

Evaluation of a Novel Vaccine Based on Siderohpore Receptor Proteins and porins (SRP Technology) for Controlling Klebsiella Mastitis in a Dairy Herd

2016 AABP Annual Meeting

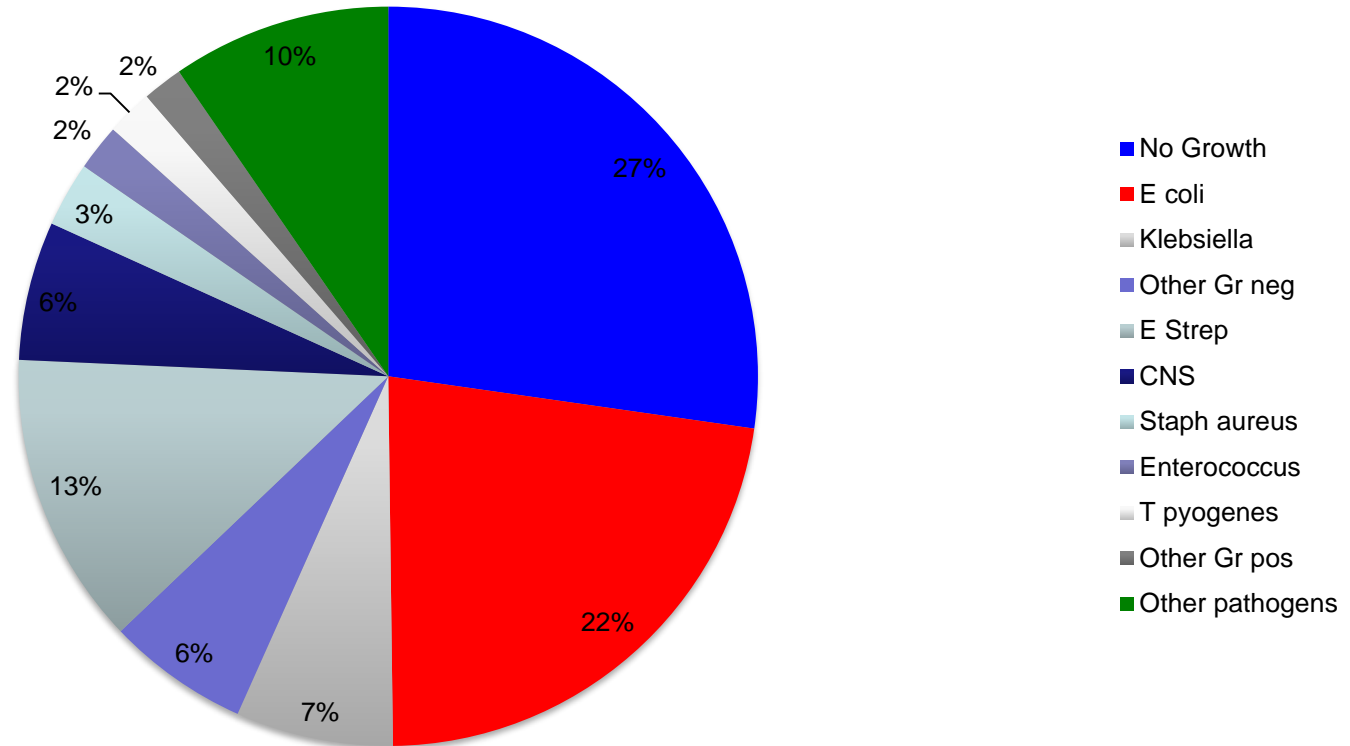
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L Slinden, and D Burkhardt



Food Supply Veterinary Medicine
Veterinary Diagnostic and Production Animal Medicine
Iowa State University

**IOWA STATE
UNIVERSITY**
College of Veterinary Medicine

Large WI Dairy Farms



Oliveira, et al, 2013, J. Dairy Sci. 96:7538–7549

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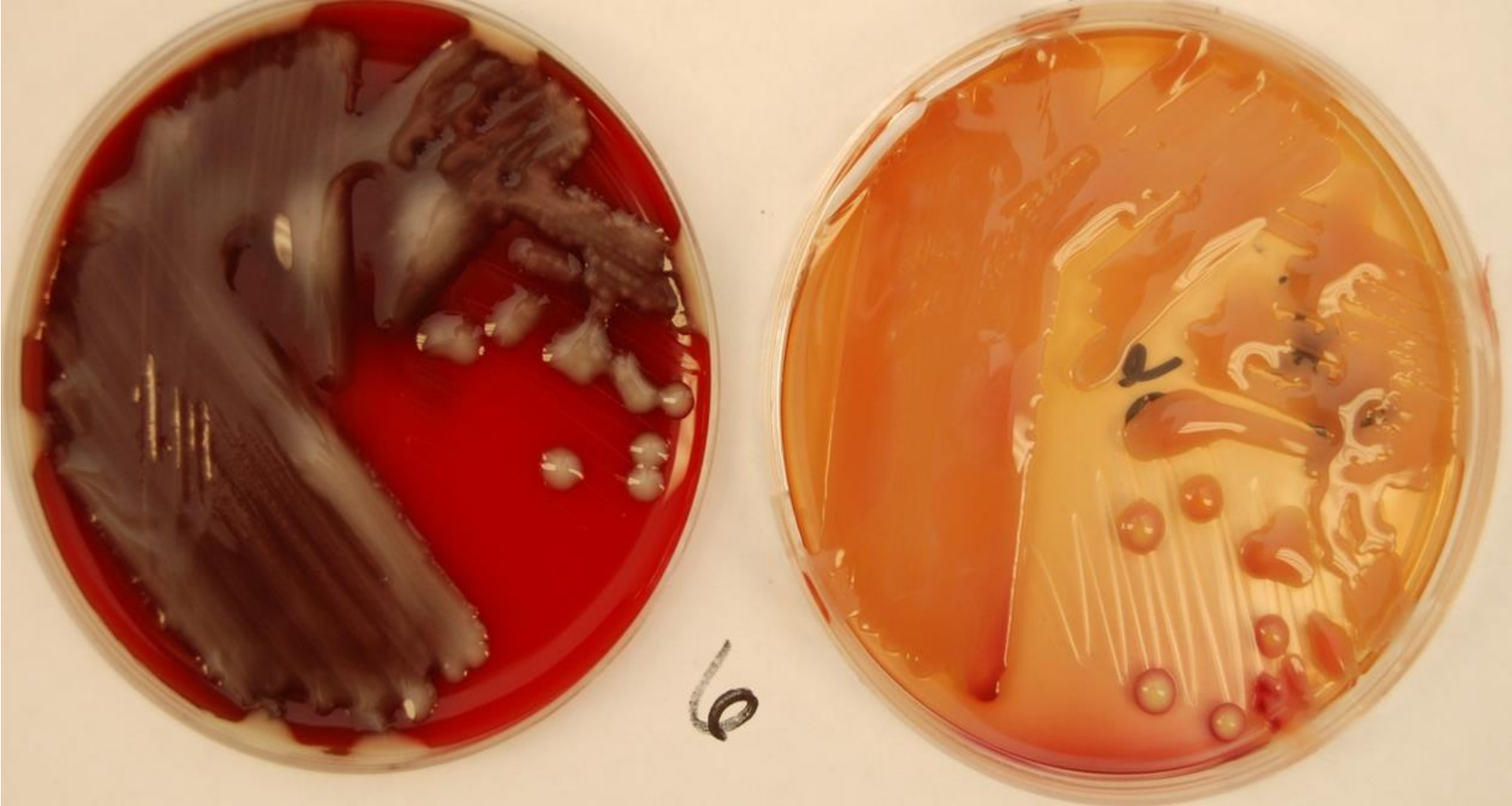


Klebsiella sp.

