Does the time of hypocalcemia diagnosis matter?

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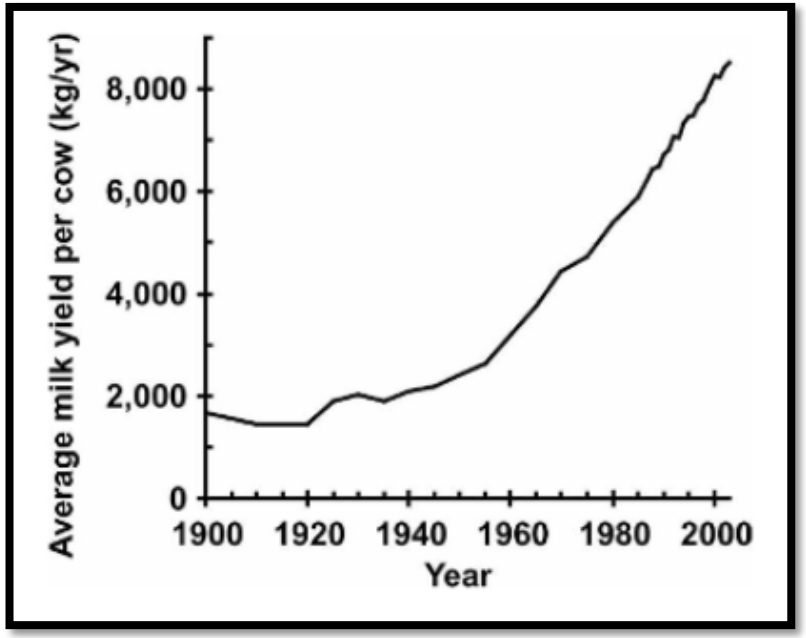
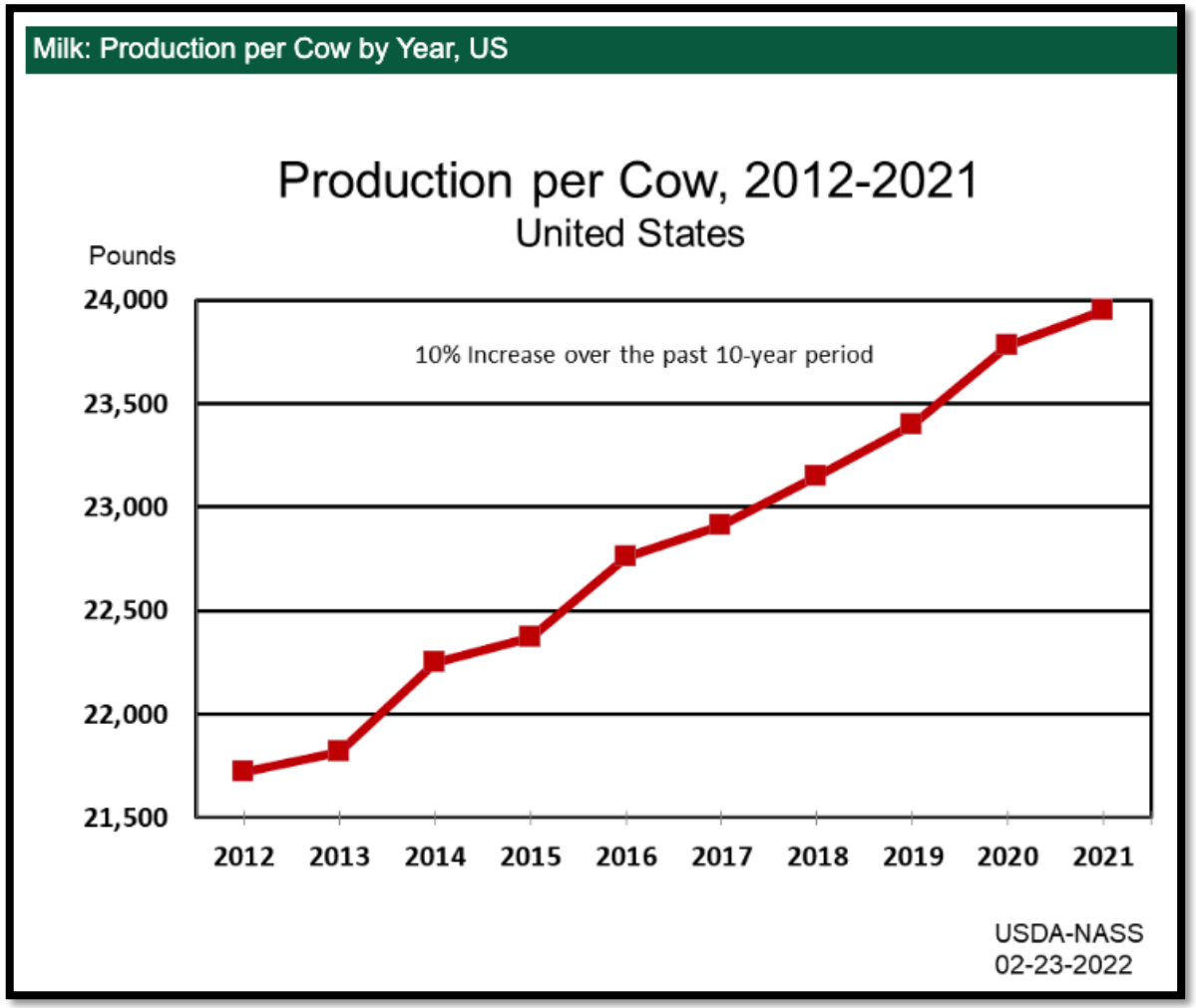
Overview

- Calcium demands of milk production
- Subclinical hypocalcemia and calcium dynamics
- Dyscalcemia and dry matter intake
- Dyscalcemia and reproduction
- Association with inflammation

The average cow of today:



VandeHaar and St-Pierre, J Dairy Sci, 2006

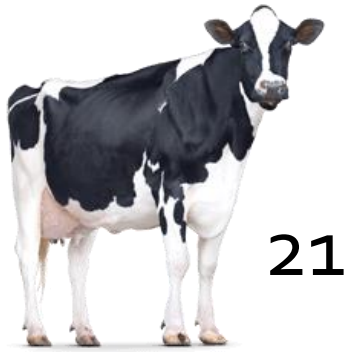


- Many cows producing >45 kg by end of 1st week
- Lactation initiates massive change in nutrient and macromineral demands

- Our job: provide the environment to support needs
- Today: focus on calcium

Calcium demands of milk production

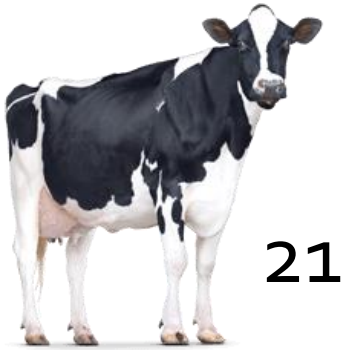
Prior to calving:



21 g Ca

21 g Ca

At calving:



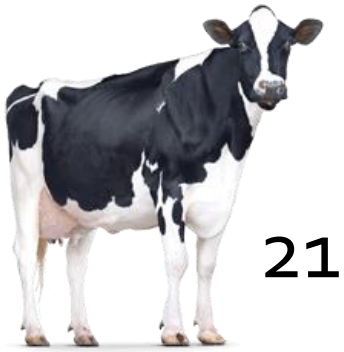
21 g Ca

+

23 g Ca

44 g Ca

7 days in milk:



