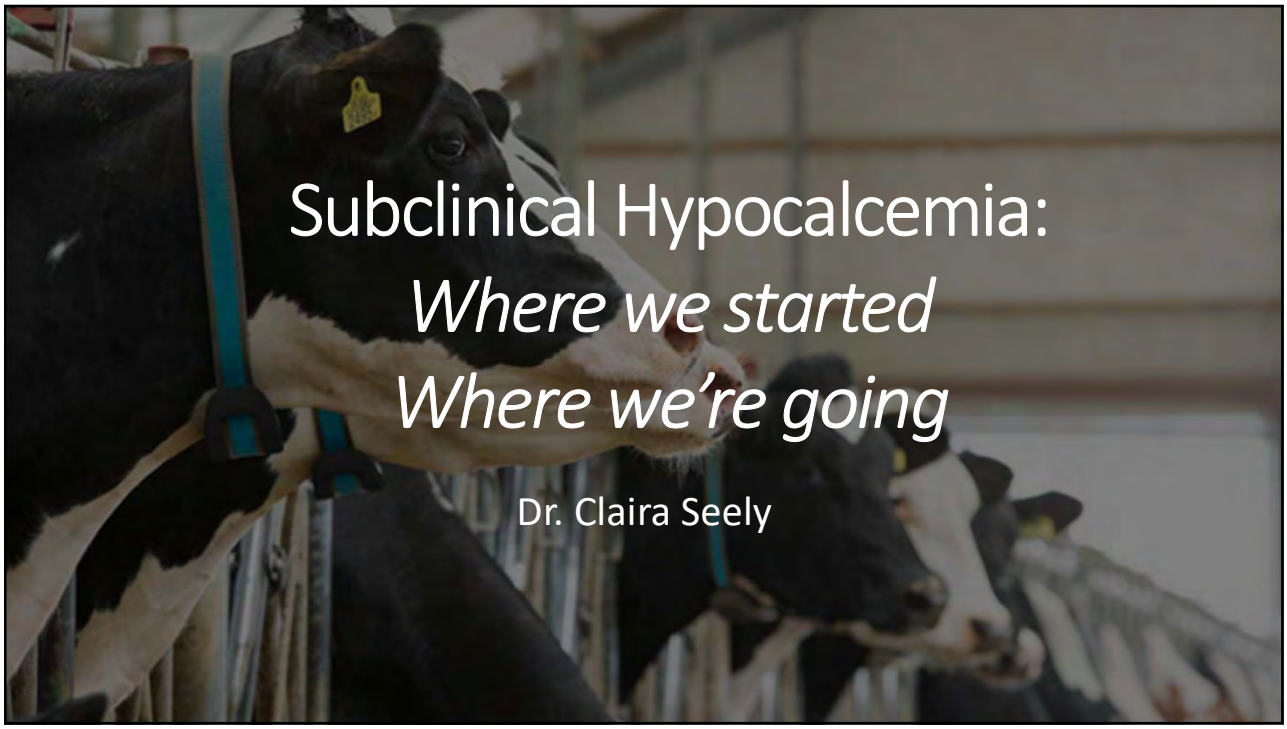


Subclinical Hypocalcemia: *Where we started* *Where we're going*

Dr. Claira Seely

Outline

- What is behind subclinical hypocalcemia?
- Understanding importance of early lactation blood Ca dynamics
- How can we treat or prevent subclinical hypocalcemia?
- Future directions

Ca Challenge of Early Lactation

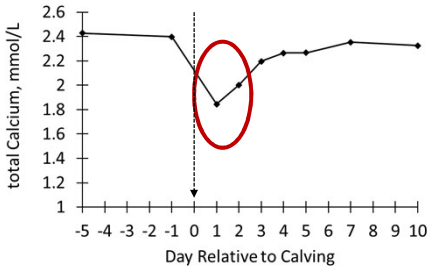
Cow
21 g Ca/d

Colostrum
23 g Ca/d

45 lb/d milk
33 g Ca/d

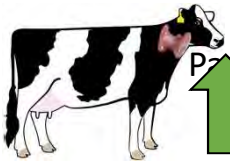
56 g Ca/d

Intake ↓30%



3

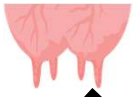
Calcium Homeostasis



Parathyroid gland
↑Blood Ca

↓

parathyroid hormone
(PTH)

