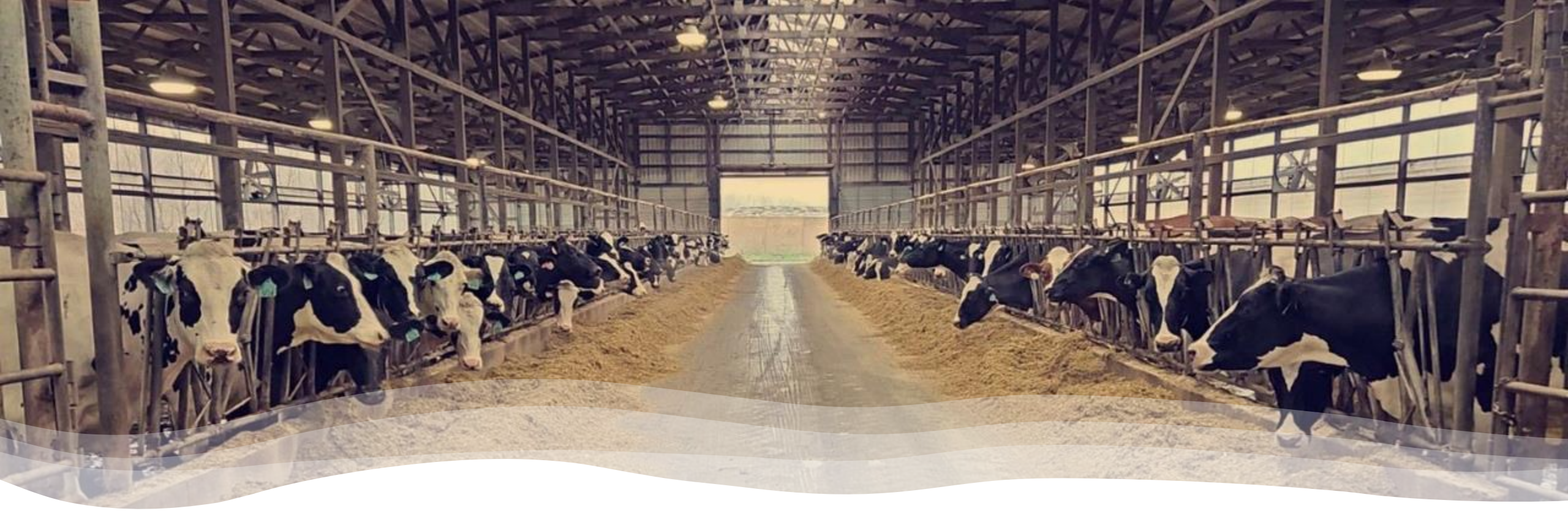


# Prevention & Treatment of Subclinical Hypocalcemia to Optimize Health & Production in Dairy Cattle

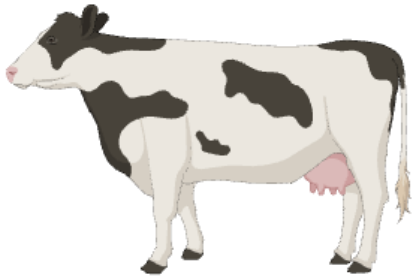
Dr. Claira Seely

University of New Hampshire

# Overview

- Ca challenge and homeostasis
- Importance of blood Ca dynamics in early lactation
- Subclinical hypocalcemia prevention/mitigation strategies
- Next steps

# Calcium Challenge of Early Lactation



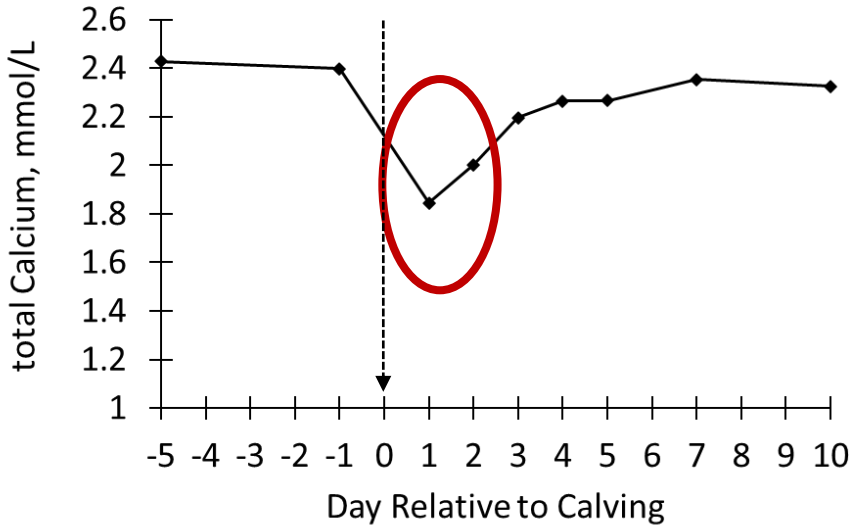
Cow
**21 g Ca/d**

Colostrum
**23 g Ca**

45 lb/d milk
**33 g Ca/d**

More than doubles Ca requirement!

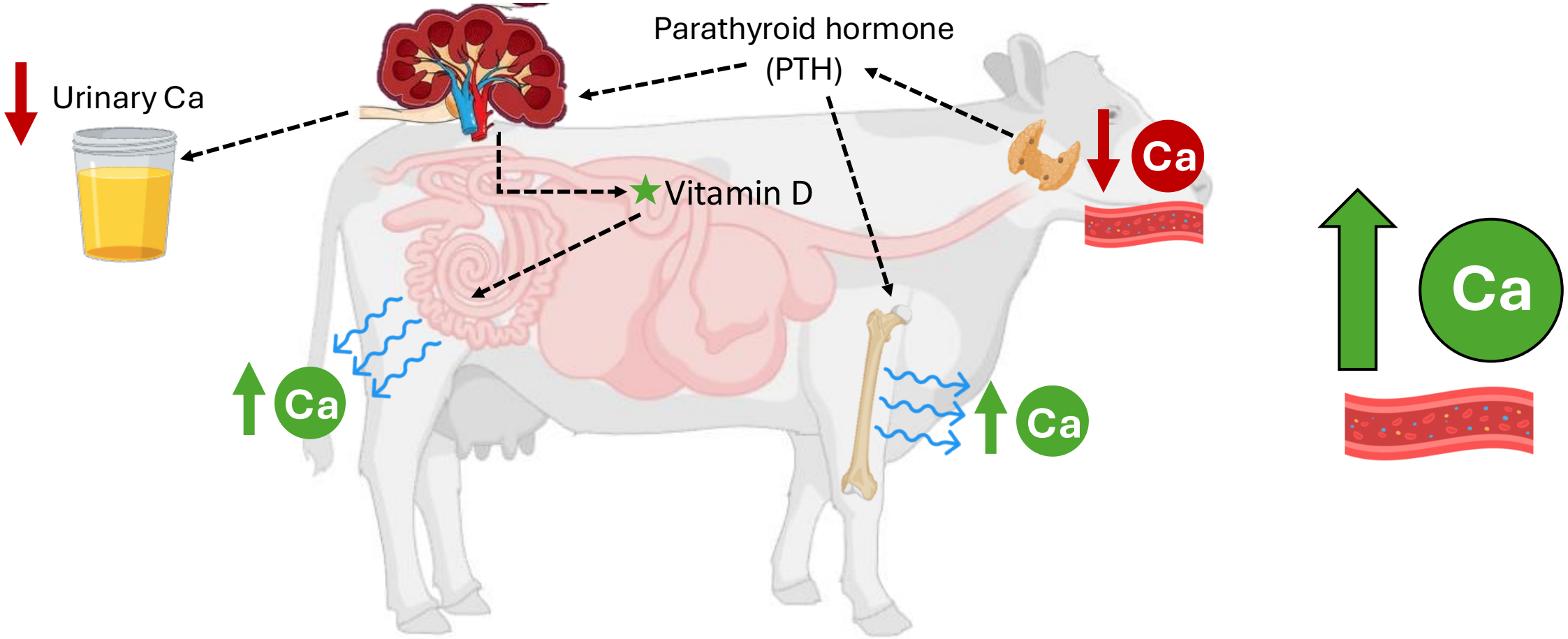
Intake ↓ 30%






*Adopted from Seely and McArt , 2023*

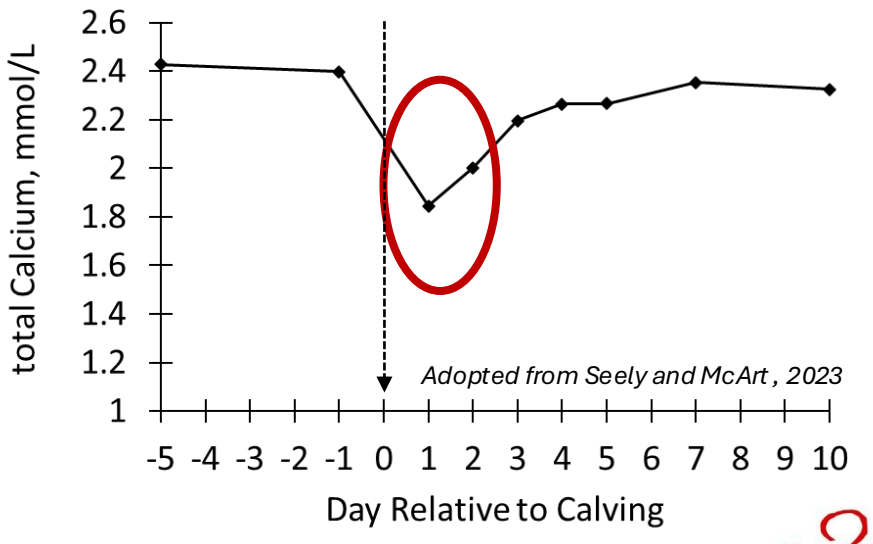
# How does the cow restore blood Ca?

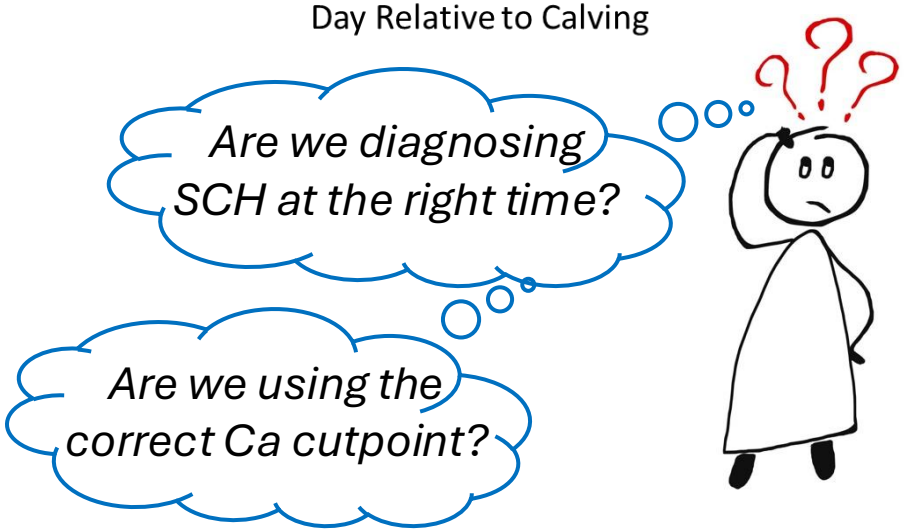


# What happens when things don’t go to plan?

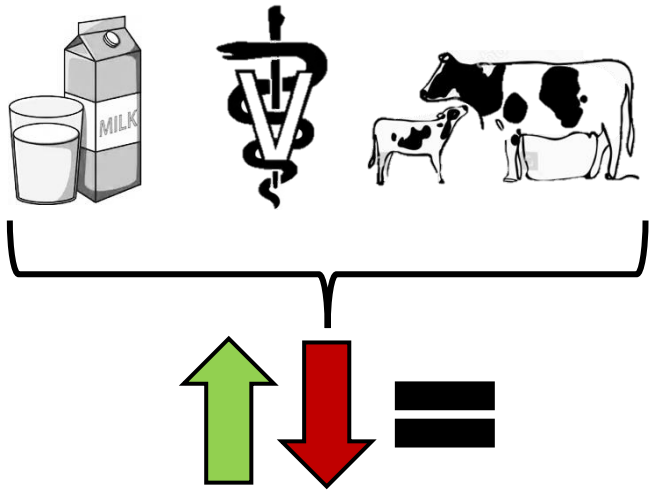

- Clinical hypocalcemia- Milk Fever
  - Obvious clinical symptoms
    - Down cow
  - Usually at blood Ca < 5.5 mg/dL (1.37 mmol/L)
  - Requires treatment to avoid death
    - 500 mL Ca gluconate IV
    - Oral Ca bolus when she stands and again 12 h later
- Subclinical hypocalcemia (SCH)
  - No physical signs of disease
  - Blood sample required for true diagnosis

# Defining Subclinical Hypocalcemia

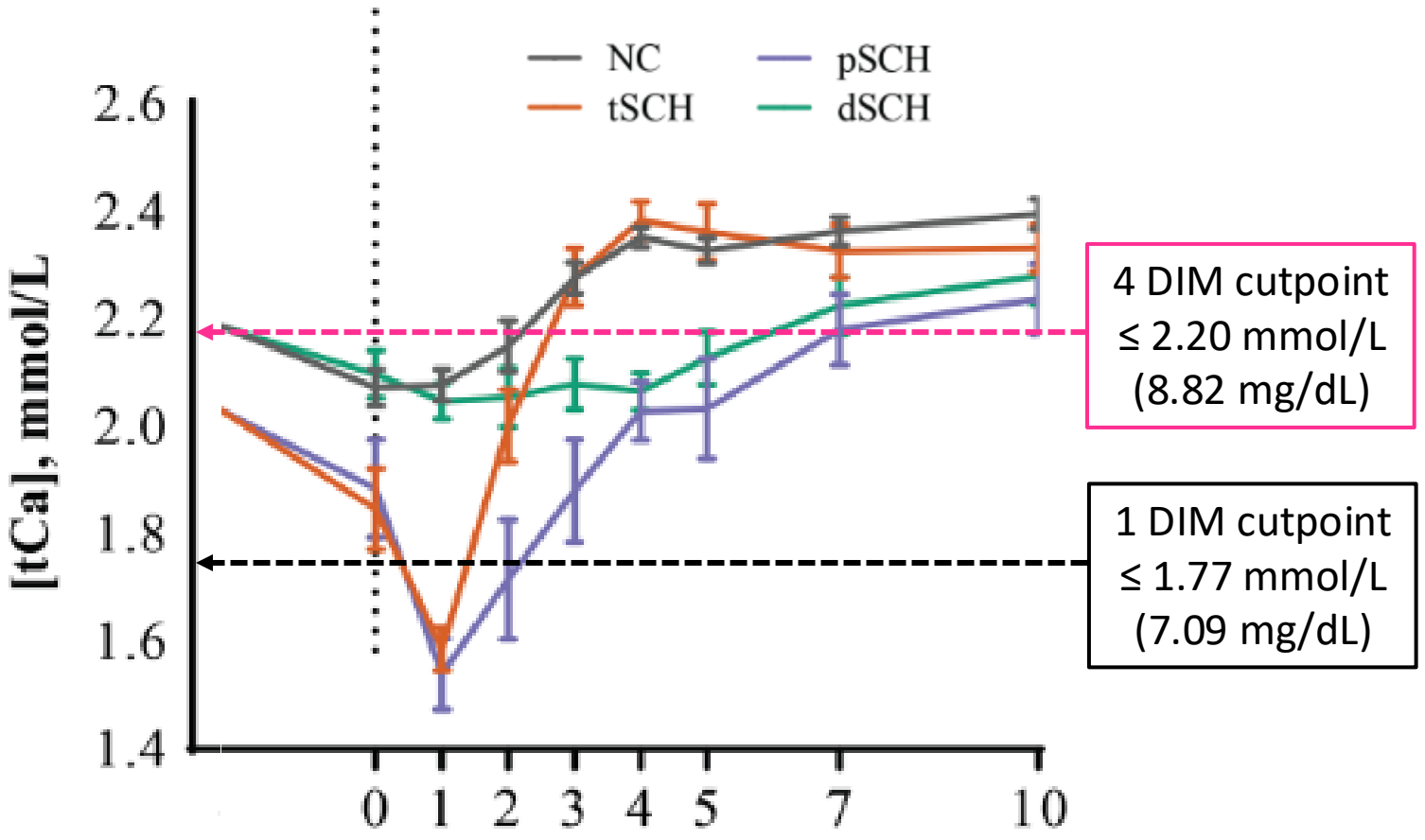



- Historically we have focused on blood Ca at 0-24 h post calving
  - Varying blood Ca cutpoints from 7.2 – 8.8 mg/dL
    - Aka 1.8 – 2.2 mmol/L
- Associated outcomes varied