21 g Ca

+

56 g Ca

77 g Ca

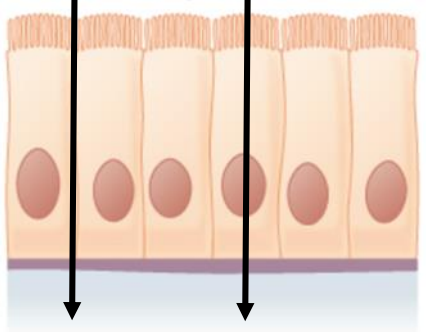
Increasing blood calcium

↑ PTH secretion

↓ Ca excretion
25-OH vit D → 1,25(OH)$_2$D
(minutes)

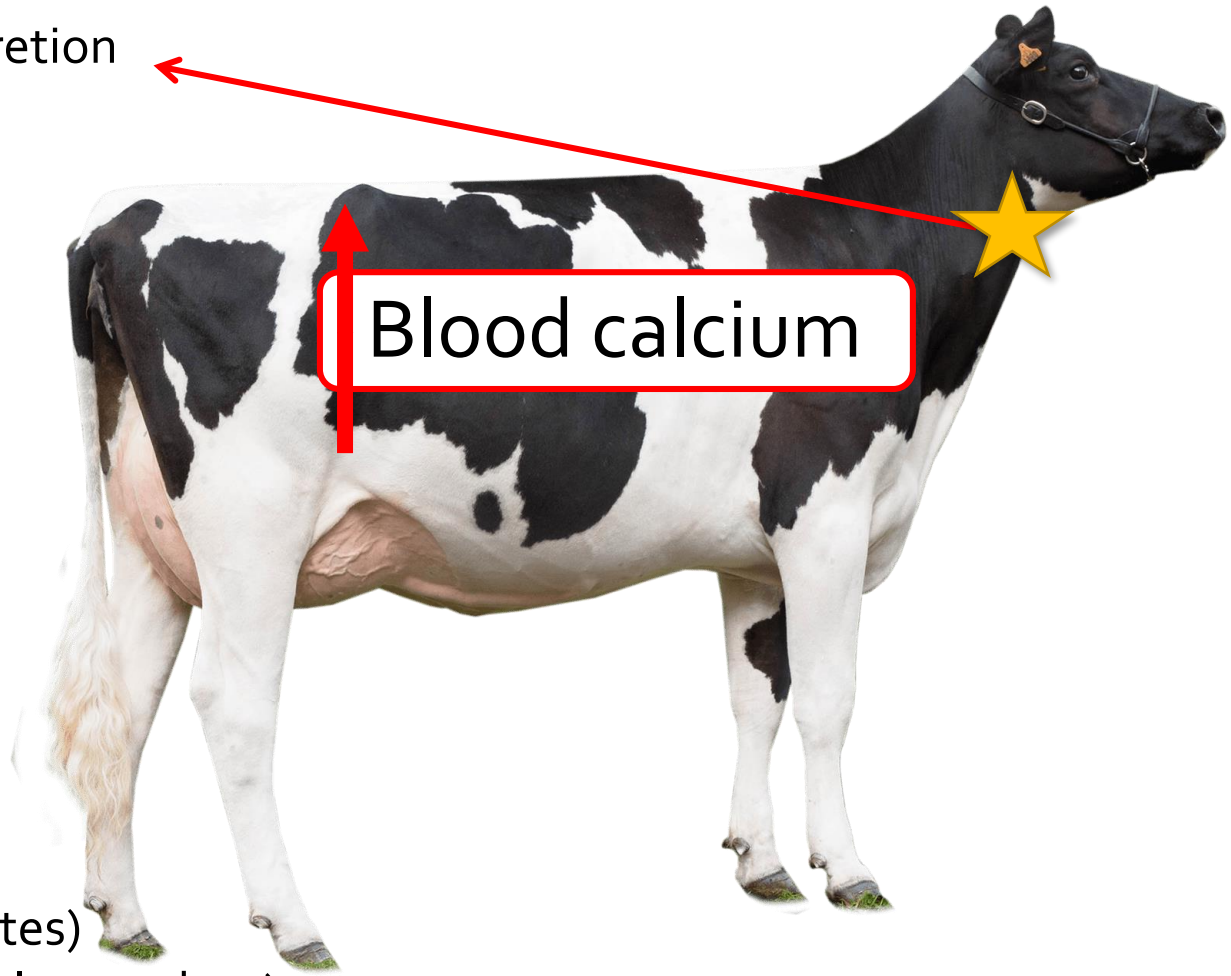
Paracellular Ca transport

Transcellular Ca transport



↑ Ca absorption
(days)

↑ Ca release
(osteocytes = minutes)
(osteoblasts/osteoclasts = days)



What is subclinical hypocalcemia?

Subclinical hypocalcemia (SCH)

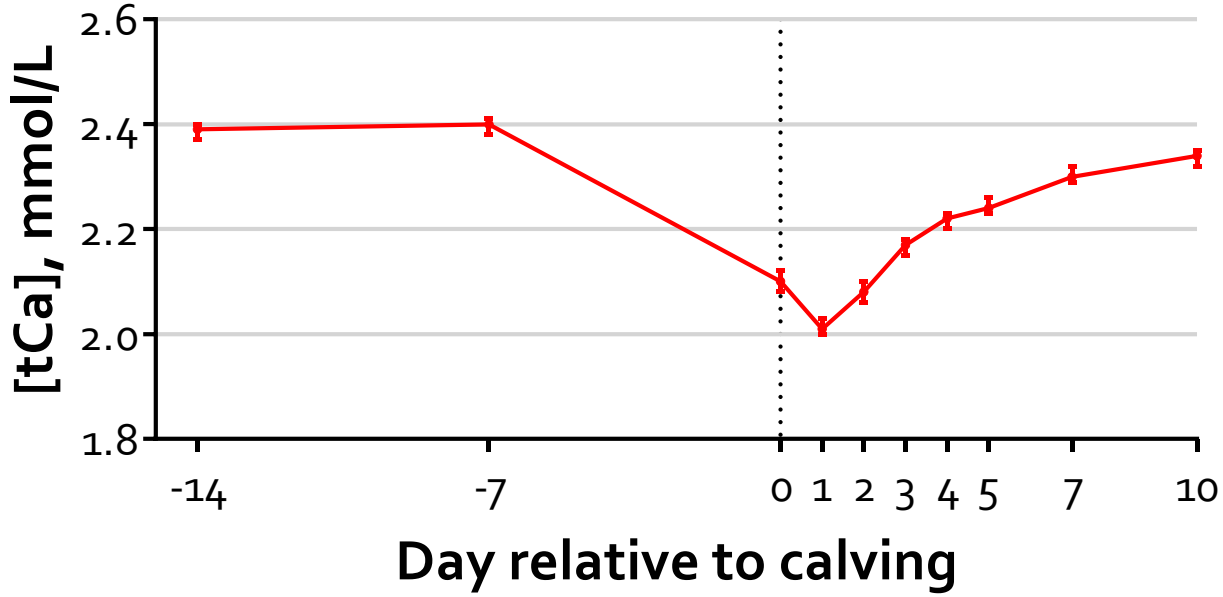
- Multiple studies have explored categorization of blood calcium concentrations in early lactation
  Oetzel et al., 1988; Oetzel et al., 1996; Martinez et al., 2012

- Recent studies use epidemiologic outcomes to improve characterization
  Chapinal et al., 2011; Rodriguez et al., 2017; Wilhelm et al., 2017; Neves et al., 2018; Venjakob et al., 2018

- No consensus on optimal test day or what cut point to use for classification of SCH

Is subclinical hypocalcemia bad?

- When to test:
  - At calving?
  - At 24 hrs?
  - At 48 hrs?
  - Later?



