Bones & Lameness – The Importance of Vitamin D and Ca/P

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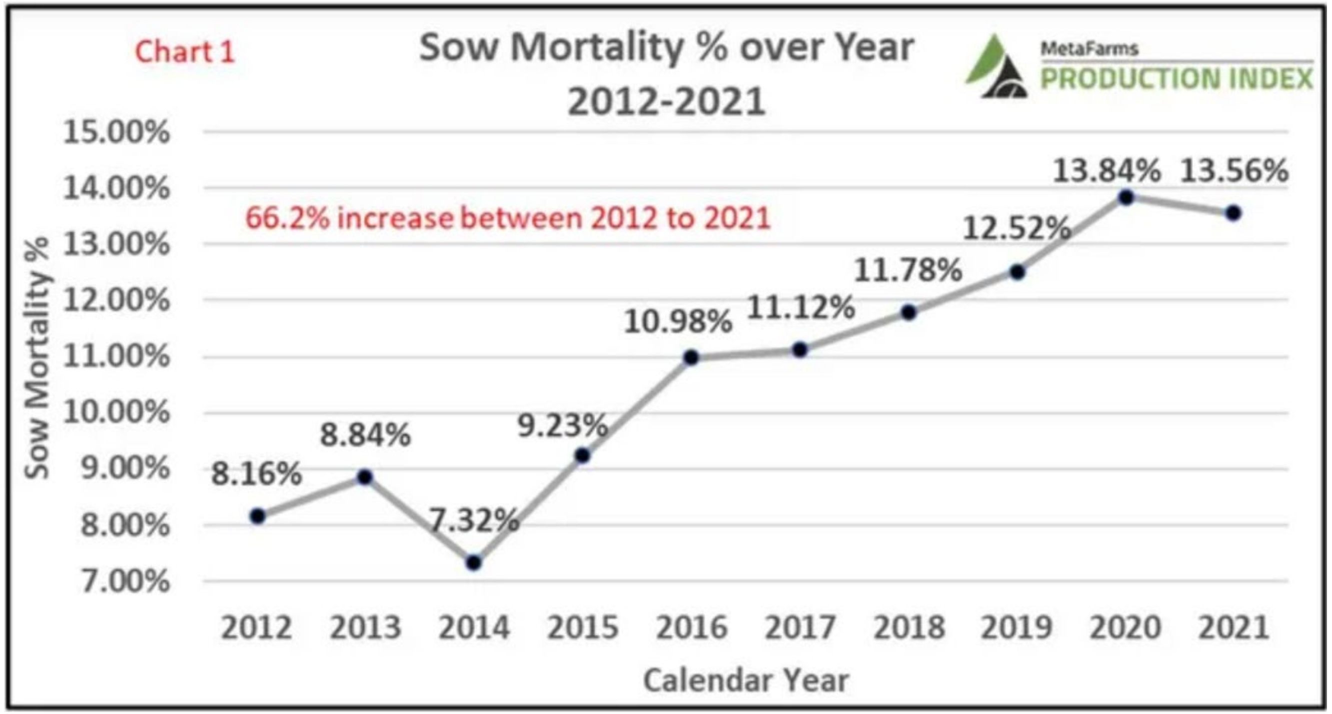
dsm-firmenich

Why does it matter?

Primary reasons for sow mortality are: **Sudden death**, death resulting from **lameness**, or death resulting from **prolapse**



Source: 2021 Sow mortality analysis (nationalhogfarmer.com)

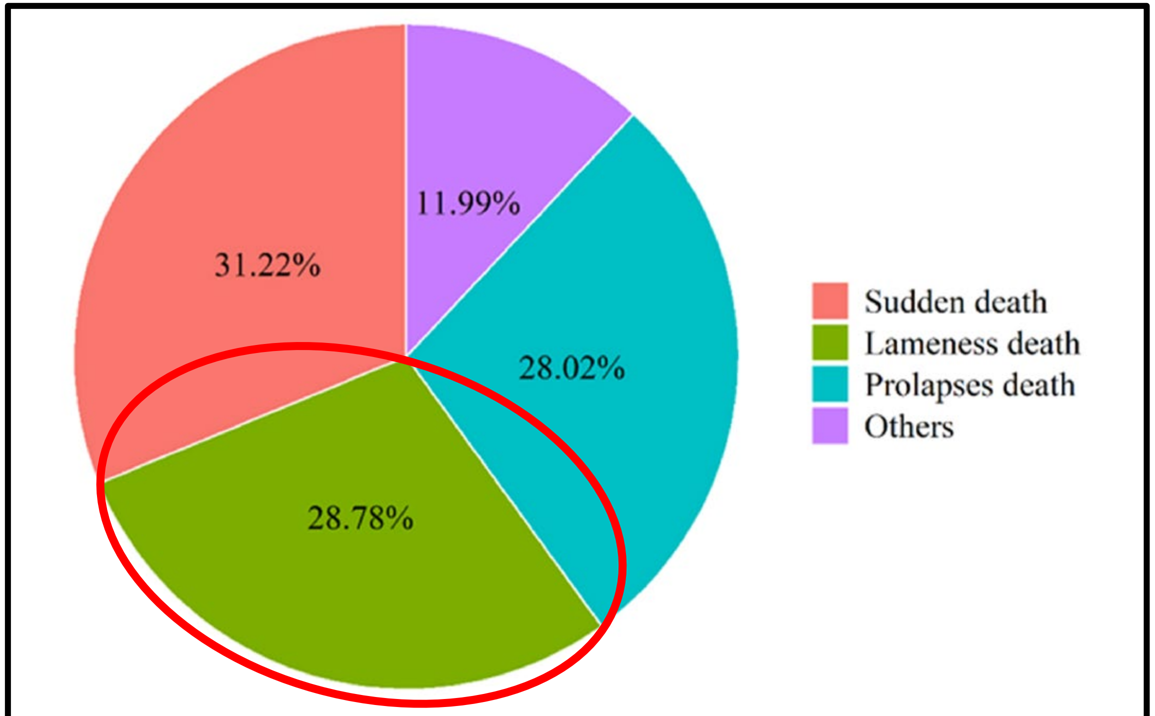


Fig. 2. Main reasons for sow mortality from the 48 breeding herds in the Midwestern U.S from 2019 to 2021.

Source: https://doi.org/10.1016/j.prevetmed.2023.105883

Many sow mortalities occur within the period surrounding parturition

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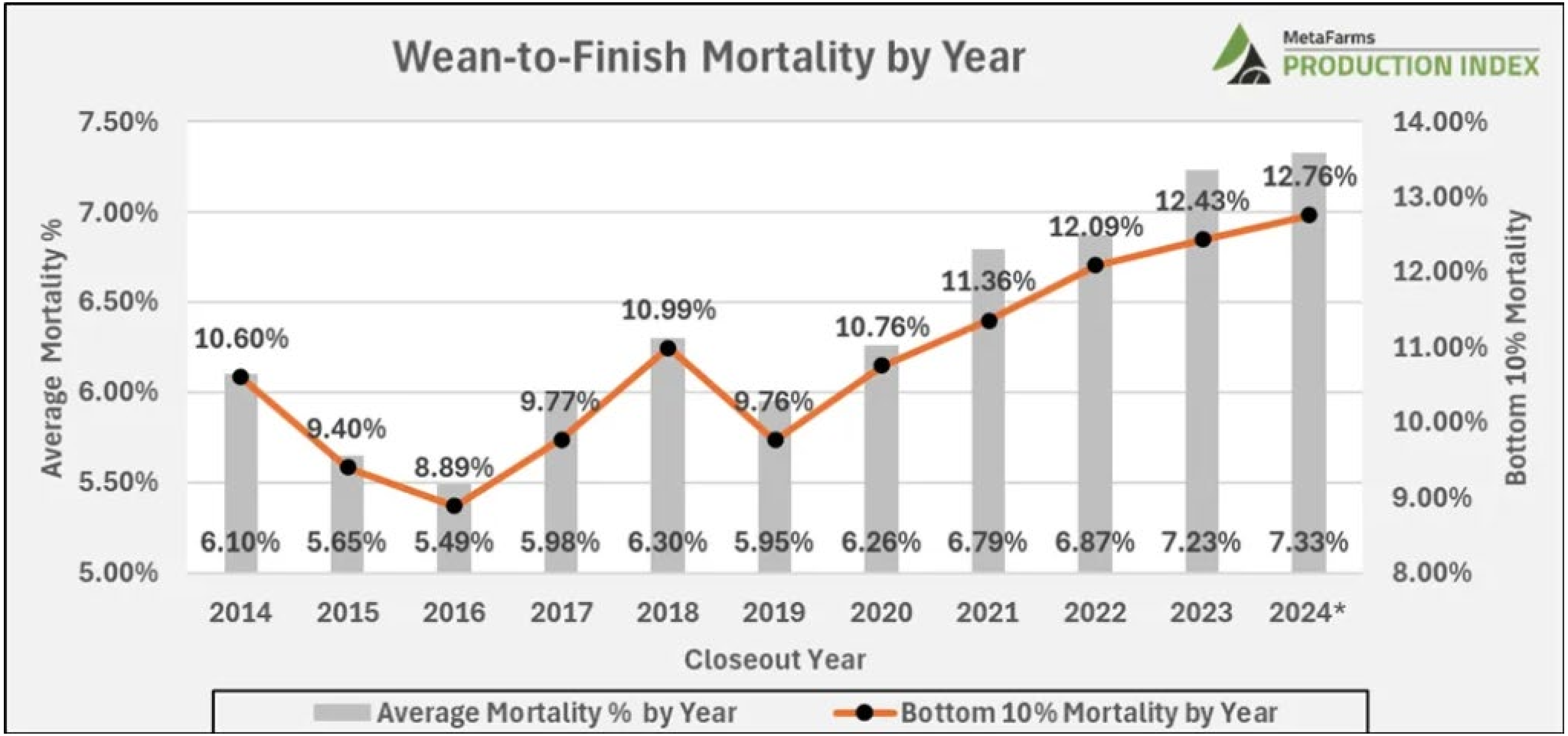
June 5, 2024 What and when: Deeper look at wean-to-finish mortality (nationalhogfarmer.com)



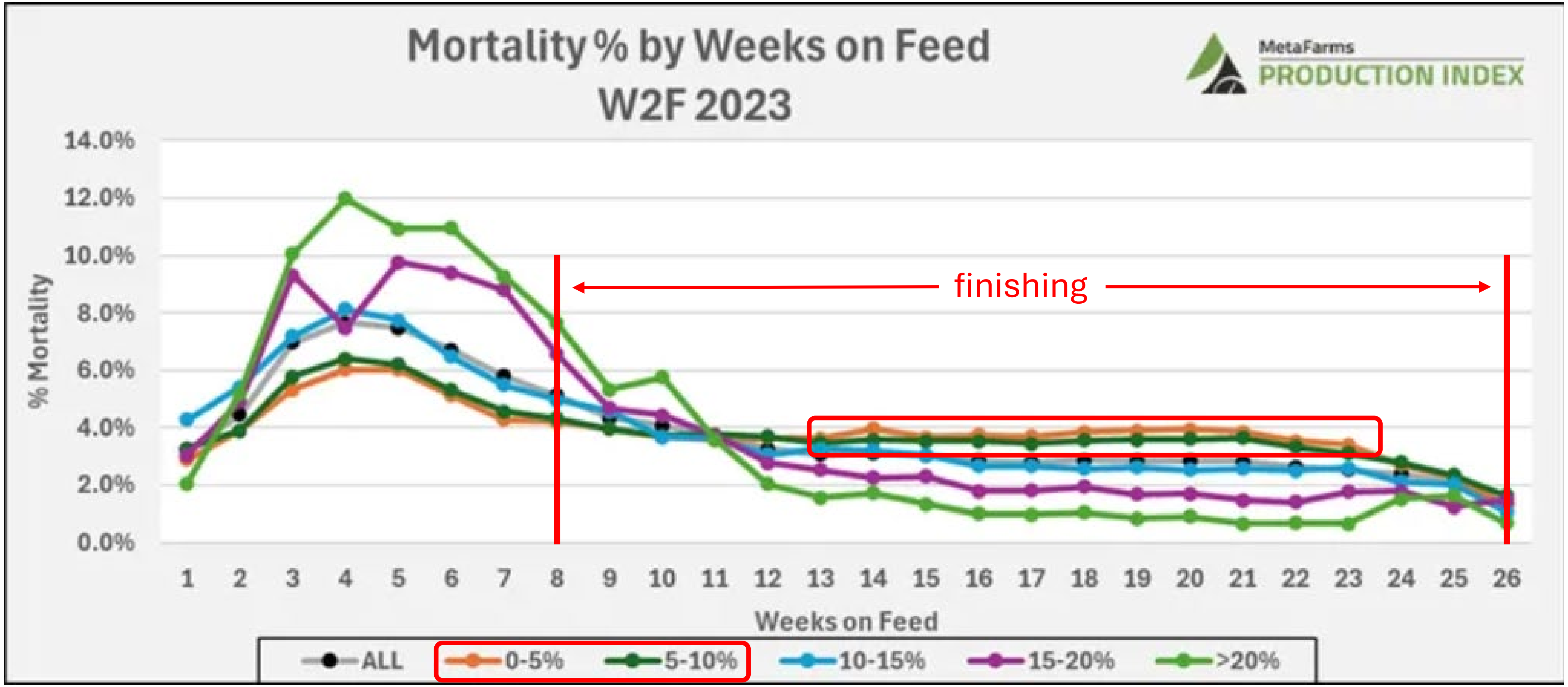
February 7, 2023 Key findings regarding post-weaning mortality (nationalhogfarmer.com)

Factors associated with Wean-to-Finish Mortality:

Sow herd – Pre-weaning mortality, weaning age, PRRSv status, *Mycoplasma hyopneumoniae*

Post-weaning – various infectious and non-infectious causes (Gebhardt et al., 2020)

June 5, 2024 What and when: Deeper look at wean-to-finish mortality (nationalhogfarmer.com)



*"**Lameness** is a frequent health and welfare problem **in finishing pigs**. It also **causes great economic losses**."

Lameness in finishing pigs may account for 11-15% of the recorded clinical problems…

Primary causes of Lameness – Nutritional, Environment/Management, Infectious, other Non-Infectious (i.e., rapid growth)

*Heinonen, M.; Pluym, L.; Maes, D.; Olstad, K.; Zoric, M. Lameness in Pigs.
In *Production Diseases in Farm Animals: Pathophysiology, Prophylaxis and Health Management*;
Gross, J.J., Ed.; Springer International Publishing: Cham, Switzerland, **2024**; pp. 405–450.

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NEWS / HOG PRODUCTION

Stiffness Isn't Normal: A Field Perspective on Lameness in Grow-Finish Pigs

By November 13, 2020

Lameness is the No. 1 cause of mortality in mid- to late-finishing stage pigs, Kathleen Wood, DVM, Christensen Farms, said in a recent webinar sponsored by the Swine Health Information Center (SHIC) and American Association of Swine Veterinarians (AASV).