# RE-defining Subclinical Hypocalcemia




4 DIM cutpoint
≤ 2.20 mmol/L
(8.82 mg/dL)

1 DIM cutpoint
≤ 1.77 mmol/L
(7.09 mg/dL)

263 multiparous Holstein cows
2 farms in New York state

Normocalcemic; n = 109
NC: 1 DIM [Ca] ↑
4 DIM [Ca] ↑

Transient SCH; n = 50
tSCH: 1 DIM [Ca] ↓
4 DIM [Ca] ↑

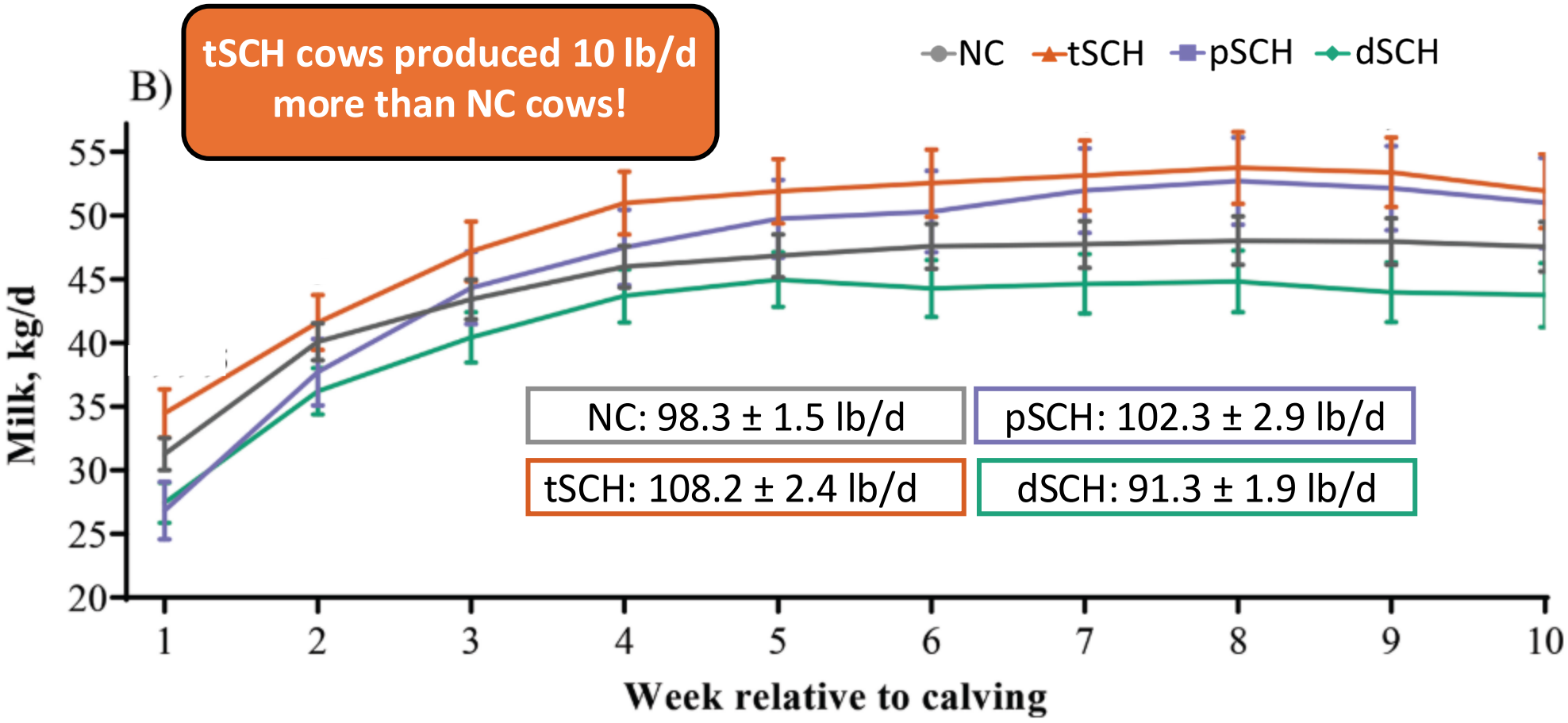
Persistent SCH; n = 34
pSCH: 1 DIM [Ca] ↓
4 DIM [Ca] ↓

Delayed SCH; n = 70
dSCH: 1 DIM [Ca] ↑
4 DIM [Ca] ↓



McArt and Neves, 2020, http://dx.doi.org/10.3168/jds.2019-17191

# Dynamics of SCH; Milk Production




*Error bars represent 95% confidence intervals*



McArt and Neves, 2020, http://dx.doi.org/10.3168/jds.2019-17191

# Dynamics of SCH; Health

| | Incidence, % | | | |
|---|---|---|---|---|
| | NC (n=109) | tSCH (n=50) | pSCH (n=34) | dSCH (n=70) |
| Hyperketonemia | 30.3 | 48.0 | 50.0 | 50.0 |
| Metritis | 5.5 | 4.0 | 17.6 | 12.9 |
| Displaced abomasum | 1.8 | 2.0 | 11.8 | 8.6 |
| Herd removal | 0.9 | 2.0 | 2.9 | 12.9 |
| Adverse event* | 33.0 | 50.0 | 61.8 | 60.0 |

*Adverse event = one or more of hyperketonemia, metritis, DA, or herd removal diagnosis

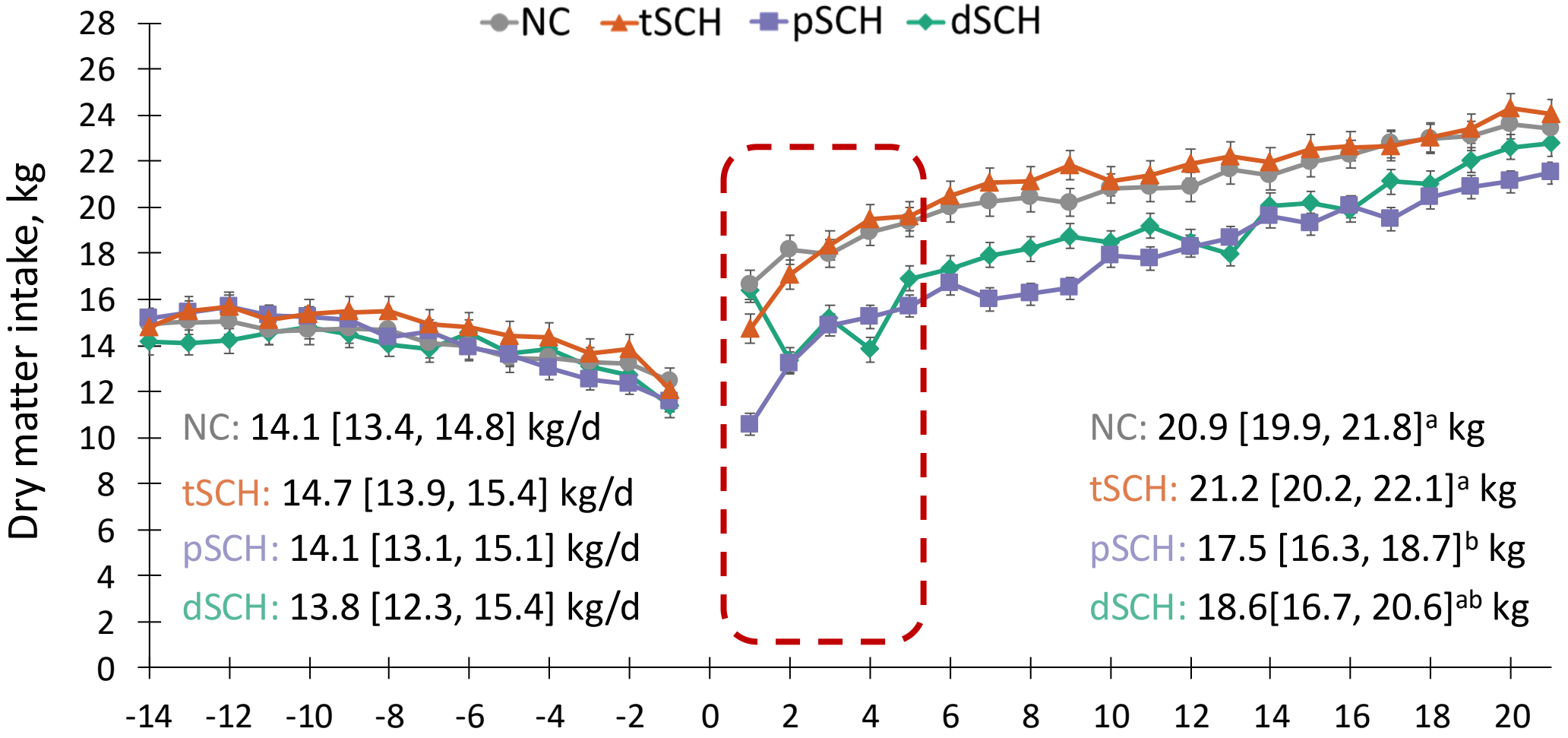
**pSCH and dSCH = twice as likely to experience Adverse Event compared to NC cows**



McArt and Neves, 2020, http://dx.doi.org/10.3168/jds.2019-17191

# Where does dry matter intake fit in?

# Dynamics of SCH; Dry Matter Intake




78 multiparous Holstein cows
Cornell research herd- tie stalls

*Error bars represent standard error*

Seely et al., 2021, 10.3168/jds.2020-19344

# What about Reproduction?

# Dynamics of SCH; Reproduction

Normocalcemic (NC; n = 515): tCa > 2.2 mmol/L (8.82 mg/dL) at **4 DIM**
Subclinical hypocalcemia (SCH; n = 182): tCa ≤ 2.2 mmol/L (8.82 mg/dL) at **4 DIM**

| Variable | Incidence (%)[1] | OR[2]/HR[3] | 95% CI | *P*-value |
|---|---|---|---|---|
| Time of first AI, DIM | | | | |
| NC | 64.1 days | | 62.3-65.4 | 0.28 |
| SCH | 65.1 days | | 63.4-66.8 | |
| Pregnant to 1st service | | | | |
| NC | 27.4% | Ref | - | - |
| SCH | 18.1% | 0.75 | 0.61-0.93 | 0.01 |
| Pregnant by 150 DIM | | | | |
| NC | 70.7% | Ref | - | - |
| SCH | 65.4% | 0.82 | 0.67-1.01 | 0.06 |

[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



Seely and McArt, 2023, http://dx.doi.org/10.3168/jdsc.2022-0279

# Dynamics of SCH; Reproduction

Normocalcemic (NC; n = 515): tCa > 2.2 mmol/L at **4 DIM**
Subclinical hypocalcemia (SCH; n = 182): tCa ≤ 2.2 mmol/L at **4 DIM**

Median time to pregnancy

NC = 103 ± 11 d

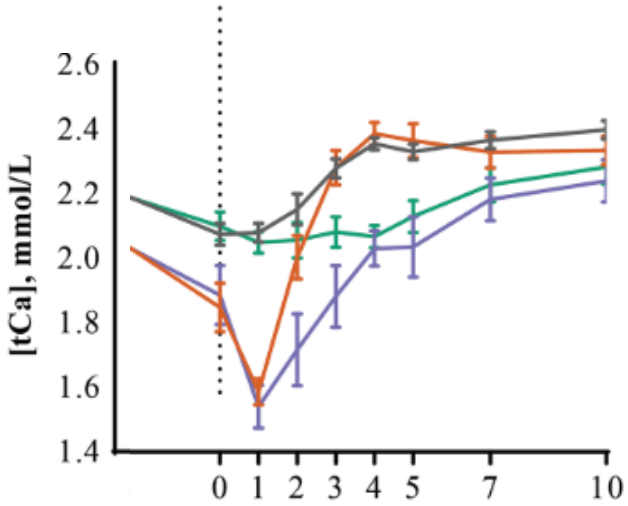
SCH = 119 ± 16 d

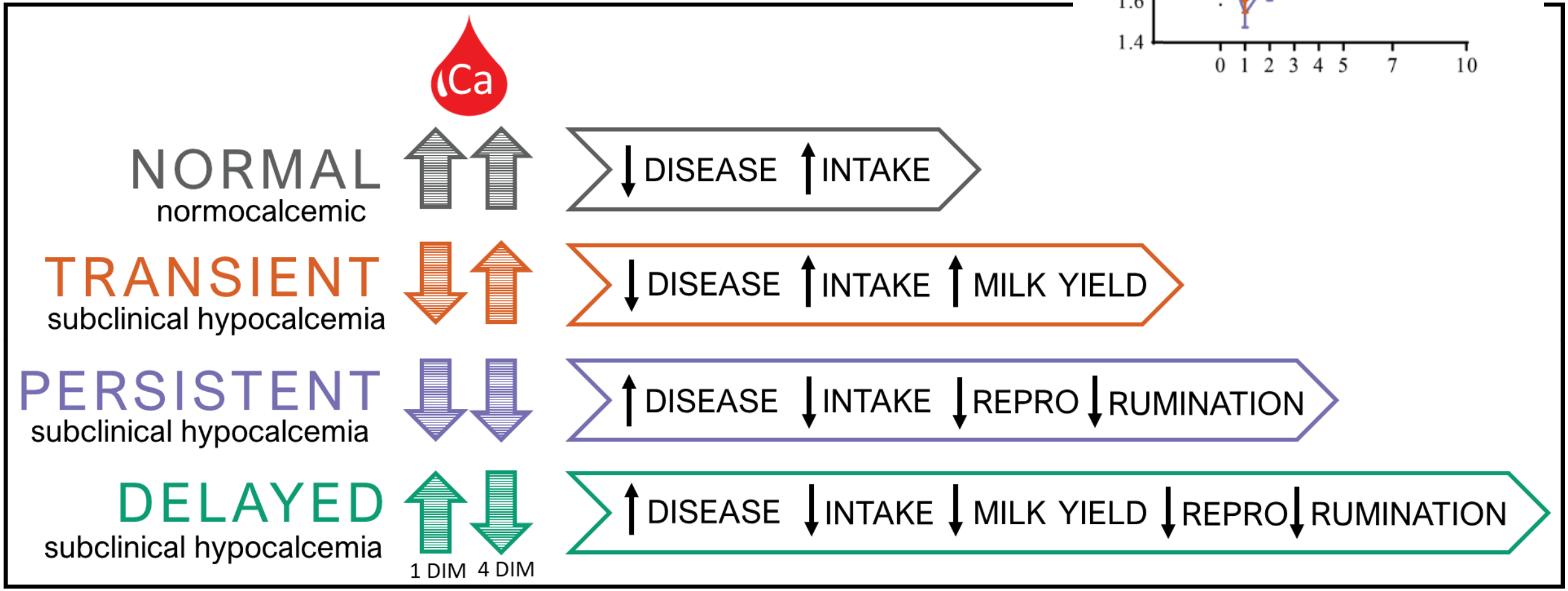
16 days!