- What cut-point to use:
  - Definition of "normal"
  - Based on health and production outcomes

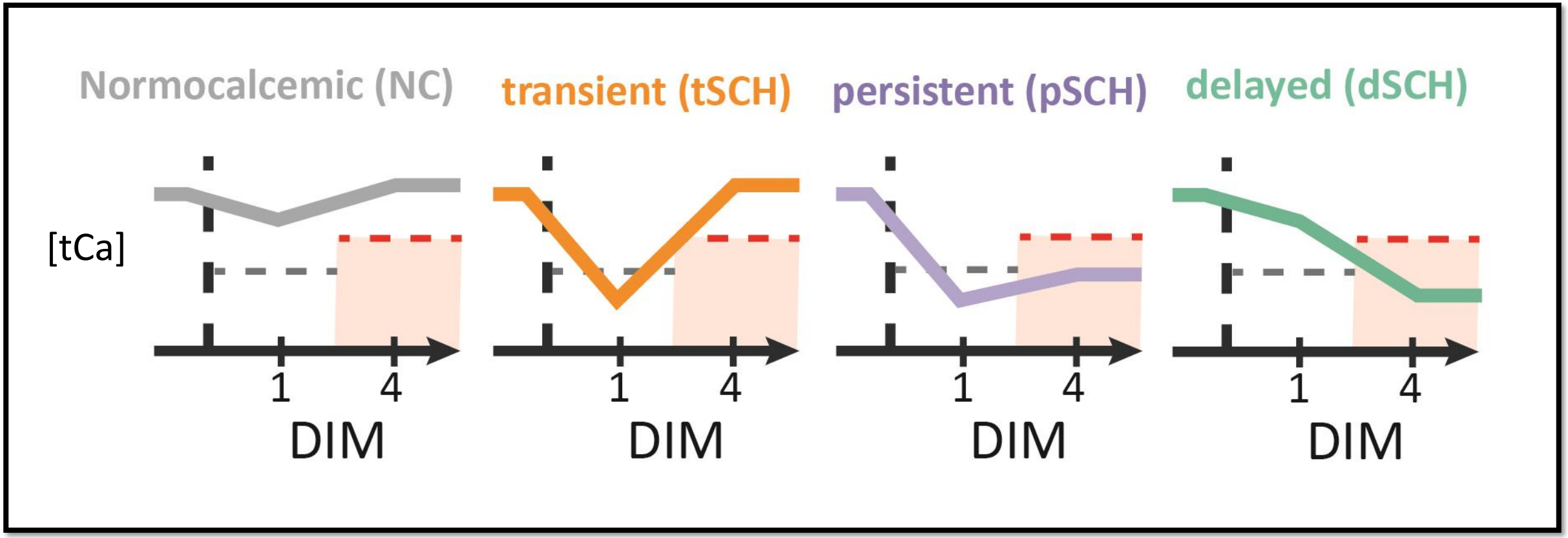
Calcium dynamics by "cohort"

- Can we quantify differences in calcium dynamics between cows?
- Parity ≥2: cohort based on DIM 1 & 4

Normocalcemic	1 DIM [Ca]	↑
	4 DIM [Ca]	↑
Transient SCH	1 DIM [Ca]	↓
	4 DIM [Ca]	↑
Persistent SCH	1 DIM [Ca]	↓
	4 DIM [Ca]	↓
Delayed SCH	1 DIM [Ca]	↑
	4 DIM [Ca]	↓

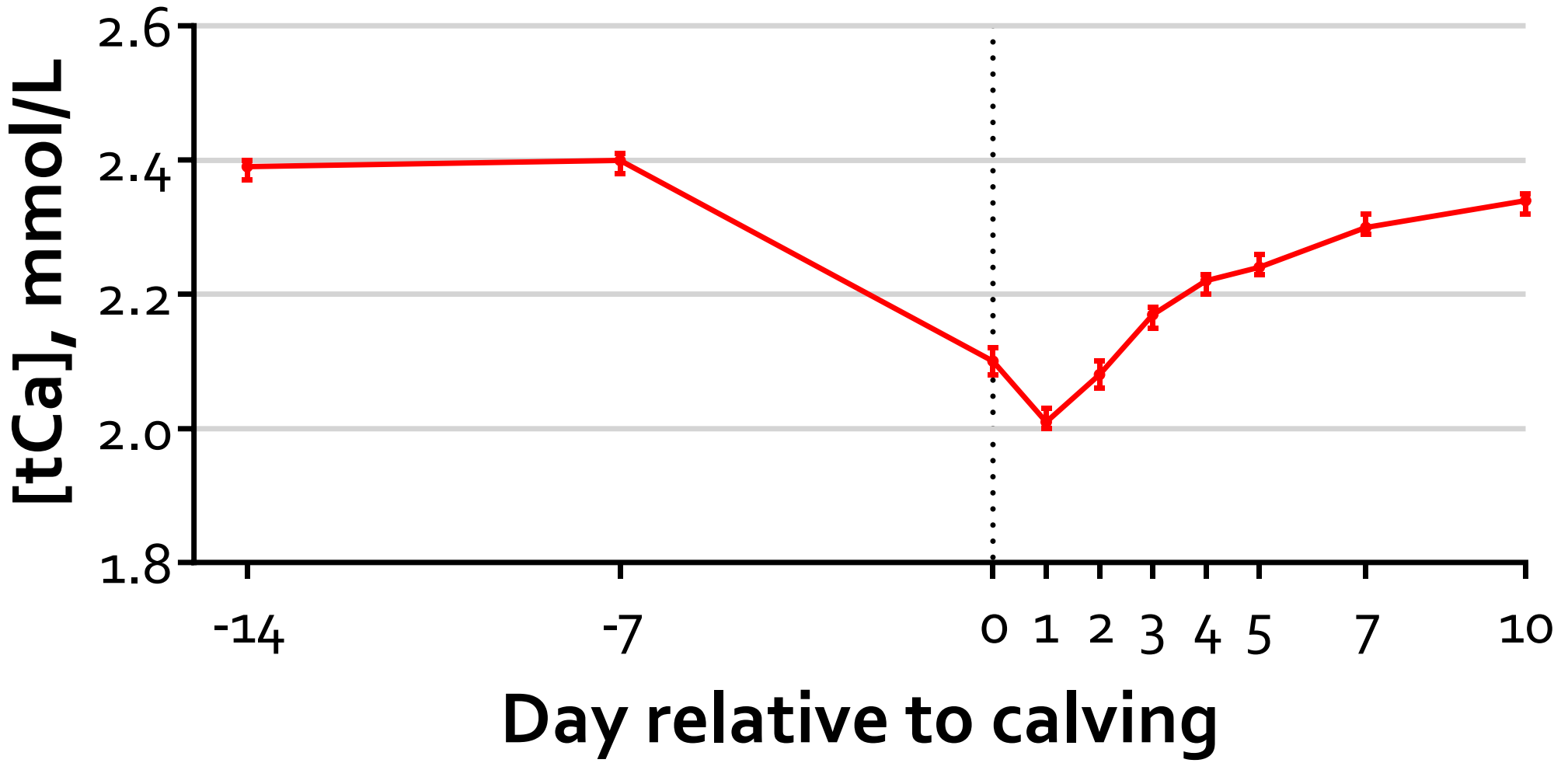
Neves et al., JDS, 2018; McArt and Neves, JDS, 2020

