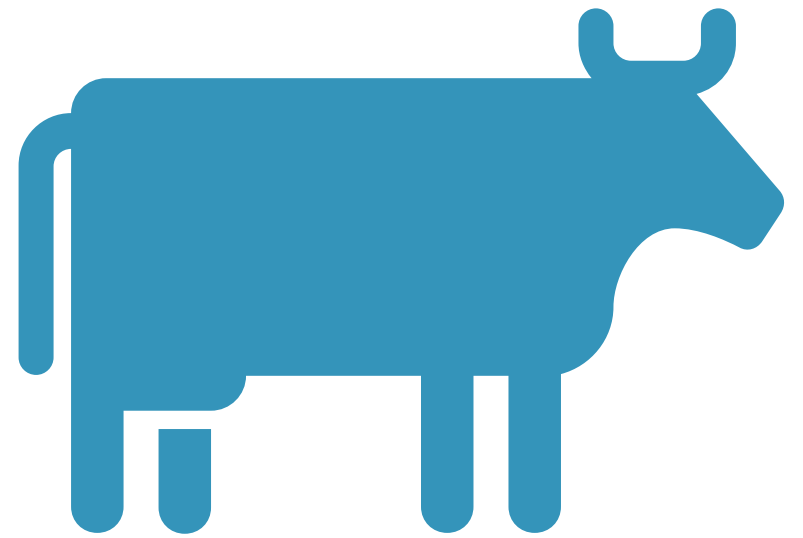


**ADVANCED POTION
MAKING: TREATING
COWS FOR
SUBCLINICAL
HYPOCALCEMIA**

**CYNTHIA MILTENBURG, DVM,
DVSC.**



QUESTIONS TO ANSWER TODAY

Are Ontario dairy cattle at risk of subclinical hypocalcemia after calving?

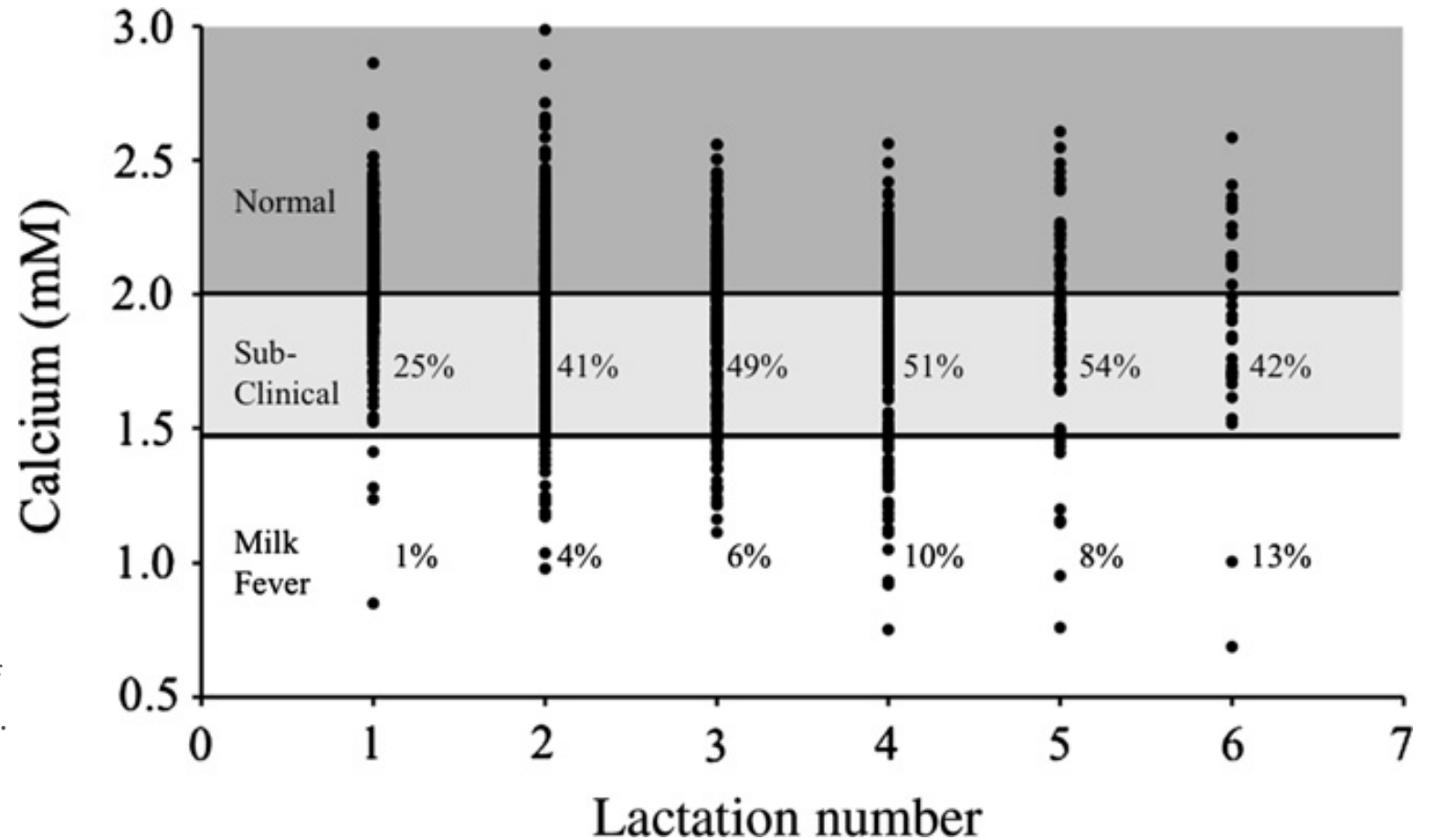
What are the treatment options for subclinical hypocalcemia?

Who should be treated?