Stiffness Isn't Normal: A Field Perspective on Lameness in Grow-Finish Pigs | Pork Business

1. **Hidden mortality** - "Continuous mild mortality doesn't raise red flags like an acute PRRS outbreak. Lameness has been there the whole time. ...it's accepted."
2. **Injectable treatments are variable and difficult to accomplish** - "Anti-inflammatory are an important treatment, relieving pain and related issues. ...injectables may be difficult to manage for grow-finish pigs... ...withdrawal times."
3. **Determine the source** – "Look upstream. ...possible origins in the sow farm? Is there an upstream intervention that will help downstream interventions more effective?"
4. **Communicate** – Practitioner time in the field (enough for a thorough investigation?)
   a) Train to recognize and identify issues – lameness/stiffness are not "normal" – more necropsies
   b) Provide diagnostic labs with more information – detailed history – give the full story and what you're seeing – opening joints, identifying broken bones/abnormalities, presence of infection/abscess,...

Each 1% loss in saleable pigs is worth approximately $1.50 of lost revenue/head marketed

Journal of Swine Health and Production — May and June 2019

ORIGINAL RESEARCH PEER REVIEWED

Retrospective study of lameness cases in growing pigs associated with joint and leg submissions to a veterinary diagnostic laboratory

Paisley Canning, DVM; Nicole Costello, DVM; Emily Mahan-Riggs, DVM; Kent J. Schwartz, DVM, MS; Kristin Skoland; Bret Crim; Alex Ramirez, DVM, MPH, PhD, Diplomate ACVPM; Daniel Linhares, DVM, MBA, PhD; Phillip Gauger, DVM, PhD; Locke Karriker, DVM, MS, Diplomate ACVPM

M & M: All cases of lameness or locomotor dysfunction in 7- to 40-week-old pigs submitted to the ISU VDL between May 1, 2010, and April 30, 2015. **(Did not include sows, boars, gilts, or pigs <7 weeks of age)**

Results: Of the 1847 cases retrieved, 464 met the inclusion criteria. The **4 most common primary diagnosis…**

1) ***Mycoplasma hyosynoviae*** (93 cases; **20%**),
2) **metabolic bone disease** (86 cases; **18.5%**),
3) infectious **arthritis due to non-*Mycoplasma* bacterial infection** (81 cases; **17.5%**), and
4) lameness with **inconclusive findings** (101 cases; **21.8%**).

23.3% of the cases (108 of 464 cases) had a secondary diagnosis with **metabolic bone disease** (**28.7%**; 31 of 108 cases) identified **as the most common secondary diagnosis**.

Caution: …not prevalence data …sources of bias …requested tests …reveals the importance of careful clinical examination, sampling, testing, and accurate diagnosis.

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In Sows – What are other identified risk factors for lameness?

Season	Fall	Winter	Spring	Summer		
		+1%	+6%	+11%		
PRRSv status	Negative	Endemic	Epidemic			
		+35%	+65%			
SVA status	Negative	Positive				
		+26%				
Gestation housing	Stalls (Individual)	Pens (Grouped)				
		+21%				
"Bump" feeding	Yes	No				
		+14%				
Feed medication	Yes	No				
		+8.5%				
PRRSv x SVA status	Neg-Neg	Neg-Pos	Endemic-Neg	Epidemic-Neg	Endemic-Pos	Epidemic-Pos
		+1%	+13%	+37%	+59%	+97%

?

Risk factors associated with sow mortality in breeding herds under one production system in the Midwestern United States – ScienceDirect 2023

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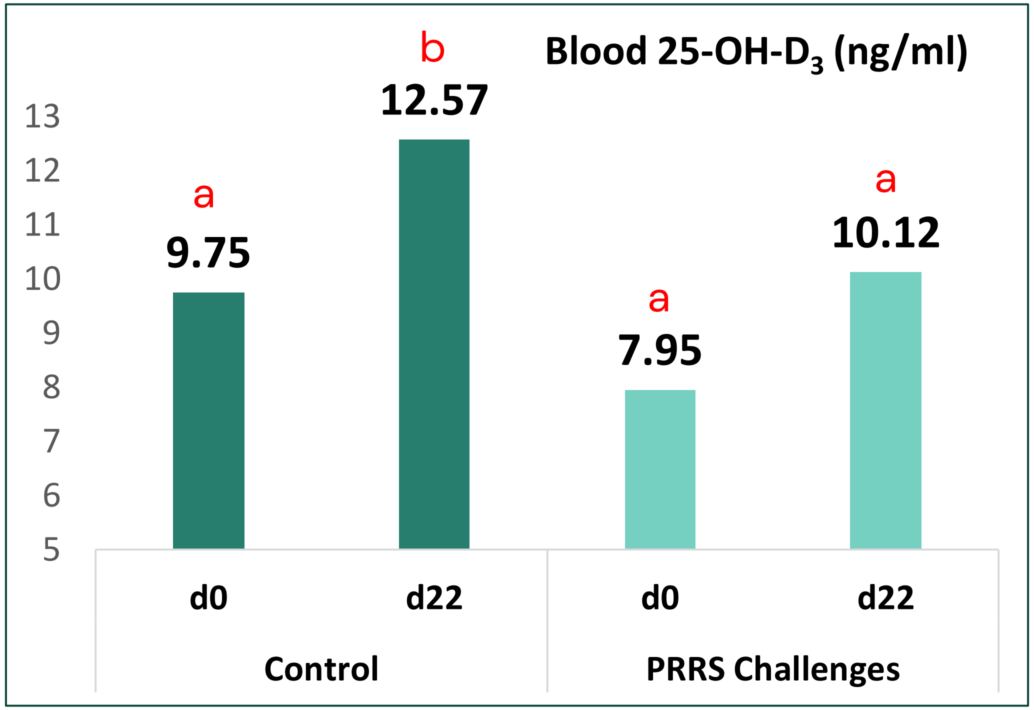
Relationship of health with bone and vitamin D status



Treatment $P<0.013$ days $P<0.04$

For the bone samples analysed, the PRRS-challenged pigs had bone with lower percent Ash, lower percent Ca, and lower density; but the percent P of bone was not different.

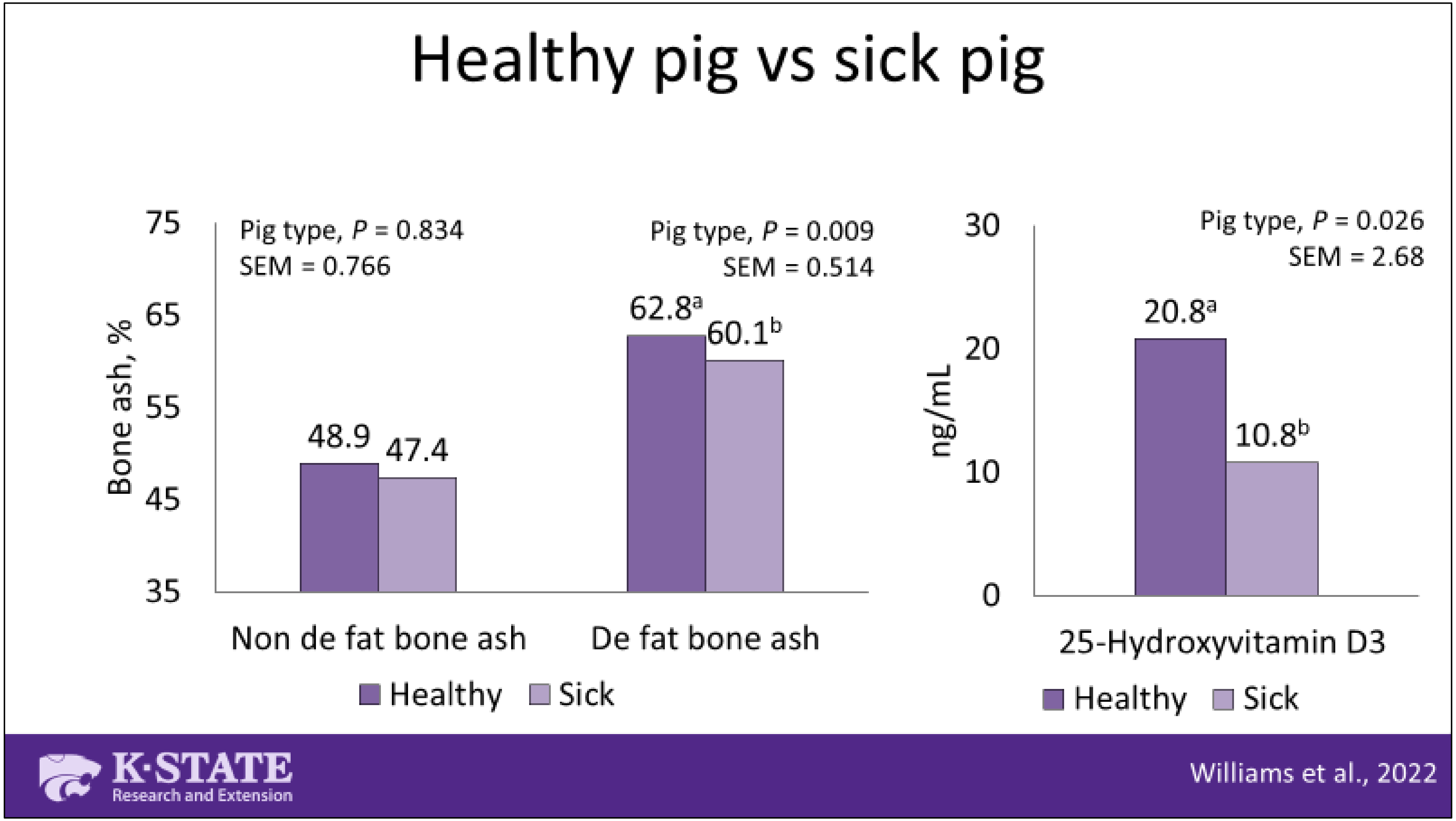
	Control	PRRS-Challenged	*P≤*
Ash, %	57.25	54.20	***0.003***
Ca, %	34.91	32.11	***0.007***
P, %	16.16	15.99	***0.725***
density, g/ml	1.36	1.28	***0.00001***

Pigs assigned to the PRRS-challenge group environment were inoculated intra-muscularly with a heterologous PRRS virus (n=20). The challenge dose was 103 viral logs. The pigs in the non-challenged (Control) group were not inoculated with virus (n=20).
On d 9 post-weaning, or 2 days post-challenge, blood samples were collected from all pigs to confirm that pigs in the PRRS-challenge group were PRRS+ and that pigs in the control group remained PRRS-.

2019 AASV Proceedings

Jacob Baker[1], BSc; Mark Wagner[2], DVM; David Baumert[3], DVM
[1]Iowa State University College of Veterinary Medicine, Ames, Iowa; [2]Fairmont Veterinary Clinic, Fairmont, Minnesota;
[3]Zoetis, Parsippany, New Jersey

Relationship of health with bone and vitamin D status



Factors contributing to lameness...

"...Among the reasons for lameness, **osteochondrosis** is a major factor contributing to leg weakness in pigs"

— Supakorn et al. (2018, Lameness: a principal problem to sow longevity in breeding herds)

U.S. Pork Nexus Mtg.
Nov. 2016

Experiences from diagnosing cases of metabolic bone disease, rickets, and/or kyphosis and lameness in pigs from commercial farms

Darin Madson
Iowa State University
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Body systems affected

Skeletal system
- **Bone and joints**

Muscular system
- Weak muscles
- Heart issues

Nervous system
- Nerves
- Spinal cord
- Brain

Common swine etiologies

Osteochondrosis dissecans (OCD)

Metabolic bone disease
- **Calcium, phosphorus, or vitamin D**

Mycoplasma spp.
- *Mycoplasma hyosynoviae* and *Mycoplasma hyorhinis*

Trauma

Bacterial sepsis
- *Haemophilus parasuis*
- *Erysipelothrix*
- etc.

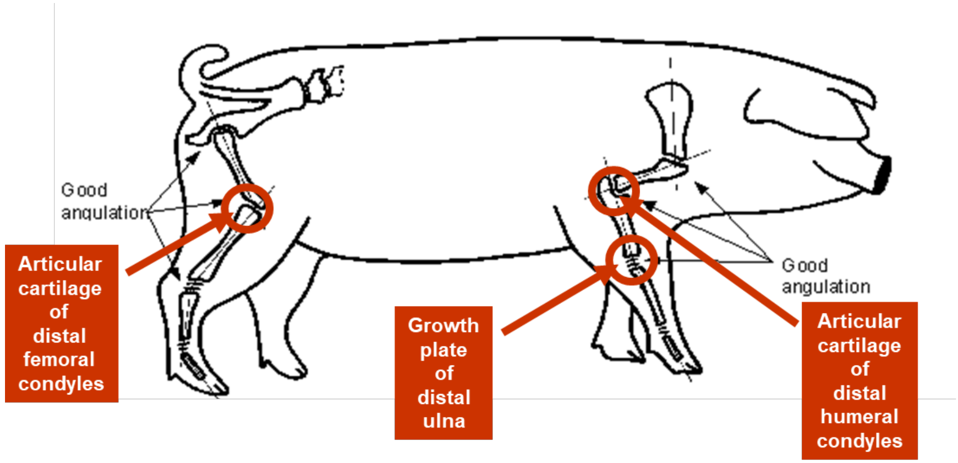
What is osteochondrosis dissecans (OCD)?