Calcium dynamic groups



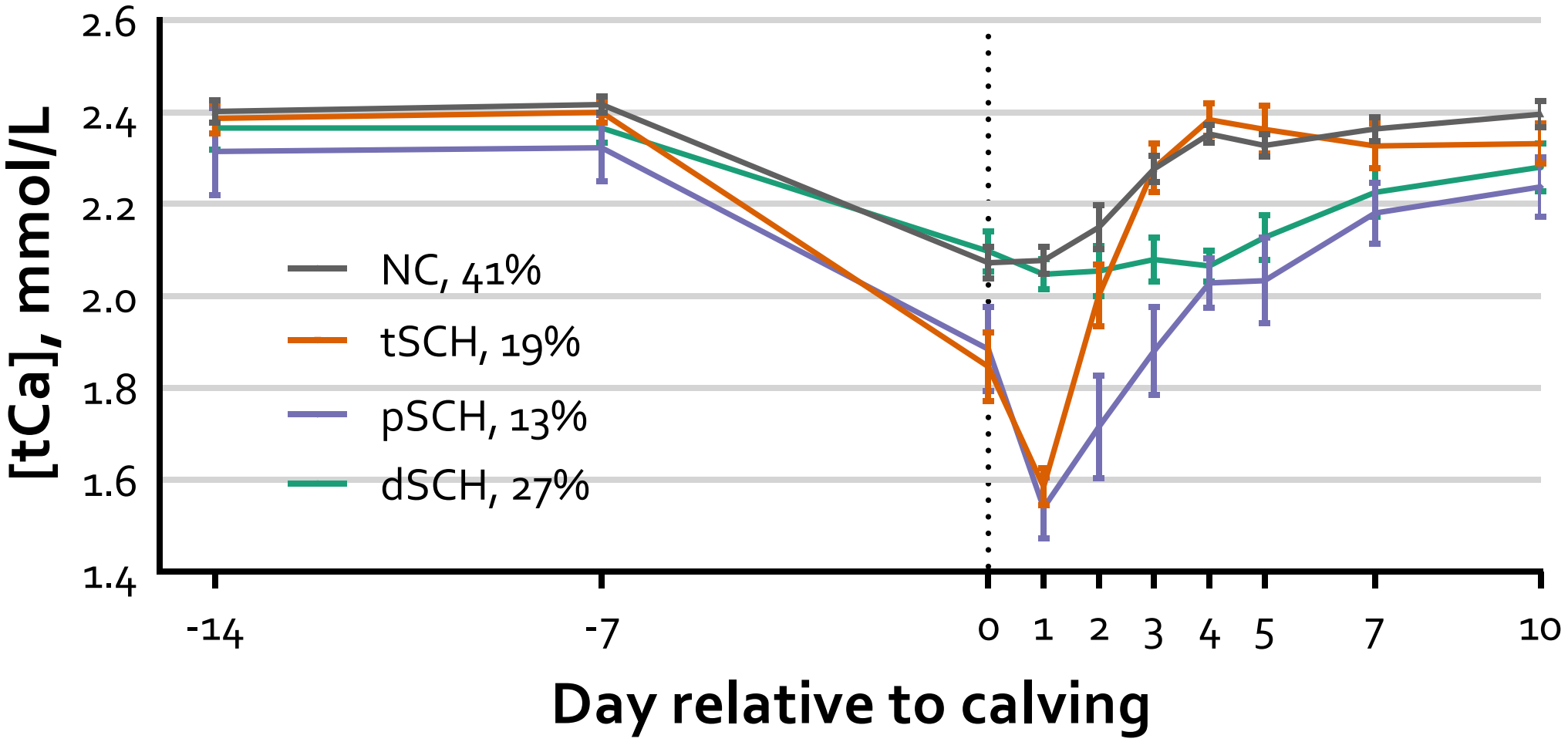
Courtesy: J. A. Seminara; McArt and Oetzel, *VCNA*, 2023

Calcium dynamics



(tCa: 1 mmol/L = 4 mg/dL)

Calcium dynamics: parity ≥2



Error bars represent ± SD.

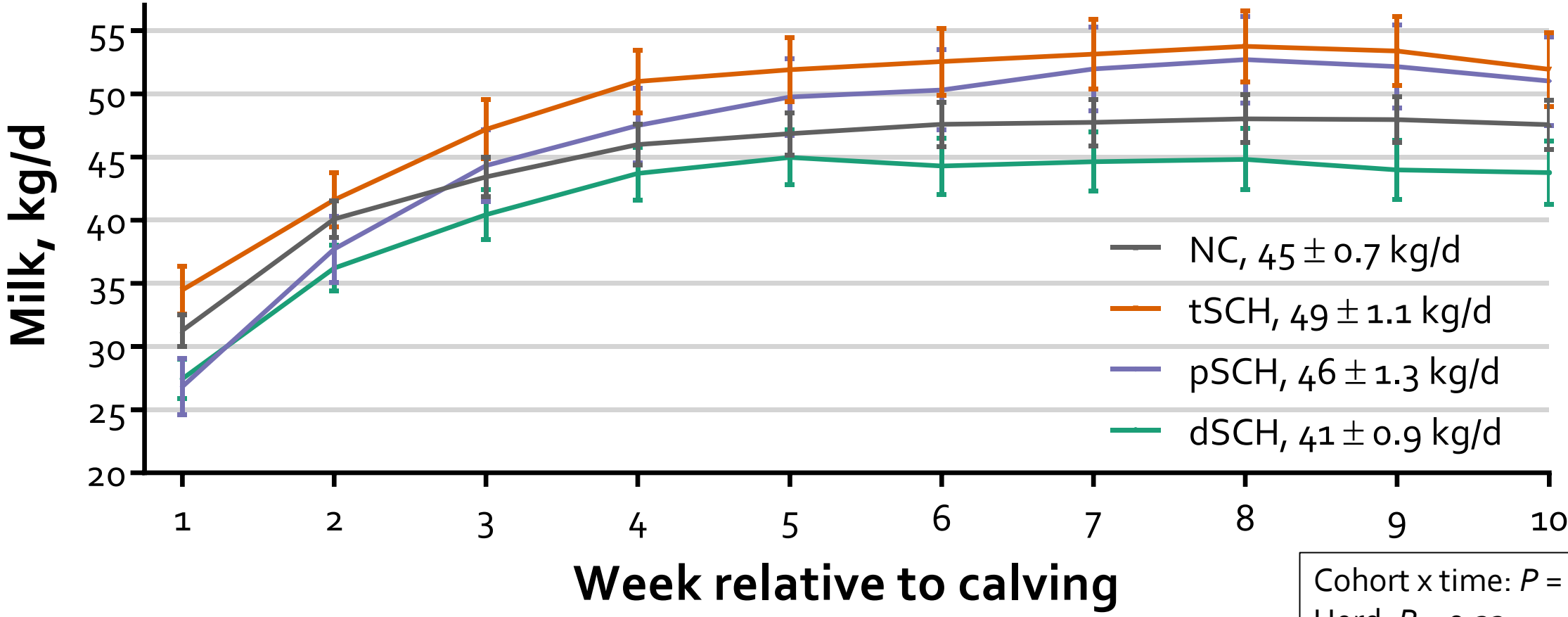
McArt and Neves., J Dairy Sci 103:690-701.