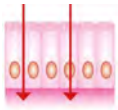


Serotonin
PTHrP

↓ Ca excretion
in urine

↑ Ca release
from bone

25-OH vit D →
$1,25(OH)_2D$



↑ Ca absorption
in intestine

4

Goff et al., 2002

Coordination Gone Wrong

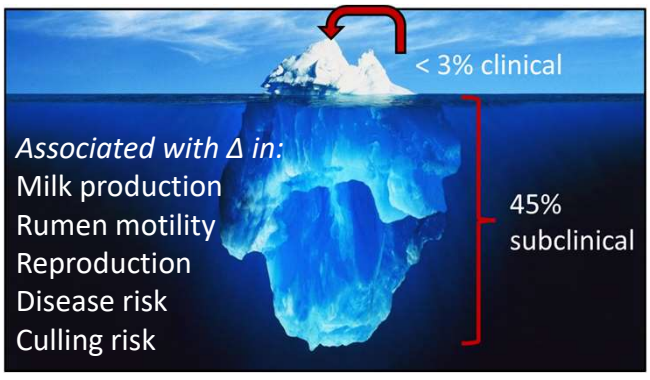
- Decrease in blood Ca below physiologically normal range
- Clinical hypocalcemia (milk fever)
  - Blood Ca < 1.37 mmol/L (5.5 mg/dL)
  - Down cow, risk of death if not treated
- Treatment of milk fever
  - 500 mL of calcium gluconate intravenously
  - Oral Ca bolus after she stands and again 12 h later

5

Coordination Gone Wrong

Subclinical hypocalcemia (SCH)

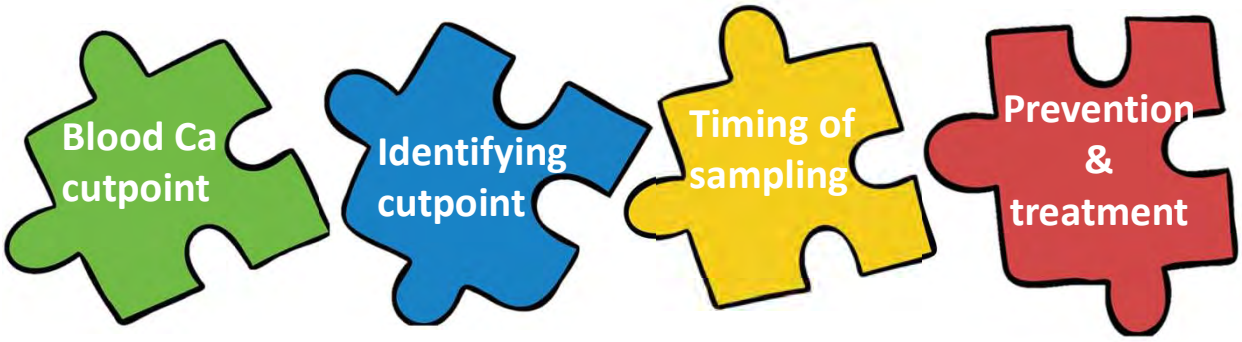
- No physical signs of disease
- Need blood sample to diagnose



6

Seely & McArt 2022; Seely et al., 2021, McArt & Neves, 2020; Caixeta et al., 2017; USDA-NAHMS, 2018; Reinhardt et al., 2011

Solving the SCH Puzzle

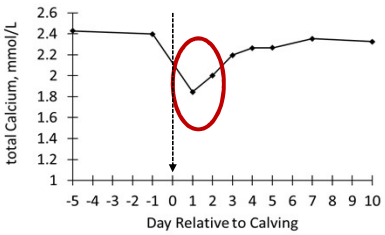


7

Diagnosing SCH

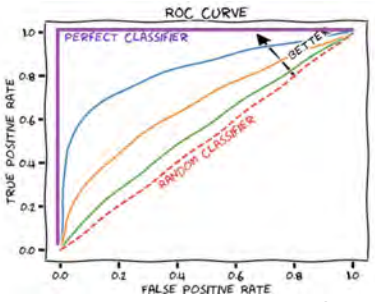
Varying cutpoints

- Blood [Ca] of 1.8 – 2.2 mmol/L
- Aka 7.2 – 8.8 mg/dL



Identifying a cutpoint

- Nadir concentrations; 0 to 24 h postpartum
- Population averages
- Previously published reference values
- ROC curves → i.e. statistics