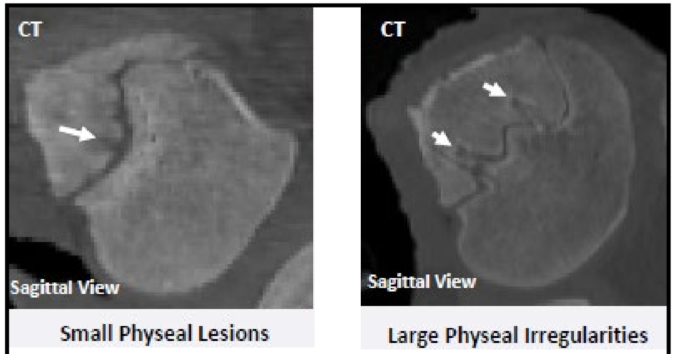
- **A common and clinically important joint disorder, defined more specifically as a focal disturbance of endochondral ossification of cartilage to bone.**

- **May affect, at some point in time, as many as 85 to 90% of all pigs.**

– Considered to have a **multifactorial etiology**:
  - **heredity**
  - **rapid growth**
  - **anatomic conformation**
  - **trauma**
  - ***dietary imbalances**

– That result in the initiation of **disturbance via**:
  - **failure/interruption of blood supply to the growth cartilage**
  - **fragile cartilage**
  - **failure of chondrocyte differentiation**
  - **subchondral bone necrosis**





From Kokinos et al., 2023

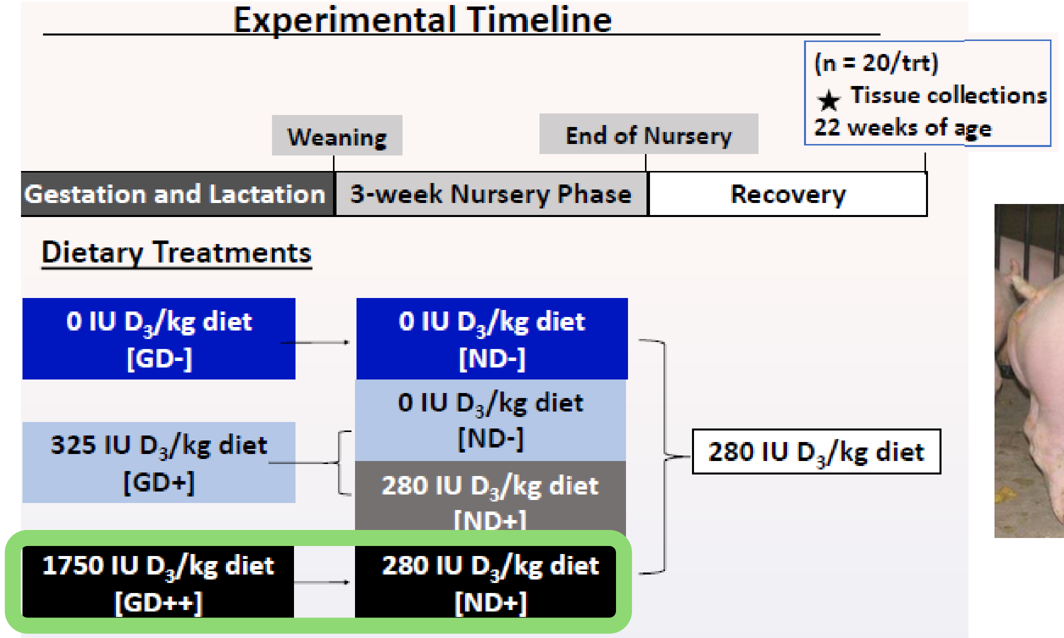

mild

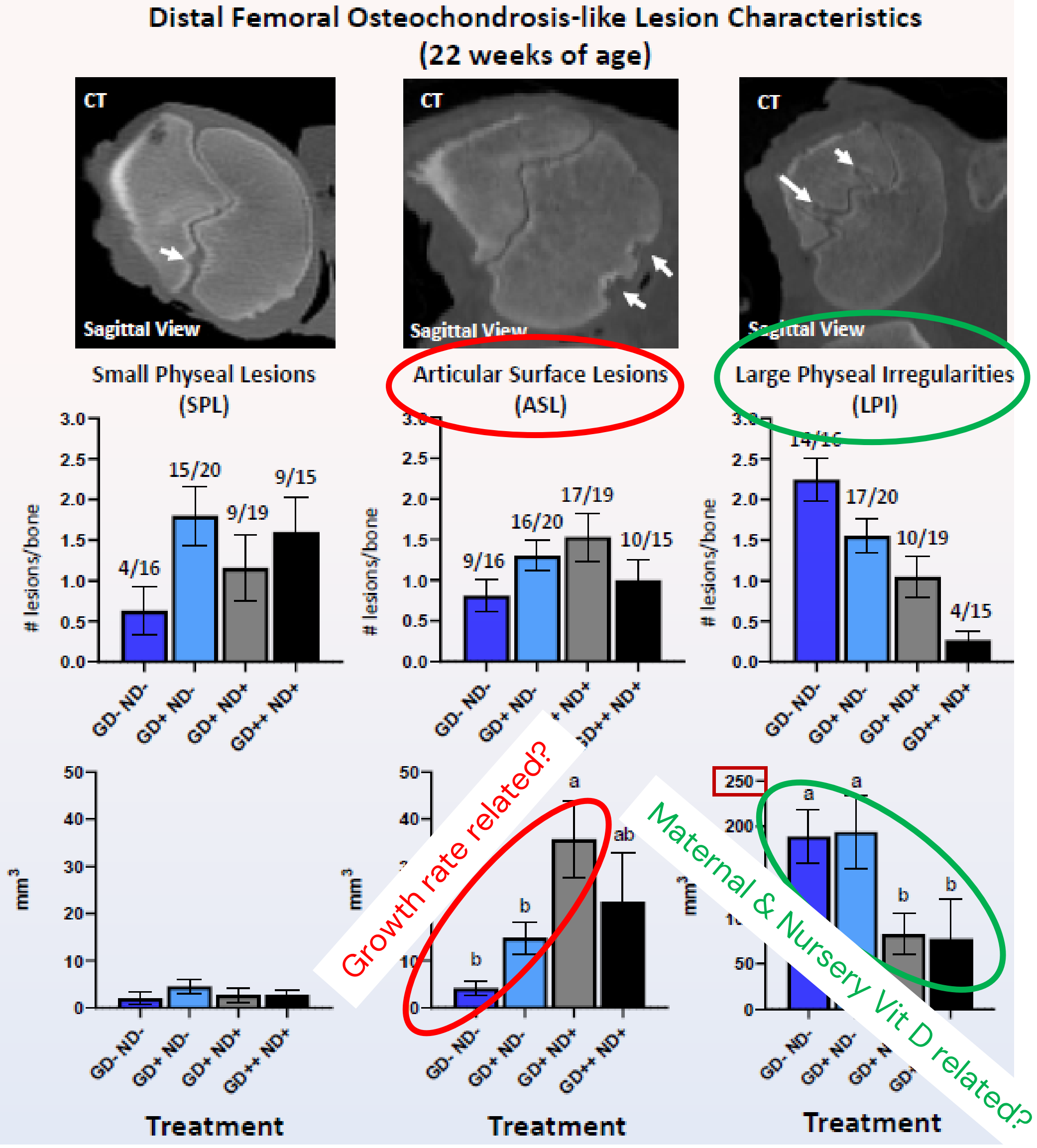

severe

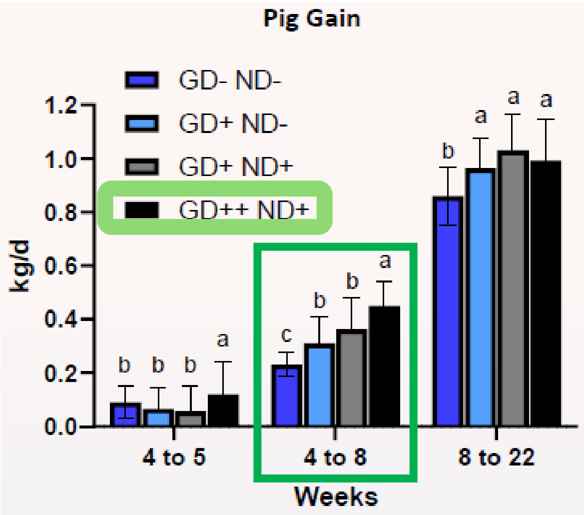

very severe

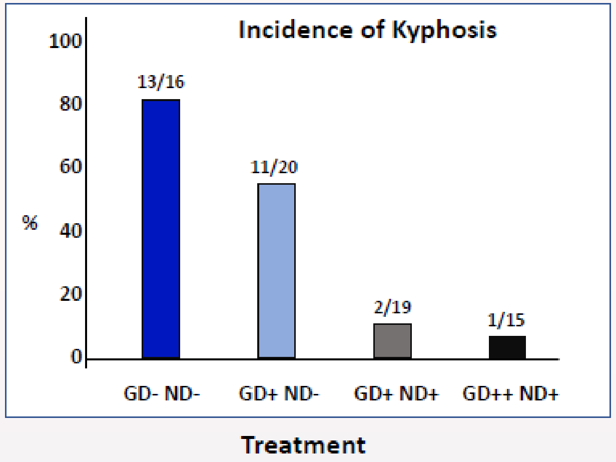
Maternal vitamin D deficiency increases the incidence of osteochondrotic-like lesions in the distal femur of growing pigs

Kokinos et al., 2023









What is metabolic bone disease?

- **Body disturbances related to:**
  1. Vitamin D
  2. Ca
  3. P
  4. Parathyroid hormone

- **To maintain body functions, a disturbance results in**
  1. Depletion of bone storage
  2. Delayed formation/modeling

- Metabolic bone disease
  - *AKA*: **Osteodystrophy**
  - Disturbance in bone:
    - Growth
    - Modeling
    - Remodeling

- **Rickets –** Abnormal endochondral ossification in a **growing** animal – **Defective mineralization of growing bone**
- **Osteomalacia –** Like rickets, but in **adult** animals – **Defective mineralization of bone remodeling**
- **Fibrous osteodystrophy –** Extensive bone resorption with replacement by fibrous connective tissue
- **Osteoporosis/Osteopenia –** Reduced bone mass – Quality of remaining bone is normal

Causes of metabolic bone disease

*Most **common suspected mechanisms** in cases of metabolic bone disease:*

1. **Inadequate** ~~dietary supplementation of~~ **vitamin D_3**
   (low serum 25-OH-D_3)

   Nutritionist – "But there's (2 to 10) X times more supplemental Vitamin D_3 in the diet than the 2012 NRC requirement estimates!"

2. **Inadequate** absorption of **P** due to low P in diet, P bound to phytate and therefore unavailable, and inadequate or ineffective phytase usage

3. **Imbalance** of feed **Ca to P ratio; improper formulation of Ca:P ratio** in diet

4. **Inadequate** dietary **Ca** can also contribute to rachitic lesions, though these are also often confounded by accompanying osteoporosis

Assessing Vitamin D Status – One of the Essentials in Metabolic Bone Disease Diagnosis

- Serum vitamin D reference ranges considered "normal"

Age of animal	25-OH-D3 ng/ml
Neonate	5-15
10 days	8-23
3-4 weeks old	25-30
Finishing pigs	30-35
Mature	35-70
Parturition	35-100

"This is more of general guide"

What needs to be collected and/or assessed

- Rib strength
- Serum
- Bone
  - Second rib
- Joints
  - Fluid and/or synovial tissue
- Normal tissues
  - Rule out other disease
- Feed

“There’s plenty of vitamin D_3 in the diets – why do my pigs have a lower status than what is suggested?”

Survey of Data from the ISU-VDL

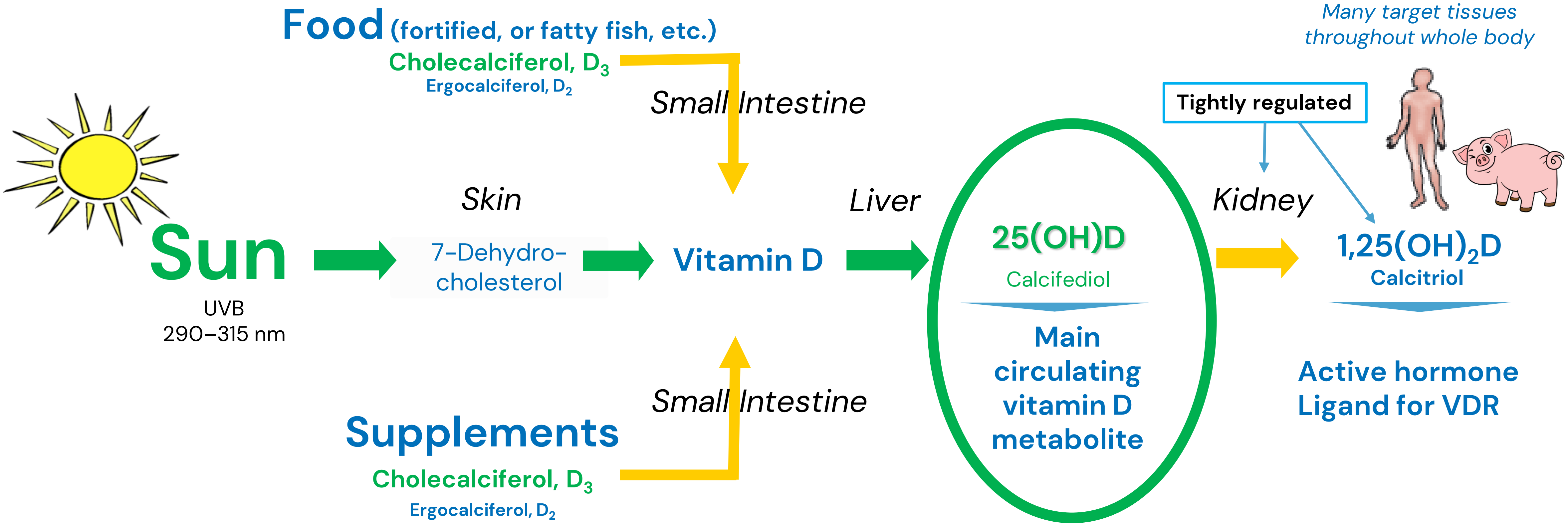
Hough, S., 2021. American Assoc. of Swine Vet. Annual Meeting

Data from **2016 - 2020**	**Serum 25-OH-D_3 (ng/ml)**		
Age	Mean	Median	June Outdoor - Mean
Nursery	15.3	7.4	**58.6**
Grower	14.6	12.4	**61.1**
Finishing	31.5	26.6	**86.0**
Mature/Sow	40.23	33.5	**57.2**
			(Arnold et al., 2015)

Jakobsen et al., 2022. *Animals*. 12, 299.