Disease: parity ≥2

	Metritis	DA	Herd Removal
NC, n = 109	6%	2%	1%
tSCH, n = 50	4%	2%	2%
pSCH, n = 34	18%	12%	3%
dSCH, n = 70	13%	9%	13%

McArt and Neves, J Dairy Sci, 2020

Milk yield: parity ≥2



Cohort x time: $P = 0.009$
Herd: $P = 0.22$

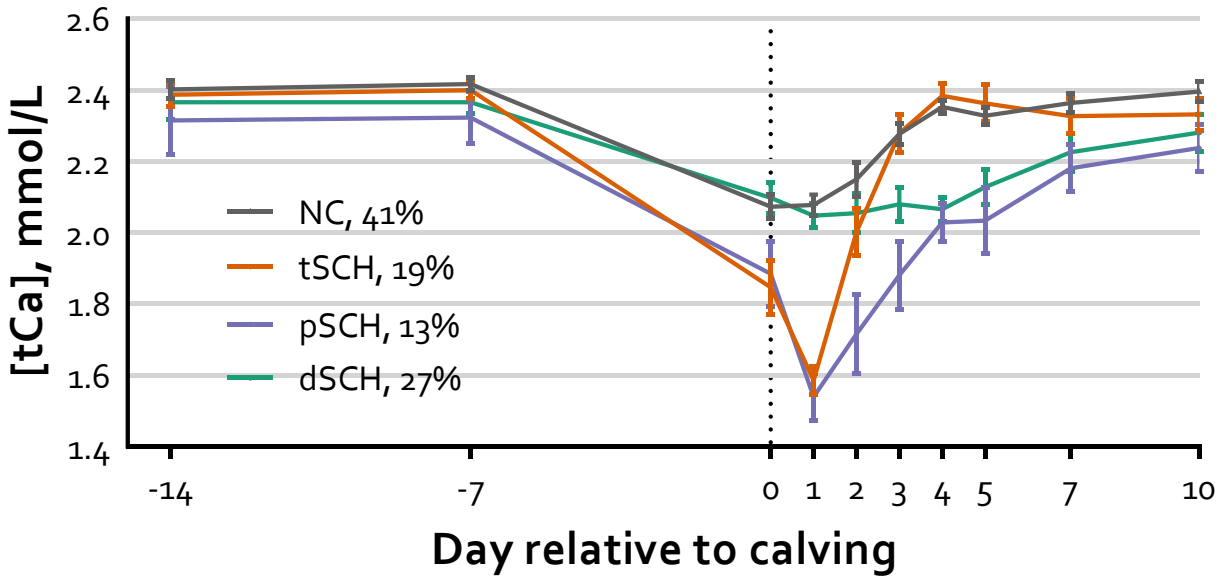
Error bars represent 95% confidence intervals.

McArt and Neves., J Dairy Sci, 2020

What did we learn?

- Conclusions:
  - Cows differ in dynamics of calcium change in early lactation
  - Differences associated with risk of adverse events and milk yield

- Why?
  - Dry matter intake?
  - Failure of homeostatic regulation?
  - Cause or effect of disease?



Association of subclinical hypocalcemia dynamics with dry matter intake, milk yield, and blood minerals during the periparturient period

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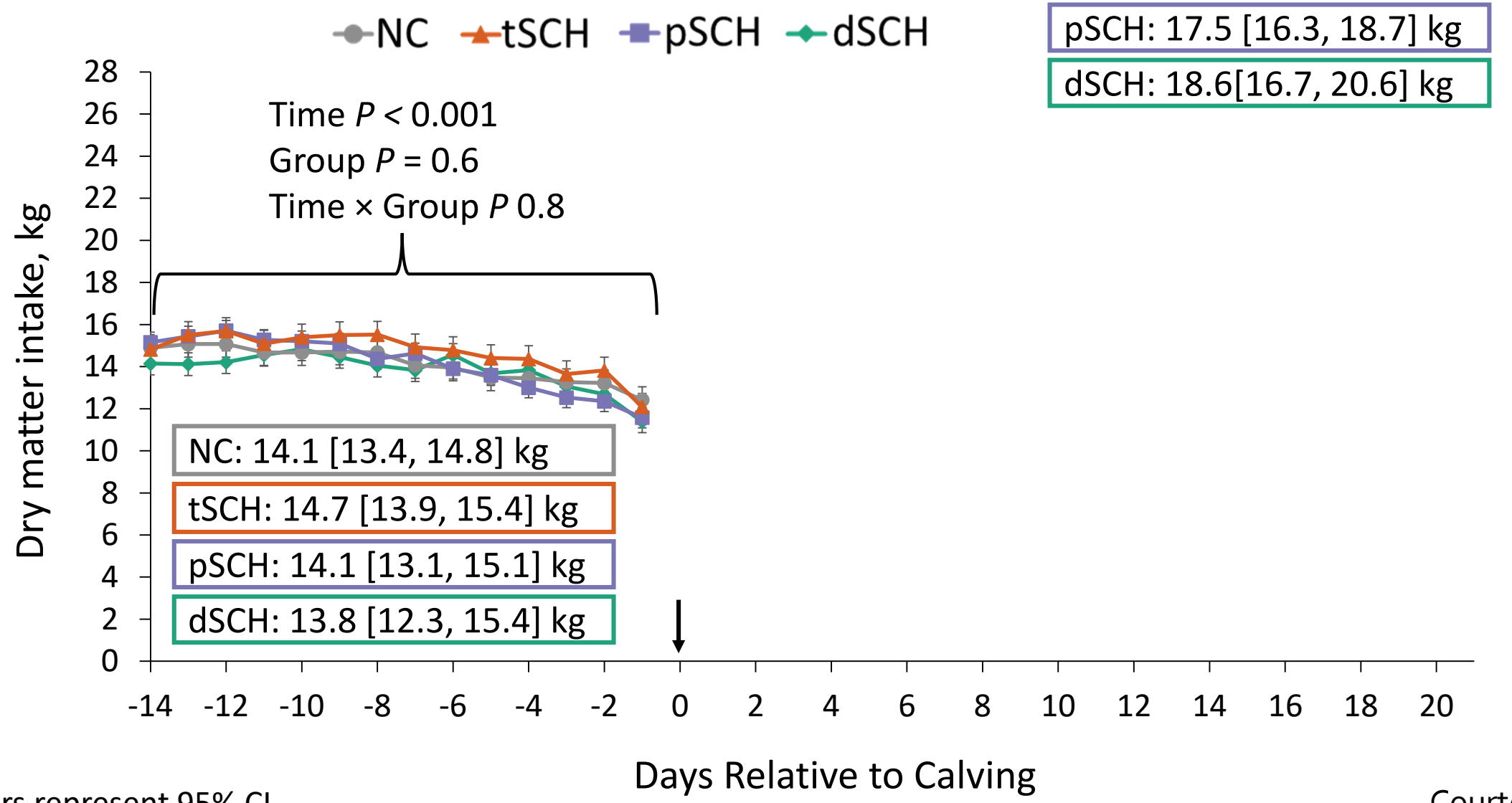
Materials and methods

- Multiparous Holstein cows (n = 78)
  - Leno et al. (2017a;b)
  - Kerwin et al. (2019)
- Housed in tie-stalls at the Cornell University Ruminant Center
- Individual DMI recorded daily from 14 d prior to parturition → 21 DIM
- Blood sampled from 1-6, & 10 DIM

Normocalcemic (NC; n = 28)	1 DIM [Ca] ↑	4 DIM [Ca] ↑
Transient SCH (tSCH; n = 27)	1 DIM [Ca] ↓	4 DIM [Ca] ↑
Persistent SCH (pSCH; n = 17)	1 DIM [Ca] ↓	4 DIM [Ca] ↓
Delayed SCH (dSCH; n = 6)	1 DIM [Ca] ↑	4 DIM [Ca] ↓