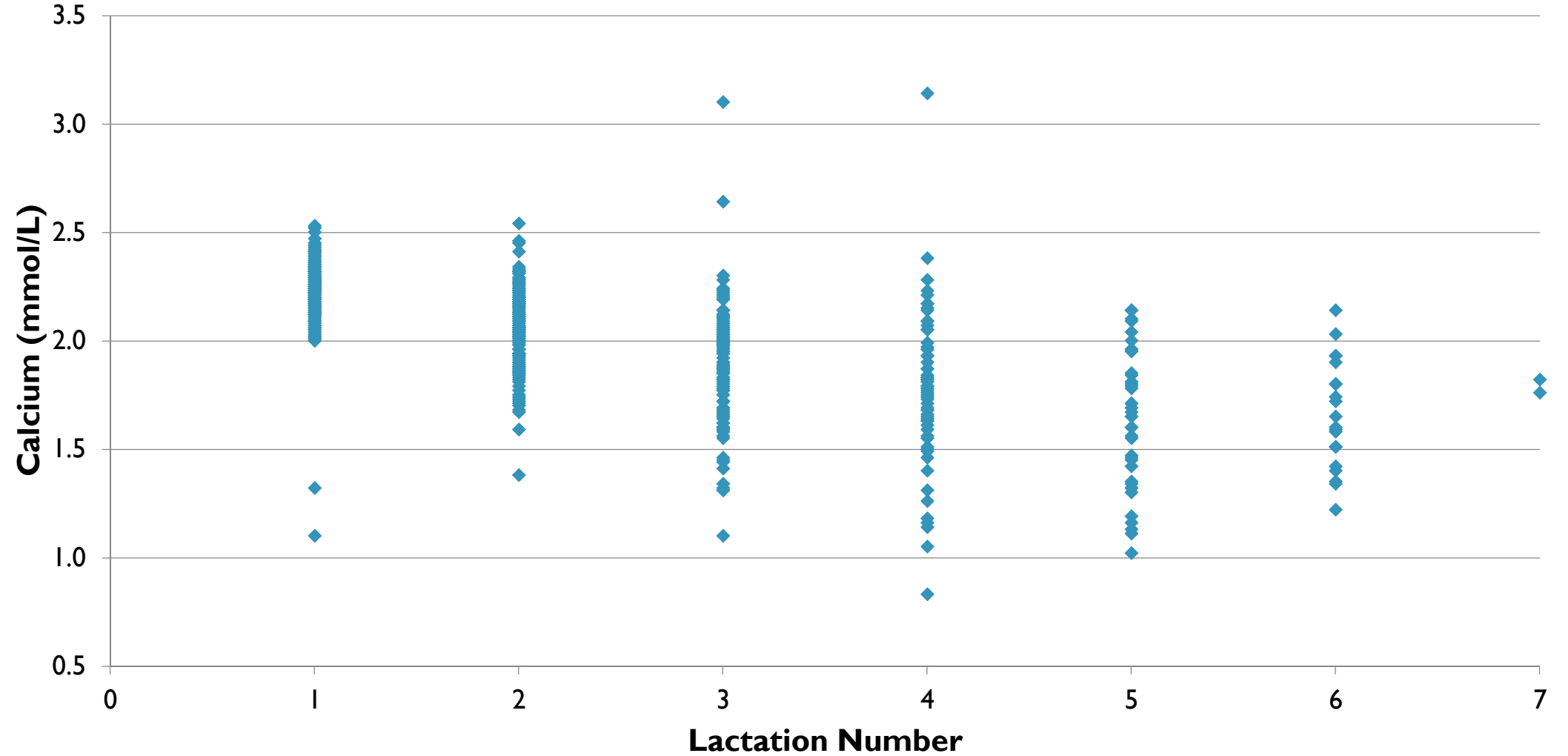
**ARE ONTARIO DAIRY CATTLE AT RISK OF
SUBCLINICAL HYPOCALCEMIA AFTER
CALVING?**

Serum samples collected from 1462 cows within 48 h postpartum, representing 480 dairy herds from 21 States.

Reinhardt, T.A., J. D. Lippolis, B. J. McCluskey, J. P. Goff, and R. L. Horst. 2011. Prevalence of subclinical hypocalcemia in dairy herds. *Vet. J.* 188:122–124.