Danish outdoor sows, Jun-Aug 2020 survey of serum 25-OH-D_3, ng/mL	
Mean	**67**
Range	**32 – 134**

Vitamin D – "The Sunshine Vitamin"

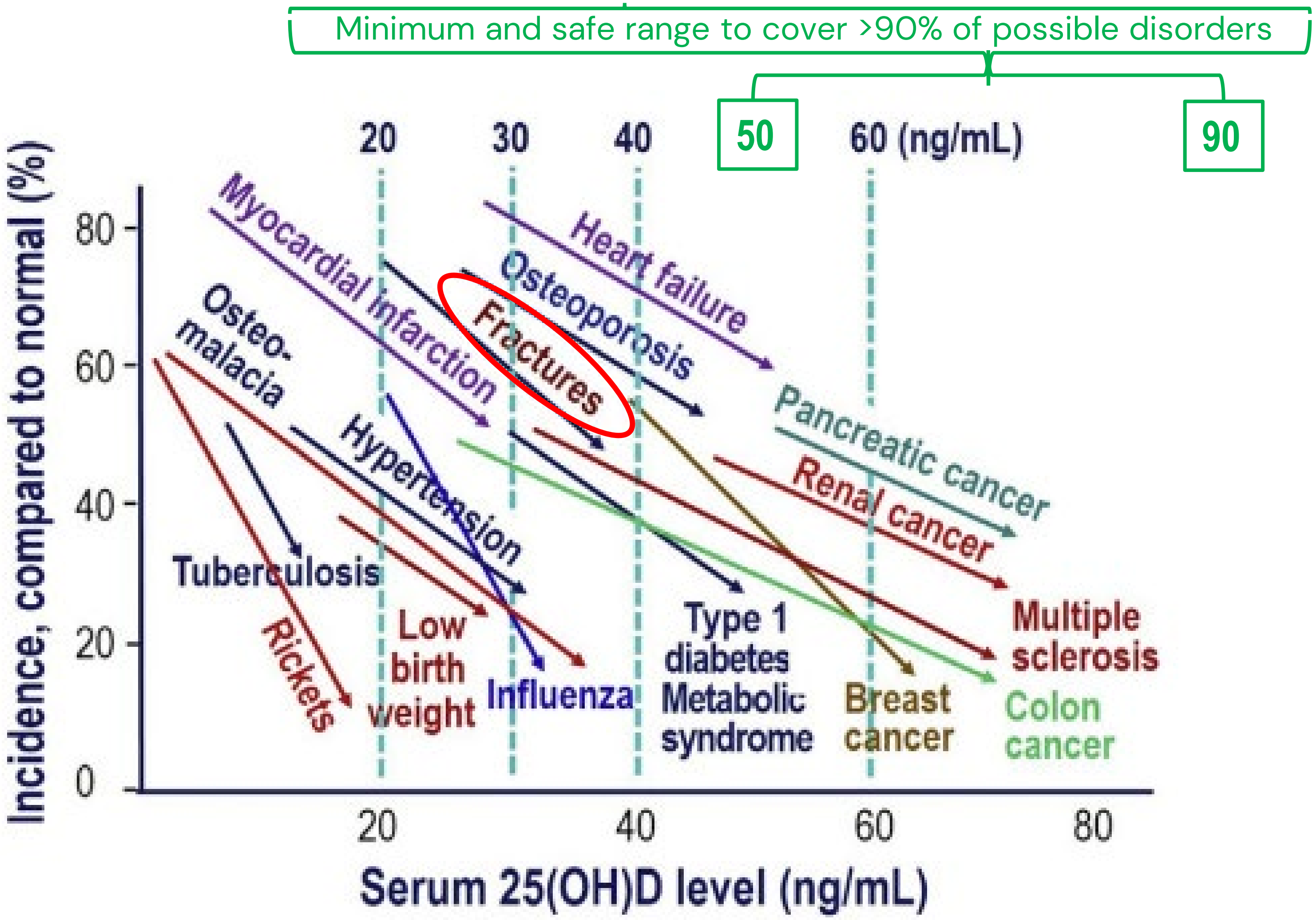


"… **a lot of debate as to whether dietary vitamin D_3 is equivalent to vitamin D_3 made in the skin**. Although both have the same biologic activity once they are metabolized, the half-life of vitamin D_3 produced in the skin is prolonged in the circulation because 100% is bound to the vitamin D binding protein whereas **when vitamin D_3 is ingested, only about 60% is bound to the vitamin D binding protein and 40% is rapidly cleared in the lipoprotein bound fraction.**" – Holick, M. F., 2008. Sunlight, UV-radiation, vitamin D and skin cancer: how much sunlight do we need? - PubMed (nih.gov)

Where do reference values for 25-OH-D_3 status come from?

Evidence from human studies

Skeletal and "extra-skeletal" effects of vitamin D	
Musculoskeletal	Extra-skeletal
- Essential for Ca homeostasis	- Improved immunity
- Enhanced GI absorption of Ca	- Decreased severity of autoimmune and neurological disorders
- Enhanced osteoblast function	- Prevention of type 1 and type 2 diabetes
- Necessary for bone mineralization	- Prevention of cancer
- Prevent rickets & osteomalacia	- Decreased cardiovascular disease
- Decrease sarcopenia	- Decreased all-cause mortality
- Improve balance and prevention of falls	- Decreased pulmonary morbidities
- Prevention of osteoporosis and fractures	- Less morbidities and improved survival



Sunil J. Wimalawansa, Review: Non-musculoskeletal benefits of vitamin D, J Steroid Biochem. Mol. Biol. 175 (2018) 60–81.
http://dx.doi.org/10.1016/j.jsbmb.2016.09.016

Bone Characteristics that are Relevant in Metabolic Bone Disease Diagnosis

Bone analysis reference ranges

Swine - rib bone	
Bone ash	58-62 %
Bone density	1.4-1.5 g/ml.
Bone ash - Calcium	32-39%
Bone ash - Phosphorus	13-22%

"Bone ash can sometimes be misleading"

- "I don't get excited until ash is less than 45%"
- "Typically, microscopic changes are seen when ash is <40%"

Rickets (growing pigs)	
↓ Phosphorus	Rubbery bones
↓ Calcium	Fragile bone; Break easy, but snap
↓Vitamin D	Rubbery bones

Cases of Metabolic Bone Disease in Growing Pigs

Darin Madson,
Iowa State Univ.

Table 1. Summary of vitamin D–dependent rickets cases submitted to the Iowa State University Veterinary Diagnostic Laboratory (Ames, Iowa) from January 2010 through March 2012.

Case	Year	Month	State*	Age† (wks)	Weight† (kg)	Reported history	Bone ash (%)	25 (OH)D_3‡ (ng/ml)	No. of pigs submitted
1	2010	January	IL	15	64	Sudden death and weakness	40–42	<2.5	2
2	2010	April	IA	11	23	Sudden death, tetany, seizure-like activity	26–37	<2.5	10
3	2010	May	IA	14	64	Sudden death	28–40	<2.5	3
4	2010	July	NE	15	68	Sudden death, tremors, weakness, and recumbency	15–35	<2.5	10
5	2011	March	IL	13	59	Recumbency, dog-sitting, and sudden death	29–35	<2.5	5
6	2011	March	IA	11	36	Lameness, dog-sitting, and sudden death	18–29	<2.5	3
7	2011	May	IA	14	57	Lameness	27–33	6–15	3
8	2011	May	IA	10	23	Tremors, weakness, lameness, and fractures	21	9	1
9	2011	June	MN	17	55	Lameness	22–25	9–13	2
10	2011	June	IA	9	23	Lameness	34–58	5–14	3
11	2011	August	MN	9	36	Lameness	35–50	9–11	2
12	2011	August	IA	10	32	Recumbent and lame with bone fractures	40–42	9–15	2
13	2011	September	IA	13	55	Lameness with bone fractures	35–50	6–9	6
14	2011	September	IA	11	41	Recumbent and lame	29–45	12–29	8
15	2012	January	MN	11	41	Lameness, humpbacks, and sudden death	37–44	3–11	2
16	2012	February	IA	11	36	Lameness	41–44	10–15	2
17	2012	March	IA	12	45	Recumbency and sudden death	11–17	5–6	4

Cases of Metabolic Bone Disease?
Why?
Health status? Nutrition? Both?

- **Nutrition** – a late nursery/early finisher case with metabolic bone disease (bone, low serum vitamin D, etc.) like those described in the previous table

Vitamin and Phytase investigation, % of expected

Vitamin D Analysis ✓OK	8/12/2014 Week 0	8/26/2014 Week 2	9/9/2014 Week 4	9/23/2014 Week 6	10/7/2014 Week 8	11/4/2014 Week 12	12/2/2014 Week 16
Starter Base - QB			135.3%	150.0%	147.0%	127.0%	124.0%
Sow Premix - QB			151.4%	131.0%	94.0%	154.0%	100.0%

Sow Premix - Phytase Analysis		Week 0	Week 2	Week 4	Week 6	Week 8	Week 12	Week 16
QB40	X	51.0%	59.7%	46.1%	46.9%	37.7%	48.9%	45.8%
HP (M)	X	85.0%	86.0%	76.3%	58.9%	66.2%	69.9%	68.6%
HP (GT)	✓OK	115.2%	123.5%	126.7%	104.2%	103.4%	100.2%	129.8%

Vitamin A Analysis	8/12/2014 Week 0	8/26/2014 Week 2	9/9/2014 Week 4	9/23/2014 Week 6	10/7/2014 Week 8	11/4/2014 Week 12	12/2/2014 Week 16
Starter Base - QB	101.0%	115.0%	138.2%	99.0%	123.0%	87.0%	115.0%
Sow Premix - QB	108.0%	96.0%	90.8%	65.0%	68.0%	46.0%	63.0%
Sow Premix - HP(M)	103.0%	96.0%	79.3%	62.0%	71.0%	43.0%	39.0%
Sow Premix - HP(GT)	114.0%	101.0%	81.2%	63.0%	48.0%	30.0%	47.0%

KSU – Premix Research - Vitamins and Phytase, % of expected

Effect of the premix type × oil type × **environmental condition × storage time interaction on the stability of vitamins and phytase.**

% of Initial	Storage time	Vitamin premix				Vitamin trace mineral				SEM	*P*=
		Mineral oil		MCFA		Mineral oil		MCFA			
		22°C	40°C	22°C	40°C	22°C	40°C	22°C	40°C		
Vitamin A	d30	106.58	76.99	91.55	76.49	106.14	91.60	114.22	94.30	4.782	0.1211
	d60	105.32	71.71	102.60	79.50	117.59	80.11	91.84	80.93		
	d90	100.00	55.28	111.59	68.72	110.20	75.44	93.40	74.09		
Vitamin B_{12}	d30	102.55	55.69	92.02	51.61	94.67	29.61	88.16	32.02	5.356	0.4879
	d60	94.51	38.31	83.91	29.76	98.74	13.00	93.04	14.72		
	d90	92.23	31.07	92.66	19.46	110.24	9.20	97.63	10.73		
Vitamin B_2	d30	97.24	84.69	105.46	94.97	88.85	80.12	78.38	84.48	4.215	0.1731
	d60	95.86	94.93	97.32	101.49	85.58	89.31	86.23	83.36		
	d90	88.84	80.65	96.94	80.70	79.71	71.44	70.88	73.17		
Vitamin B_3	d30	90.84	91.56	95.30	94.19	93.17	94.53	93.96	91.87	2.388	0.4180
	d60	99.53	94.89	97.58	96.70	97.22	96.95	93.87	88.54		
	d90	94.30	90.76	94.66	93.61	98.09	90.28	94.30	92.86		
Vitamin B_5	d30	100.28	92.80	109.01	104.83	97.05	88.47	91.09	84.95	2.607	0.7388
	d60	86.54	86.09	90.49	88.47	84.26	79.60	85.27	73.48		
	d90	82.29	77.97	82.33	82.50	81.09	61.49	74.68	50.62		

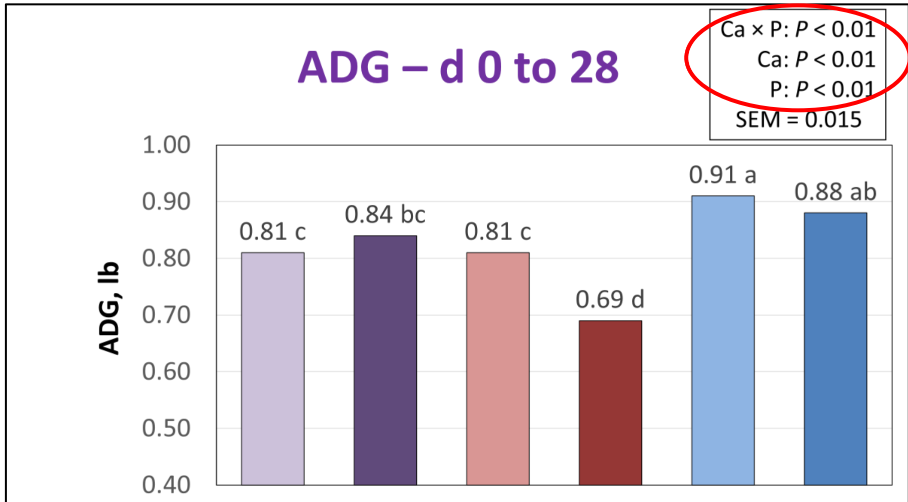
KSU – Premix Research - Vitamins and Phytase, % of expected

Effect of the premix type × oil type × **environmental condition × storage time interaction on the stability of vitamins and phytase.**

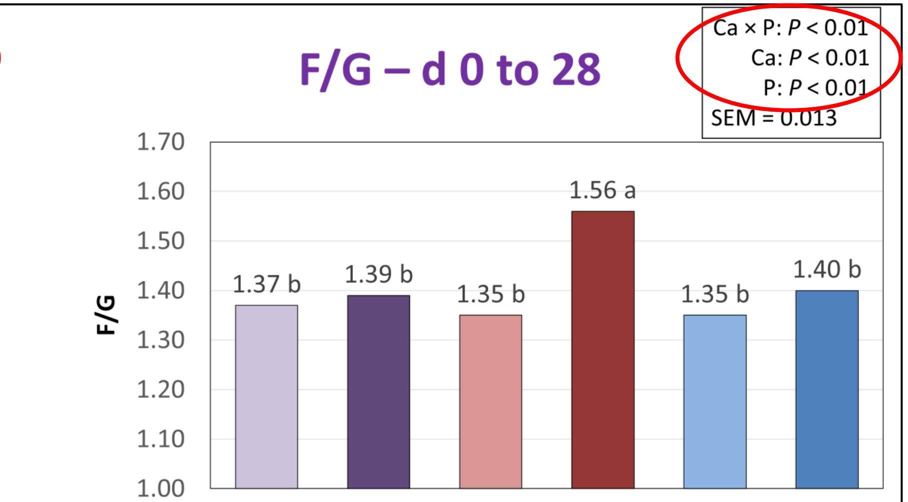
% of initial or % of claim	Storage time	Vitamin premix				Vitamin trace mineral				SEM	*P*=
		Mineral oil		MCFA		Mineral oil		MCFA			
		22°C	40°C	22°C	40°C	22°C	40°C	22°C	40°C		
Vitamin D_3	d30	89.48	92.76	94.21	87.77	93.71	79.48	91.73	91.35	4.085	0.0729
	d60	86.94	82.40	88.36	77.85	84.03	84.21	87.69	76.30		
	d90	93.33	75.53	90.34	75.91	86.09	82.03	87.74	74.37		
Vitamin E	d30	94.98	90.79	95.29	90.55	96.33	99.19	101.00	103.40	1.726	0.6282
	d60	90.73	84.09	91.50	80.53	89.17	83.88	92.47	87.02		
	d90	85.76	74.76	90.45	76.24	86.29	80.58	89.14	86.95		
Vitamin K	d30	68.20	55.73	75.36	47.65	79.24	83.23	77.20	79.14	5.165	0.6493
	d60	77.81	51.64	73.72	44.27	76.79	75.46	81.08	70.96		
	d90	91.51	47.55	90.80	36.09	87.52	76.79	95.20	73.52		
Phytase	d30	92.65	41.15	87.32	37.54	90.56	49.73	95.09	45.74	2.665	0.5015
	d60	102.42	6.44	100.40	6.33	103.11	27.03	104.30	23.96		
	d90	106.87	0.62	109.09	0.65	111.90	14.03	111.26	13.32		

High Heat with High Relative Humidity destroys vitamins and enzymes!!!