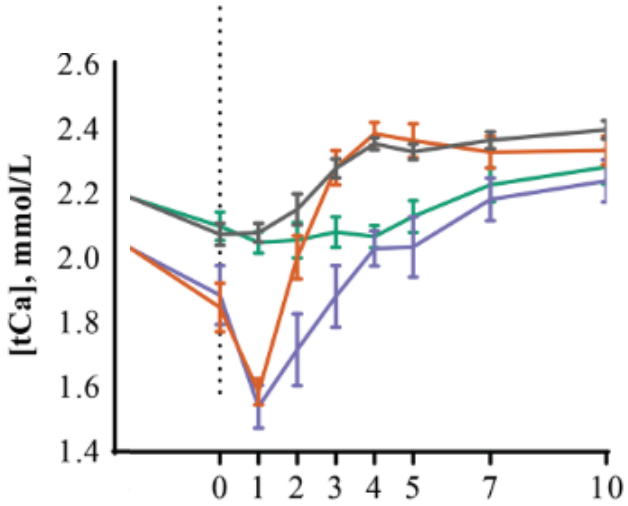
Seely and McArt, 2023, http://dx.doi.org/10.3168/jdsc.2022-0279

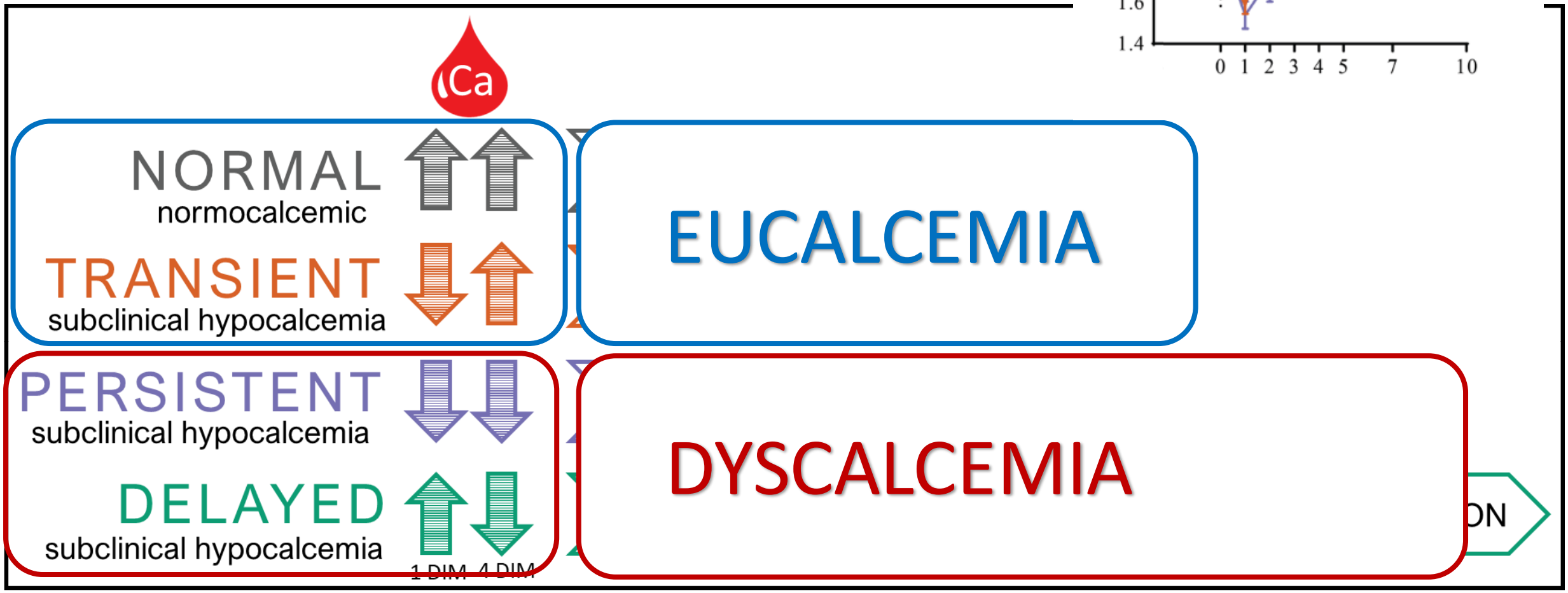
# Is low Ca at 1 DIM really that bad?



# Is low Ca at 1 DIM really that bad?



# Can we improve blood Ca status in early lactation?

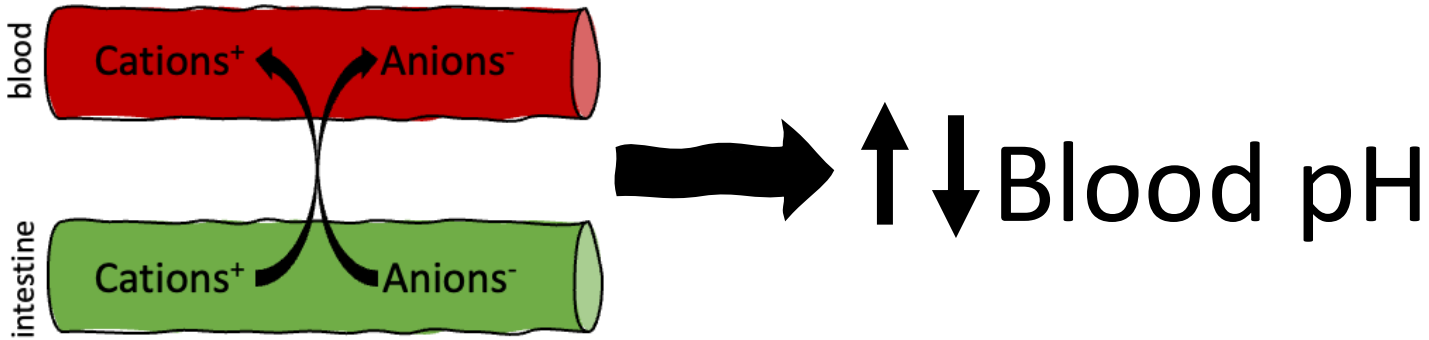

Ration formulation for prepartum cows

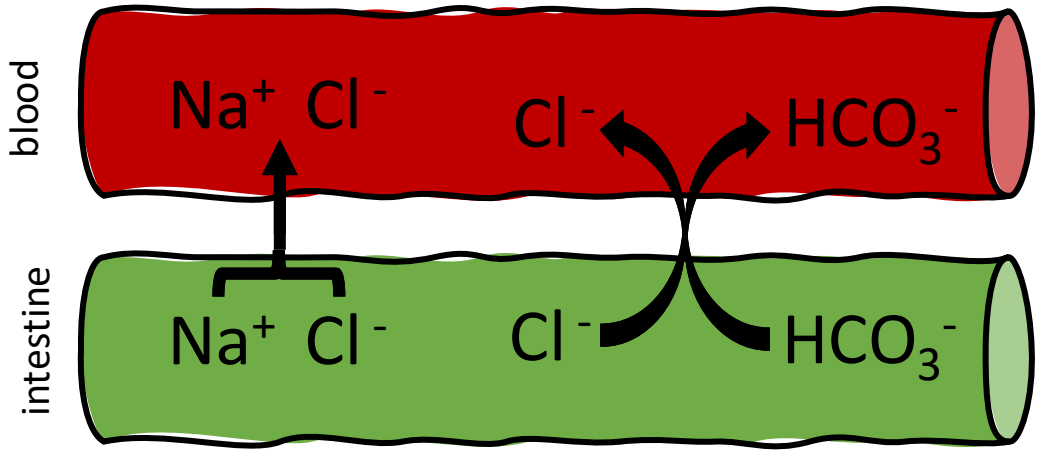

Ca supplementation at or after calving as treatment/prophylaxis

# Evaluating the success of Ca supplementation

- Blood Ca concentrations?
- Milk production
- Health events/culling
- Reproductive success

# Dietary Cation Anion Difference



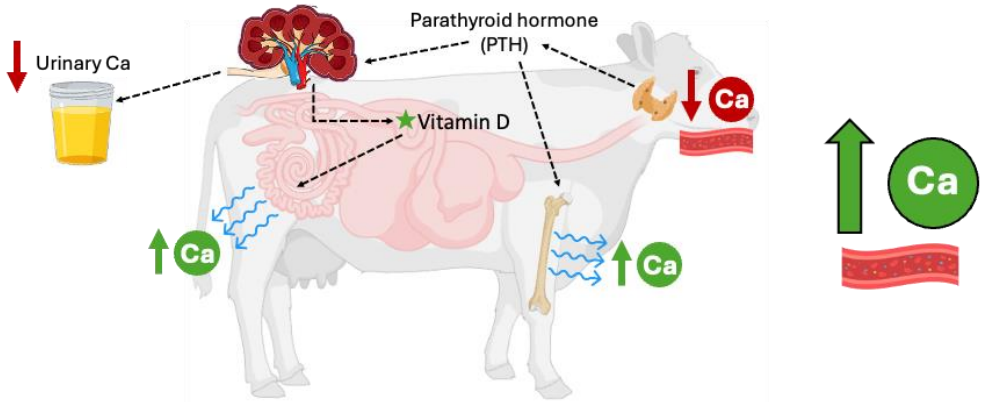




## Negative DCAD

strong anions > strong cations

blood pH ↓

# Improving Ca status via nDCAD





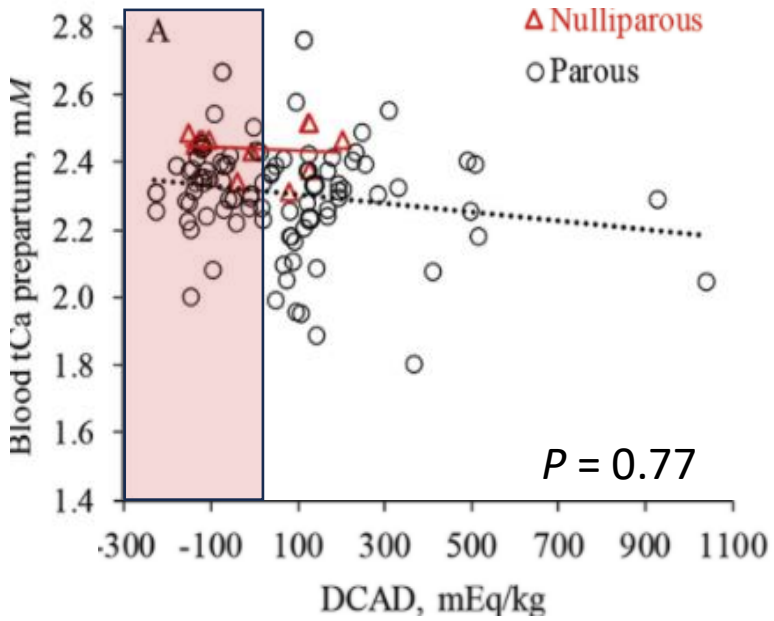


**Priming cow for low blood Ca post calving**

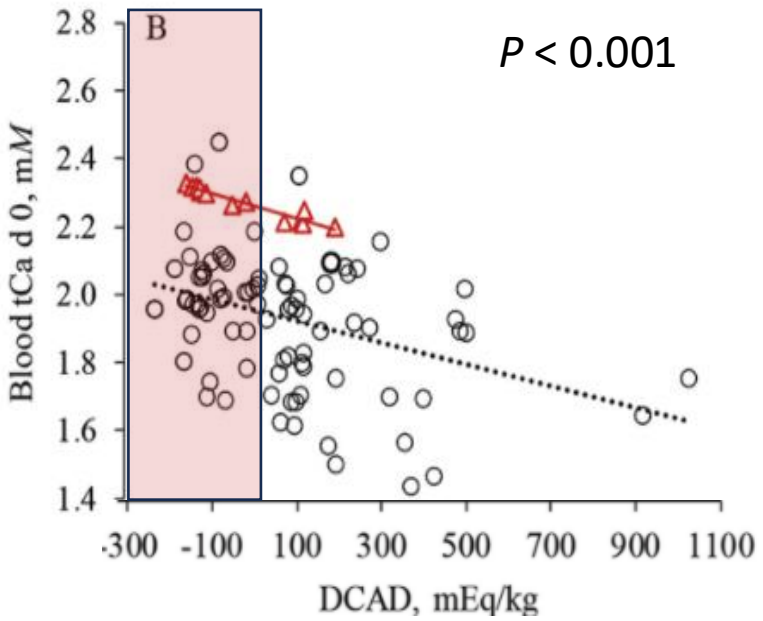
- Acidification improves sensitivity of PTH receptor
- Decrease in urine pH → increase in Ca excretion in urine → increase Ca flux
- Systemic pH reduction → stimulation of Ca release from bone