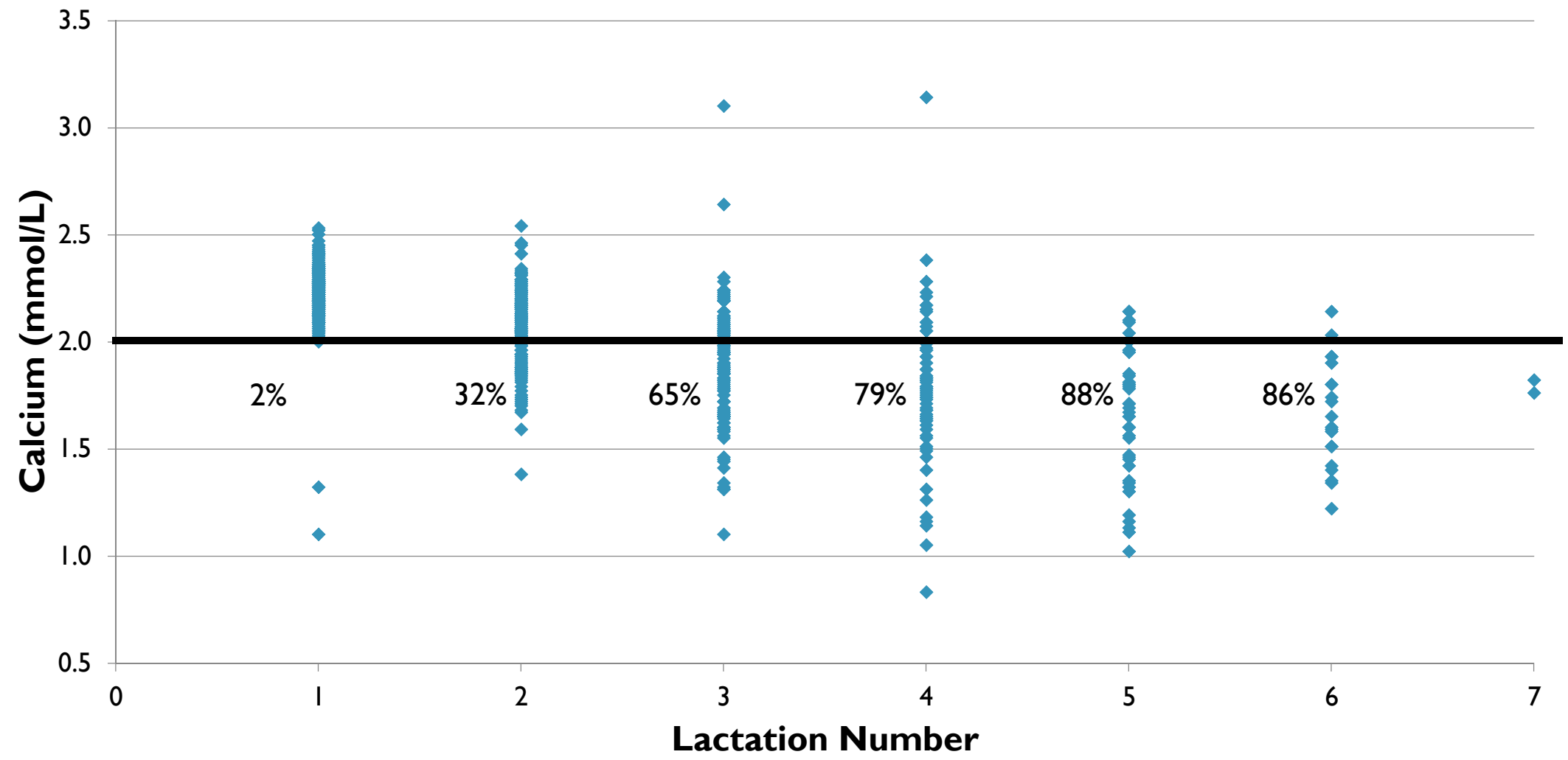


Serum calcium concentration between 0 – 12h post calving for 657 cows



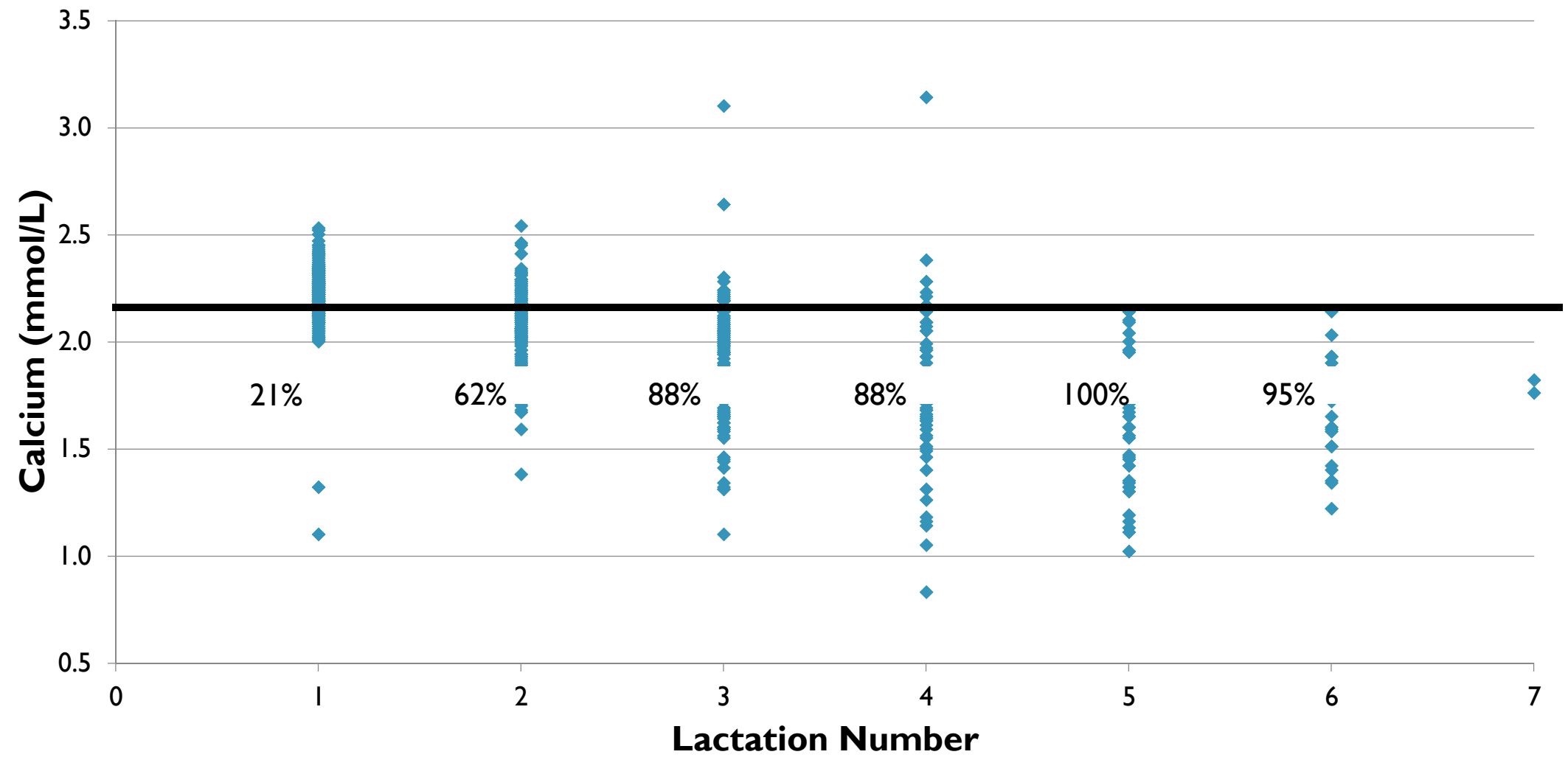
Miltenburg et al., 2016

Serum calcium concentration between 0 – 12h post calving for 657 cows



Miltenburg et al., 2016

Serum calcium concentration between 0 – 12h post calving for 657 cows



Miltenburg et al., 2016

IS SUBCLINICAL HYPOCALCEMIA A REAL DISEASE?

ANIMAL CARE

Hypocalcemia is more than a "low calcium" problem

Milk fever cannot be overcome in a reactive fashion. Prevention programs must be in place to help cows successfully transition into lactation.

by J.A. Shire and D.K. Beede

The authors are a graduate research assistant and professor in the department of animal science at Michigan State University, respectively.



HIDDEN HEALTH RISK

Feeding a negative dietary cation-anion difference (DCAD) diet for approximately 21 days prior to parturition can reduce the incidence of subclinical hypocalcemia in dairy cows.