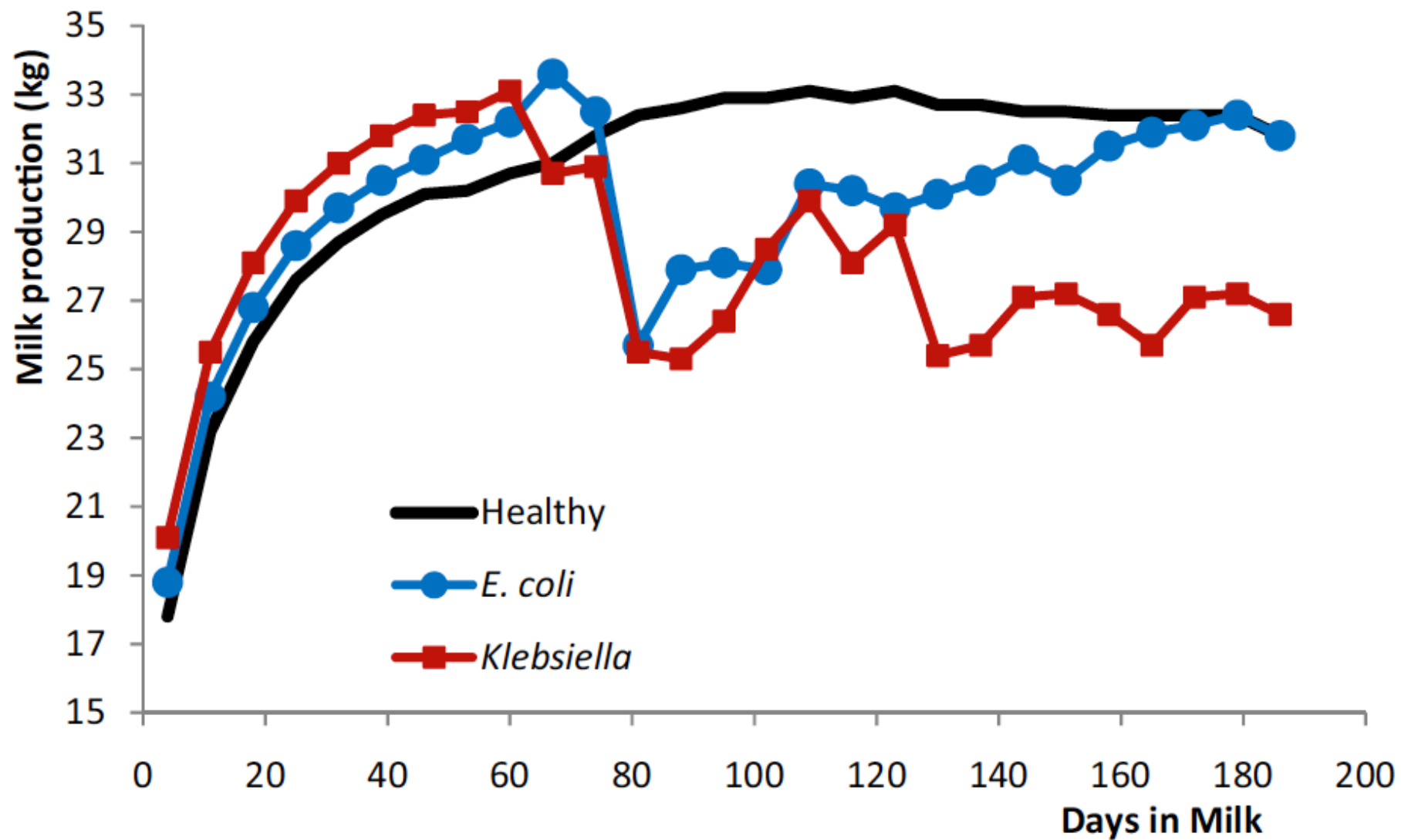
- *K. pneumoniae* – most common
- *K. oxytoca* – Occasionally seen.
- *Raoultella sp*
- Virulence factors:
 - Thick polysaccharide capsule – Reduces phagocytosis.
 - LPS – Lipopolysaccharide
 - O Ag – Prevents complement fixation.