# Effect of DCAD on blood tCa

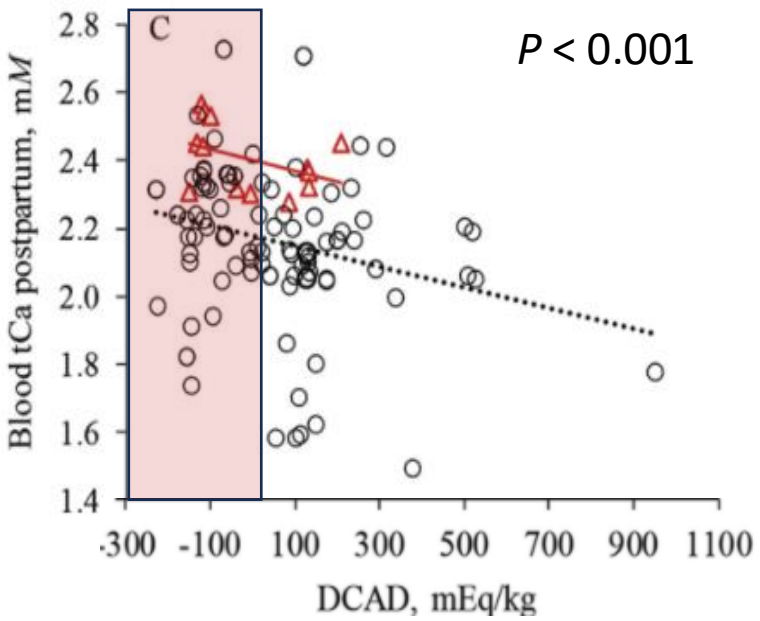
Prepartum Blood tCa




Day 0 blood tCa




Postpartum blood tCa

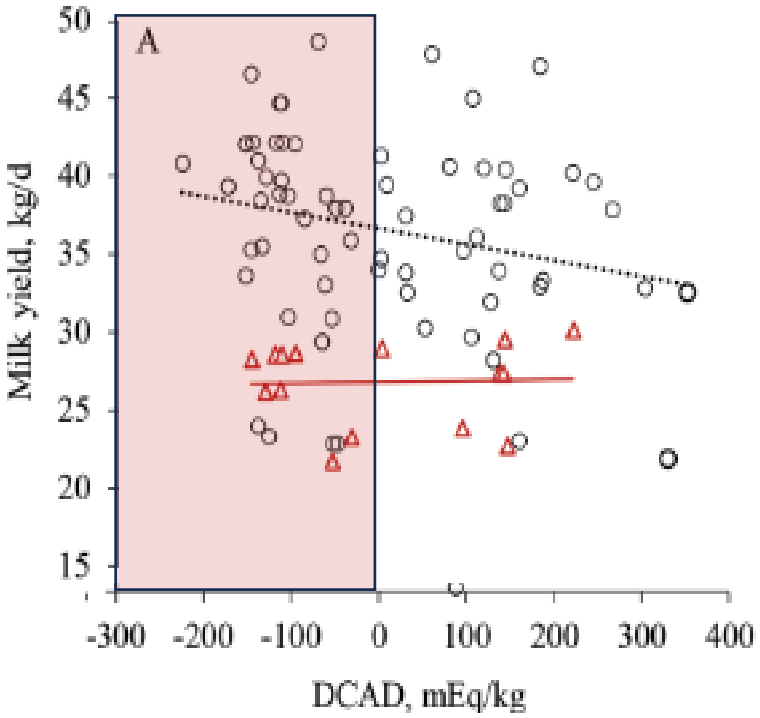





Santos et al., 2019; https://doi.org/10.3168/jds.2018-14628

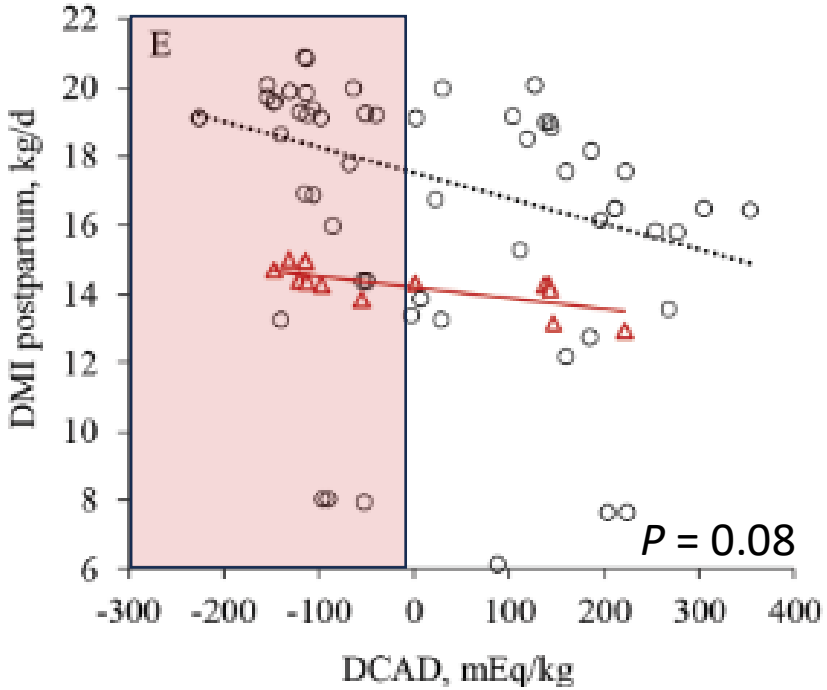
# Effect of DCAD on Milk and Intake

Milk Production




Multiparous
$P < 0.001$

Postpartum DMI

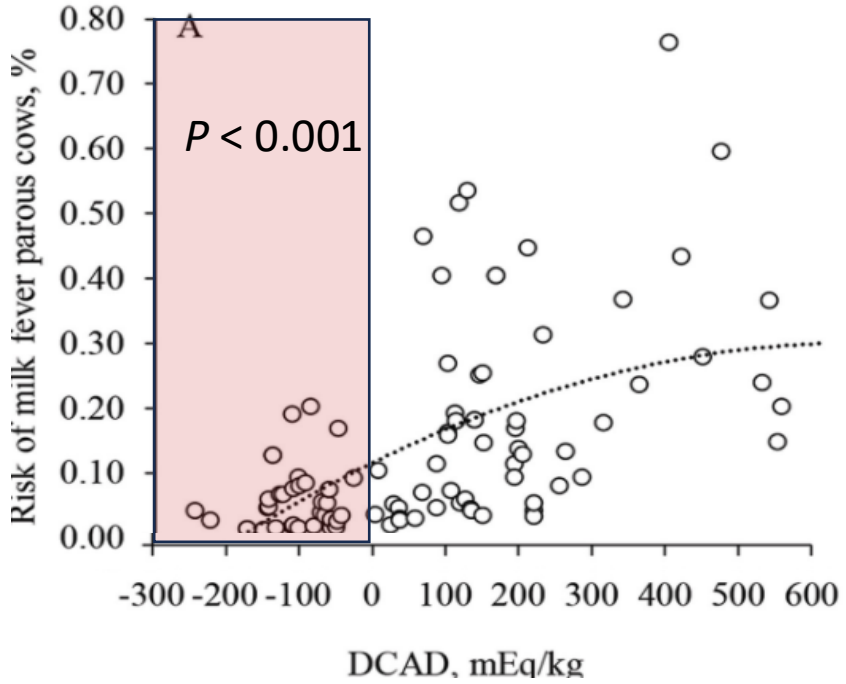




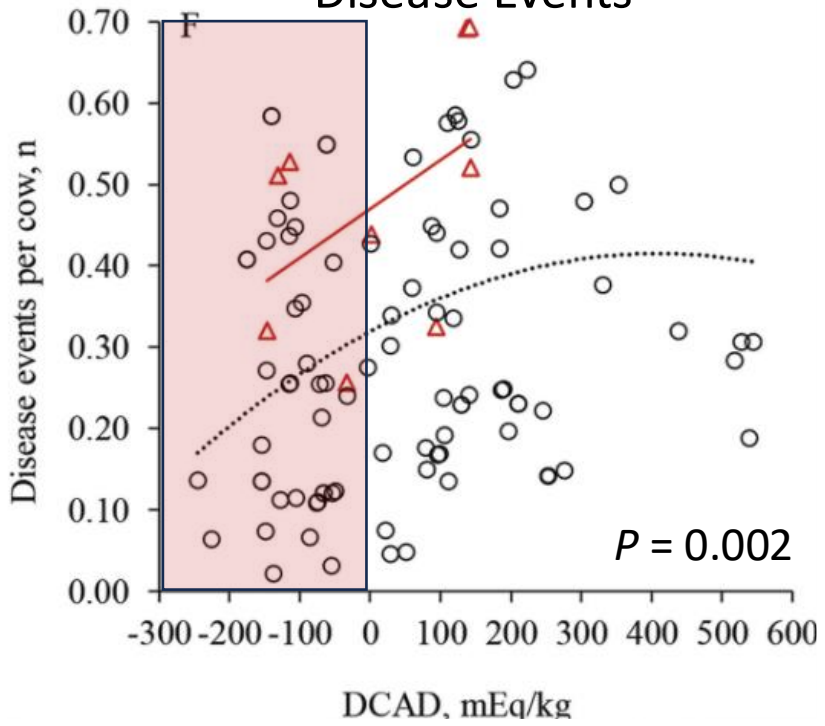

Santos et al., 2019; https://doi.org/10.3168/jds.2018-14628

# Effect of DCAD on health outcomes

Risk of Milk Fever




Disease Events

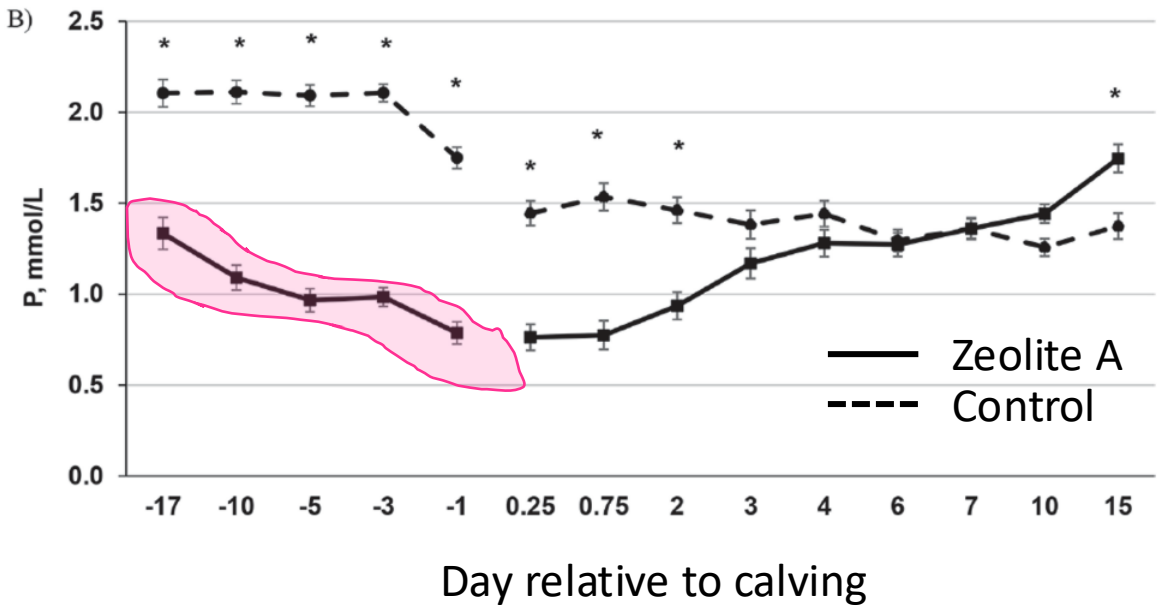


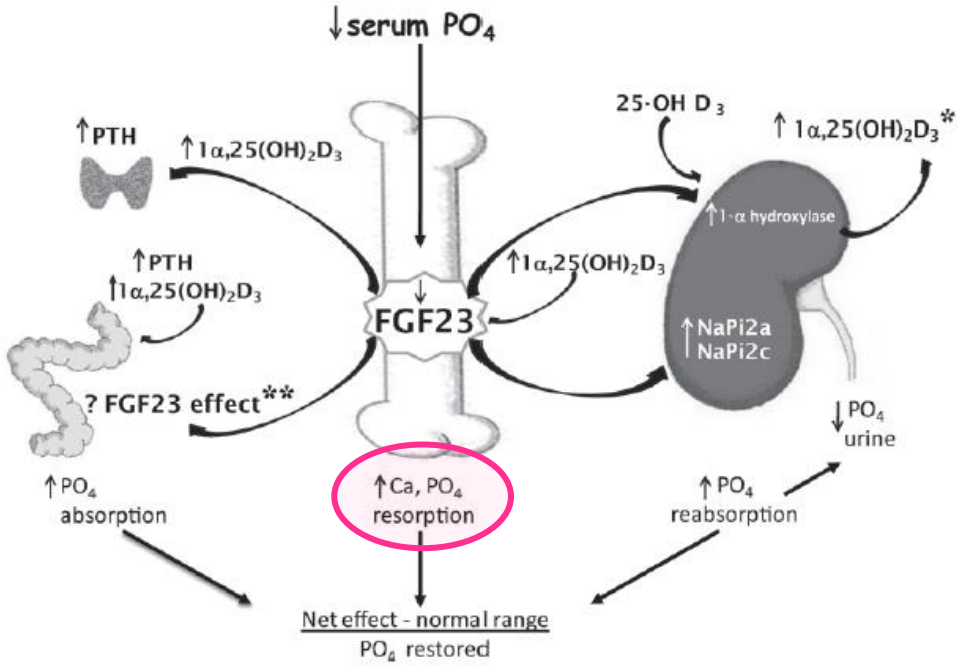



Santos et al., 2019; https://doi.org/10.3168/jds.2018-14628

# Improving Ca Status via Zeolite A

- Binds P (and Ca and Mg) in the rumen
- Elicits a hypophosphatemic state



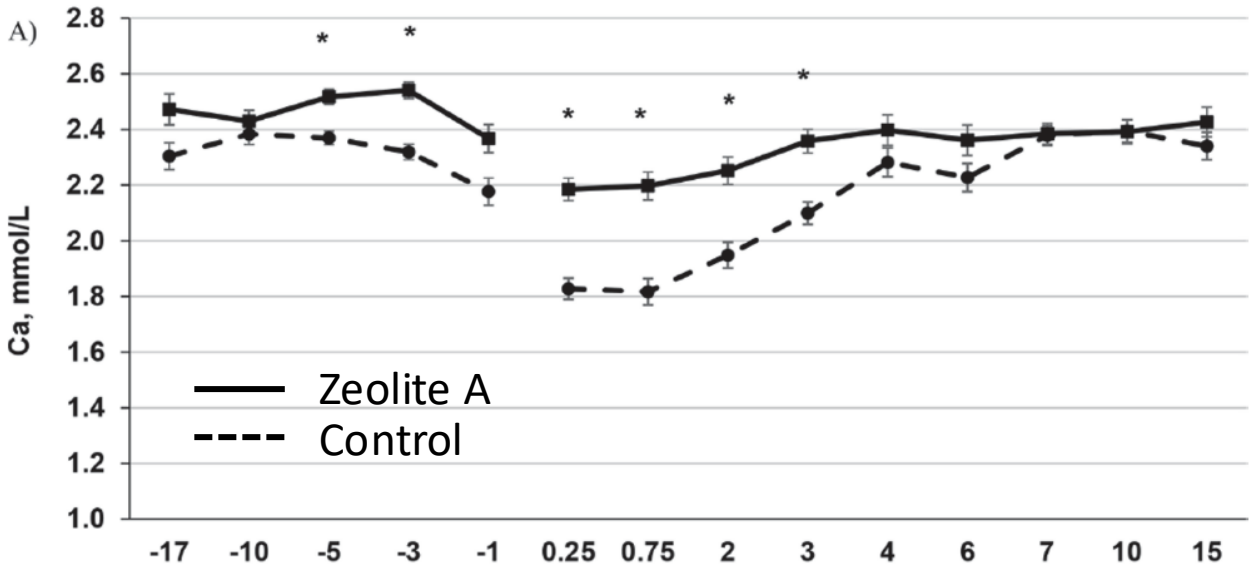



Kerwin et al., 2019; https://doi.org/10.3168/jds.2019-16272

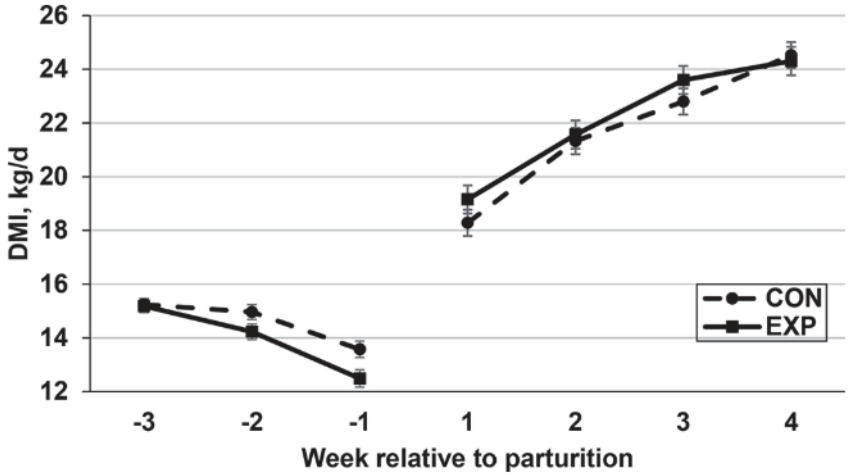
# Effect of Zeolite A on blood Ca & Production