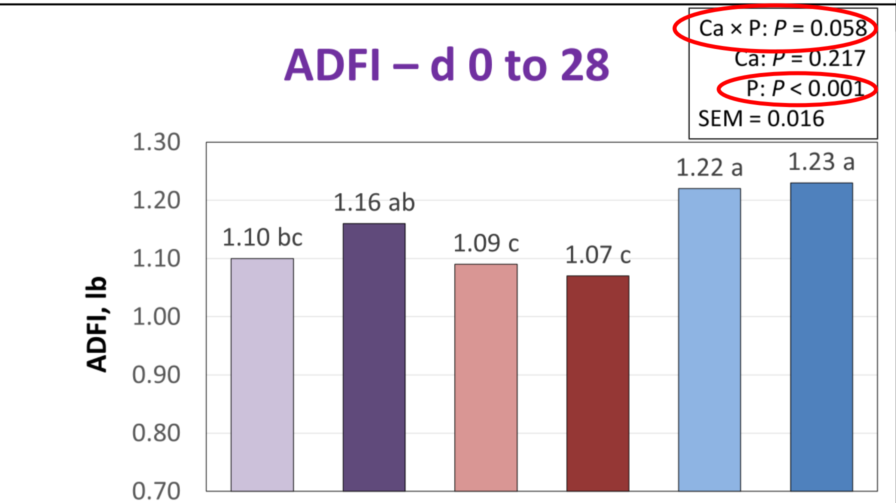
Wu et al. 2018. Effects of dietary calcium to phosphorus ratio and addition of phytase on growth performance of nursery pigs. J. Anim. Sci. 96:1825–1837.

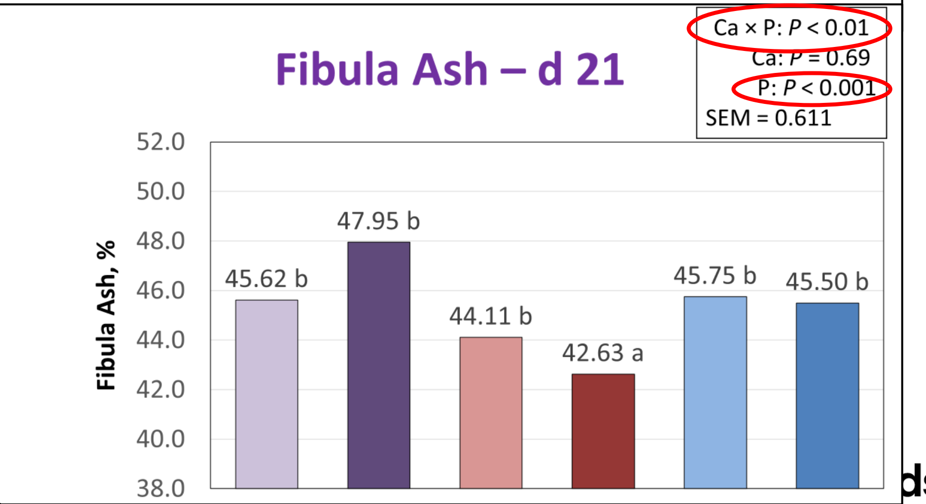


Analyzed Ca	0.58	1.03	0.58	1.03	0.46	0.91
STTD P no phytase	0.45	0.45	0.33	0.33	0.33	0.33
STTD P w/phytase	-	-	-	-	0.45	0.45
Analyzed Ca:STTD P	1.29	2.29	1.76	3.12	1.02	2.02
Analyzed Ca:Analyzed P	0.79	1.41	1.07	1.91	0.85	1.69



Analyzed Ca	0.58	1.03	0.58	1.03	0.46	0.91
STTD P no phytase	0.45	0.45	0.33	0.33	0.33	0.33
STTD P w/phytase	-	-	-	-	0.45	0.45
Analyzed Ca:STTD P	1.29	2.29	1.76	3.12	1.02	2.02
Analyzed Ca:Analyzed P	0.79	1.41	1.07	1.91	0.85	1.69





Vier et al. – 2019 Midwest Section Meetings. ASAS

Kansas State University | applied swine nutrition

Effects of storing three phytase sources for 90 days under high temperature and humidity on phytase stability, growth performance, and bone mineralization of nursery pigs

American Dairy Science Association® MIDWEST American Society of Animal Science

PSV-10

Material and Methods

- Three phytases were used: HiPhos GT (HP, 20,000 FYT/g, DSM Nutritional Products, Parsippany, NJ); Axtra Phy TPT (AP, 20,000 FTU/g, Dupont, Wilmington, DE), and Quantum Blue G (QB, 40,000 FTU/g, AB Vista, Plantation, FL).
- A phytase-free VTM premix, the three pure phytase products, and the three phytases mixed in a VTM premix were stored for 90 d in an environmentally controlled chamber set at 29.4°C and 75% humidity.
- Samples were taken on d 0, 30, 60, and 90 of storage and phytase activity was measured. Phytase activity results are expressed as a percentage of the original formulated values.
- Afterward the 90 d storage period, a total of 300 pigs (DNA; 241 × 600, initially 11.7 kg) were assigned to 1 of 8 treatments in a RCBD with 4 to 5 pigs/pen and 8 pens/treatment.

TREATMENTS

- Phytase-free VTM: Negative Control, Positive Control
- Stored as pure phytase: Hiphos, Quantum Blue, Axtra Phy
- Stored in VTM premix: Hiphos, Quantum Blue, Axtra Phy

0.12% aP (Negative Control) | 0.27% aP (achieved with monocalcium P or aP release from phytase)

- * The negative and positive control diets were formulated with a phytase-free VTM premix. The phytases were added as part of a corn-soybean meal-based diet such that 0.15% of the VTM premix or the comparable amount of pure phytase would provide the phytase recommended by the manufacturer to release 0.15% aP (1,000 FYT/kg of HiPhos, 651 FTU/kg of Axtra Phy, and 500 FTU/kg of Quantum Blue in the final diet).

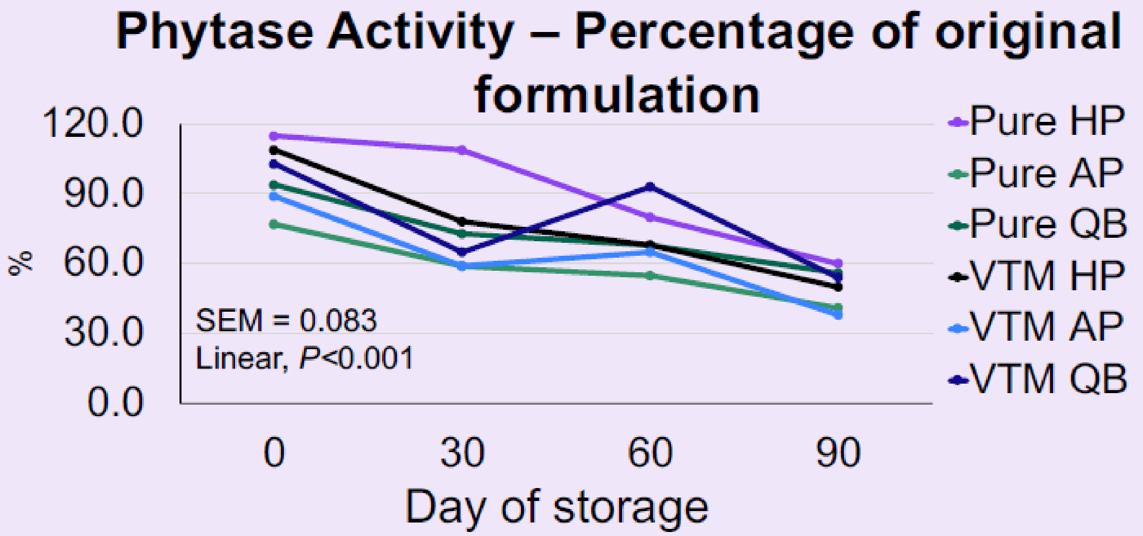
Diet composition (as fed basis)

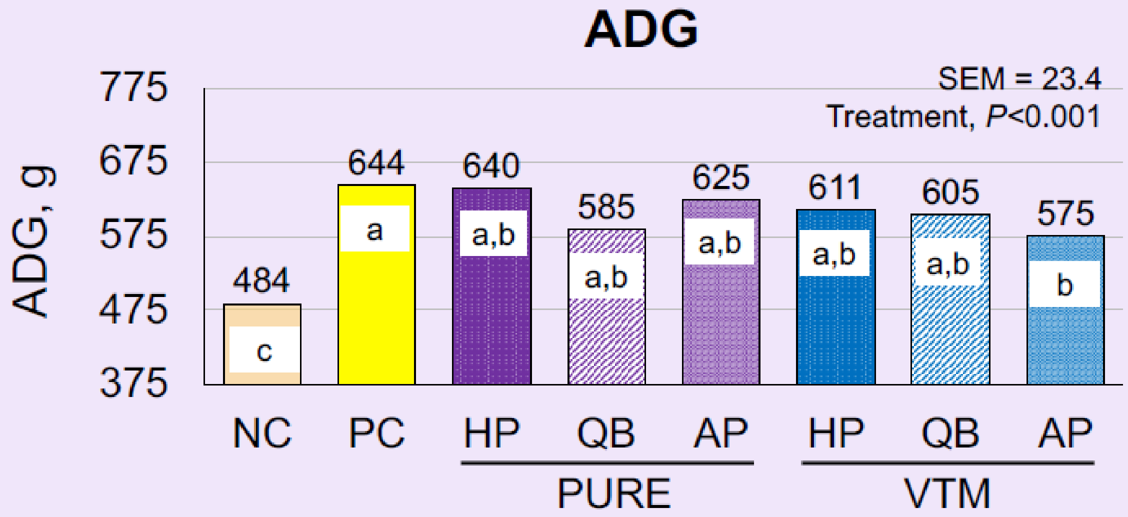
	Negative Control	Positive Control	Phytase Treatments
Corn	60.09	60.10	60.09
Soybean meal	36.45	36.45	36.45
Limestone	1.04	1.19	1.04
Monocalcium P	0.19	0.93	0.19
Salt	0.65	0.65	0.65
L-lysine	0.29	0.29	0.29
DL-methionine	0.14	0.14	0.14
L-threonine	0.10	0.10	0.10
Sand	0.90	-	0.90
Phytase-free VTM	0.15	0.15	-
VTM with phytase*	-	-	0.15
Total	100.00	100.00	100.00
Calculated analysis			
SID Lysine, %	1.30	1.30	1.30
Total Lysine, %	1.46	1.46	1.46
NE, kcal/kg	2,414	2,414	2,414
CP, %	22.8	22.8	22.8
Ca, %	0.54	0.72	0.54
P, %	0.47	0.62	0.47
Available P	0.12	0.27	0.27

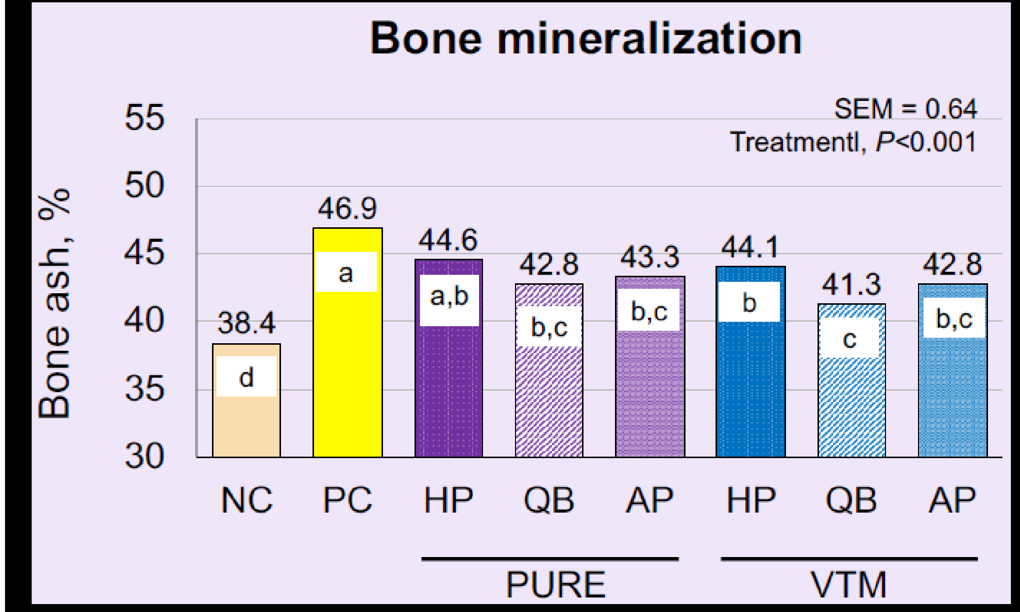
Next | Main

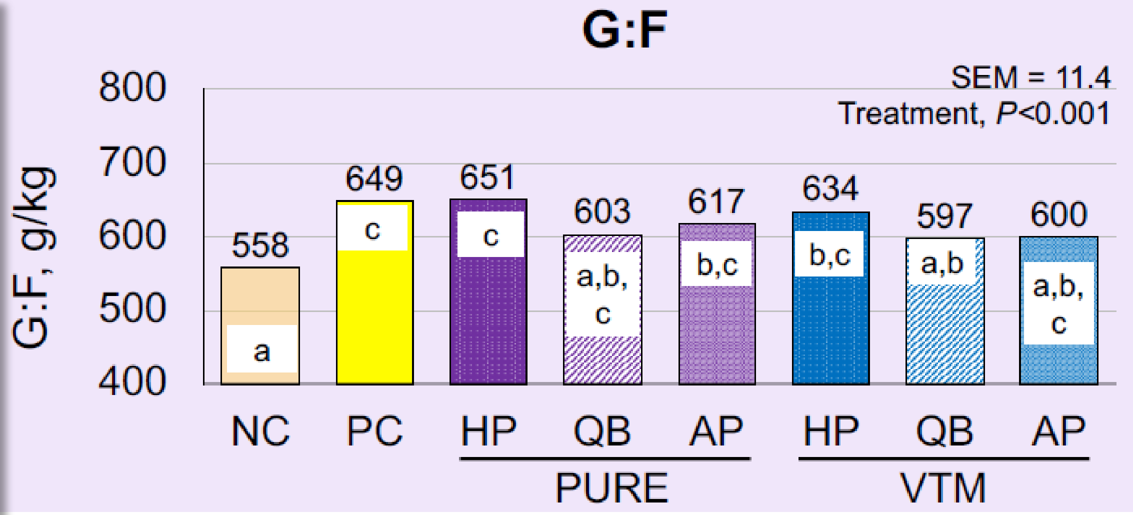
Vier et al. – 2019 Midwest Section Meetings. ASAS

Results









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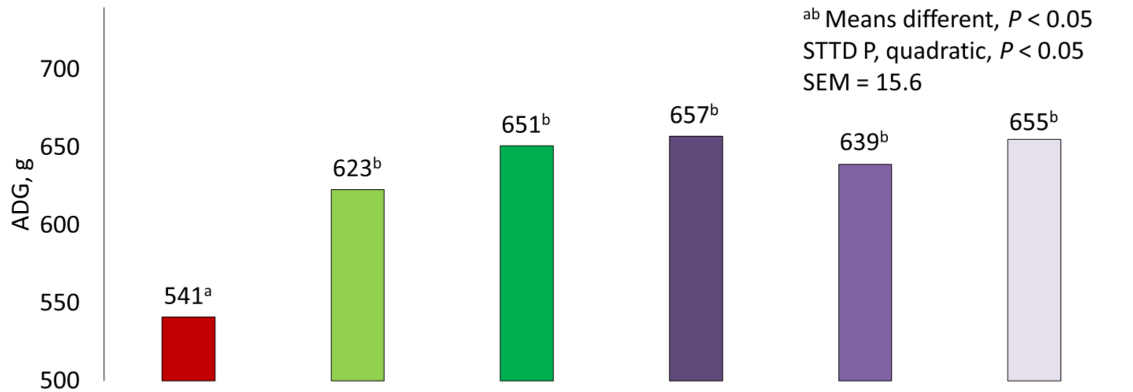
Williams et al. 2023. The effect of bone and analytical methods on the assessment of bone mineralization response to dietary phosphorus, phytase, and vitamin D in nursery pigs.

