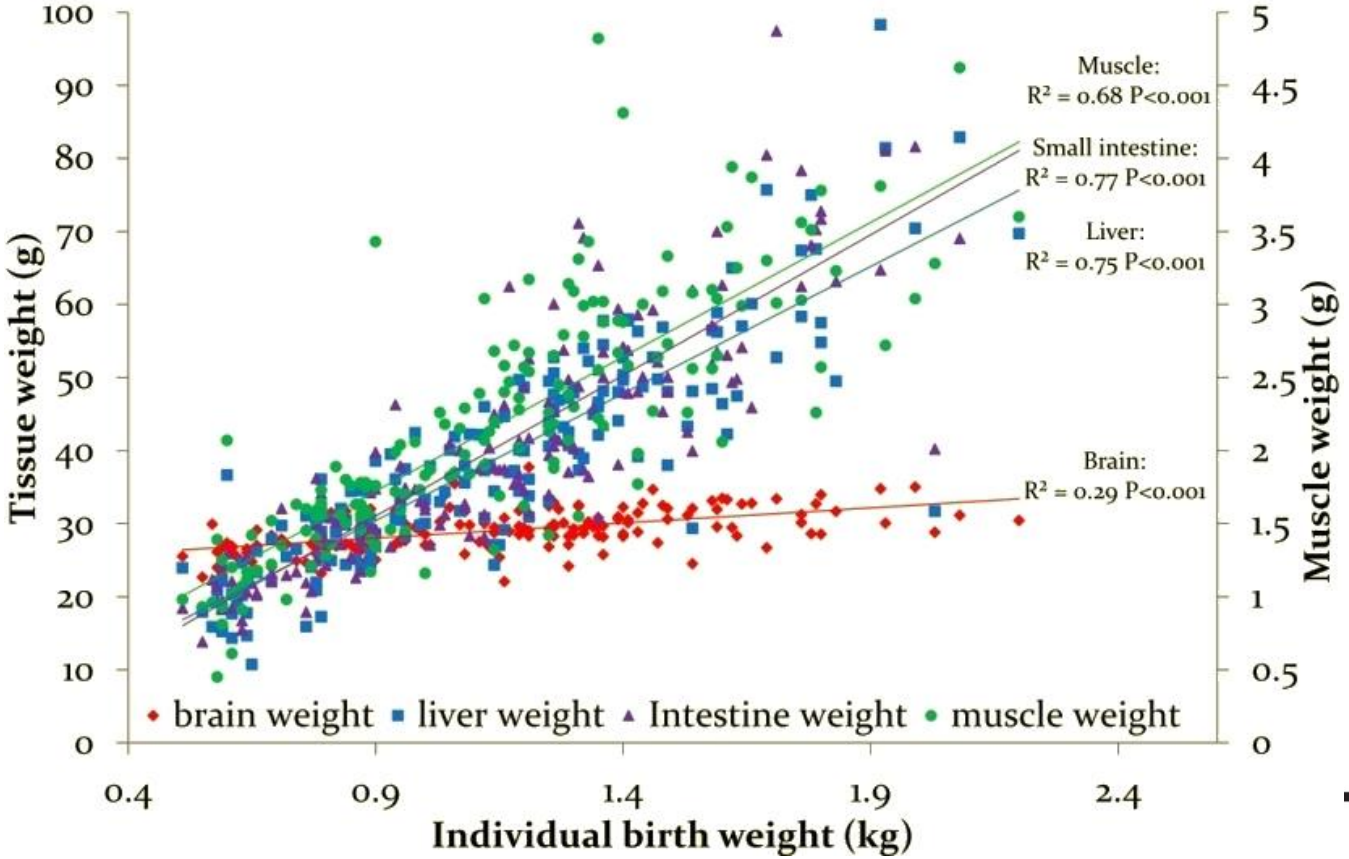
Tonisity Px

From a Liquid Supplement

To a Soluble Powder Formula

Tonisity Px

Effect of birth weight on organ development



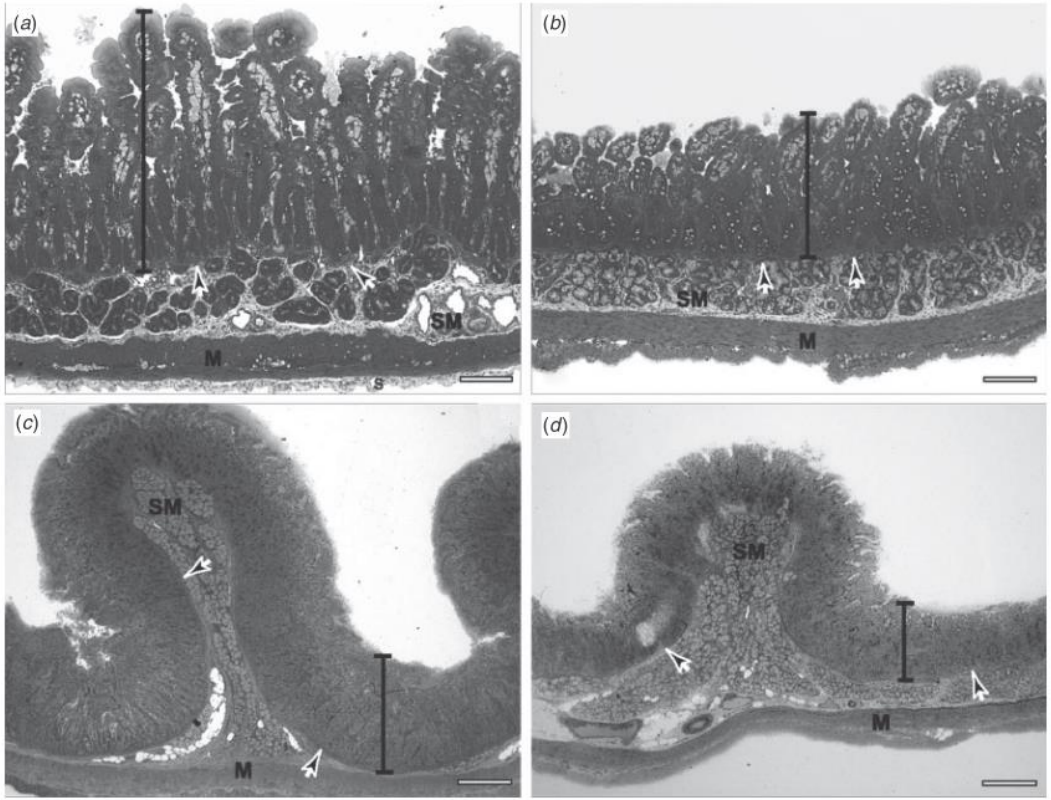
Source: Miranda Smit, University of Alberta, Saskatchewan Pork Industry Symposium 2012

Small intestine development of high- (HW) and low- (LW) birthweight pigs

high-birthweight low-birthweight

Newborn pigs

150-day-old pigs



Photomicrographs of the duodenal mucosa of (a) high- and (b) low-birthweight newborn and (c) high- and (d) low-birthweight 150-day-old pigs, comparing the differences in the height of the intestinal mucosa (vertical bar). Observe the muscularis mucosa (arrowheads), submucosa (SM), muscular layers (M) and serosa (S). Toluidine blue–sodium borate staining. Bars represent: (a) and (b), 180 mm; (c) and (d), 550 mm.

Alvarenga et al., 2012

Tonisity Px