By Angela Rowson, DVM

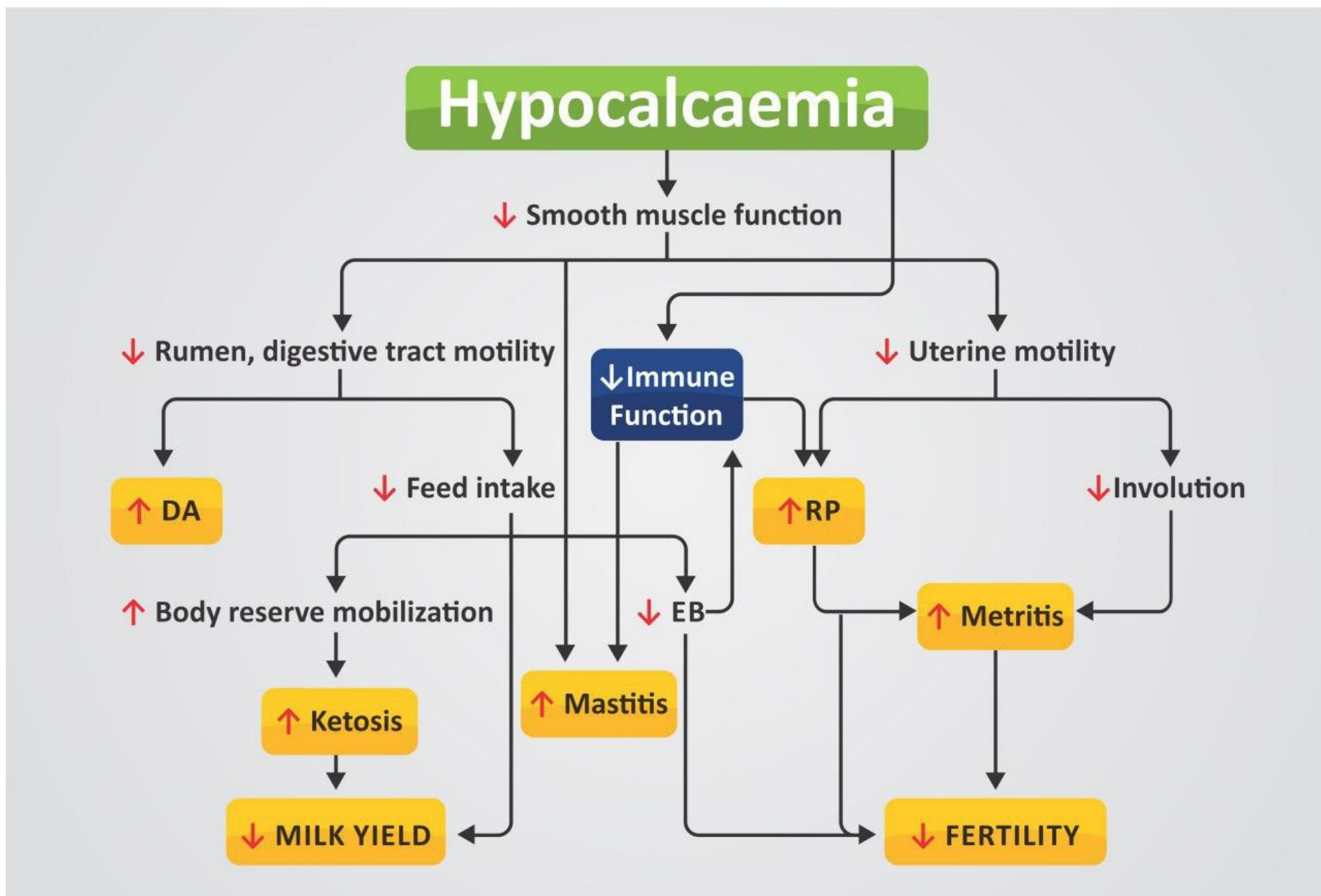
Subclinical hypocalcemia reduces dairy cow productivity and profitability.

The transition from gestating to lactating results in a sudden, dramatic physiological demand for calcium by dairy cows due to the production and secretion of colostrum and milk. Inadequate blood calcium concentrations at this time can result in the metabolic condition hypocalcemia, or milk fever. Clinical hypocalcemia (blood calcium concentrations below 5.5 mg/dL) affects approximately 5 percent of dairy cows in the United States and is often associated with recumbancy, depression and partial paralysis.



To better control subclinical hypocalcemia, producers should consider using a higher blood calcium threshold to identify cows at risk. Managing the problem with the aid of a negative DCAD diet can lessen losses from reduced milk production, disease and impaired reproduction.





Schematic view of consequences of hypocalcemia in dairy cows (modified chart from Howard, JL; Smith RA (1999) Current Veterinary Therapy: Food Animal Practice. W.B. Saunders) as published in Selfi et al., 2017

EFFECTS OF SCH - EARLY LACTATIONAL METABOLISM

- Caixeta et al., 2015
 - SCH cows had significantly higher NEFA on d 0 and significantly more lipid in hepatocytes on d 7 and 35 postpartum
 - Cows with SCH lost weight faster than those with normocalcemia
- Chapinal et al., 2012
 - The odds of displaced abomasum after calving were higher in herds that had $\geq 35\%$ of the animals with calcium ≤ 2.1 mmol/L in wk +1 (OR = 2.4; CI = 1.3–4.3)
- Rodriguez et al., 2017
 - Occurrence of displaced abomasum, ketosis, retained placenta, and metritis was 3.7, 5.5, 3.4, and 4.3 times more likely, respectively, in cows that had SCHC than in cows with normocalcemia

EFFECTS OF SCH - REPRODUCTIVE HEALTH AND SUCCESS

- Martinez et al., 2012
 - Cows with SCH were at a greater risk of developing fever, metritis, and puerperal metritis compared with normocalcemic cows.
- Caixeta et al., 2017
 - Cows with chronic SCH had negative effect on return of ovarian function during the voluntary waiting period and decreased the odds of pregnancy at first service
- Chapinal et al., 2012
 - Lower odds of pregnancy at first AI ($\geq 25\%$ of the herd SCH)
- Heppelmann et al., 2015
 - Cows with SCH had delayed reduction of uterine length, presumably related to reduction of myometrial contractility

EFFECTS OF SCH - IMMUNE FUNCTION

- Martinez et al., 2012
 - Neutrophil phagocytosis and oxidative burst were all reduced in cows with SCH compared with normocalcemic cows
- Martinez et al., 2013
 - Induction of SCH reduced the percentage of neutrophils undergoing phagocytosis and the oxidative burst response after incubation of pathogenic bacteria

EFFECTS OF SCH - PRODUCTION

- Chapinal et al., 2012
 - Lower average milk production at first DHIA test ($\geq 15\%$ of herd)
- Gild et al., 2015
 - Israeli cows with SCH produced significantly more milk when compared with normocalcemic cows - 3.17, 2.71 and 1.90 kg more on first, second and third test days
- Jawor et al., 2012
 - Cows with SCH produced, on average, 5.7 kg/d more milk during wk 2, 3, and 4 compared with control cows

EFFECTS OF SCH - BEHAVIOUR

- Martinez et al., 2013
 - Cows with induced SCH had reduced DMI and rumen contractions
- Hansen et al., 2003
 - SCH depresses the feed intake and ruminative activity of dairy cows when induced
- Jawor et al., 2012
 - Cows with SCH stood for 2.6 h longer during the 24-h period before parturition



WHAT ARE THE TREATMENT OPTIONS FOR SUBCLINICAL HYPOCALCEMIA?