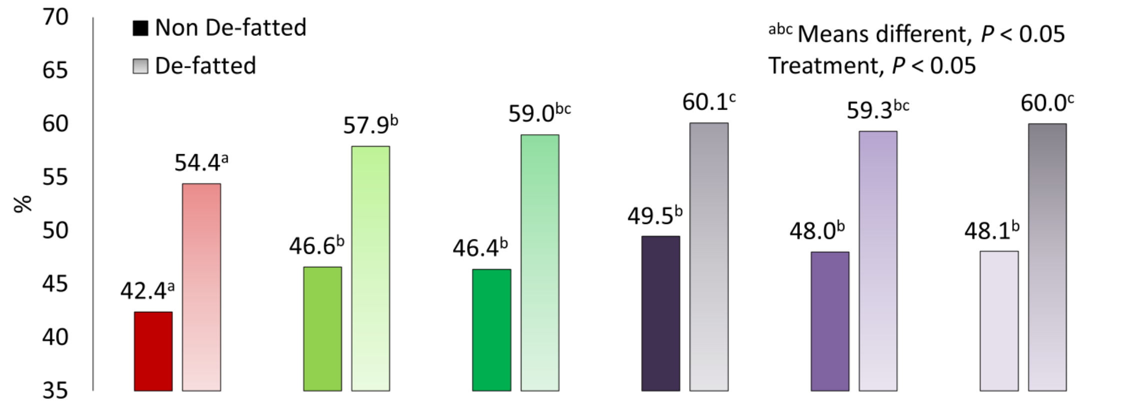
J. Anim. Sci. 101:1–15.

Dietary P, phytase, and vitamin D on overall growth performance



STTD P, %	0.19	0.33	0.33	0.44	0.44	0.44
Vitamin D, IU/kg	1,653	1,653	1,653	0	1,653	1,653 + HyD
Phytase, FYT/kg	0	0	2,000	2,000	2,000	2,000

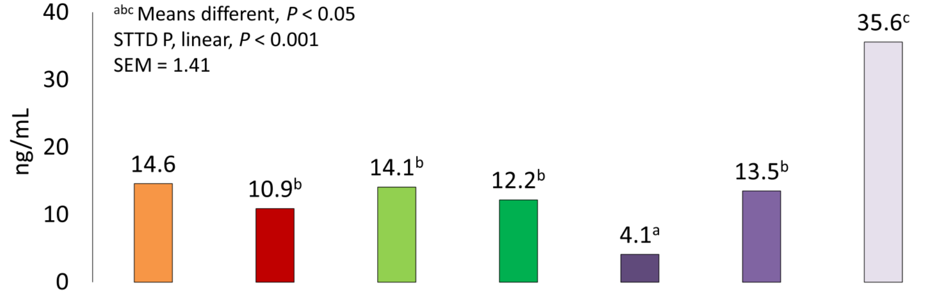
Dietary P, phytase, and vitamin D on bone ash %



STTD P, %	0.19	0.33	0.33	0.44	0.44	0.44
Vitamin D, IU/kg	1,653	1,653	1,653	0	1,653	1,653 + HyD
Phytase, FYT/kg	0	0	2,000	2,000	2,000	2,000

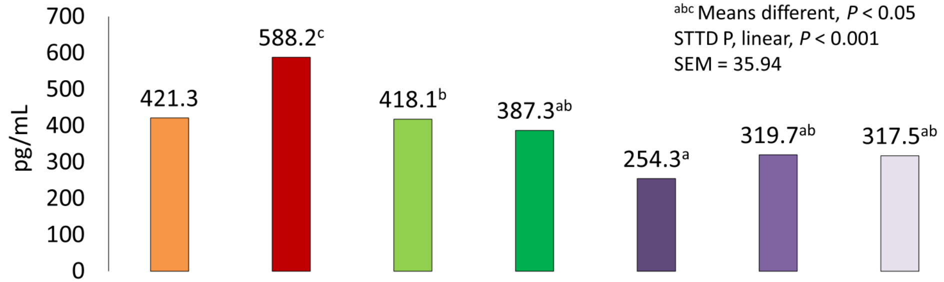
Williams et al. 2023. The effect of bone and analytical methods on the assessment of bone mineralization response to dietary phosphorus, phytase, and vitamin D in nursery pigs. J. Anim. Sci. 101:1–15.

Dietary P, phytase, and vitamin D on 25-Hydroxyvitamin D_3 serum chemistry (d 28)



STTD P, %	Baseline d 0	0.19	0.33	0.33	0.44	0.44	0.44
Vitamin D, IU/kg		1,653	1,653	1,653	0	1,653	1,653 + HyD
Phytase, FYT/kg		0	0	2,000	2,000	2,000	2,000

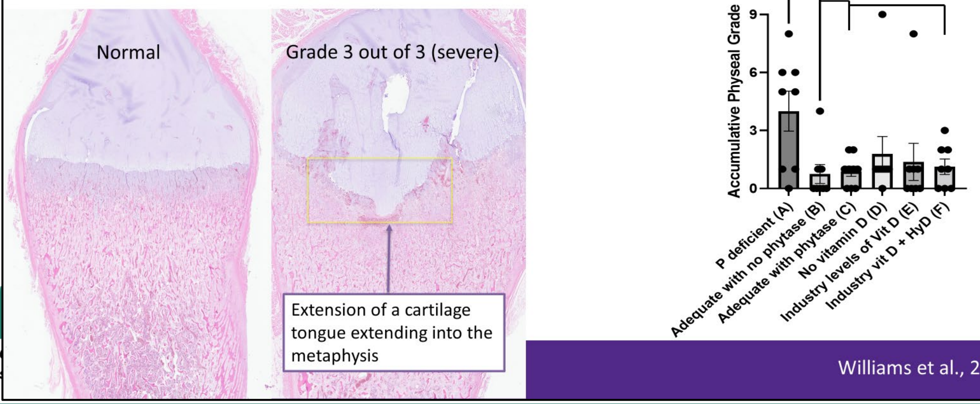
Dietary P, phytase, and vitamin D on 1,25-dihydroxyvitamin D_3 serum chemistry



STTD P, %	Baseline d 0	0.19	0.33	0.33	0.44	0.44	0.44
Vitamin D, IU/kg		1,653	1,653	1,653	0	1,653	1,653 + HyD
Phytase, FYT/kg		0	0	2,000	2,000	2,000	2,000

Histopathology of 10th rib – physeal grade

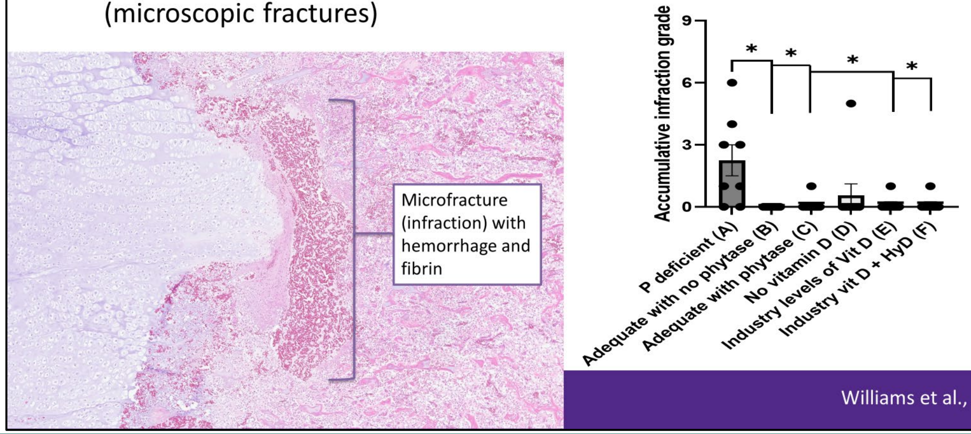
- 10th rib was more sensitive than 2nd rib or fibula for lesions
- The physis (growth plate) was scored for evidence of failure of endochondral ossification (rickets)



Williams et al., 2022

Histopathology of 10th rib – infraction grade

- 10th rib was more sensitive than 2nd rib or fibula for lesions
- Bones were scored for severity of fracture and/or infractions (microscopic fractures)



Williams et al., 2022

25-OH-D_3 supplementation improved vitamin D status and bone mineralization, especially when dietary P was deficient or marginal

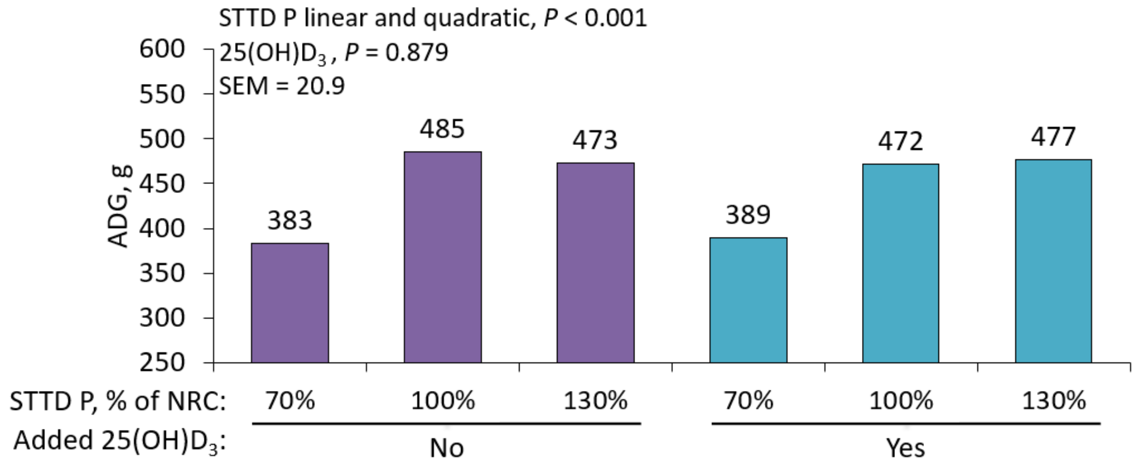
K·STATE Research and Extension | dsm-firmenich | Becker et al., 2024

Serum Vitamin D_3 Metabolite Concentrations

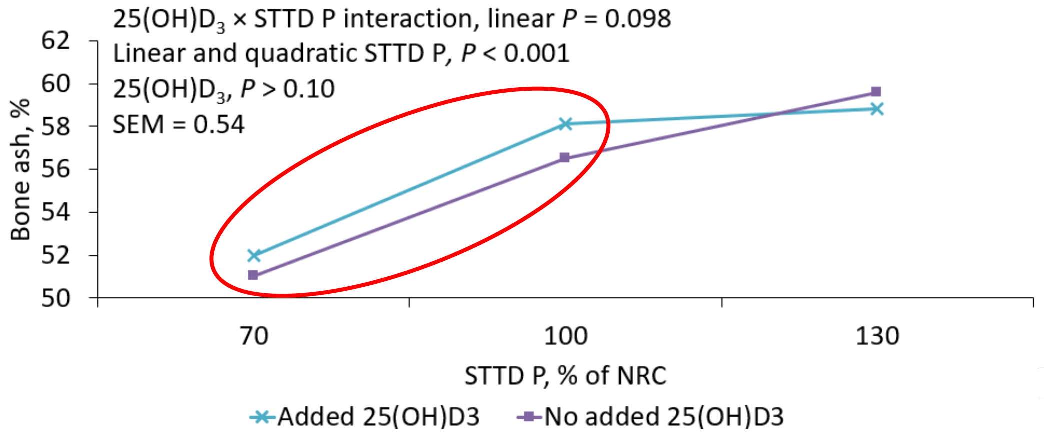
Vitamin D_3, IU/kg	1,653							*P* =		
Added 25(OH)D_3	No			Yes					STTD P	
STTD P, % of NRC	70%	100%	130%	70%	100%	130%	SEM	25(OH)D_3	Linear	Quadratic
25(OH)D_3, ng/mL	7.2	7.2	8.2	18.7	29.2	25.0	2.07	< 0.001	0.082	0.057
24,25(OH)$_2D_3$, ng/mL	1.6	1.3	2.0	9.8	10.0	8.6	0.52	< 0.001	0.455	0.777
1,25(OH)$_2D_3$, pg/mL*	339	257	181	394	203	180	14.8	0.986	< 0.001	0.001

*Quadratic 25(OH)D_3 × STTD P interaction, *P* = 0.002.