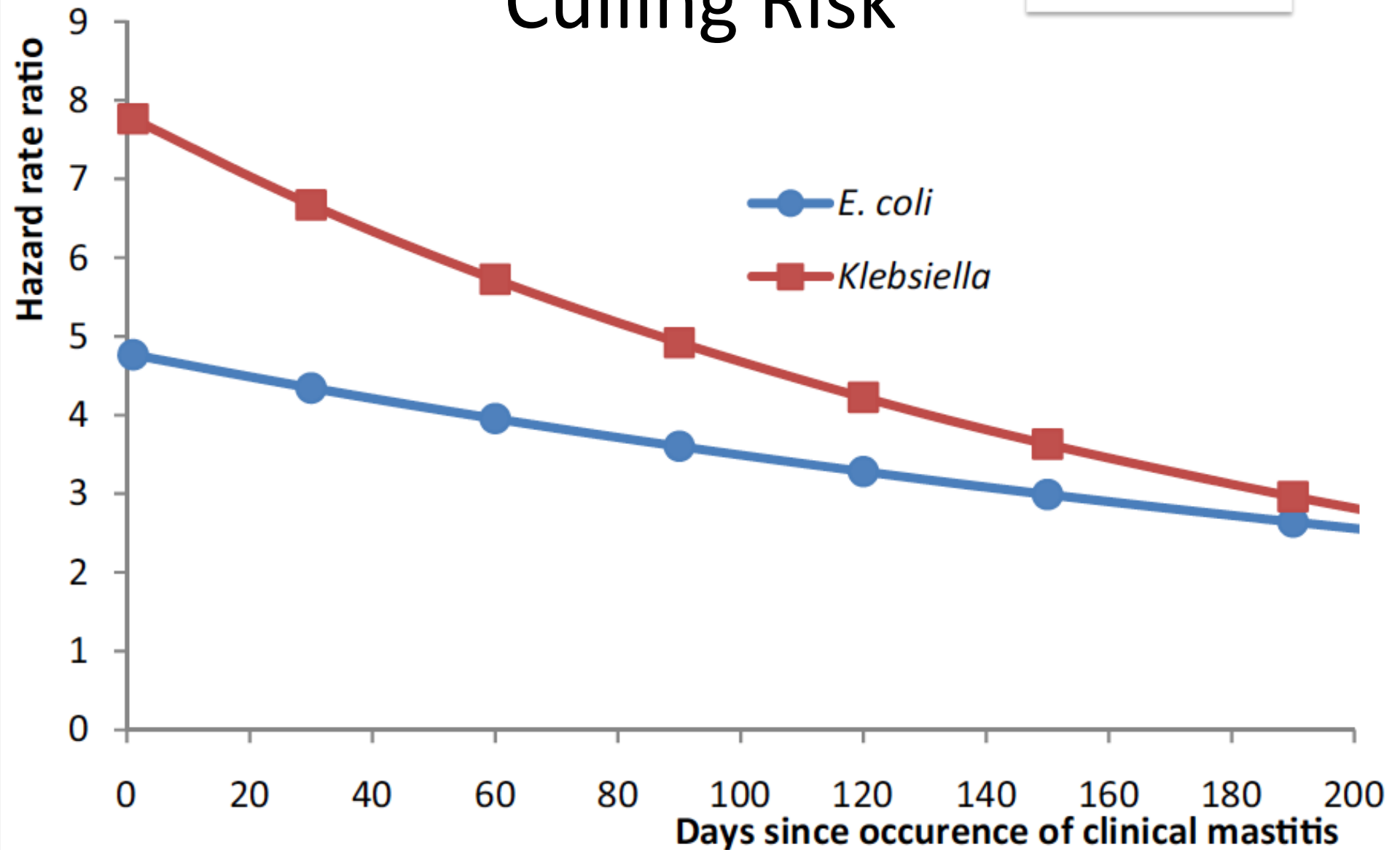
Capsule

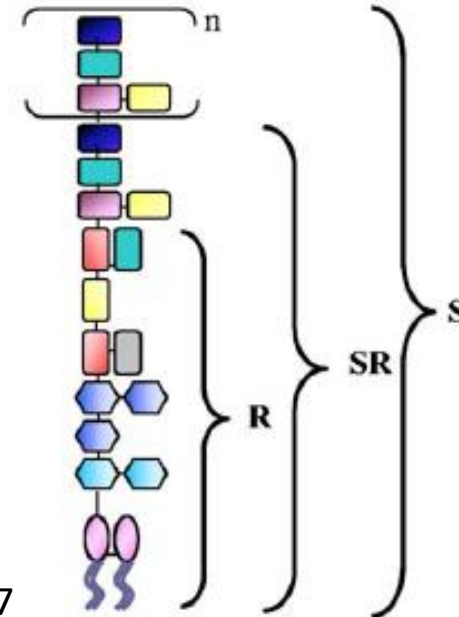
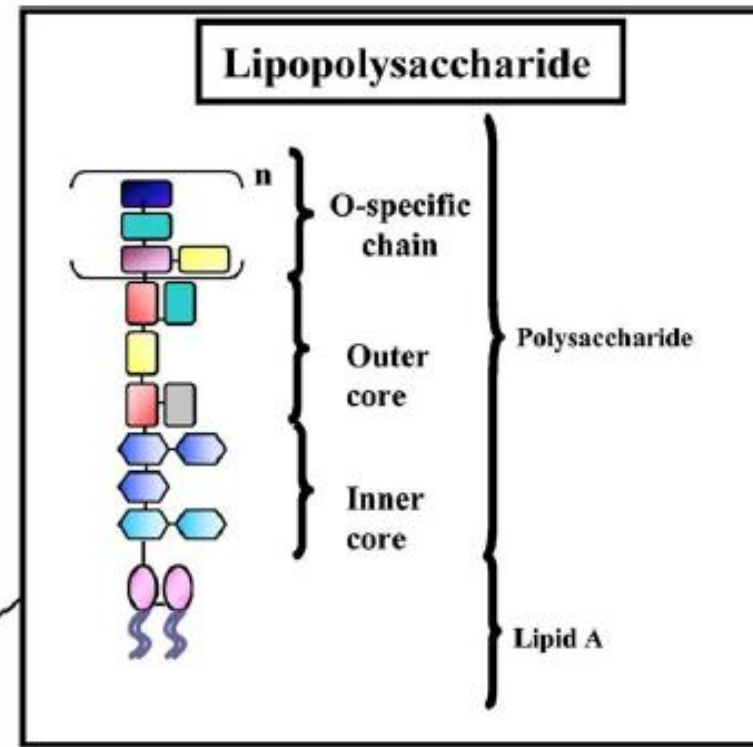
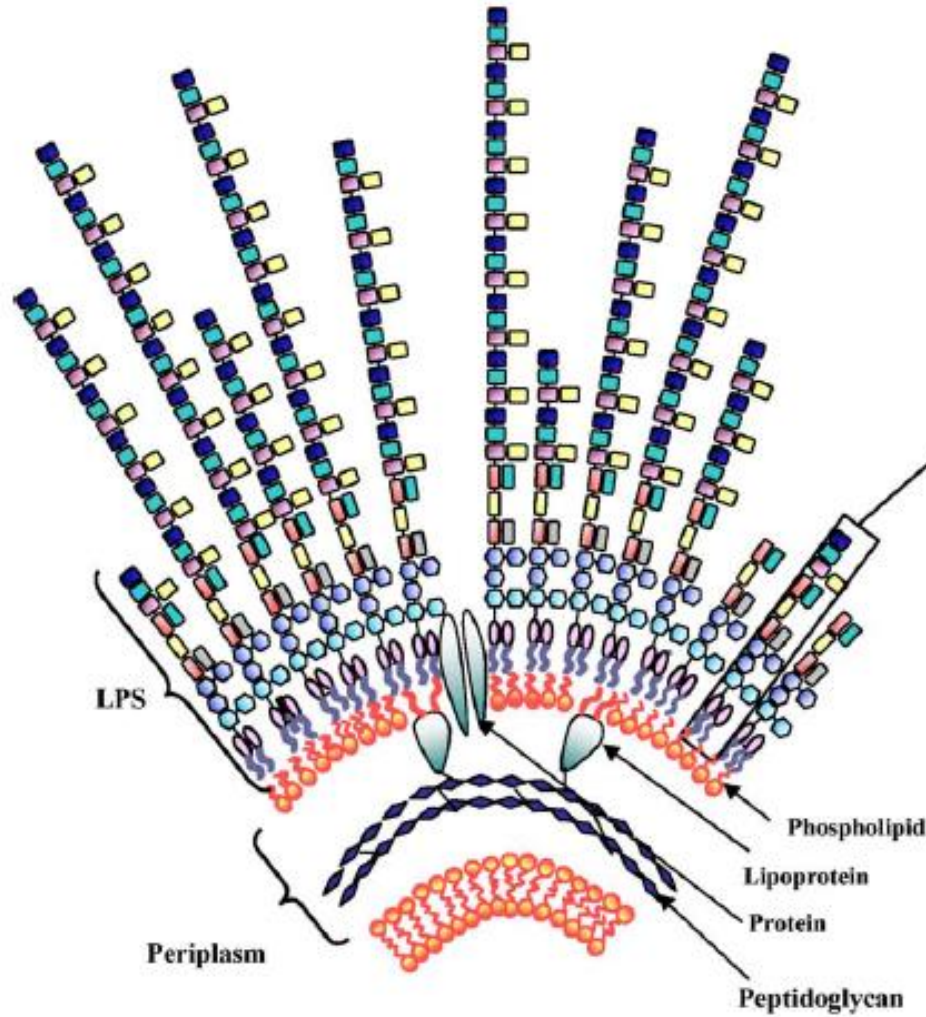


Milk Loss



Culling Risk





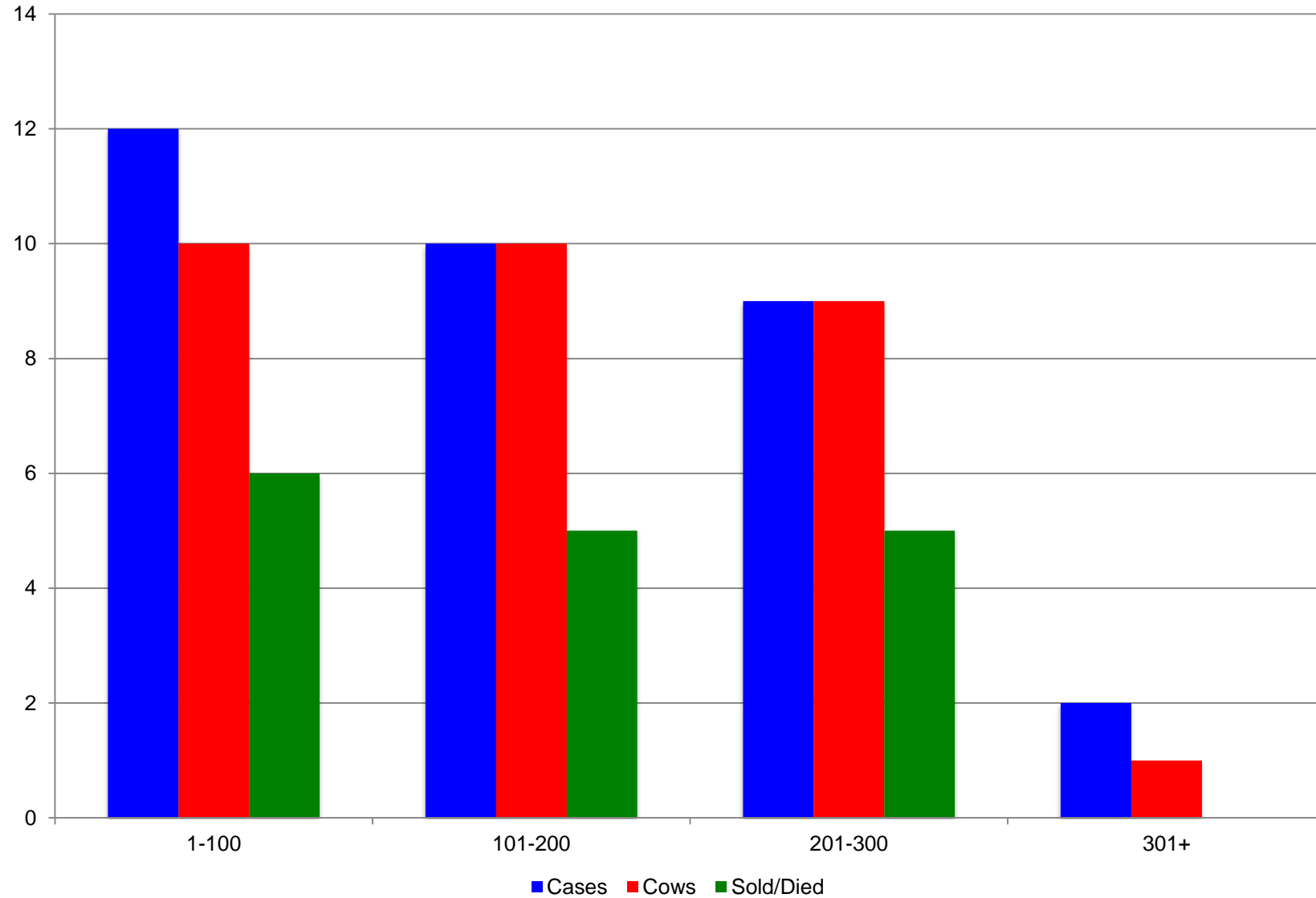
Overview of ISU Dairy

- 429 cows
- 378 milking
- Free stall barn houses all lactating cows with manger headlocks
- Currently bedded with manure solids (not heat treated)
 - Approximately 30% dry matter coming off the separator.
 - Stalls are re-bedded 3x/week.
- J5 Vaccination
 - 4 x/lactation (-45, -28, 25, & 90 DIM)