CALCIUM SUPPLEMENTATION PRODUCTS IN CANADA

Calcium boluses

- Bovicalc - Calcium chloride, Calcium sulfate
- Transition – Calcium chloride, calcium carbonate, calcium proprionate

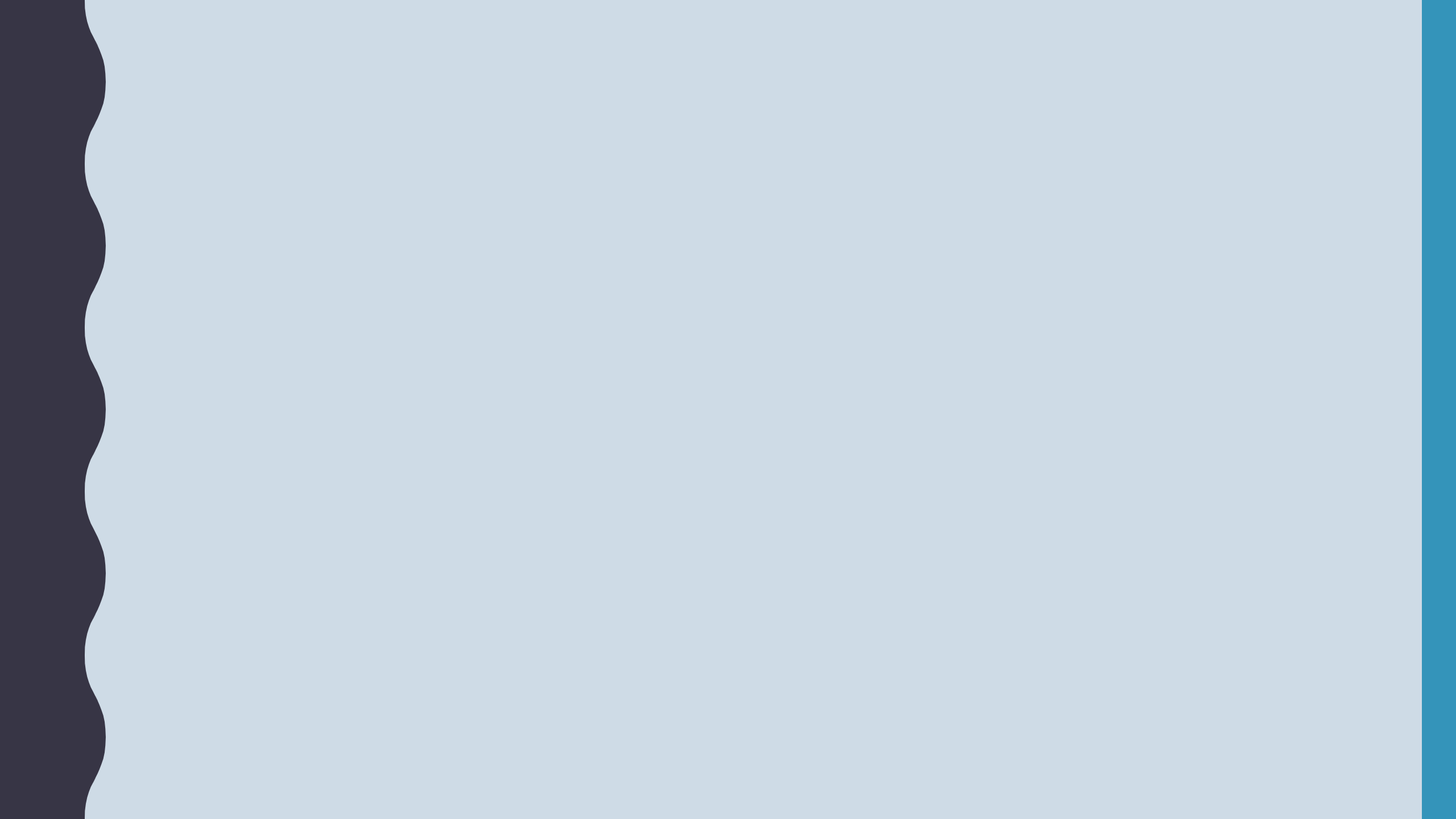
Calcium drenches/pastes

- Dr. Register Calcium Supplement – Calcium chloride, calcium proprionate (liquid)
- Lyte P - Di-Calcium phosphate, Calcium chloride (paste)
- Cal Paste Plus – Di-calcium phosphate, calcium chloride (paste)

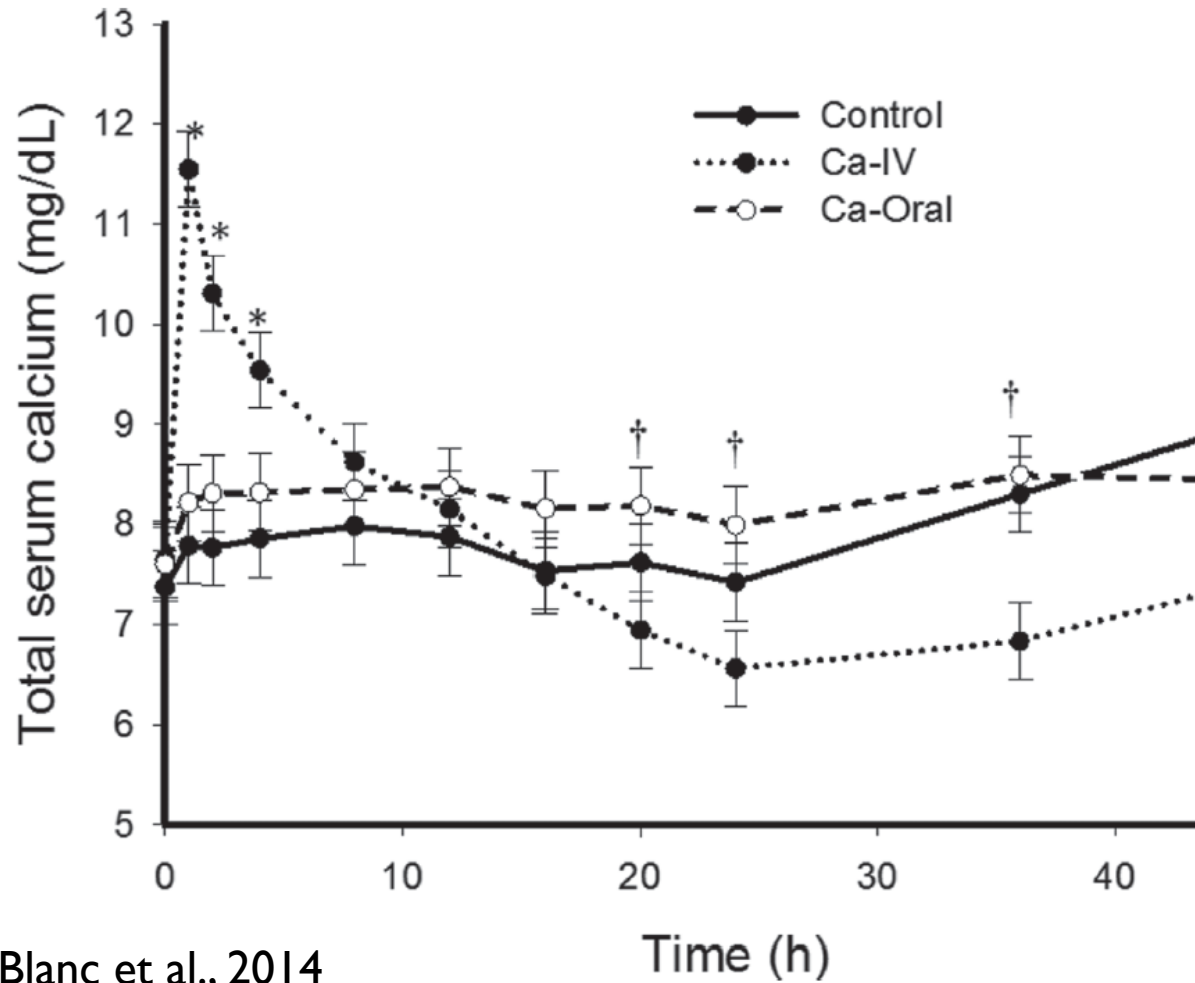
Calcium injectables

- Calcium borogluconate 23%
- Calcium, phosphorus, magnesium dextrose products
- Theracalcium – Calcium gluconate and calcium glucoheptonate