Overall Average Daily Gain, d 0 to 45



Percentage Bone Ash



25-OH-D_3 and phytase (HiPhorius) improved digestibility of Ca and P in the 25 kg growing pig

Jaramillo et al., (2024) unpublished

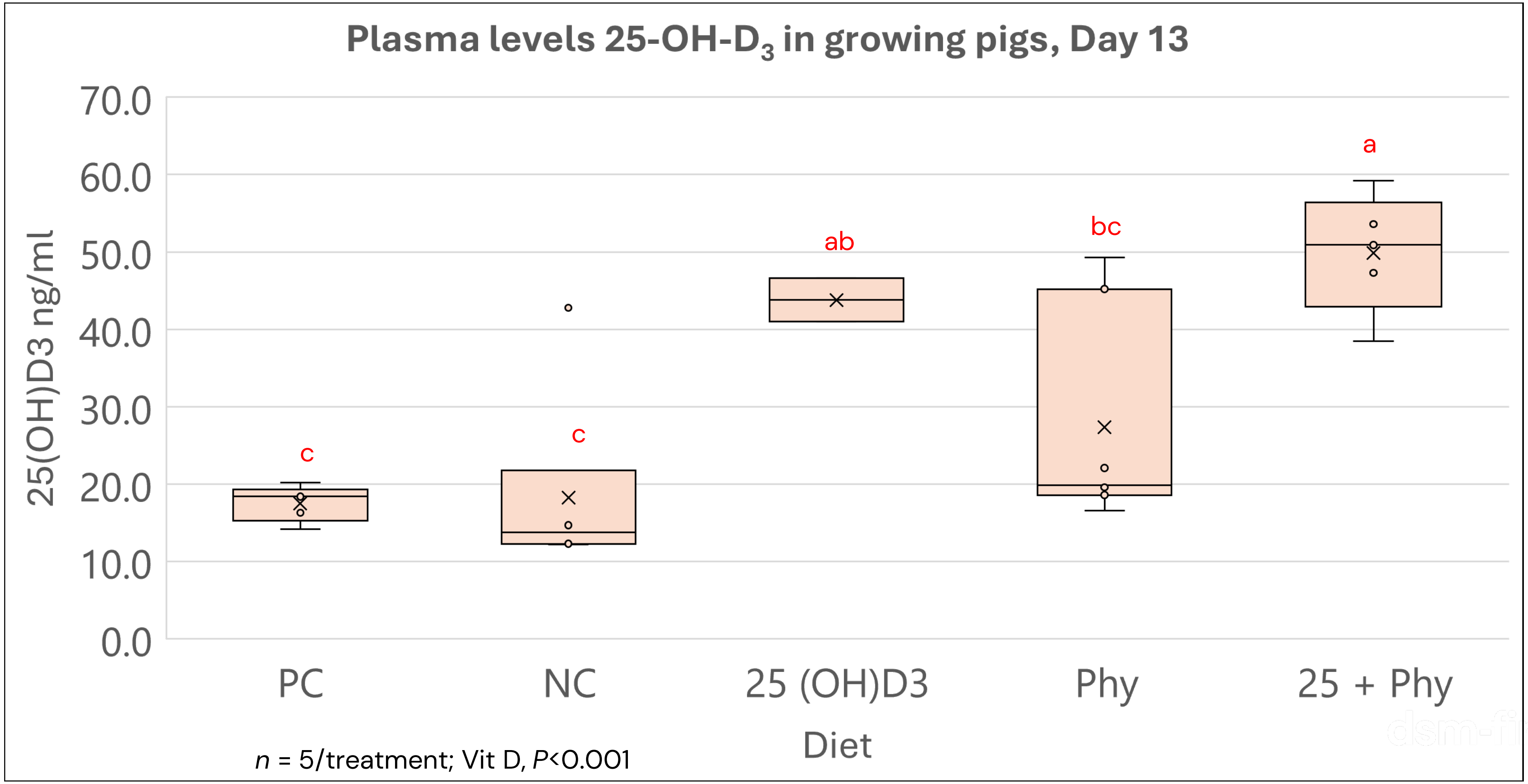
NC basal diet – 25% less total Ca and STTD P compared with PC (i.e., -0.17% total Ca and -0.08% digestible P, respectively). The calculated ratio between total Ca and digestible P was 2.13:1 in all diets.

Item	Positive control (PC)	No phytase		500 unit/kg of phytase		SEM	Contrast *P*-value			
		NC	25(OH)D_3	-	25(OH)D_3		NC vs. PC	Vit D	Phy	Vit D × Phy
ATTD of Ca, %	**68.40[b]**	**67.20[b]**	**72.92[b]**	**79.96[a]**	**80.26[a]**	**1.45**	0.550	**0.041**	**< 0.001**	**0.064**
BEL of Ca, mg/d	518	515	512	506	515	13	0.550	0.441	0.509	0.092
STTD of Ca, %	**74.87[c]**	**75.23[bc]**	**80.65[b]**	**88.07[a]**	**88.23[a]**	**1.45**	0.857	**0.056**	**< 0.001**	**0.072**
Absorbed Ca, g/d	**5.47[a]**	**4.31[c]**	**4.79[b]**	**4.99[b]**	**5.19[ab]**	**0.13**	**< 0.001**	**0.006**	**< 0.001**	0.226
ATTD of P, %	**54.64[bc]**	**48.53[c]**	**56.78[b]**	**69.24[a]**	**66.68[a]**	**1.57**	**0.008**	**0.078**	**< 0.001**	**0.001**
BEL of P, mg/d	227	226	225	222	226	6	0.550	0.442	0.509	0.093
STTD of P, %	**57.62[bc]**	**52.05[c]**	**60.15[b]**	**72.78[a]**	**70.11[a]**	**1.57**	**0.015**	**0.093**	**< 0.001**	**0.001**
Absorbed P, g/d	**4.16[ab]**	**3.11[c]**	**3.76[b]**	**4.34[a]**	**4.39[a]**	**0.12**	**< 0.001**	**0.007**	**< 0.001**	**0.019**

n = 12 per dietary treatment. Initial BW = 26 kg.
PC diet analyzed 1.1-to-1 Ca/P ratio
NC diets analyzed 1-to-1 Ca/P ratio

25-OH-D_3 and phytase (HiPhorius) improved plasma concentrations of 25-OH-D_3 in the 25 kg growing pig

Jaramillo et al., (2024) unpublished



25-OH-D_3 and phytase (HiPhorius) increased the bone formation biomarker, osteocalcin, in blood of the 25 kg growing pig

Jaramillo et al., (2024) unpublished

Blood concentrations of bone formation [osteocalcin (OC) and bone alkaline phosphatase (BAP)] and bone resorption (carboxyterminal cross-linked telopeptide of type I collagen; CTX-I) biomarkers, and biomarker for 25(OH)D_3-hydrolase (fibroblast growth factor; FGF23) in serum of growing pigs

Item	Positive control	No phytase		500 unit/kg		SEM	Contrast *P*-value			
	(PC)	**NC**	25(OH)D_3	-	25(OH)D_3		NC vs. PC	**Vit D**	**Phy**	**Vit D × Phy**
Day 13										
OC, µg/L	38.11[bc]	**35.98**[c]	39.47[abc]	**40.13**[ab]	**42.83**[a]	1.51	0.111	0.002	< 0.001	0.680
BAP, µg/L	64.90	62.75	65.83	61.52	60.82	6.16	0.629	0.721	0.360	0.564
CTX-I, µg/L	0.14	0.13	0.15	0.14	0.11	0.03	0.905	0.768	0.652	0.426
OC to CTX-I ratio	364	305	353	342	395	36	0.167	**0.115**	0.215	0.930
FGF-23, µg/L	0.42	0.42	0.44	0.41	0.43	0.04	0.900	0.526	0.754	0.997

n = 12 per dietary treatment. Initial BW = 26 kg.
PC diet analyzed 1.1-to-1 Ca/P ratio
NC diets analyzed 1-to-1 Ca/P ratio

(2022, Translational Animal Science, https://doi.org/10.1093/tas/txac124)

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JOURNAL ARTICLE ACCEPTED MANUSCRIPT

Use of fixed calcium to phosphorus ratios in experimental diets may create bias in phytase efficacy responses in swine

H Zhai, J R Bergstrom, J Zhang, W Dong, Z Wang, K Stamatopoulos, A J Cowieson

Comparison of available P release values based on different response variables, g/kg feed[1]

Response variable	1.05 Ca/P Phytase, FYT/kg feed				1.20 Ca/P Phytase, FYT/kg feed				SEM[2]	P-value 1.05 Ca/P		P-value 1.20 Ca/P		
	500	1000	1500	3000	500	1000	1500	3000		L[3]	Q[3]	L	Q	Ca/P ratio[4]
ADG[5], g/d	0.158	0.210	0.199	0.221	0.139	0.180	0.216	0.204	0.03	< 0.01	0.23	< 0.01	< 0.01	0.12
Gain:feed, g/kg	0.177	0.234	0.212	0.262	0.119	0.176	0.249	0.226	0.05	0.02	0.98	< 0.01	0.01	0.05
Bone ash, %	0.117	0.110	0.192	0.182	0.132	0.149	0.193	0.180	0.05	< 0.01	0.40	0.07	0.28	0.39
Bone P, g	0.125	0.148	0.198	0.197	0.131	0.184	0.207	0.221	0.04	< 0.01	0.17	< 0.01	0.13	0.09

[1]There were 6 replicates.
[2]SEM: standard error of the mean.
[3]Linear and quadratic effects of phytase.
[4]The effect of Ca/P ratio compares between the ratios of 1.05 and 1.20, and no significant interaction between phytase and the Ca/P ratio was observed.
[5]ADG, average daily gain.

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(2023, Translational Animal Science, https://doi.org/10.1093/tas/txad006)

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JOURNAL ARTICLE

The effects of increasing dietary total Ca/total P ratios on growth performance, Ca and P balance, and bone mineralization in nursery pigs fed diets supplemented with phytase

Hengxiao Zhai, Jon Bergstrom, Jingcheng Zhang, Wei Dong, Zhenzhen Wang, Kostas Stamatopoulos, Aaron J Cowieson

	PC	Ca/P ratio 0.55	0.73	0.90	1.07	1.24
Formulated						
Ca	0.62	0.23	0.30	0.37	0.44	0.52
P	0.56	0.41	0.41	0.41	0.41	0.41
Ca/P	1.10	0.55	0.73	0.90	1.07	1.24
Phytase	0	1000	1000	1000	1000	1000
Analyzed						
Ca	0.63	0.24	0.31	0.38	0.45	0.52
P	0.58	0.42	0.42	0.41	0.41	0.40
Ca/P	1.09	0.58	0.75	0.93	1.11	1.30
Phytase	0	1083	1077	1033	1121	1101

	PC	Ca/P ratio					SEM	PC *vs* others	Ca/P ratio	
		0.55	0.73	0.90	1.07	1.24			L	Q
IBW, kg	8.3	8.3	8.3	8.3	8.3	8.3	0.01	0.756	0.823	0.531
FBW, kg	19.7	19.8	19.9	20.2	19.8	19.6	0.22	0.624	0.528	0.123
ADG, g/d/pig	546	548	553	570	548	540	10.2	0.617	0.531	0.107
ADFI, g/d/pig	720	724	723	735	729	726	14.0	0.659	0.836	0.666
Gain: feed, g/kg	758	758	766	776	751	744	5.7	0.920	0.029	0.006
Bone ash, g	6.1	5.0	5.3	5.5	5.6	5.8	0.17	0.002	< 0.001	0.719
Bone Ca, g	2.2	1.8	1.9	2.0	2.0	2.1	0.06	< 0.001	< 0.001	0.756
Bone P, g	1.1	0.9	1.0	1.0	1.0	1.1	0.03	0.003	0.001	0.670
Bone Ca/P	1.98	1.92	1.94	1.95	1.96	1.99	0.011	0.023	< 0.001	0.656

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(2023, Translational Animal Science, https://doi.org/10.1093/tas/txad122)

HiPhorius™

JOURNAL ARTICLE

The effects of concurrent increases in supplementation of calcium and phytase on growth performance, balance of Ca and P, and bone mineralization in nursery pigs

Hengxiao Zhai, Jon Bergstrom, Jingcheng Zhang, Wei Dong, Zhenzhen Wang, Kostas Stamatopoulos, Aaron J Cowieson

Analyzed Ca and P content (as-is, %) and phytase activity (FYT/kg) of dietary treatments

Diet[1]	Ca	P	Ca/P ratio	Phytase
PC 1	0.65	0.63	1.04	48
PC 2	0.84	0.64	1.31	67
NC	0.49	0.45	1.09	52
Ca/phytase, %/FYT				
0.48/1,750	0.48	0.44	1.10	1,822
0.52/2,000	0.51	0.44	1.17	2,038
0.55/2,250	0.56	0.44	1.28	2,301
0.59/2,600	0.59	0.44	1.35	2,668
0.63/3,000	0.65	0.44	1.48	3,003

[1]NC, negative control; PC, positive control.

Summary and Conclusions

"Increasing the dietary addition of phytase in coordination with increased levels of Ca increased the digestible Ca/P ratio of the diet but prevented a compromise in P absorption.

The higher digestible Ca/P ratios with increasing Ca and phytase did not markedly impair or improve growth or bone mineralization while extra Ca was voided through urine."

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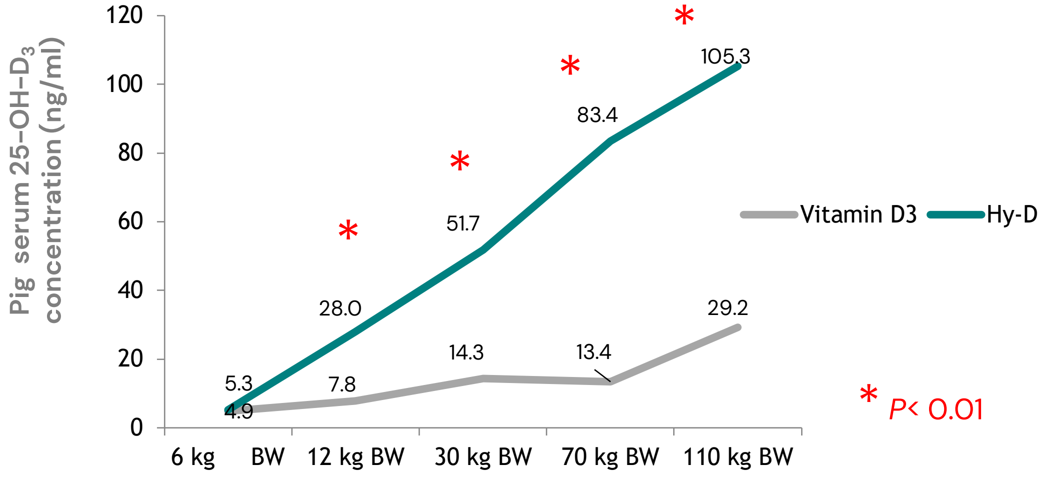
Increased vitamin D status is associated with reduced incidence of osteochondrosis (OCD) in pigs

Sugiyama et al., 2013

Treatments:

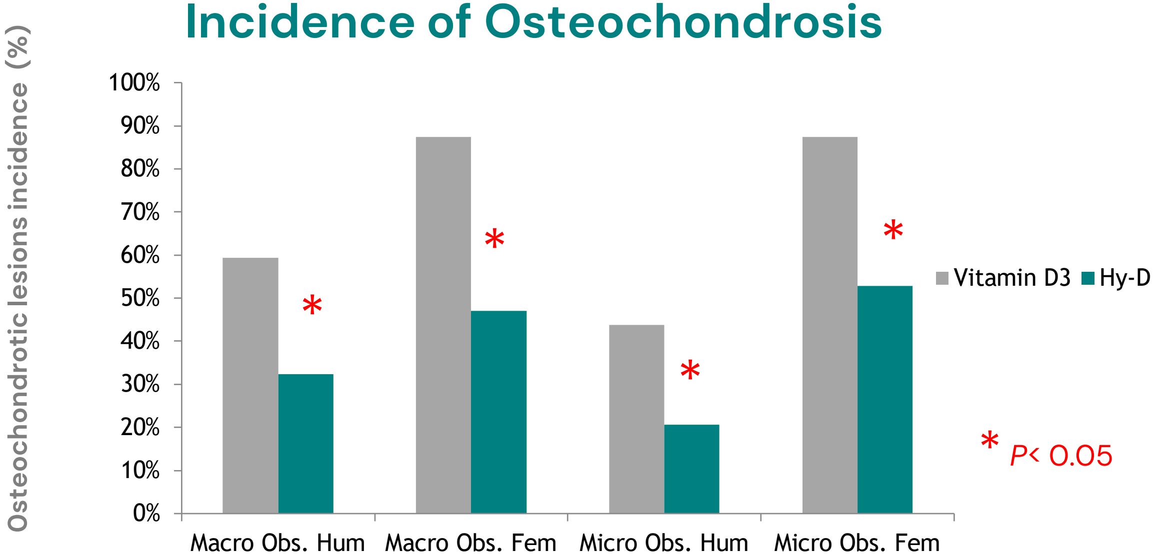
- ✓ **Vitamin D3 (D3)**: Vitamin D_3 according to existing Japan Feed Standards; 1,800 – 1,500 IU/kg feed
- ✓ **Hy-D: D3** + 25-OH-D_3 at 50 µg/Kg feed (Rovimix Hy•D®)

25-OH-D_3 in Blood Serum



Significant increase in the serum concentration of 25-OH-D_3 for pigs fed diets supplemented with Hy-D®

Incidence of Osteochondrosis



Dietary supplementation with Hy-D® significantly reduced the incidence of osteochondrosis lesions

Hy-D® supplementation demonstrated a tendency for promoting normal endochondral ossification, inhibited progression of osteochondrosis, and possibly increased healing of destroyed cartilage tissue.