8

Couto-Serrenho et al.,2021

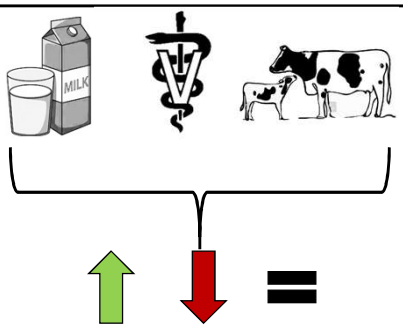
Timing of SCH Diagnosis

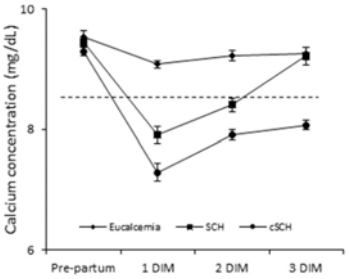
Single timepoint

- Generally, 0 – 24 h post calving
- Associated outcomes varied

Multiple timepoints

- 0 – 4 days in milk
- 2 to 3 samples/cow

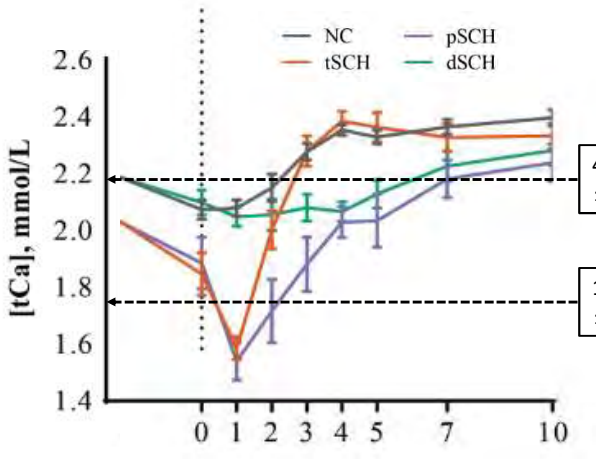




Chamberlin et al., 2013;Caixeta et al., 2017; Neves et al., 2018; McArt and Neves, 2020

9

Dynamics of SCH



4 DIM cutpoint
≤ 2.20 mmol/L

1 DIM cutpoint
≤ 1.77 mmol/L

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] ⬇

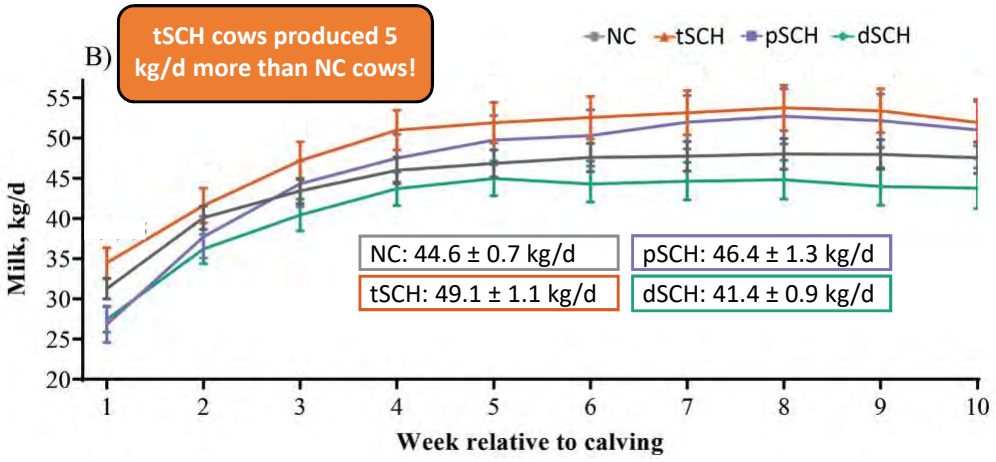
Delayed SCH; n = 70
dSCH: 1 DIM [Ca] ⬆
4 DIM [Ca] ⬇

McArt and Neves, 2020

10

Dynamics of SCH; Milk Production

tSCH cows produced 5 kg/d more than NC cows!