Tie-stall research herd
Zeolite A: n = 26
Control: n = 29

**Blood Ca**




**Dry Matter Intake**




**Milk Production**

1-9 weeks of lactation
Zeolite A = 50.7 kg/d
Control: 51.7 kg/d

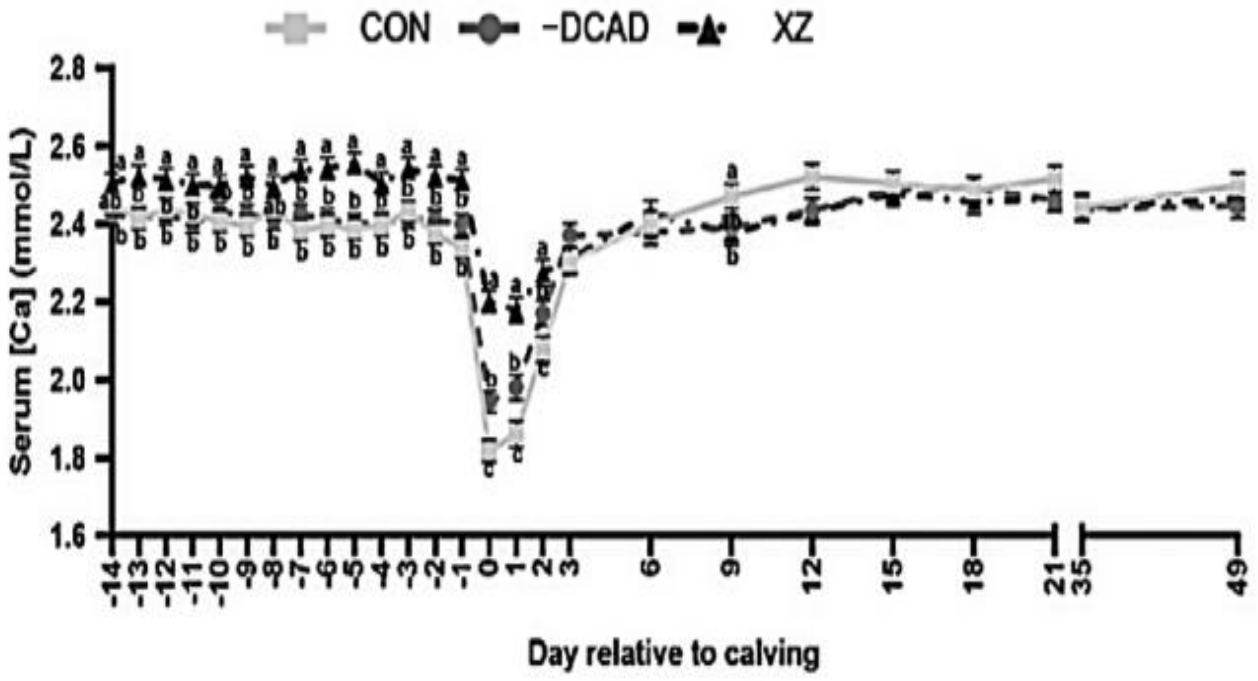


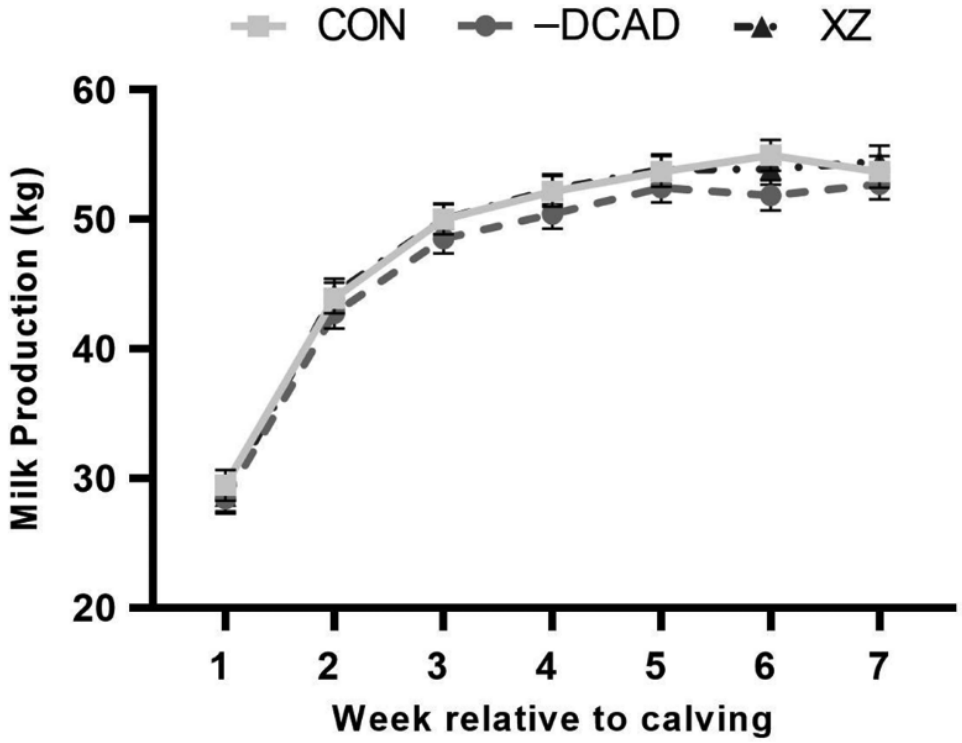
Kerwin et al., 2019; https://doi.org/10.3168/jds.2019-16272

# Comparison of Zeolite A and nDCAD

CON; n = 40
-DCAD = urine pH 6; n = 41
XZ = Zeolite A; n = 40

**Prepartum Intake**
* similar between nDCAD and CON
* Zeolite A cows consumed less than nDCAD& CON






Frizzarini et al., 2024a & b; https://doi.org/10.3168/jds.2024-24056, https://doi.org/10.3168/jds.2024-24057

# nDCAD vs Zeolite- Dyscalcemia Outcomes

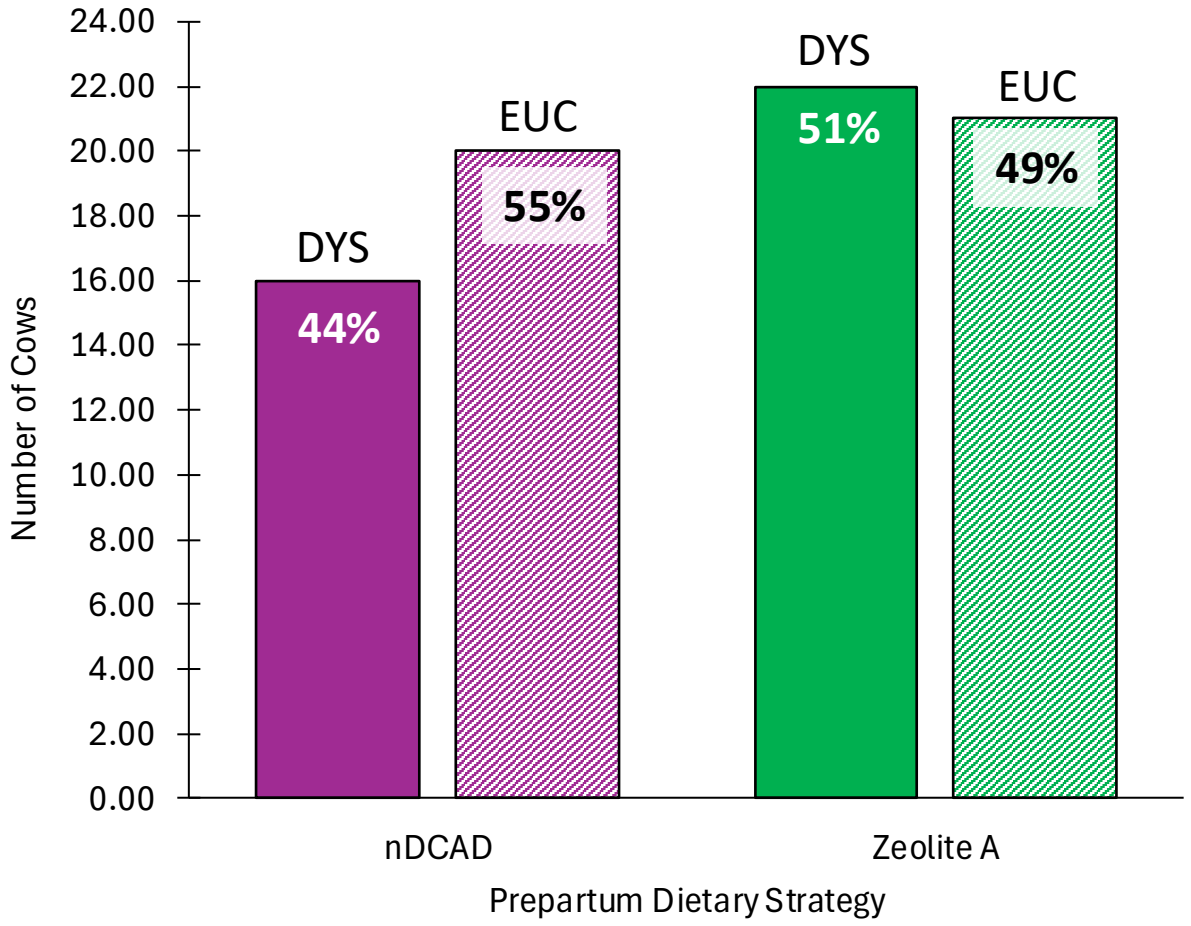
4 herds feeding nDCAD
n = 36 multiparous Holstiens

5 herds feeding Zeolite A
n = 43 multiparous Holstiens

tCa analysis at 4 DIM

Eucalcemic; 4 DIM serum Ca ≥ 2.15 mmol/L (8.62 mg/dl)

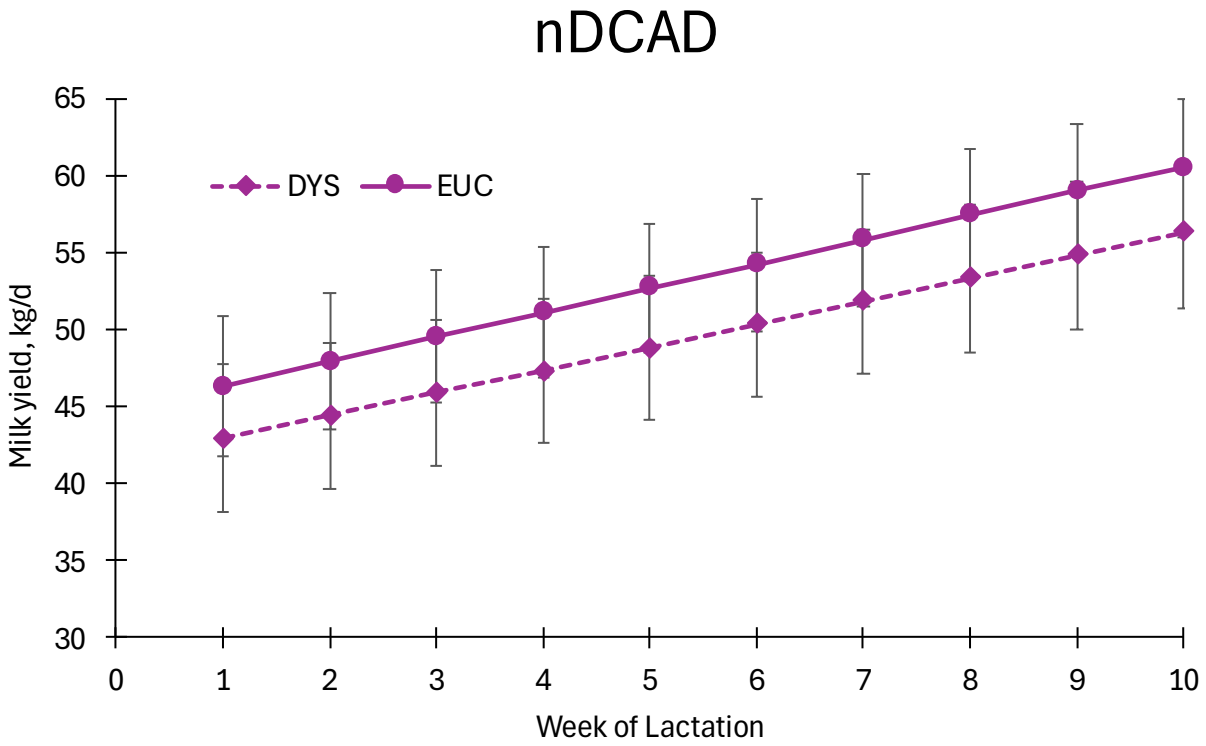
Dyscalcemic; 4 DIM serum Ca < 2.15 mmol/L