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Use of 25-OH-D_3 favors opportune and sound bone maturation in growing and developing gilts

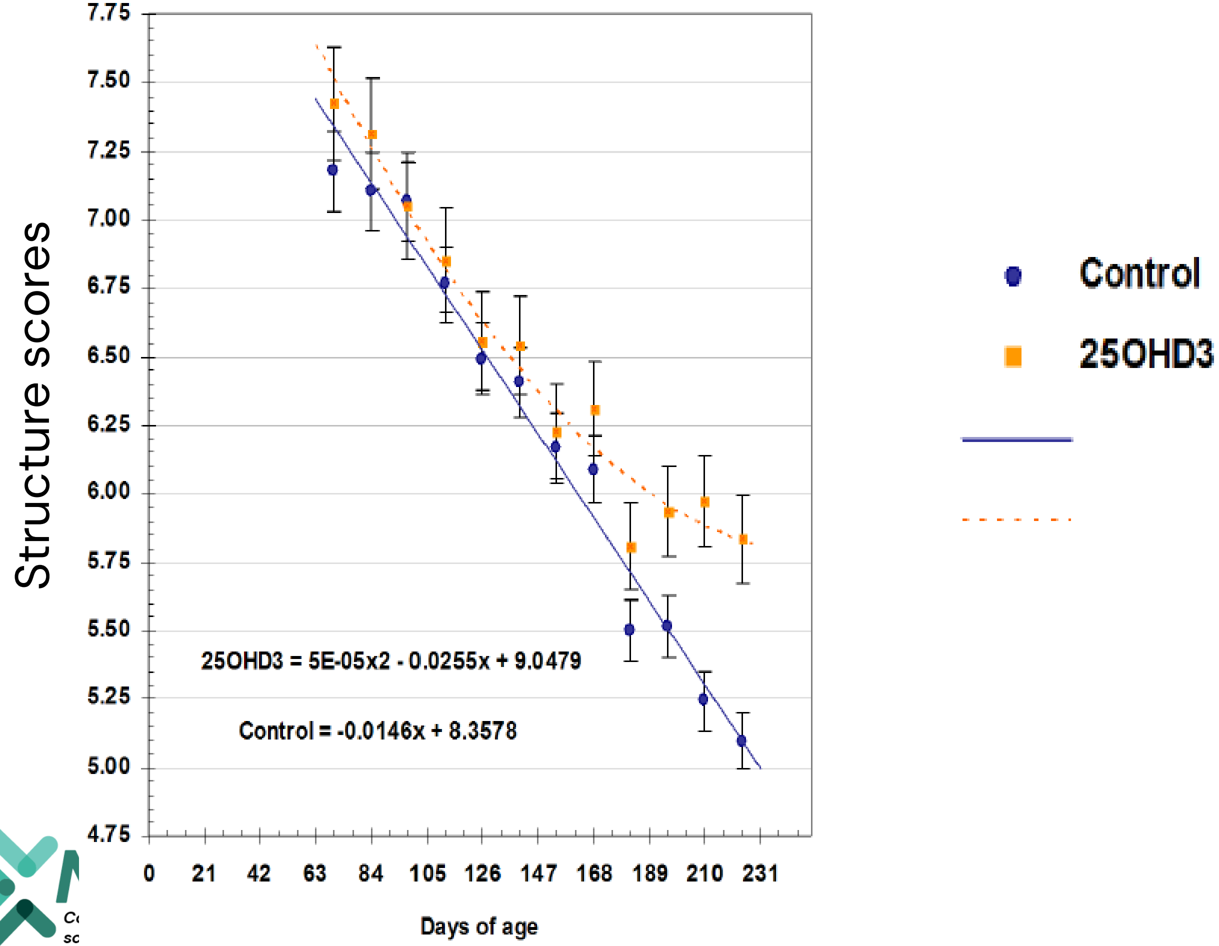
Braña et al., 2012, Midwestern Meetings of ASAS

Control: *2,000 down to 1,530 IU/kg vitamin D_3, by phase;* **25OHD3**: *Control D_3 + 50 µg/kg 25-OH-D_3 from Hy·D*

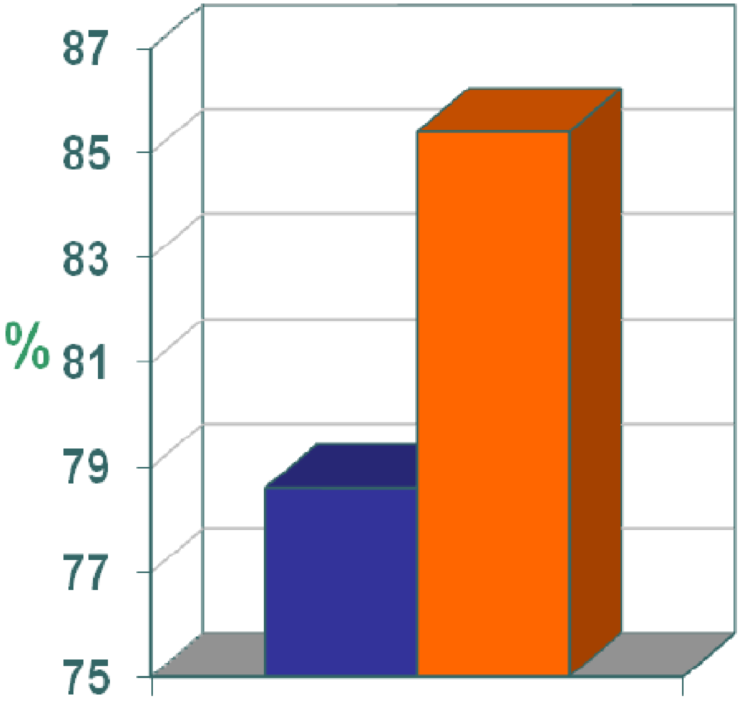
1-3, unacceptable; severe structural problems that restrict the animal's ability to move and to breed.

4-6, good; gilts with slight structural and/or movement problems.

7-9, excellent; no obvious structural or movement problems; includes even toe size, adequate length of stride, flexion of hock and pastern cushion, trueness and freeness of movement.



Proportion of gilts selected as fit for breeding, according to the mobility and structural soundness score (>6)



Note: For reproductive traits, no differences were found for the weights of ovaries (10.33 ± 4.675 g) or age at first estrus (175 ± 6.316 days).

Vitamin D – new and continuing discoveries of its important functions for healthy bone and beyond…

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24R,25-Dihydroxyvitamin D_3: An Essential Vitamin D_3 Metabolite for Both Normal Bone Integrity and Healing of Tibial Fracture in Chicks*

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JCI The Journal of Clinical Investigation

Optimal bone fracture repair requires 24R,25-dihydroxyvitamin D_3 and its effector molecule FAM57B2

Corine Martineau, … , Glenville Jones, René St-Arnaud

J Clin Invest. 2018;128(8):3546-3557. https://doi.org/10.1172/JCI98093.

Research Article | Bone Biology | Endocrinology

PLOS | ONE

RESEARCH ARTICLE

24R,25-Dihydroxyvitamin D3 Protects against Articular Cartilage Damage following Anterior Cruciate Ligament Transection in Male Rats

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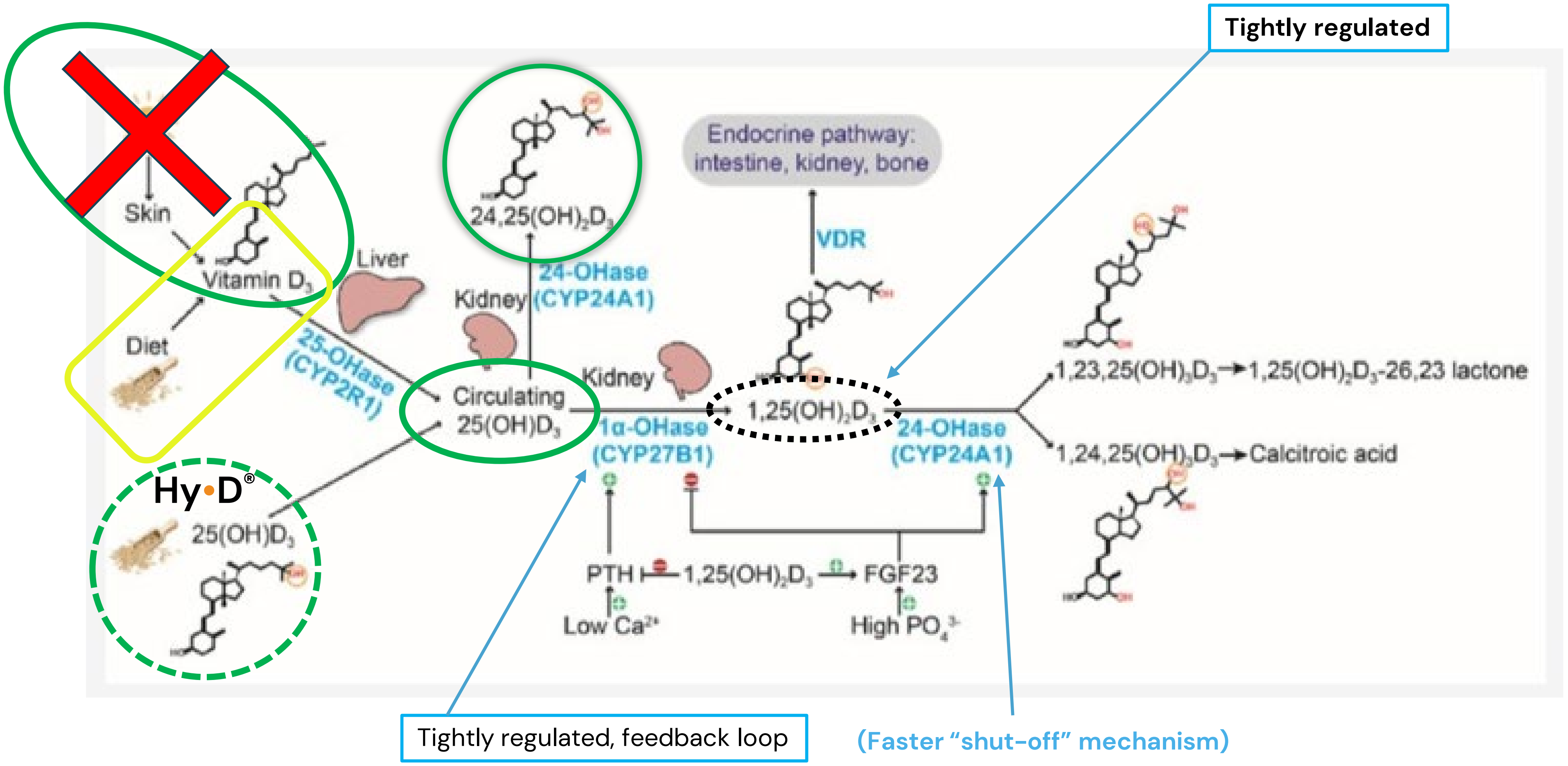
Abstract

Osteoarthritis (OA) in humans is associated with low circulating 25-hydroxyvitamin D3 [25(OH)D_3]. In vitamin D replete rats, radiolabeled 24R,25-dihydroxyvitamin D3 [24R,25(OH)$_2D_3$] accumulates in articular cartilage following injection of [^{3}H]-25(OH)D_3. Previously, we showed that 24R,25(OH)$_2D_3$ blocks chondrocyte apoptosis via phospholipase D and p53, suggesting a role for 24R,25(OH)$_2D_3$ in maintaining cartilage health. We examined the ability of 24R,25(OH)$_2D_3$ to prevent degenerative changes in articular cartilage in an OA-like environment and the potential mechanisms involved. In vitro, rat articular chondrocytes were treated with IL-1β with and without 24R,25(OH)$_2D_3$ or 1α,25(OH)$_2D_3$. 24R,25(OH)$_2D_3$ but not 1α,25(OH)$_2D_3$ blocked the effects of IL-1β in a dose-dependent manner, and its effect was partially mediated through the TGF-β1 signaling pathway. In vivo, unilateral anterior cruciate ligament transections were performed in immunocompetent rats followed by intra-articular injections of 24R,25(OH)$_2D_3$ or vehicle (t = 0, 7, 14, 21 days). Tissues were harvested on day 28. Joints treated with vehicle had changes typical of OA whereas joints treated with 24R,25(OH)$_2D_3$ had less articular cartilage damage and levels of inflammatory mediators. These results indicate that 24R,25(OH)$_2D_3$ protects against OA, and suggest that it may be a therapeutic approach for preventing trauma-induced osteoarthritis.

doi:10.1371/journal.pone.0161782

Vitamin D sources and metabolism



Summary and Conclusions

- ✓ "Lameness is a frequent health and welfare problem in pigs. It also causes great economic losses."

- ✓ Lameness is frequently associated with infectious causes or a poor health status.

- ✓ "Inconclusive findings" is a common diagnosis for Lameness cases
  - ✓ Healthy pigs – rapid growth? Injuries? - Housing / Flooring / Management – (e.g., Bos et al. 2016. https://doi.org/10.2527/jas.2015-0245)

- ✓ Metabolic bone disease and Osteochondrosis are frequently diagnosed causes for Lameness
  - ✓ Insufficient Ca, P, and/or Vitamin D are commonly associated with poor bone mineralization and metabolic bone diseases
    - ✓ After a primary diagnosis of other causes, metabolic bone disease can be a leading secondary cause for lameness – health status matters, too!

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Summary and Conclusions

- ✓ The requirements for Ca and P are fairly-well understood, but let's make sure that we're meeting them – requirements for optimizing growth are lower than those for maximizing bone mineralization, especially for Ca.
- ✓ Know the actual Ca and P (and phytase) content in your ingredients and diets. Understand phytase and how it works (or doesn't work). Higher phytase doses can provide a margin of safety.
- ✓ Vitamin D status is important, especially when Ca and P are marginal, and an improved status reduces the risk for lameness while ensuring there is a sufficient amount for bone/tissue development, repair and healing.
- ✓ Monitor your animals' vitamin D status. Feeding vitamin D_3 alone is unreliable with pigs housed indoors, feeding 25-OH-D_3 is more biologically efficient and effective.

≥ 30 ng/mL 25-OH-D_3 is sufficient for Ca/P status and bone health

60 – 90 ng/mL 25-OH-D_3 for optimizing bone health and immunity