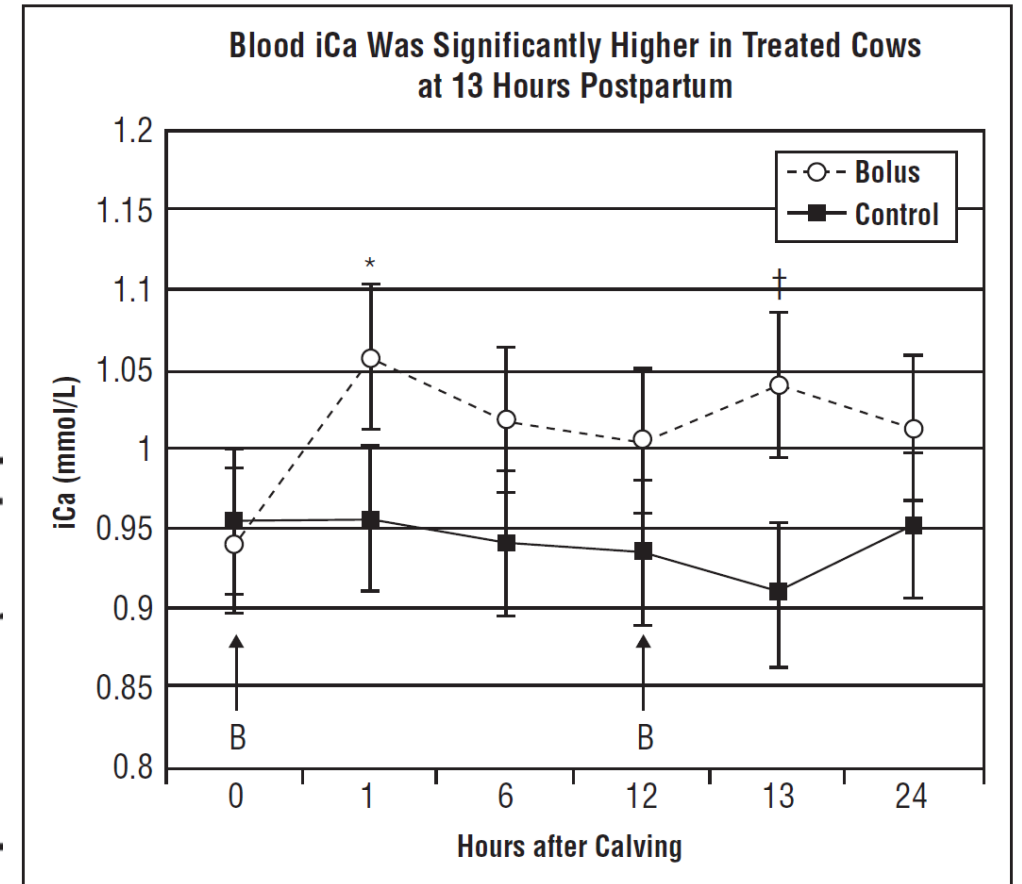
WHAT DO WE KNOW ABOUT THE EFFECTS OF CALCIUM BOLUSES?



THEY RAISE BLOOD CALCIUM



Blanc et al., 2014



Samspon et al., 2009

EFFECTS OF ORAL BOLUSES

Study and Population	Diet and Product	Relevant Outcomes
<p>Domino et al, 2017</p> <p>1,478 multiparous cows from 1 commercial dairy</p>	<p>TMR twice daily with a targeted DCAD level of -10 to -15 mEq/100 g of DM and 0 mEq/100 g of DM</p> <p>Bovicalc (0 and 12h)</p>	<ul style="list-style-type: none"> No difference in risk of metritis, displaced abomasum, early lactation disease diagnosis, or pregnancy to first insemination No effect on average daily milk yield Cows treated that had high relative herd milk rank in previous lactation were less likely to be diagnosed with mastitis in the first 60 DIM compared with control Treated second-parity cows fed a negative prepartum DCAD ration were more likely to be removed from the herd than control cows
<p>Leno et al., 2018</p> <p>3,949 cows (all parities) from 6 commercial dairies</p>	<p>TMR; DCAD varying from -6.9 to 14.1</p> <p>Quadrical (1 dose within 24h)</p>	<ul style="list-style-type: none"> No difference for plasma Ca between 1 and 24 h after treatment. Treated primiparous cows had decreased risk of one or more health disorders Treated primiparous cows with BCS >3.5 or days carried calf >277 had increased milk production Reduced risk of one or more health disorders was observed in parity ≥3 MP cows with BCS >3.5 reduced risk of RP Lame cows reduced risk of DA For MP cows with low plasma Ca, BOL decreased risk of additional Ca treatment as well as risk of one or more health disorders
<p>Martinez et al., 2016a and b</p> <p>450 Holstein cows from 1 commercial dairy – low risk and high risk for metritis</p>	<p>TMR offered for ad libitum intake; parous cow diet DCAD -153 ± 96 mEq/kg</p> <p>Bovicalc (2 boluses on d0 and d1 ± 1 boluses on d3 and d4 vs.</p>	<ul style="list-style-type: none"> Calcium supplementation decreased the prevalence of SCH on d 0 and 1 postpartum in all cows. Oral Ca increased the incidence of metritis especially in LRM primiparous cows Oral Ca increased morbidity in primiparous cows (at least one clinical disease) but not multiparous cows For multiparous cows, Ca supplementation increased milk yield in the first 30 DIM in cows of greater production potential, decreased cows with below average production potential. Primiparous cows reduced P/AI at first and all AI; multiparous cows improved P/AI at the first and all AI Extended median days to pregnancy and smaller proportion of pregnant in primiparous cows, but shorter days to pregnancy and increased proportion of pregnant cows in multiparous cows
<p>Oetzel and Miller, 2012</p> <p>927 multiparous cows from 2 commercial dairies</p>	<p>TMR; DCADs -8 and -109 mEq/kg</p> <p>Bovicalc (1 bolus <2h; 2nd bolus 8-35h after calving)</p>	<ul style="list-style-type: none"> Mean Ca²⁺ concentrations were not different between the control and oral bolus group. Lame cows supplemented averaged 0.34 fewer health events in the first 30 d in milk Cows with a higher previous lactation mature-equivalent milk production (greater than 105% of herd rank) and supplemented with oral Ca boluses produced 2.9 kg more milk at their first test