Error bars represent 95% confidence intervals

McArt and Neves, 2020

Dynamics of SCH; Health

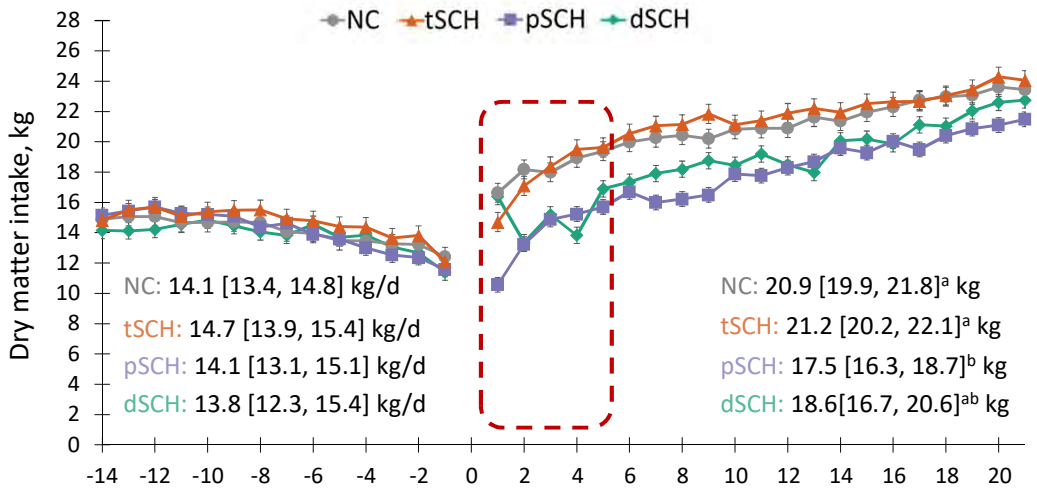
	Incidence, %			
	NC (n=109)	tSCH (n=50)	pSCH (n=34)	dSCH (n=70)
Hyperketonemia	30.3	48.0	50.0	50.0
Metritis	5.5	4.0	17.6	12.9
Displaced abomasum	1.8	2.0	11.8	8.6
Herd removal	0.9	2.0	2.9	12.9
Adverse event*	33.0	50.0	61.8	60.0

*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

Dynamics of SCH; Dry Matter Intake



78 multiparous Holstein cows
1 farm in New York state

Error bars represent standard error

Seely et al., 2021

13

Dynamics of SCH; Reproduction

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

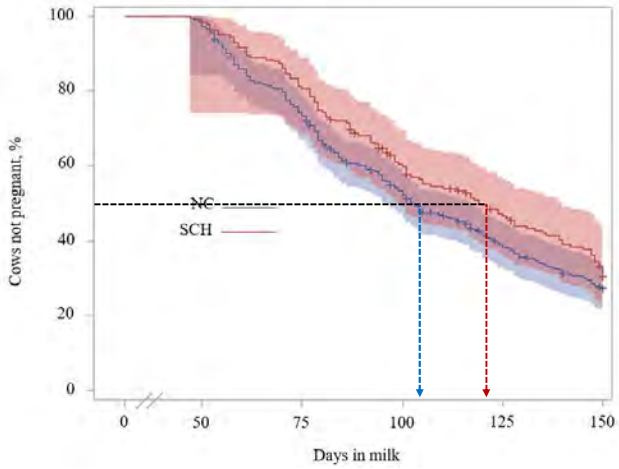
Variable	Incidence (%)[1]	OR[2]/HR[3]	95% CI	*P*-value
Time of first AI DIM				
NC	64.1 days		62.3-65.4	0.28
SCH	65.1 days		63.4-66.8	
Pregnant to 1st service				
NC	27.4%	Ref	-	-
SCH	18.1%	0.75	0.61-0.93	0.01
Pregnant by 150 DIM				
NC	70.7%	Ref	-	-
SCH	65.4%	0.82	0.67-1.01	0.06