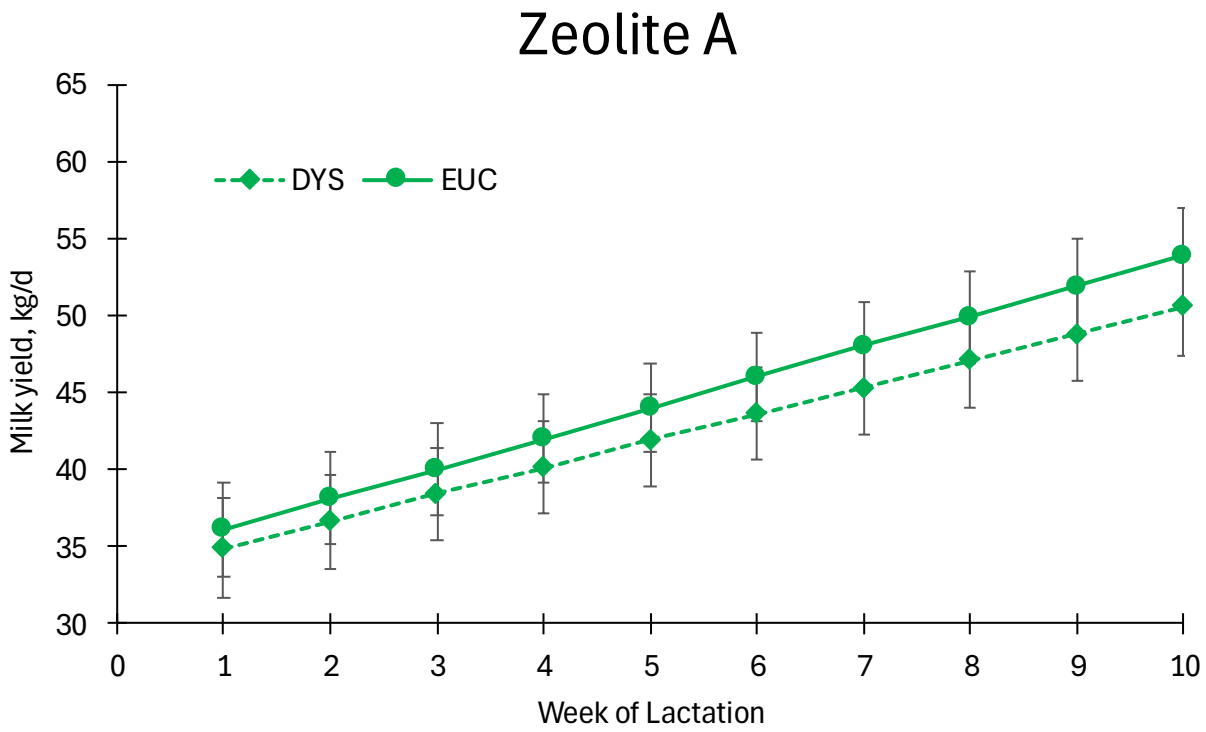



Phibro, *unpublished data*

# nDCAD vs Zeolite- Dyscalcemia Outcomes




*P* = 0.006
EUC = 53.4 ± 4.3 kg/d
DYS = 49.6 ± 4.8 kg/d



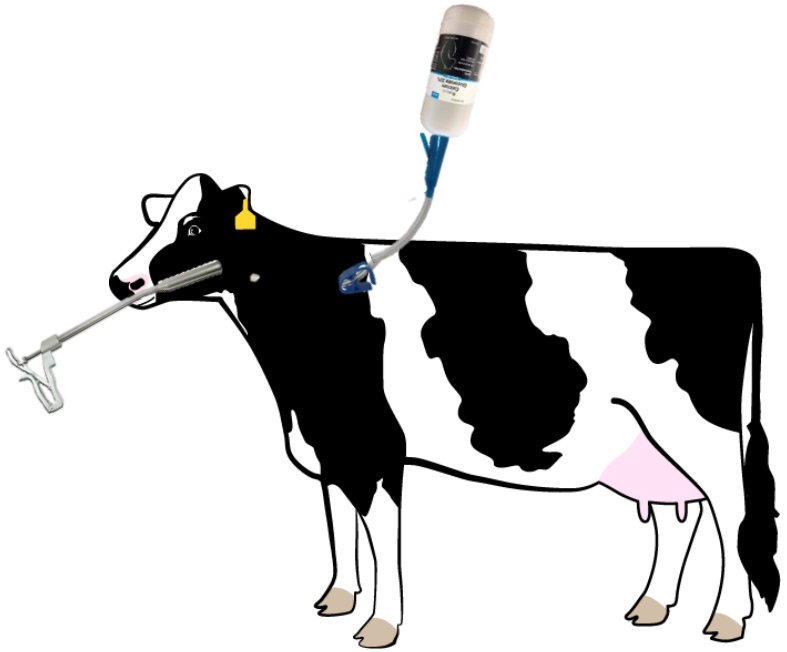

*P* = 0.4
EUC = 44.9 ± 2.9 kg/d
DYS = 42.7 ± 3.1 kg/d



Phibro, *unpublished data*

# Can we improve blood Ca status in early lactation?


Ca supplementation at or after calving as treatment/prophylaxis



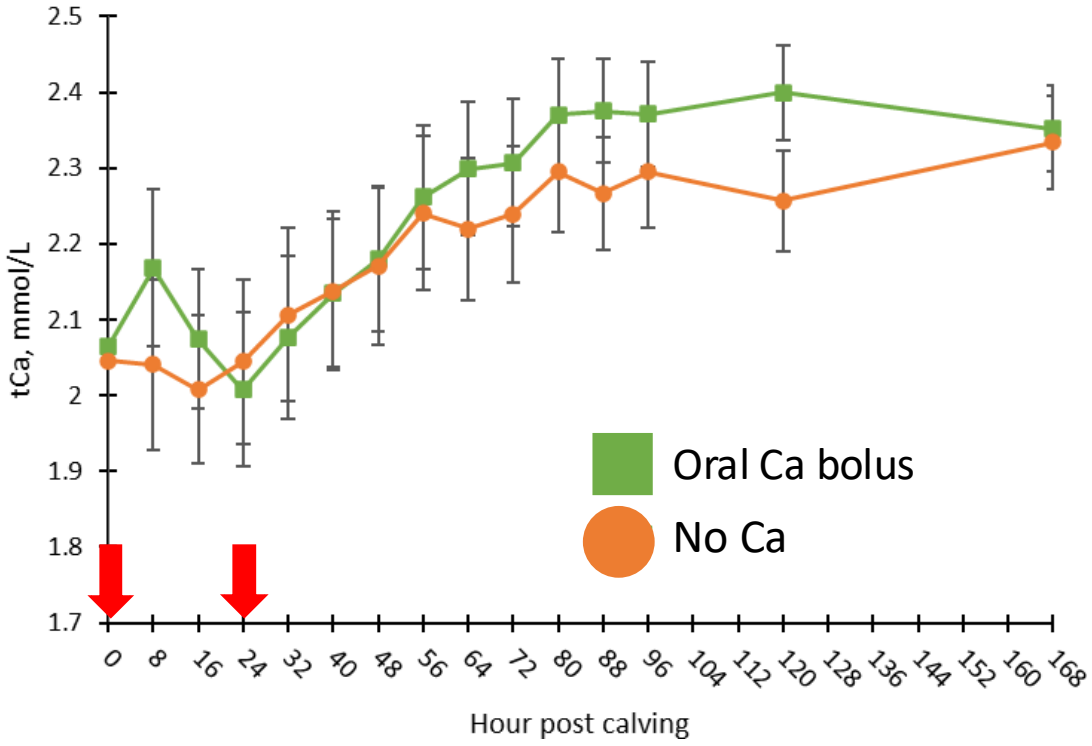
**IV/Subcutaneous Ca**

- Very steep increase in blood Ca ⇨ very fast decrease in blood Ca
- Reserve for Milk Fever!

**Oral Ca bolus**

- Slow release of Ca salts
- Sustained increase in blood Ca

# Oral Ca Supplementation

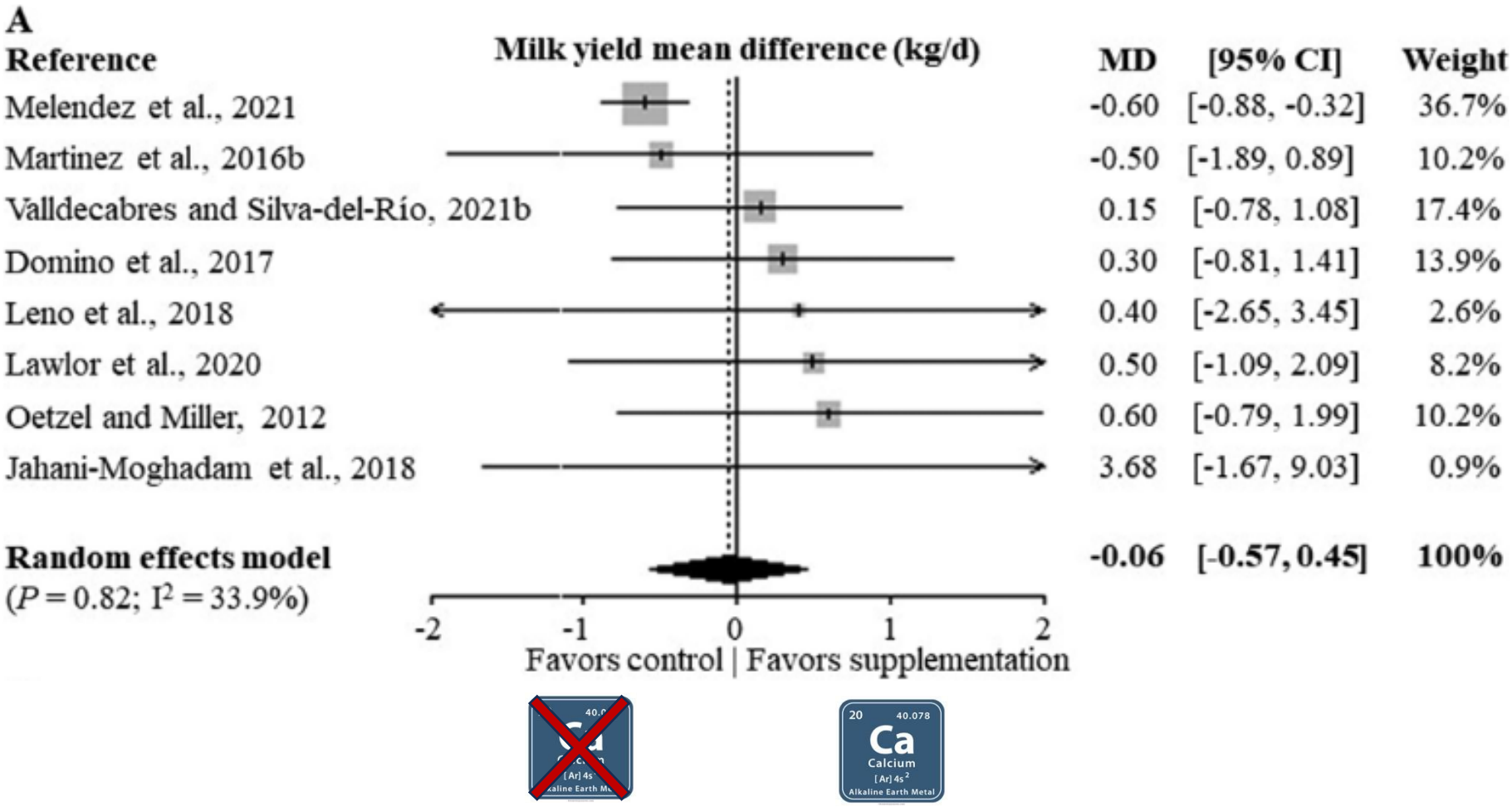



- Sustained increase in blood Ca via absorption in rumen and intestines
- What about production responses?




*Adapted from* Frost et al., 2023, https://doi.org/10.3168/jdsc.2023-0455

# Production Response to Ca Bolus






Valldecabres et al., 2023, 10.3168/jdsc.2022-0235

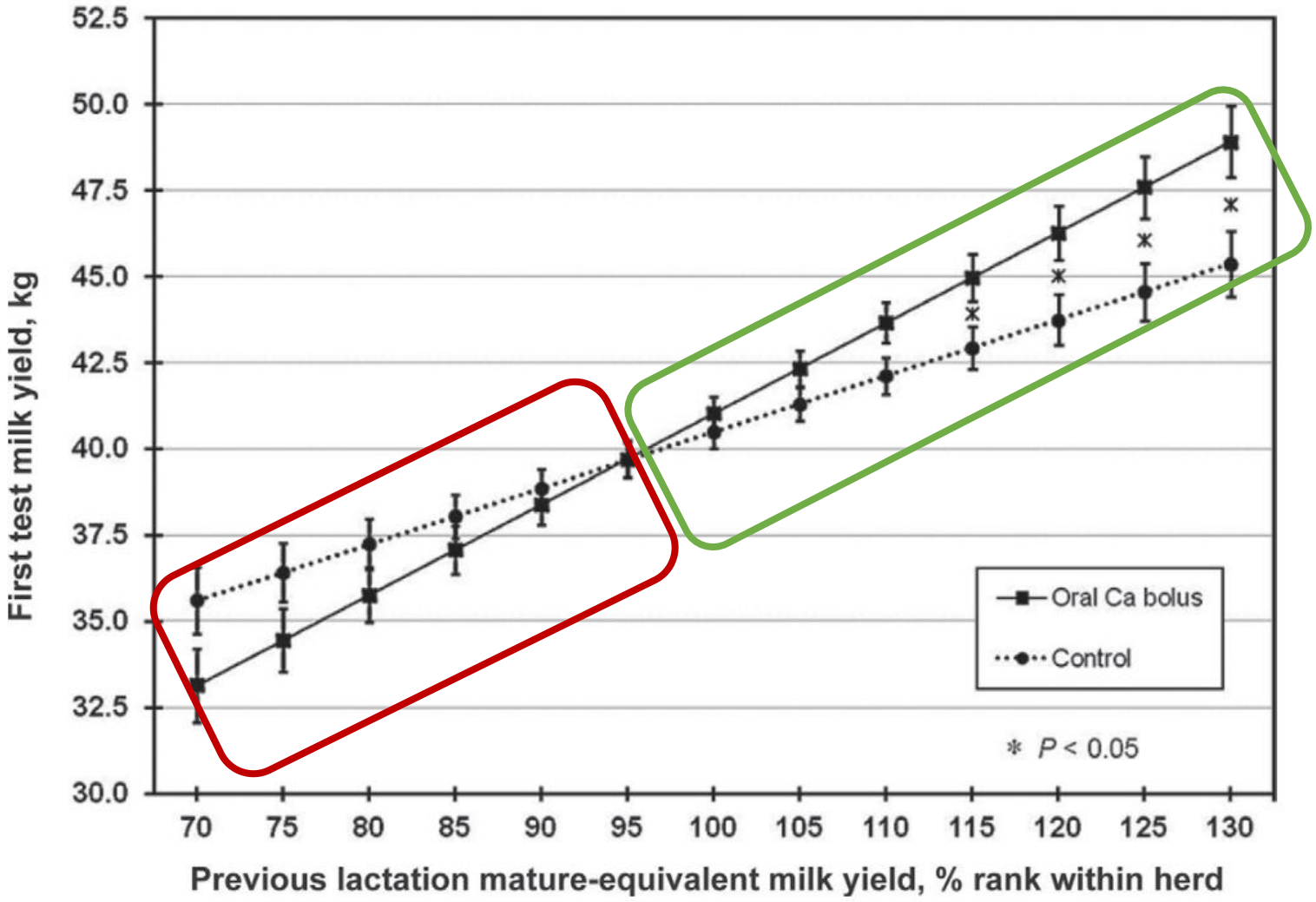
# Production Response to Ca Bolus

J. Dairy Sci. 95:7051–7065
http://dx.doi.org/10.3168/jds.2012-5510


**Effect of oral calcium bolus supplementation on early-lactation health and milk yield in commercial dairy herds**

G. R. Oetzel*[1] and B. E. Miller†
*School of Veterinary Medicine, University of Wisconsin, Madison 53706
†Boehringer Ingelheim Vetmedica Inc., St. Joseph, MO 64506