Domino et al,
2017

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multiparous
cows from 1
commercial
dairy

TMR twice daily
with a targeted
DCAD level of
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mEq/100 g of
DM and 0
mEq/100 g of
DM

Bovicalc (0 and
12h)

- No difference in risk of metritis, displaced abomasum, early lactation disease diagnosis, or pregnancy to first insemination
- No effect on average daily milk yield
- Cows treated that had high relative herd milk rank in previous lactation were less likely to be diagnosed with mastitis in the first 60 DIM compared with control
- Treated second-parity cows fed a negative prepartum DCAD ration were more likely to be removed from the herd than control cows

Leno et al., 2018

3,949 cows (all parities) from 6 commercial dairies

TMR; DCAD varying from -6.9 to 14.1

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- Treated primiparous cows had decreased risk of one or more health disorders
- Treated primiparous cows with BCS >3.5 or days carried calf >277 had increased milk production
- Reduced risk of one or more health disorders was observed in parity ≥ 3
- MP cows with BCS >3.5 reduced risk of RP
- Lame cows reduced risk of DA
- For MP cows with low plasma Ca, BOL decreased risk of additional Ca treatment as well as risk of one or more health disorders

Martinez et al.,
2016a and b

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- For multiparous cows, Ca supplementation increased milk yield in the first 30 DIM in cows of greater production potential, decreased cows with below average production potential.
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Oetzel and
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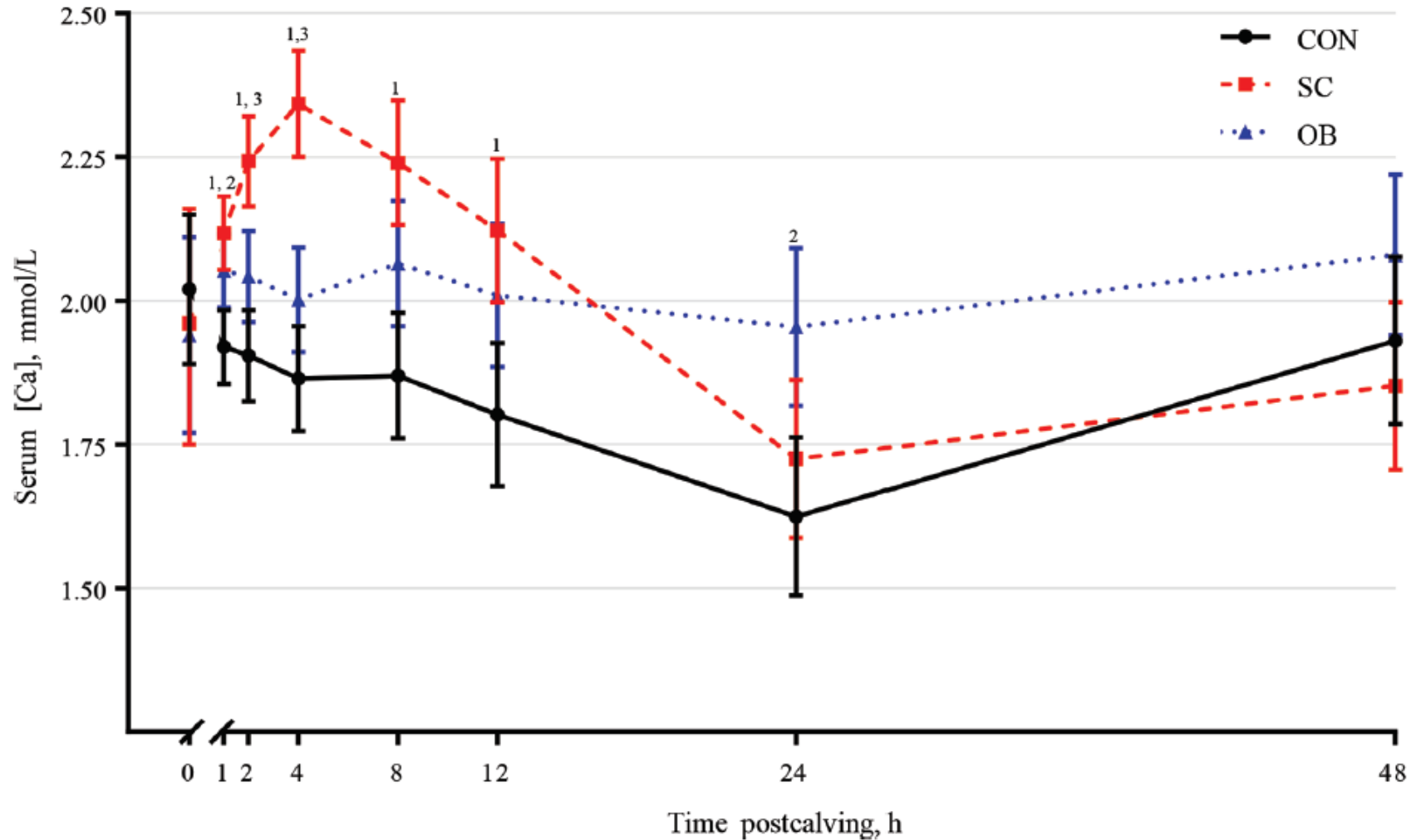
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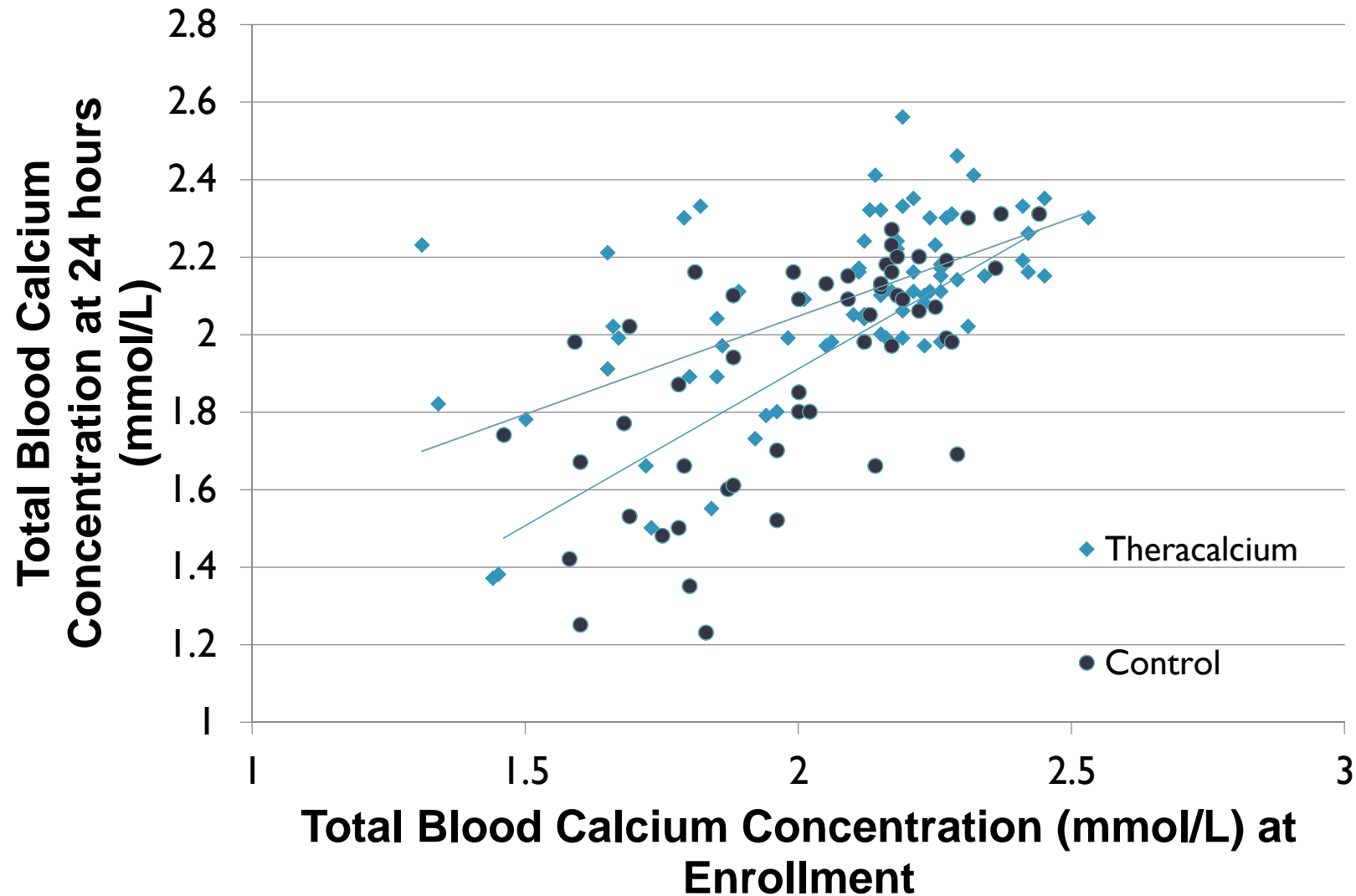