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Klebsiella Cases - Outcome by DIM



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AgriLabs® Launches Novel *Klebsiella* Vaccine

AgriLabs® Launches Novel *Klebsiella* Vaccine

Klebsiella vaccine with SRP technology is a new management tool for the dairy industry

ST. JOSEPH, Mo., August 6, 2014 — AgriLabs is teaming up with Eptopix to bring a first-of-its kind autogenous *Klebsiella* mastitis vaccine with SRP technology. With *Klebsiella pneumoniae* mastitis, cattle production losses and death due to intramammary infection (IMI) are overall higher when compared to *E. coli*.¹ Additionally, the economic impact of this disease can result in a daily milk loss of as much as 15 to 20 pounds. While this can be distressing, dairy producers now have a unique solution to help manage *Klebsiella* mastitis in their herds.

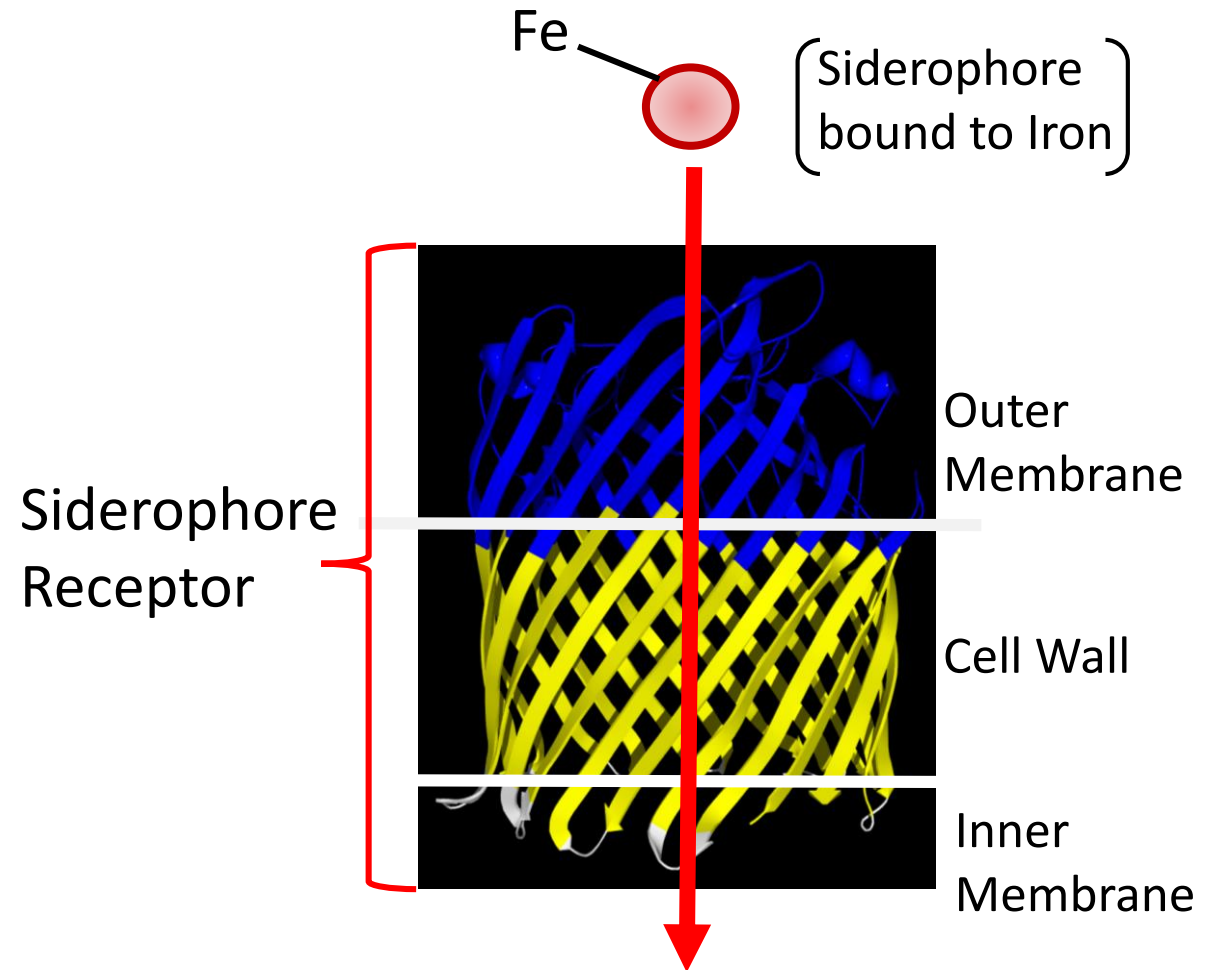
"We are proud to be partnering with Eptopix to pioneer this unique technology in the dairy industry," said Steve Schram, President and CEO of AgriLabs. "This new vaccine technology will enable us to continue to serve the needs of producers and give them access to a new tool for the management of *Klebsiella*."



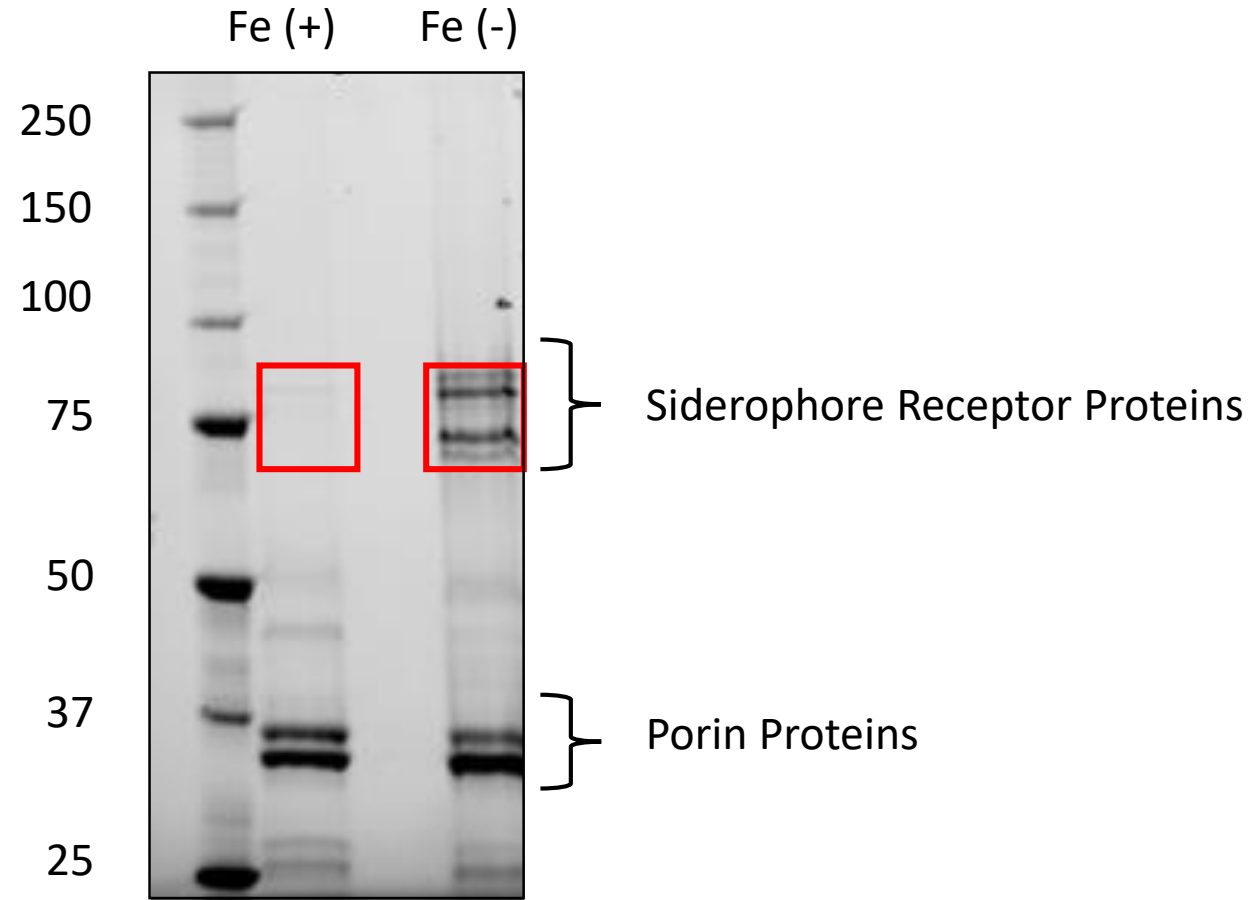
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What is SRP[®] Technology