[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

14

Seely and McArt, 2023

Dynamics of SCH; Reproduction

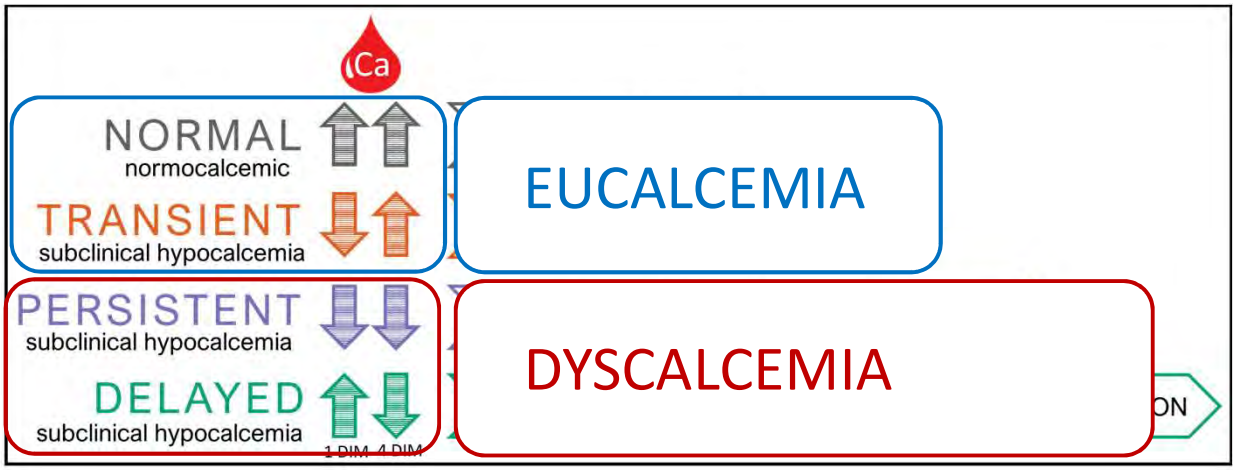


Median time to pregnancy

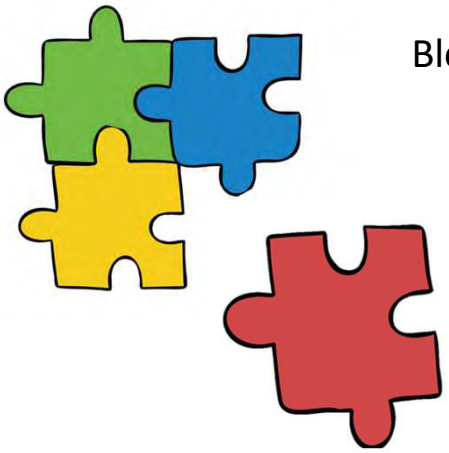
NC = 103 ± 11 d
SCH = 119 ± 16 d
P = 0.15

15
Seely and McArt, 2023

Is low Ca at 1 DIM really that bad?



Putting the SCH Puzzle Together



Blood Ca cutpoint

Identifying cutpoint

Timing of sampling

Prevention & Treatment

17

How do we improve Ca status during the transition period?

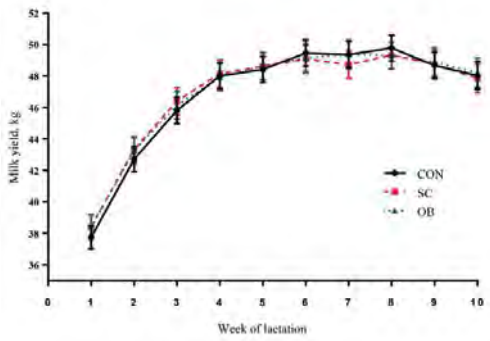
Ration formulation for prepartum cows

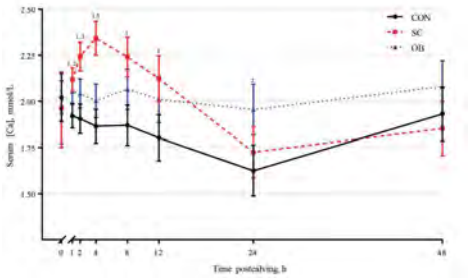
Ca supplementation at or after calving as treatment/prophylaxis