WHAT DO WE KNOW ABOUT THE EFFECTS OF SUBCUTANEOUS CALCIUM?

THEY RAISE BLOOD CALCIUM



THERACALCIUM MORE EFFECTIVE IN COWS WITH LOWER STARTING BLOOD CALCIUM



EFFECTS OF SUBCUTANEOUS CALCIUM

Study and Population	Diet and Product	Relevant Outcomes
<p>Amanalou et al., 2016</p> <p>375 Holsteins all parities from 1 commercial dairy</p>	<p>TMR with DCAD of -130 mEq/kg</p> <p>250 mL of 40% Ca borogluconate SC after calving OR 500 mL of 40% Ca borogluconate SC after calving OR 250 mL of 40% Ca borogluconate after calving and repeat 12-18 h later</p>	<ul style="list-style-type: none"> • DMI in first 24 h after calving was higher for treated cows relative to control • Milk somatic cell counts were lower for cows treated with 500mL or 2 doses compared to control • Higher risk of developing metritis, and clinical and subclinical endometritis for control cows
<p>Domino et al, 2017</p> <p>1,478 multiparous cows from 1 commercial dairy</p>	<p>TMR twice daily with a targeted DCAD level of -10 to -15 mEq/100 g of DM and 0 mEq/100 g of DM</p> <p>Subcutaneous administration of 500 mL of 23% Ca gluconate 30 min after calving</p>	<ul style="list-style-type: none"> • SC cows had greater Ca concentrations from 1 through 12 h post-treatment • Cows treated with SC that had a high relative herd milk rank in the previous lactation were half as likely to be diagnosed with mastitis in the first 60 DIM • Second-parity cows fed a negative prepartum DCAD ration and treated with SC were more likely to be removed from the herd
<p>Miltenburg et al., 2016</p> <p>984 cows of all parities from 7 commercial dairies</p>	<p>TMR with positive DCAD (no anionic salts fed)</p> <p>Theracalcium (120mL SC within 6h of calving, repeated 12-24h later)</p>	<ul style="list-style-type: none"> • tCa was significantly higher in the treated cows at 24h but no difference at 48 h • Treated cows were significantly less likely to have received supplemental Ca for exhibiting clinical signs of hypocalcemia than control cows

Amanalou et al., 2016

375 Holsteins all
parities from 1
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TMR with DCAD of -
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250 mL of 40% Ca
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after calving OR
500 mL of 40% Ca
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after calving OR
250 mL of 40% Ca
borogluconate after
calving and repeat 12-
18 h later

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Domino et al, 2017

1,478 multiparous cows from 1 commercial dairy

TMR twice daily with a targeted DCAD level of -10 to -15 mEq/100 g of DM and 0 mEq/100 g of DM

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WHO SHOULD BE TREATED WITH SUPPLEMENTAL CALCIUM?

HERD SPECIFIC SOP

What prepartum strategies are being employed?

First do no harm...

- Oral bolus – proper delivery of boluses
- Subcutaneous treatments – sterility of needles and IV hoses, appropriate amount per site

Do you have an understanding of the level of subclinical hypocalcemia on the dairy?

- Blood samples from next 10-15 cows to calve
- Unspun blood (red tops) or serum separators OK in fridge for 2-3 days; spin and freeze

DEVELOPING A HERD SPECIFIC SOP

Primiparous animals likely don't need supplementation

- Prevalence of SCH is generally low
- Mixed results for reduction of postpartum disease and milk production effects
- Some potential cautions – may be reduced P/AI and longer median days to pregnancy

Multiparous animals more appropriate to supplement

- Higher prevalence of SCH, especially among 3+ parity cows
- More likely to realize milk production benefit, especially among higher producers
- May drive improved DMI
- Data tends to show less disease, but not any one disease consistently so hard to quantify
- Mixed results for improved reproductive outcomes

WORDS OF CAUTION

- Many of the studies were conducted in conjunction with negative DCAD diets; may not see the same effects on dairies not employing prepartum strategies
- Increased milk production might get lost in the noise – only high producers, a few kg

Remember - an ounce of prevention is worth a pound of cure!



Unless you're sick.