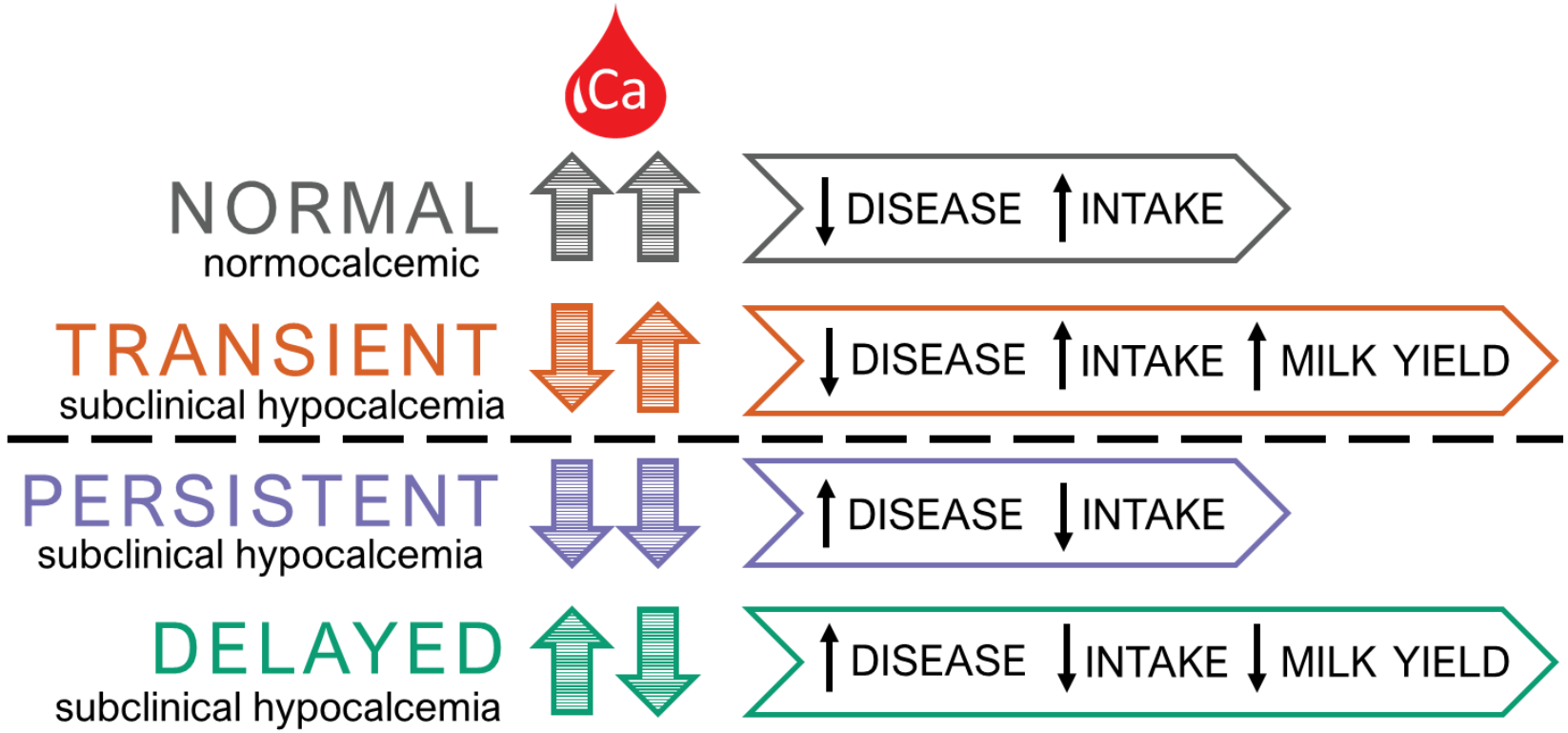
Results: DMI



Error bars represent 95% CI

Courtesy: C. Seely

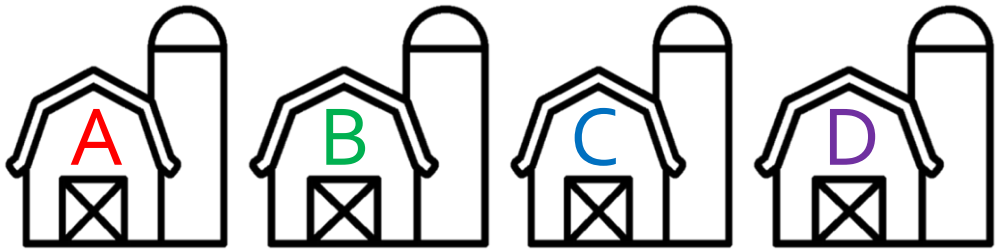
Calcium dynamics – good vs. bad



Modified from: McArt and Oetzel, *VCNA*, 2023

Is dyscalcemia associated with reproduction?

- Association of dyscalcemia with the odds of pregnancy to first service and time to pregnancy through 150 DIM

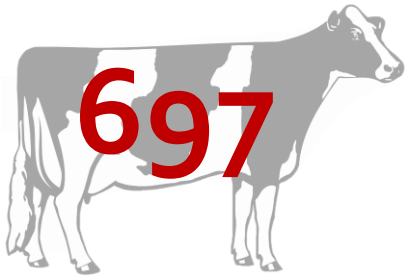


A; n = 65

B; n = 30

C; n = 87

D; n = 515



Blood collected at 4 DIM

4 DIM tCa cutpoint of 2.2 mmol/L

Normocalcemia (NC), n = 515 (74%)

Dyscalcemia (DYS), n = 182 (26%)

Results

Variable		Incidence (%)[1]	OR[2]/HR[3]	95% CI	*P*-value
Time of first AI DIM					
	NC	64 days		62.3 to 65.4	0.28
	DYS	65 days		63.4 to 66.8	

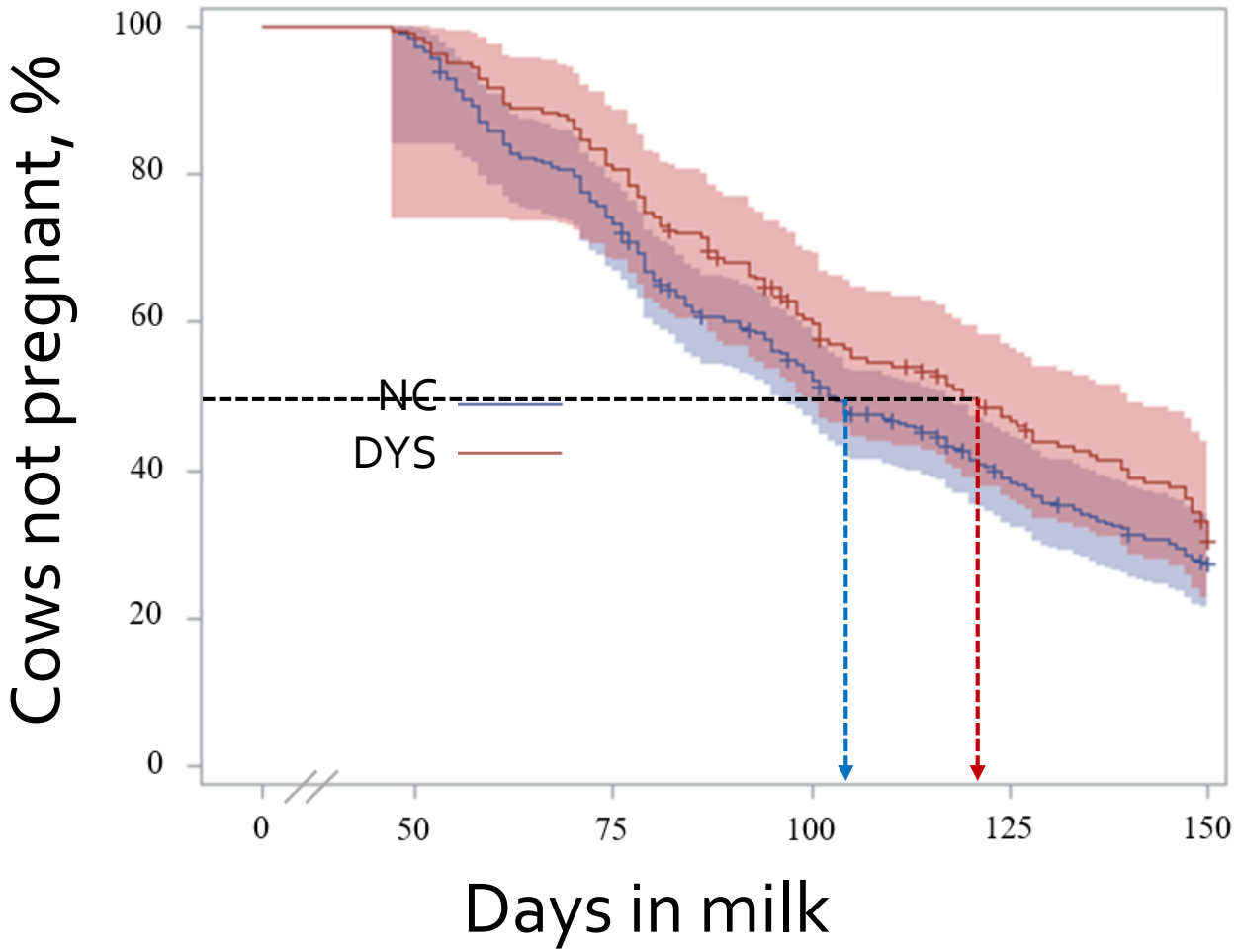
[1] Mean DIM of first AI and incidence (%) for pregnancy to 1st service and pregnant by 150 DIM