18

Ca Supplementation

Subcutaneous Ca → 500 ml of 23% Ca gluconate/borogluconate





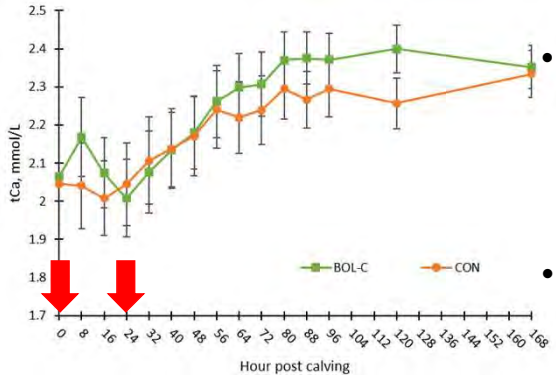
19

Domino et al., 2017; 2019; Frost et al., 2022

Ca Supplementation

Oral Ca Bolus →

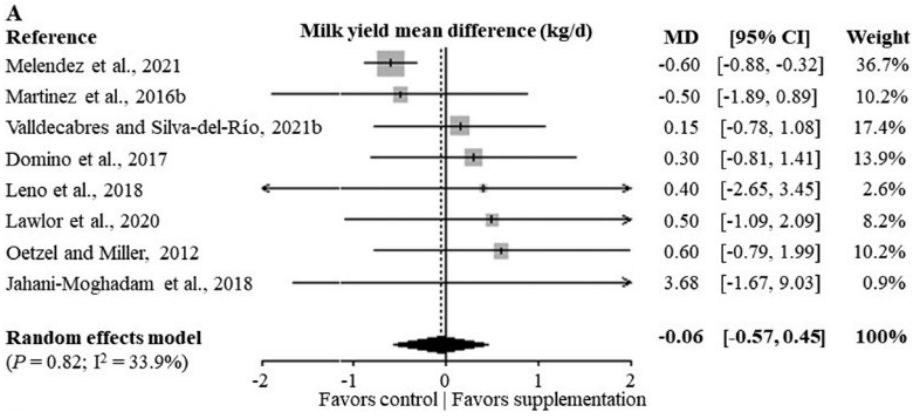
- Slow release of Ca salts
- 40 to 100 g of calcium per bolus
- Increase blood Ca by
  - Passive transport in the rumen
  - Passive or active absorption in the small intestines
- Sustained increase in blood Ca