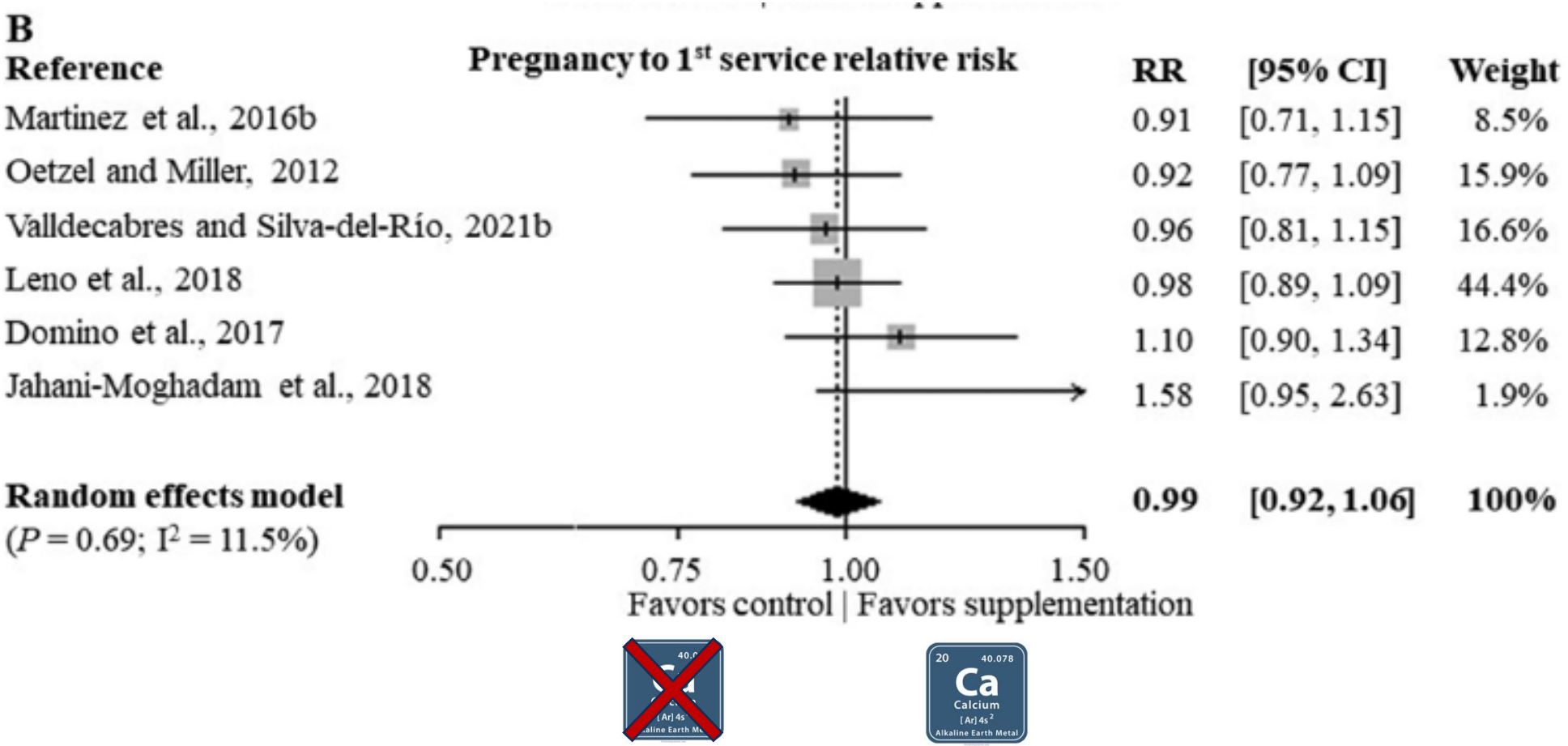
- 927 multiparous Holstein cows
  - 431 oral Ca bolus (0 h and 24 h post calving)
  - 496 control
- No effect of Ca supplementation on milk yield at study population level






Oetzel and Miller, 2012, 10.3168/jds.2012-5510

# Reproductive Response to Ca Bolus



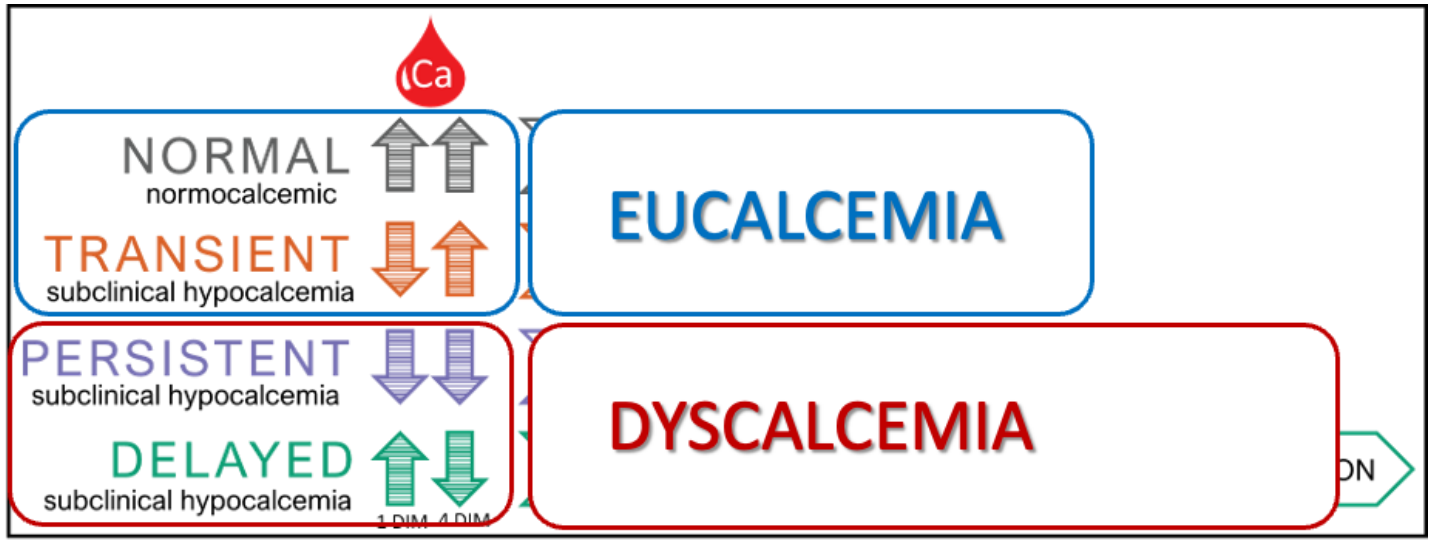


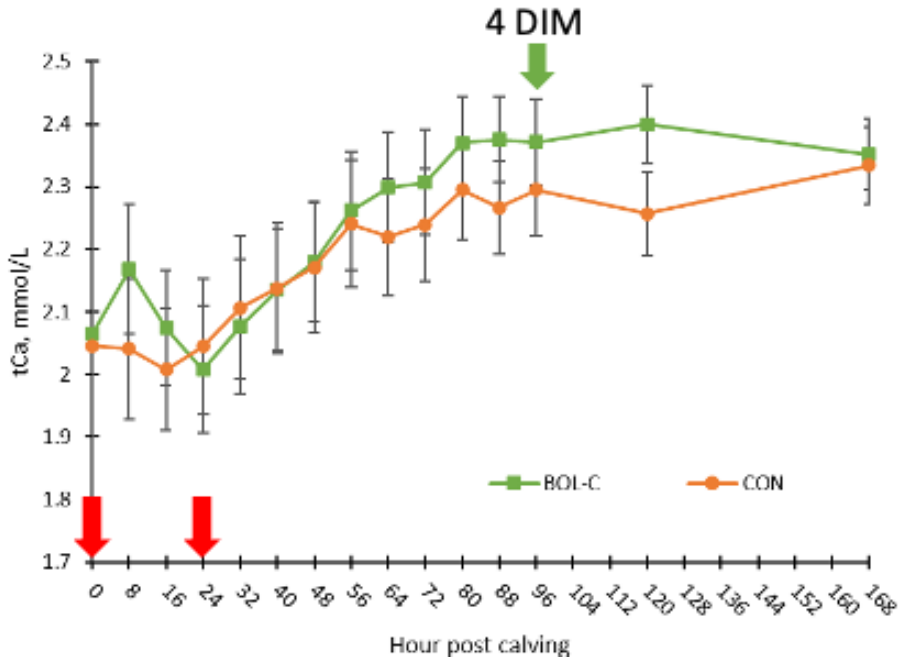




Valldecabres et al., 2023, 10.3168/jdsc.2022-0235

# Are we giving oral Ca at the right time?



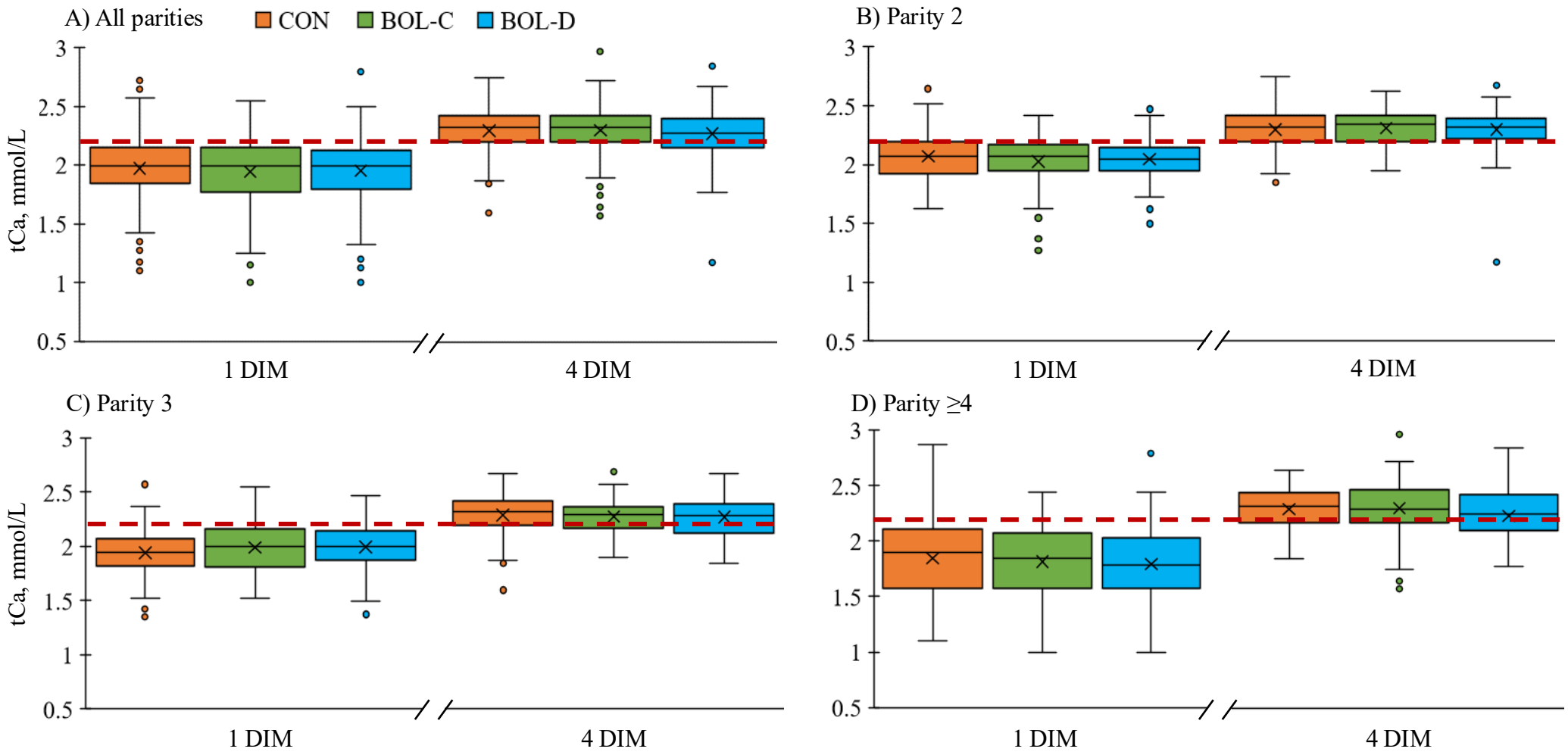
# What if we delay Ca bolus administration?