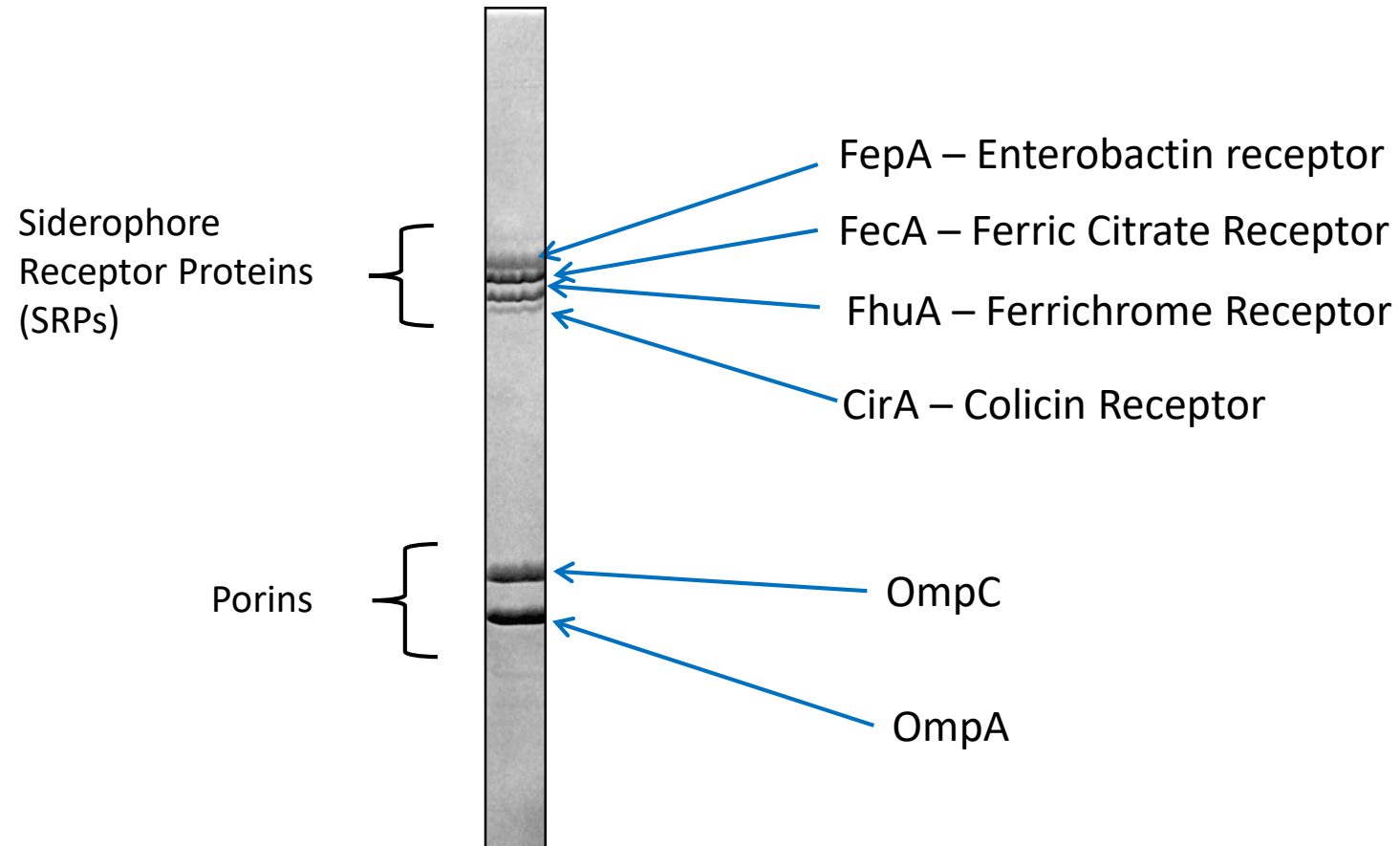
- *Bacteria need iron to grow and it's limited inside the host*
- *Bacteria use siderophores to steal iron from the host*
- Bacteria utilize Siderophore Receptors to transport iron-siderophore complexes through the cell wall.
- **SRP[®] Technology** utilizes Siderophore Receptors as the antigen for vaccine Production to stop the ability of the bacteria to acquire iron



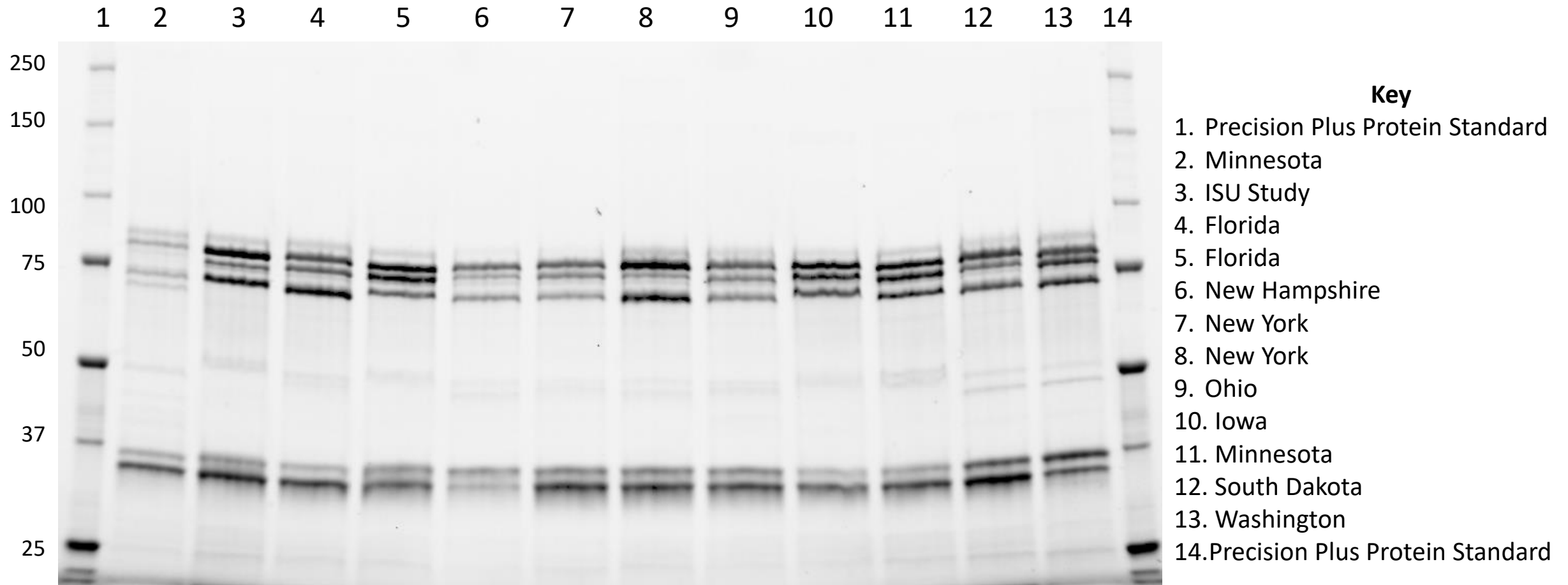
SDS-PAGE Showing Effect of Iron Restriction on Protein Expression



MALDI-TOF Identification of *Klebsiella pneumoniae* Master Seed (Vaccine Composition used in ISU Study)



Conservation of Klebsiella Siderophore Receptor and Porin Proteins Across the United States



Outcomes of Klebsiella Infection

- Recurring infections
- Culling and/or Death - 60-80% of cows with Klebsiella mastitis leave the herd within that lactation based on data at ISU dairy in the year prior to the trial. Others in the industry report similar outcomes.