[2] Odds ratio of pregnant to 1st service

[3] Hazard ratio of pregnancy by 150 DIM

Adapted from: C. Seely

Results



Median time to pregnancy

NC = 103 ± 11 d

DYS = 119 ± 16 d

P = 0.15

Adapted from: C. Seely

How do we apply this information to our herds?

- Should we test calcium dynamics at 1 & 4 DIM?
  - Pros: get a good sense of the proportion of tSCH cows
  - Cons: need to take 2 samples from same cows and twice as expensive

- Should we test for dyscalcemia?
  - Pros: only 1 blood sample needed at 4 DIM
  - Cons: less information on tSCH, pSCH, and dSCH cows

- What cut points should we use for tCa?
  - 1 DIM: ~1.9 mmol/L, better to get a sense of direction of tCa change
  - **4 DIM: <2.2 mmol/L**

Is dyscalcemia a disease or a marker of disease?

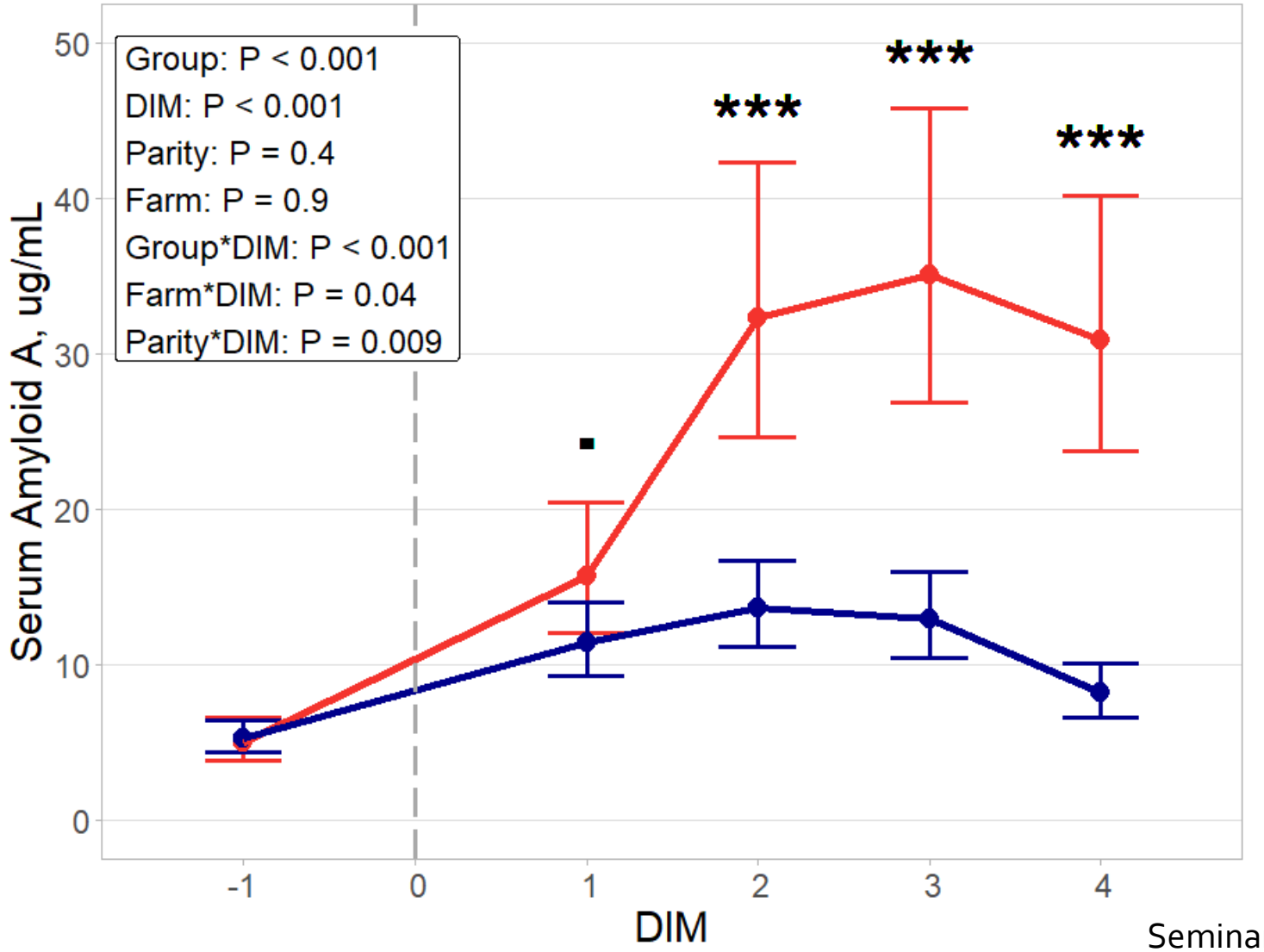
Is dyscalcemia a marker of disease?

- We know that reduced dry matter intake is associated with dyscalcemia.
- We know that mammals exposed to lipopolysaccharide (LPS) have drops in blood calcium.
- Is dyscalcemia a marker of an early disease process or excessive inflammation?
  - 56 cows on 2 commercial dairies
  - Classified as dyscalcemic or eucalcemia → markers of inflammation