- Enrolled 998 multiparous Holstein cows from 4 herds in NY at calving

| | |
|---|---|
| CON | Control; no Ca supplementation, n = 343 |
| BOL-C | Conventional bolus; oral Ca bolus (43 g Ca) at 0 & 1 DIM, n = 330 |
| BOL-D | Delayed bolus; oral Ca bolus (43 g Ca) at 2 & 3 DIM, n = 325 |

- Blood was collected from the coccygeal vessels at 1 & 4 DIM
  - Analyzed for serum total Ca (tCa)
- Milk production was recorded for the first 10 wk of lactation
- Health events and herd removal were recorded for the first 30 DIM

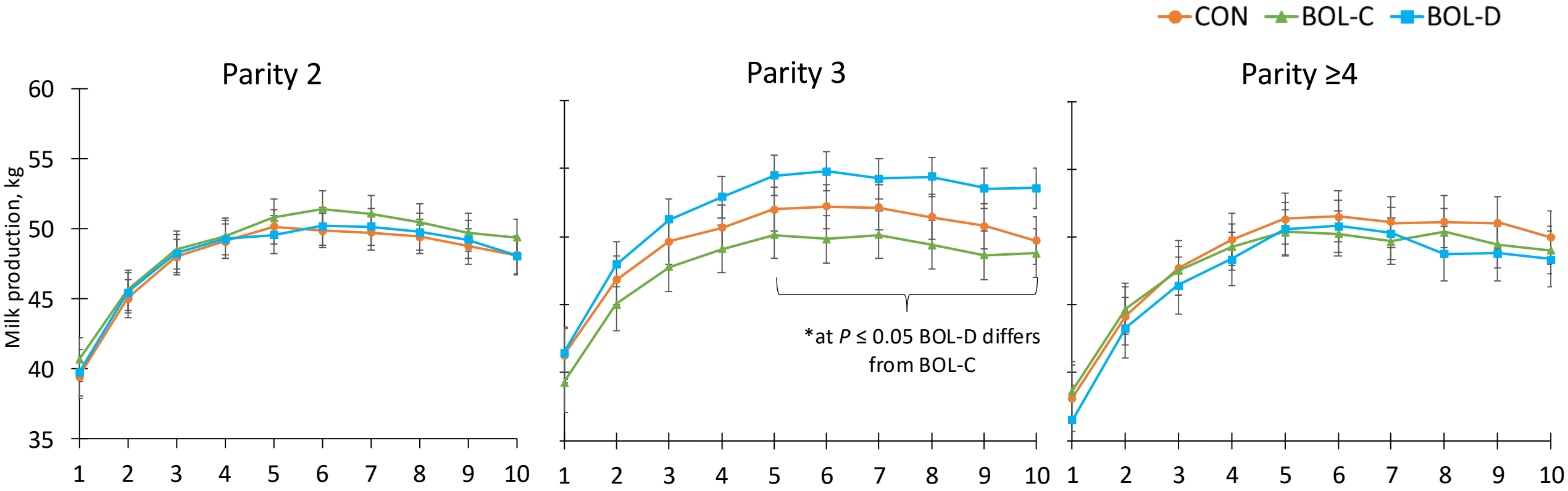
# Minimal impact of Ca bolus on 4 DIM tCa






Seely et al., 2023; http://dx.doi.org/10.3168/jds.2023-23541

# Milk production differences between parities



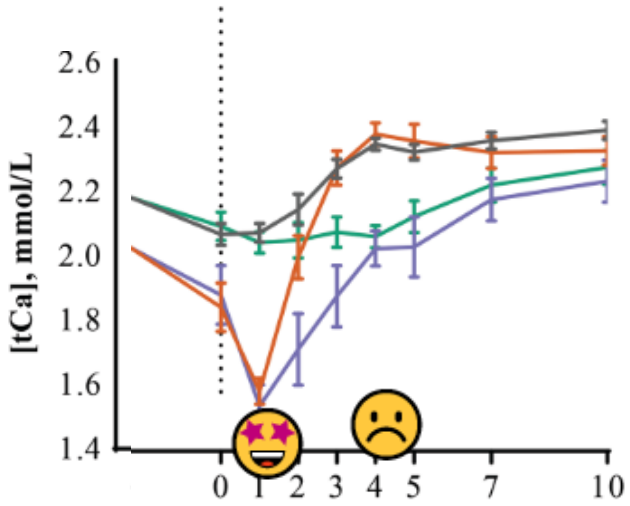

| Parity 2 | | Parity 3 | | Parity ≥4 | |
|---|---|---|---|---|---|
| CON | 47.9 [46.8, 49.0] kg/d | CON | 49.8$^{ab}$ [48.2, 51.3] kg/d | CON | 48.8 [47.0, 50.5] kg/d |
| BOL-C | 48.8 [47.7, 50.0] kg/d | BOL-C | 47.9$^{b}$ [46.3, 49.5] kg/d | BOL-C | 48.1 [46.5, 49.6] kg/d |
| BOL-D | 48.1 [46.9, 49.3] kg/d | BOL-D | 52.0$^{a}$ [50.6, 53.4] kg/d | BOL-D | 47.4 [45.5, 49.2] kg/d |

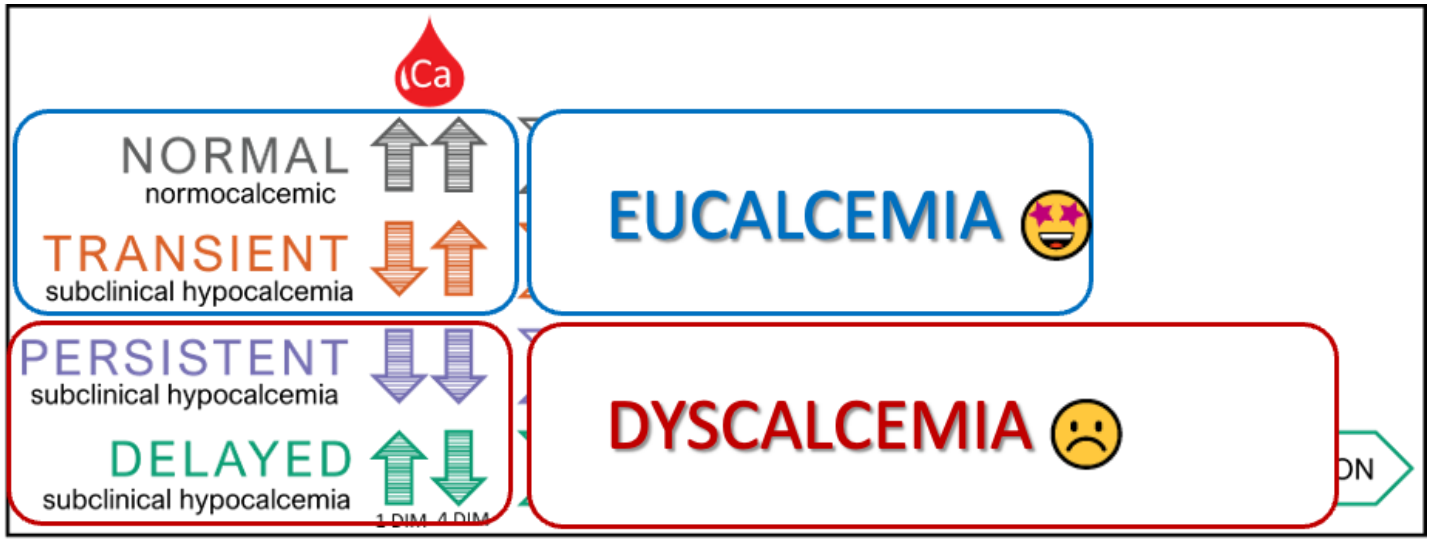
*Error bars represent 95% confidence intervals*



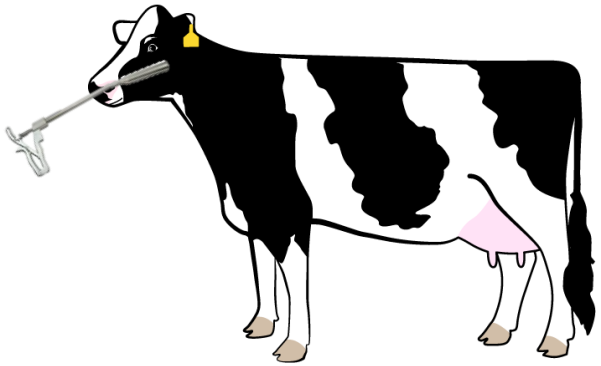
Seely et al., 2023; http://dx.doi.org/10.3168/jds.2023-23541

# What we've learned so far…



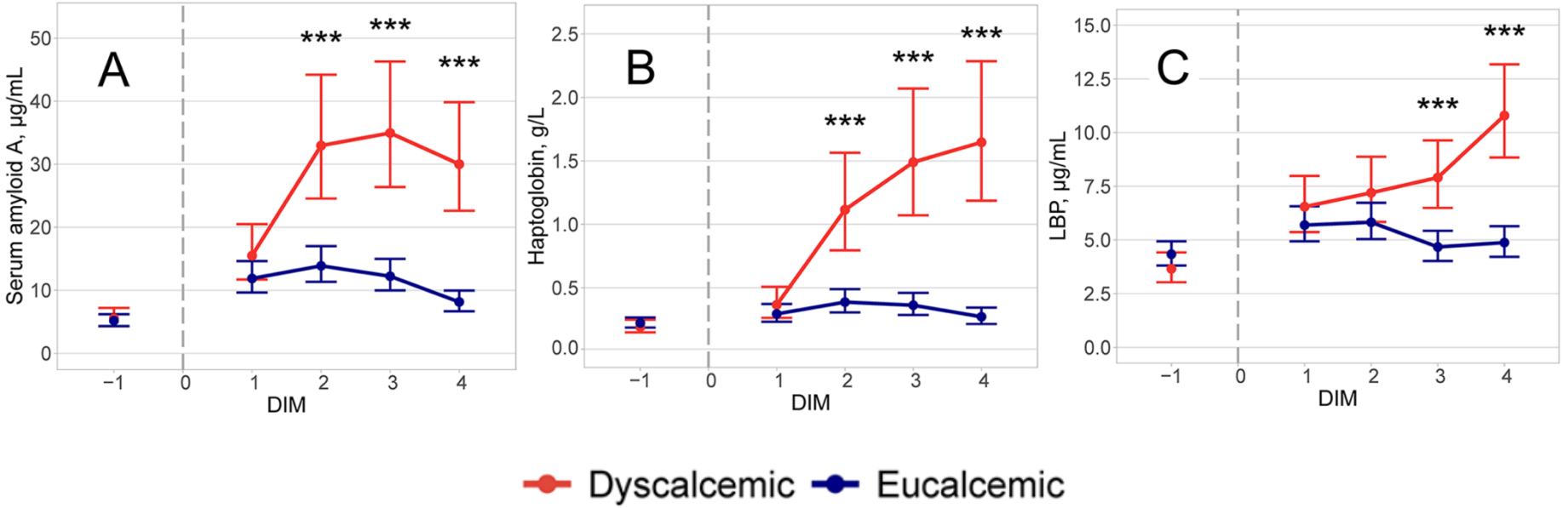




Prophylactics help sometimes…

# What are the next steps?

- What is behind Dyscalcemia?
- Is inflammation involved?

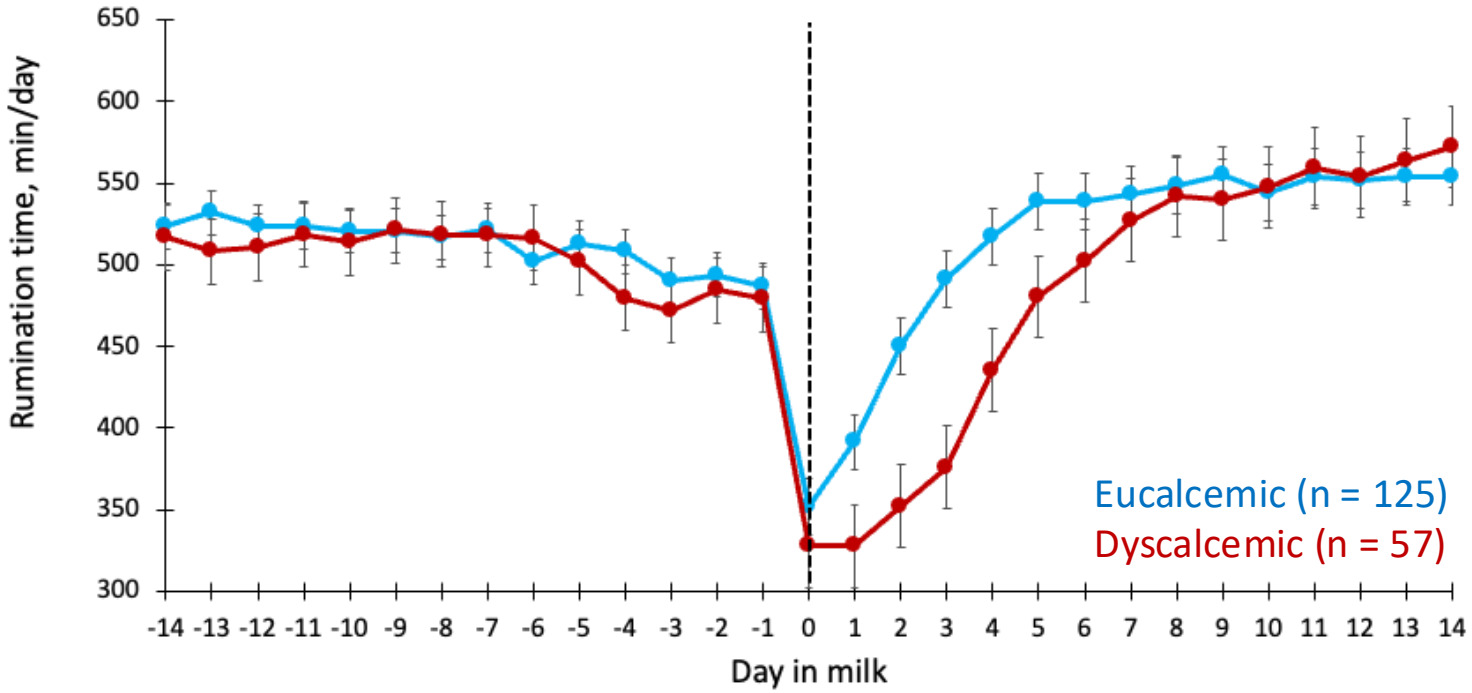





Seminara et al., 2025; https://doi.org/10.3168/jds.2024-25300

# What are the next steps?

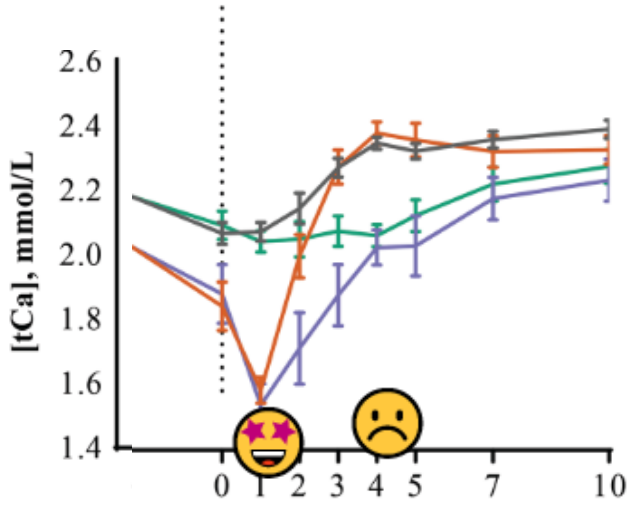
- Can we use non-invasive methods to identify cows with Dyscalcemia?

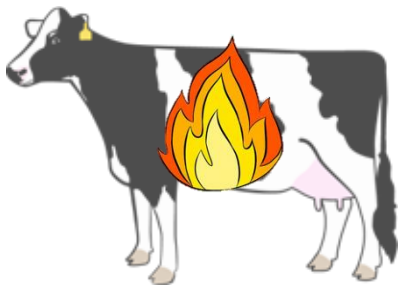






Seely and McArt, 2023; https://doi.org/10.3168/jds.2023-24139

# The future of Dyscalcemia




Make more informed management decisions to support Ca homeostasis

# Questions?

Claira.Seely@unh.edu