University
Compost Facility

A G Studies 450 Farm

260th St

260th St

260th St

260th St

260th St

Parlor

Treatment area

Free Stall Barn

Maternity/Calf

Dry Cows

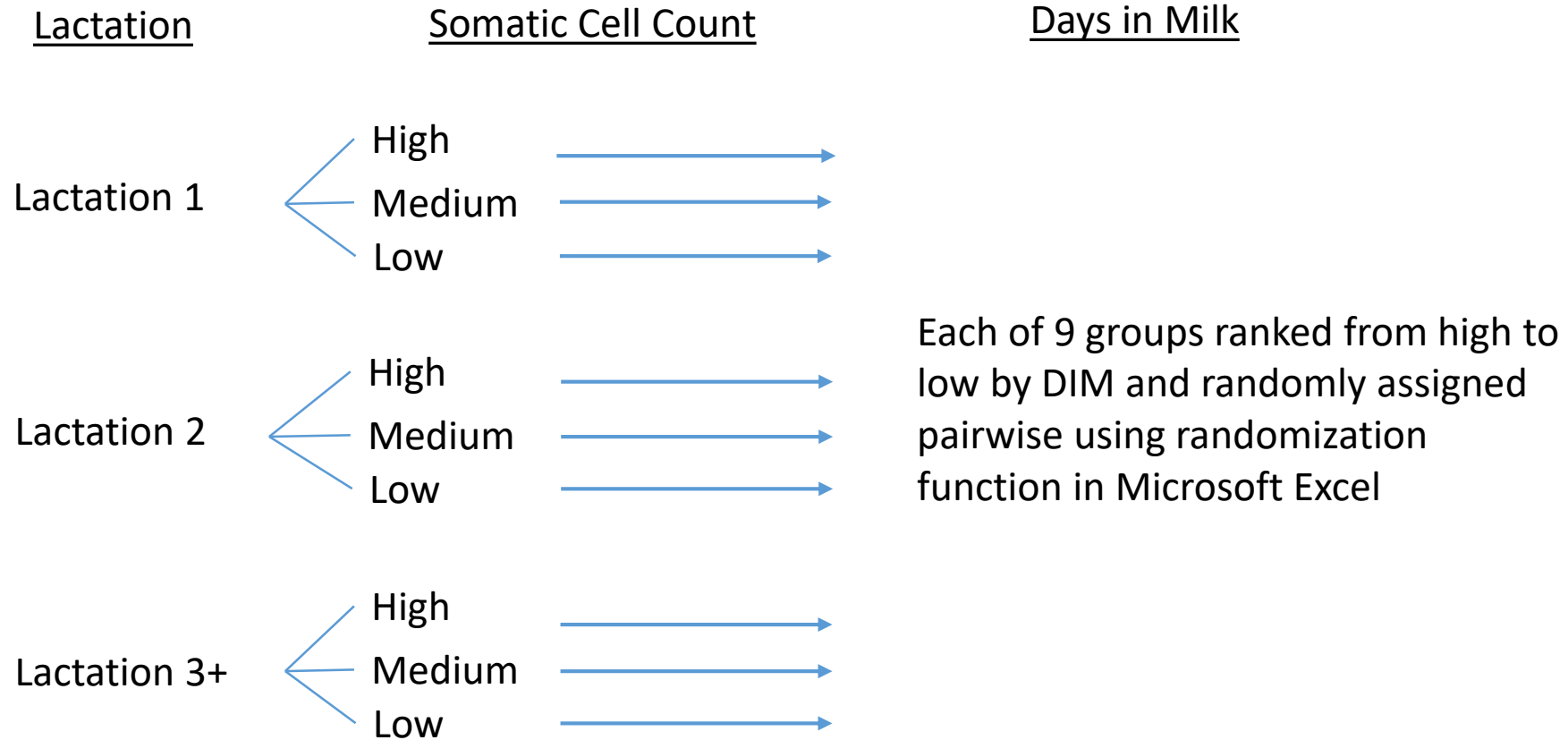
Heifers

Study Design

- 2 Groups
 - Klebsiella Pneumoniae Bacterial Extract
 - Placebo (minus antigen)
- Whole Herd vaccination to begin study
 - Some exceptions:
 - Cows within 3 weeks of dry cow protocol
 - Cows 2 weeks pre/post calving
- Dry Cow protocol (and heifer enrollment):
 - 217 DCC
 - initiated 1 week after the study began
- Clinical eligibility began 2 weeks after second dose

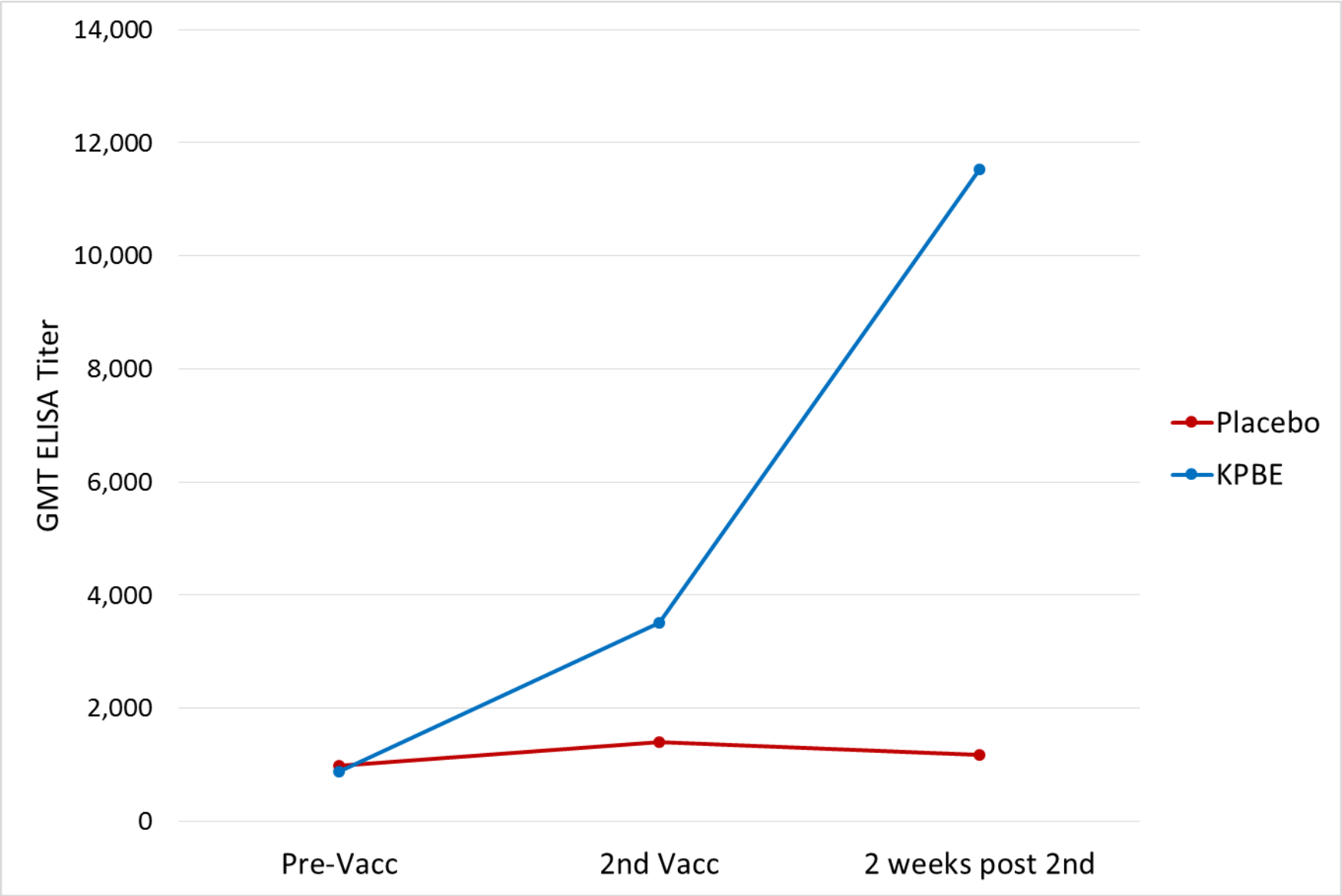
Randomization

Cows:



Heifers: assigned to treatment with simple randomization function in Microsoft Excel