Serum Amyloid A

Eucalcemic (EC; n = 36): tCa > 2.2 mmol/L at 4 DIM

Dyscalcemic (DYS; n = 20): tCa ≤ 2.2 mmol/L at 4 DIM

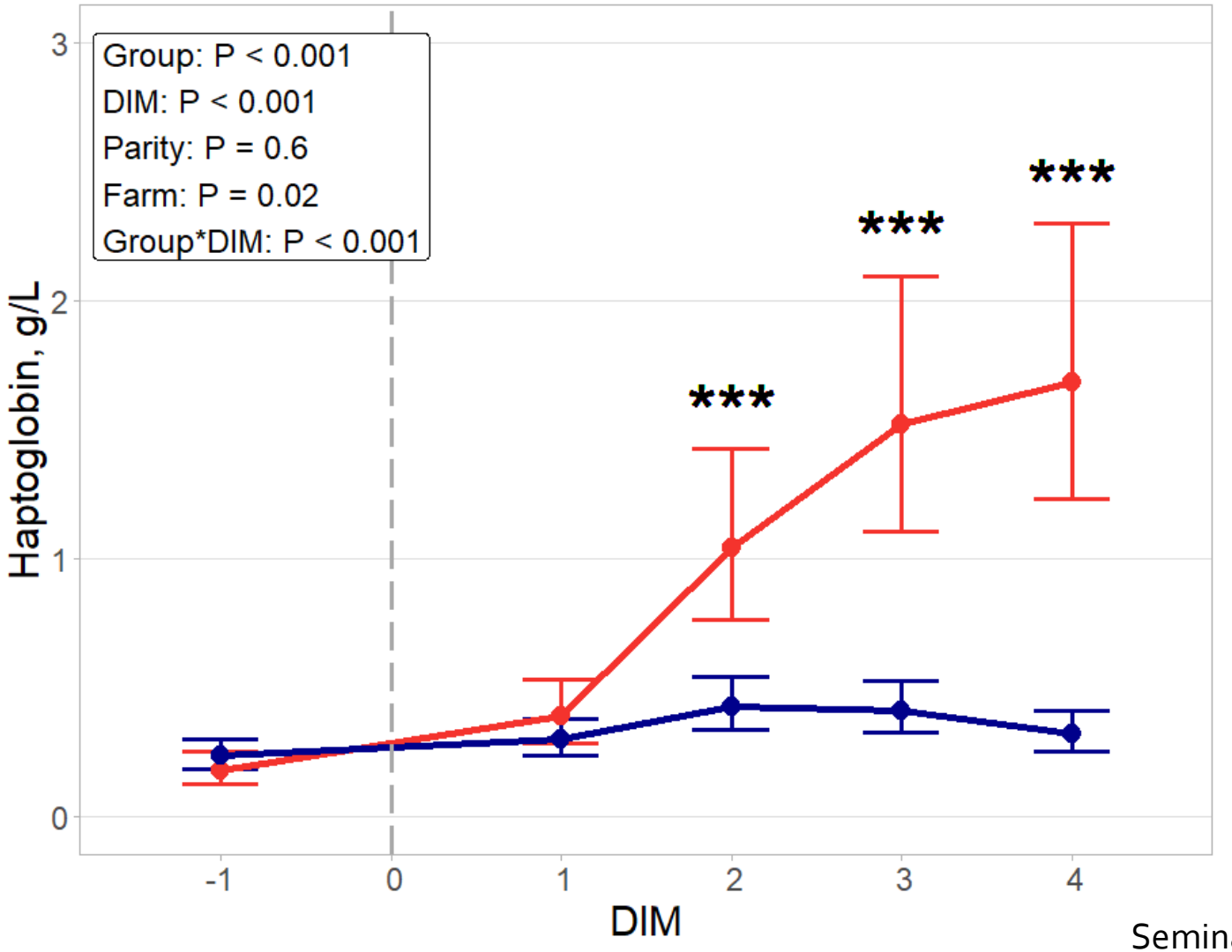


Seminara et al., *JDS*, 2025

Haptoglobin

Eucalcemic (EC; n = 36): tCa > 2.2 mmol/L at 4 DIM

Dyscalcemic (DYS; n = 20): tCa ≤ 2.2 mmol/L at 4 DIM

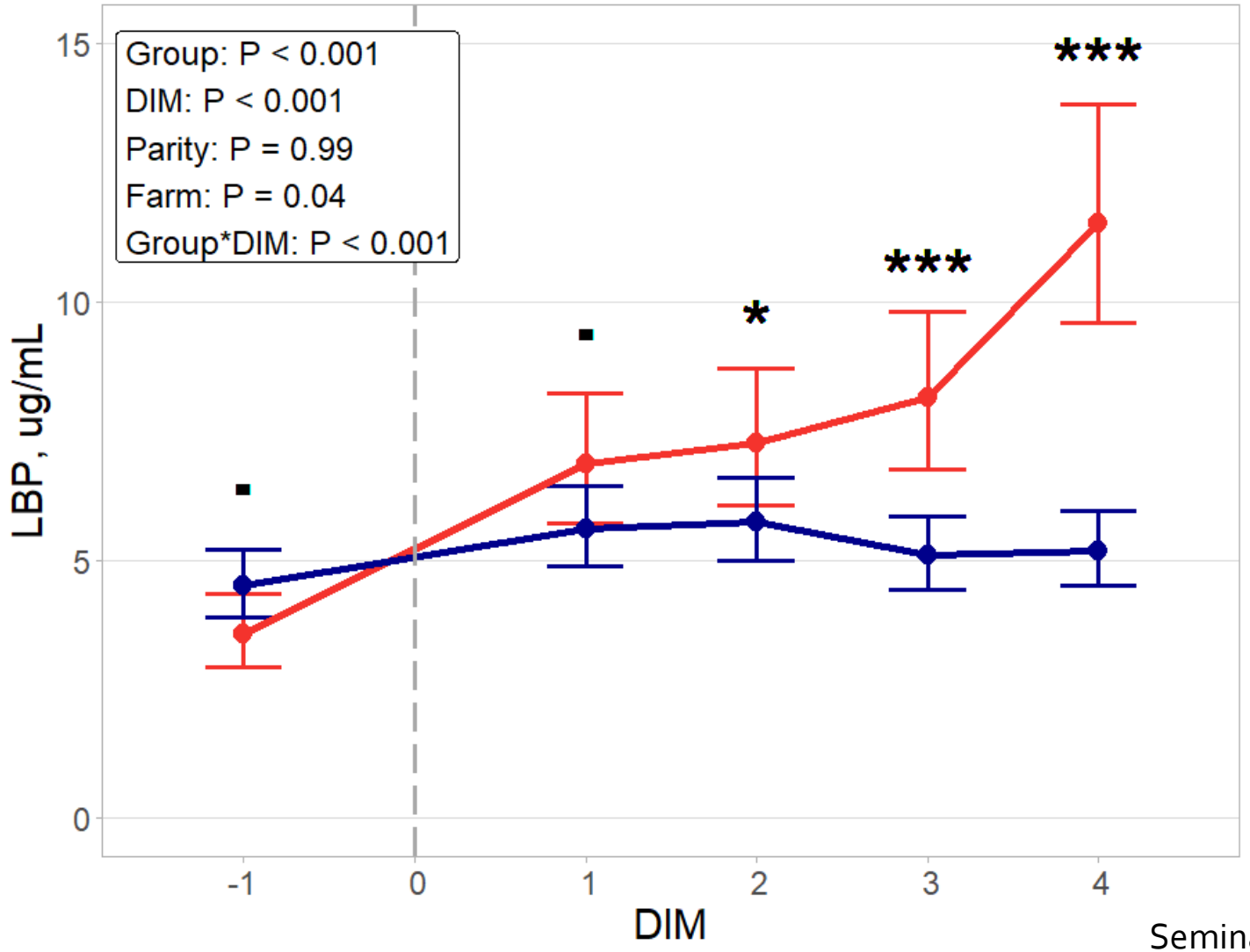


Seminara et al., *JDS*, 2025

Lipopolysaccharide binding protein (LBP)

Eucalcemic (EC; n = 36): tCa > 2.2 mmol/L at 4 DIM

Dyscalcemic (DYS; n = 20): tCa ≤ 2.2 mmol/L at 4 DIM



Seminara et al., *JDS*, 2025

Inflammation & dyscalcemia

- We know that excessive inflammation and dyscalcemia are highly associated.

- We do not know if:
  - Excessive inflammation causes dyscalcemia

  OR
  - Some process is leading to excessive inflammation and dyscalcemia

- Regardless, dyscalcemia is a good marker of this poor phenotype in early lactation cows.

Summary

- Understanding postpartum calcium dynamics and the relationship with inflammation is important
- Dyscalcemia at 4 DIM is associated with bad outcomes
- Herd-level monitoring can tell you a lot about transition management
- **Next:** how best to sample and test cows for dyscalcemia

Acknowledgements

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jmcartdvm