20

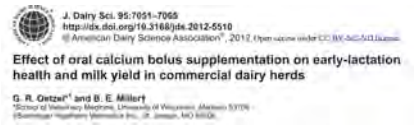
Frost et al., 2022

Production Response to Ca Bolus



Valldecabres et al., 2023

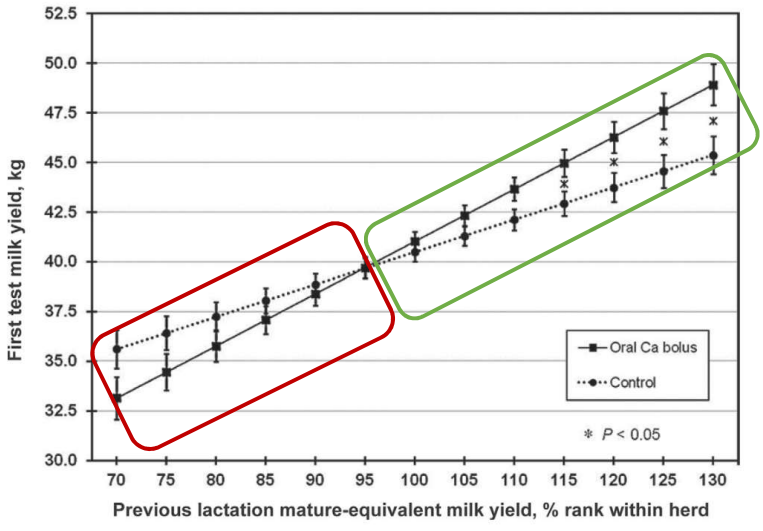
Production Response to Ca Bolus


J. Dairy Sci. 95:7051–7065
http://dx.doi.org/10.3168/jds.2012-5510
© American Dairy Science Association®, 2012.

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

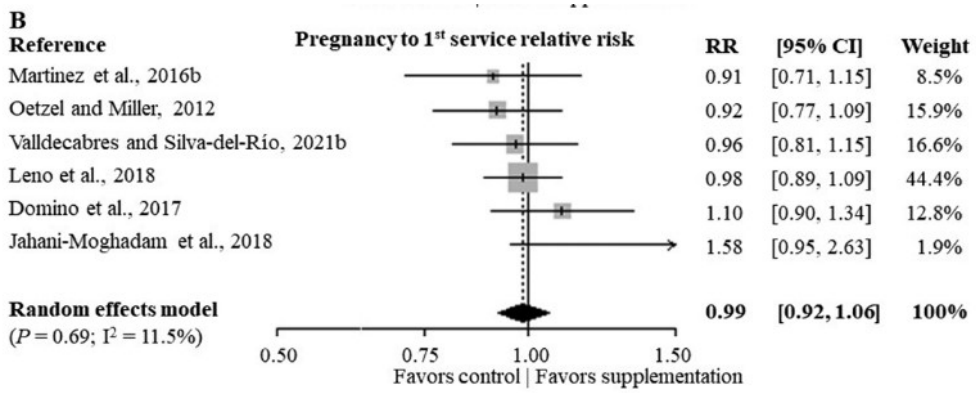
G. R. Oetzel*1 and B. E. Miller†

- 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

Reproductive Response to Ca Bolus



Valldecabres et al., 2023

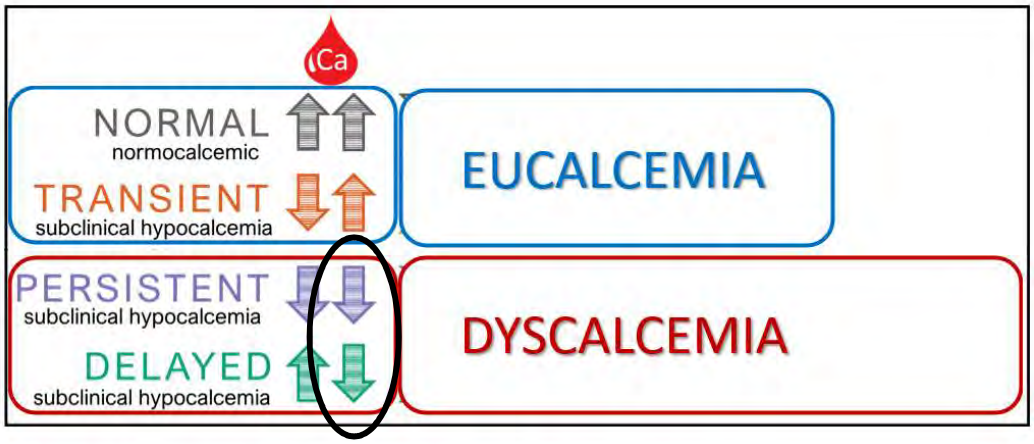
Overall impacts of Ca bolus supplementation

- Can be beneficial for
  - Lame cows (locomotion score of 3 or 4 precalving)→ reduced health disorders
  - Multiparous cows with a high previous mature equivalent milk yield → increased milk yield
  - Multiparous cows → reduced services/conception
- Can be detrimental for
  - Multiparous cows with a low previous mature equivalent milk yield → reduced milk yield
  - Primiparous cows → increased services/conception

❓ Is prophylactic Ca treatment good for herd level prevention ❓

Oetzel and Miller, 2012; Martinez et al., 2016; Leno et al., 2018; Valldecabres et al., 2023

Are we giving Ca at the right time?



25

Is there a better way to prevent SCH at 4 DIM?

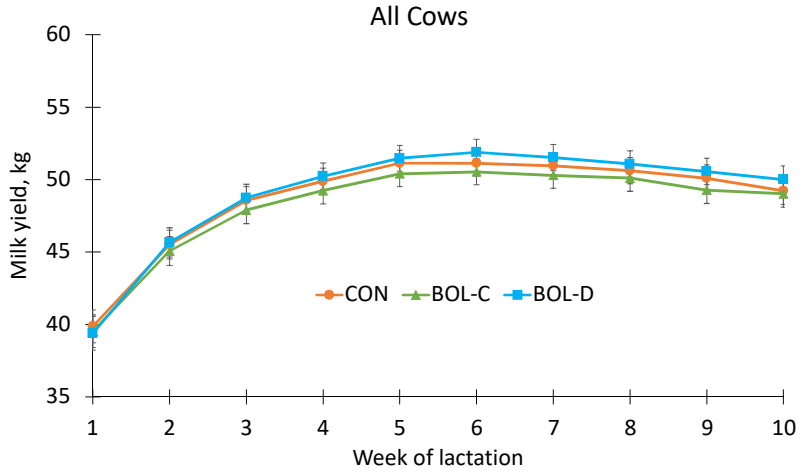
- Enrolled 998 multiparous Holstein cows from 4 herds in NY at calving

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

26

Milk production was unaffected at the study population level



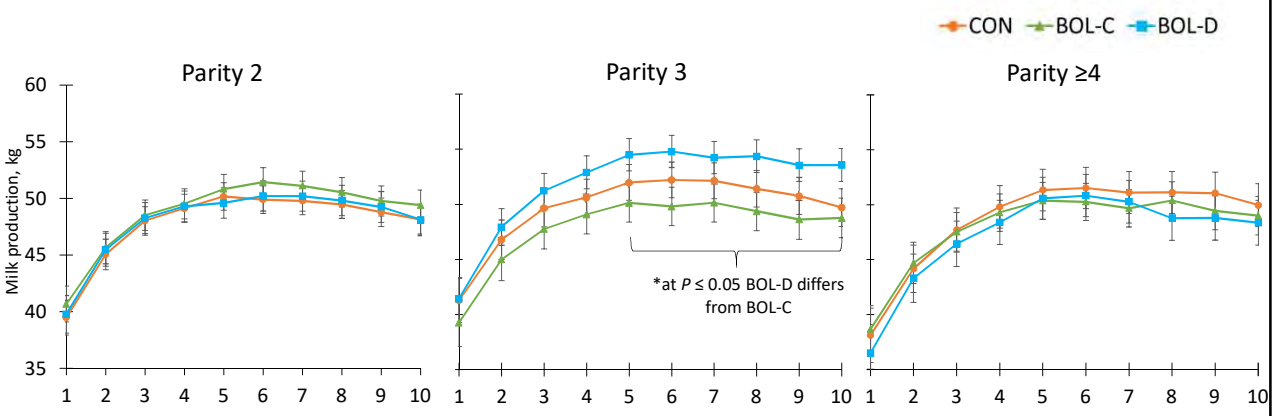
CON	48.8 [47.9, 49.6] kg/d
BOL-C	48.2 [47.4, 49.1] kg/d
BOL-D	49.2 [48.4, 50.0] kg/d