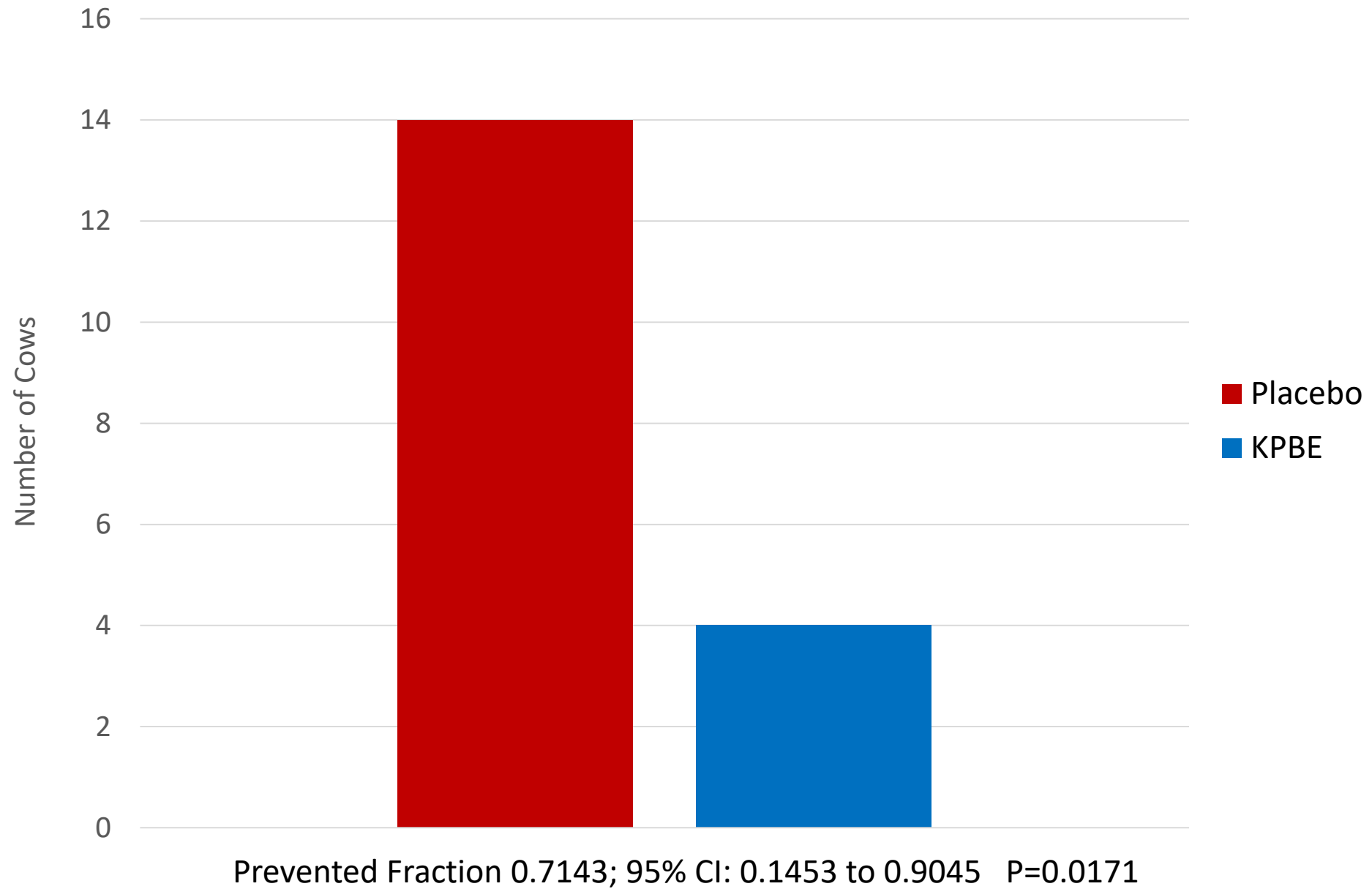
Serological Response Following Vaccination with Klebsiella Pneumoniae Bacterial Extract Versus Placebo



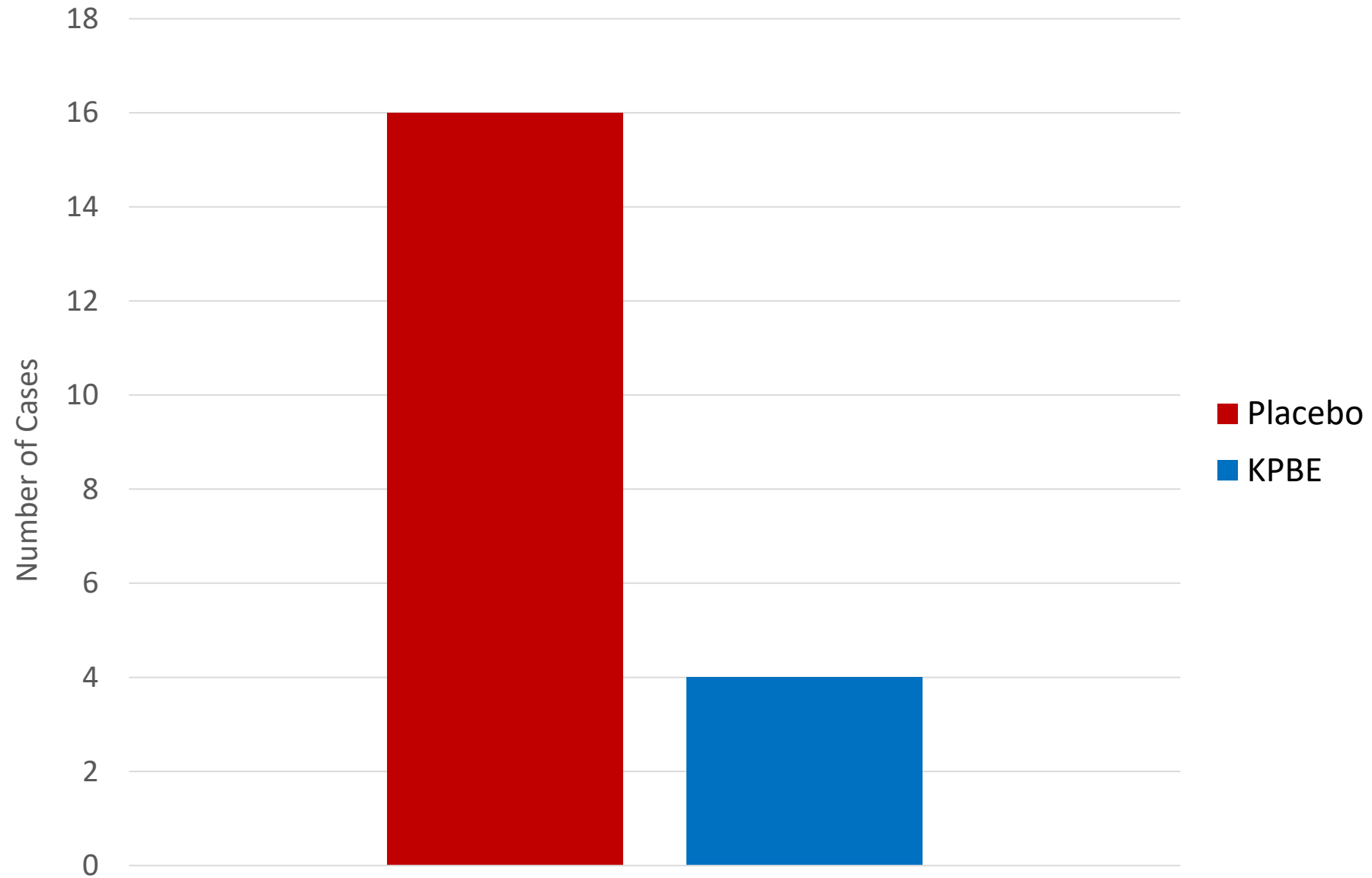
Mastitis Data Analysis

- Prevalence: Based on whether a cow had Kleb mastitis
 - Cows with mastitis were counted only once even if they had a subsequent case of mastitis.
 - Risk was calculated based the number of cows that contributed milk during their first 90 Days in Milk
- Incidence: Based on the number cases
 - Cases of mastitis were counted as new unless a previous case of mastitis in preceding 14 days.
 - Rate was calculated based on the exposure days (number of days milked)