	***P* - value**
Farm	< 0.001
Week	< 0.001
TRT	0.2
TRT × Week	0.7
TRT × Parity	0.002

Error bars represent 95% confidence intervals

27

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

28

Bolusing had no effect on health events or tCa

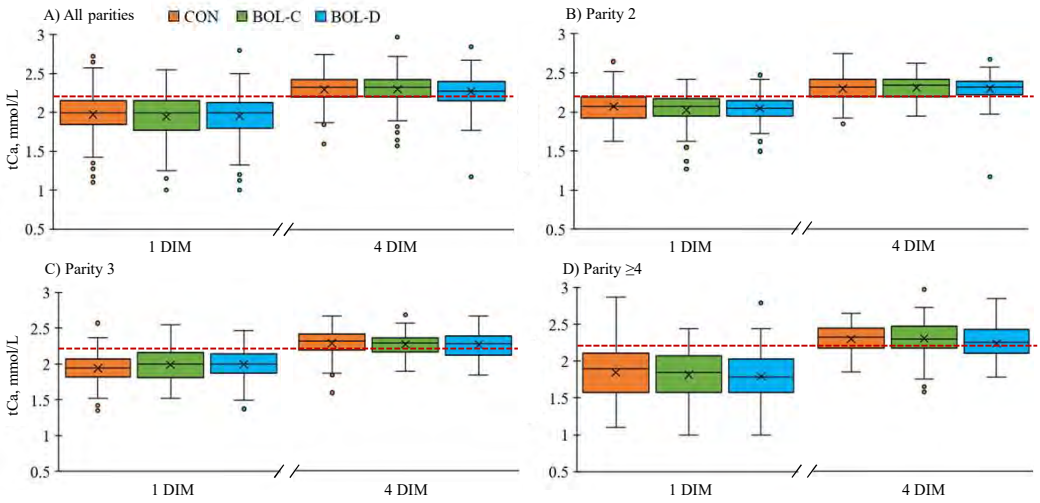
	Treatment		
	CON	BOL-C	BOL-D
Metritis, % (n)	6.3 (20)	5.4 (17)	7.0 (21)
DA, % (n)	1.9 (6)	0.6 (2)	2.3 (7)
Herd removal[2], % (n)	4.4 (14)	2.9 (9)	4.3 (13)
Adverse event[3], % (n)	10.8 (34)	8.0 (25)	11.5 (35)
tCa, mmol/L	2.11 [2.09, 2.13]	2.11 [2.09, 2.13]	2.09 [2.07, 2.11]

[2] Culled or died during 1st 10 wk of lactation

[3] Metritis, DA, and/or herd removal before 30 DIM

29

Bolusing did not improve tCa at 4 DIM



30

Ca Supplementation Conclusions

- Beneficial for sub-groups of cows
  - High producing multiparous cows
  - Lame/high BCS cows
  - Delayed bolusing 3rd lactation cows
- Likely not necessary for primiparous/parity 2 cows

- Detrimental for sub-groups of cows
  - Low producing multiparous cows
  - Primiparous cows
- Better strategy for parity 4+ cows?

31

Tying it all together

Blood Ca cutpoint
↳ 2.20 mmol/L

Identifying cutpoint

Timing of sampling
↳ 4 DIM

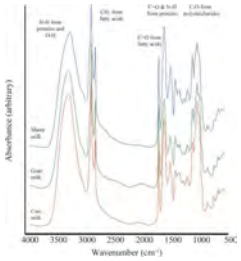
Prevention & Treatment
↳ Groups of cows that will benefit

32

What does the future hold?

- Non-invasive methods of identifying cows at risk for SCH/DYS
  - Rumination time
  - Milk constituent profiles

- Identify cows to allow for optimal management & treatment
  - Timing of Ca supplementation?
  - Optimizing intake!



33

Acknowledgements

- McArt Dairy Cow Lab
- USDA NIFA
- Cornell Institute for Digital Agriculture
- Boehringer Ingelheim
- Participating farms

QUESTIONS?

CRS336@CORNELL.EDU