Klebsiella Mastitis Prevalence From Cows 1-90 Days in Milk

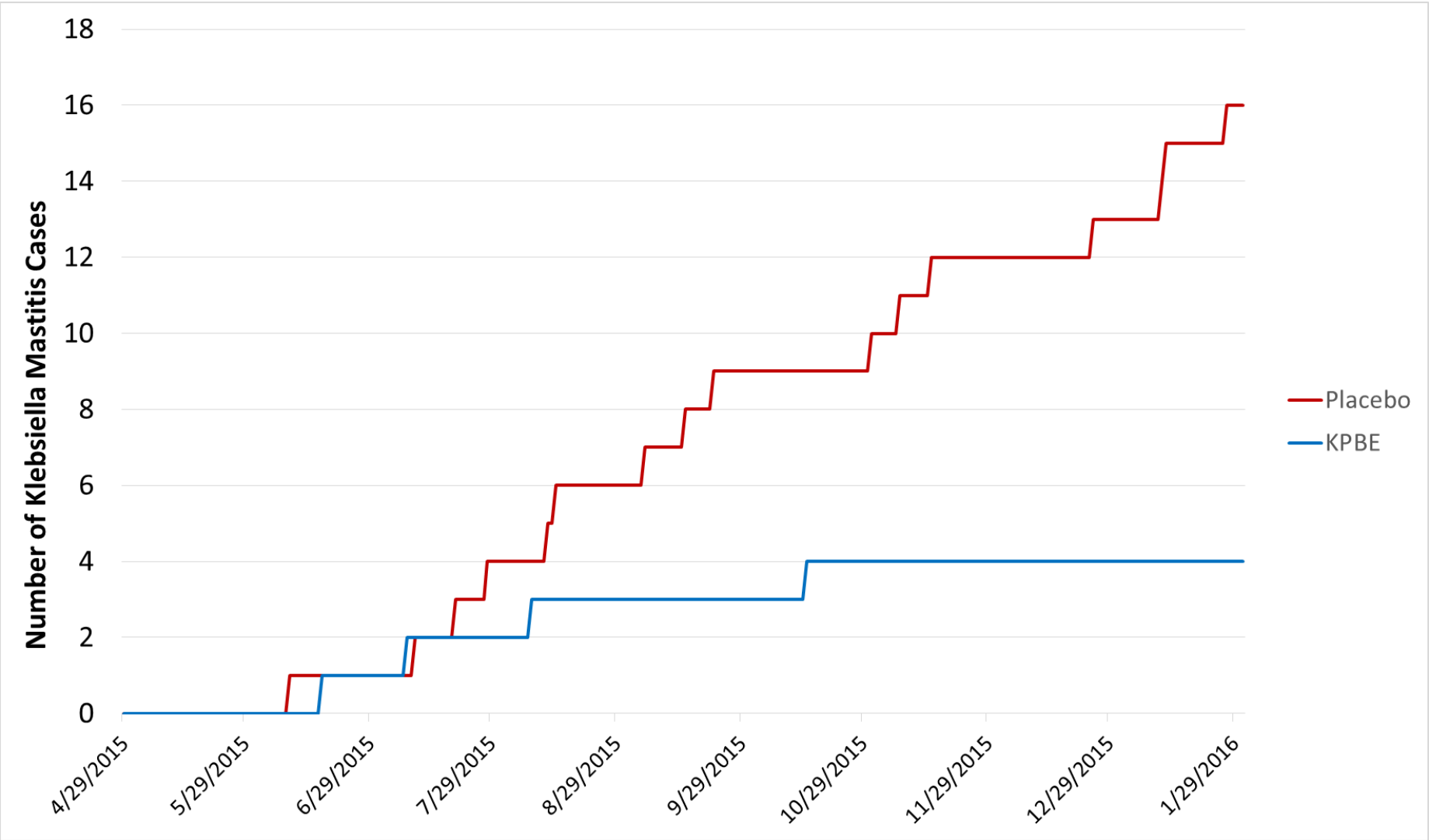


Klebsiella Mastitis Incidence From Cows 1-90 Days in Milk



Prevented Fraction 0.7594; 95% CI: 0.2804 to 0.9195. P=0.0056

Cumulative Cases of Klebsiella Mastitis in Cows 1-90 Days in Milk



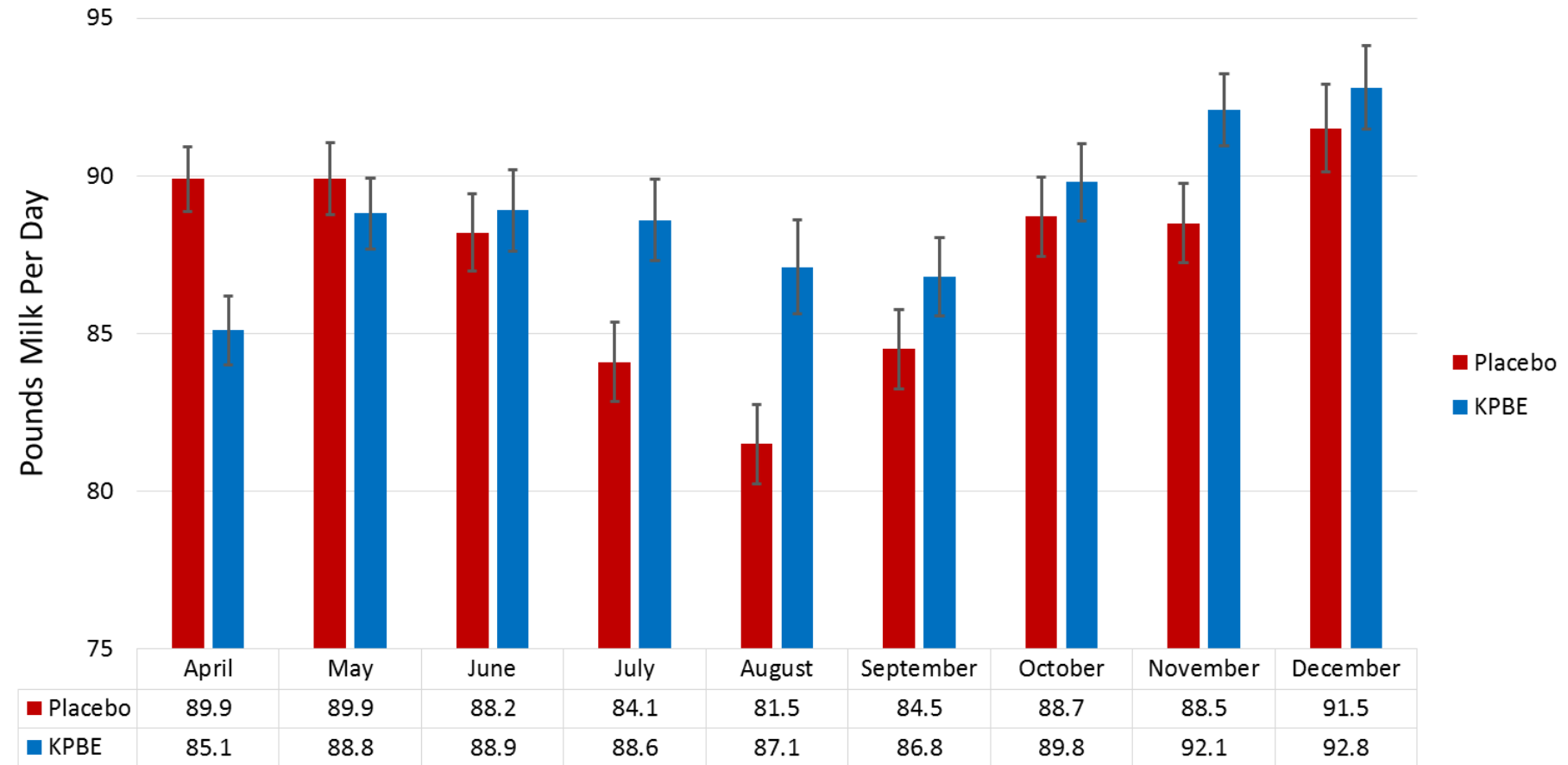
Outcomes of Cows with Klebsiella Mastitis During 1-90 DIM

		Number of cows with recurrent Klebsiella mastitis		
	Total Klebsiella mastitis cows	1 recurrence	2 recurrences	3 recurrences
Placebo	14	2	1	2
KPBE	4	1	0	0

Placebo: 5 cows were culled or died before end of lactation from Klebsiella mastitis

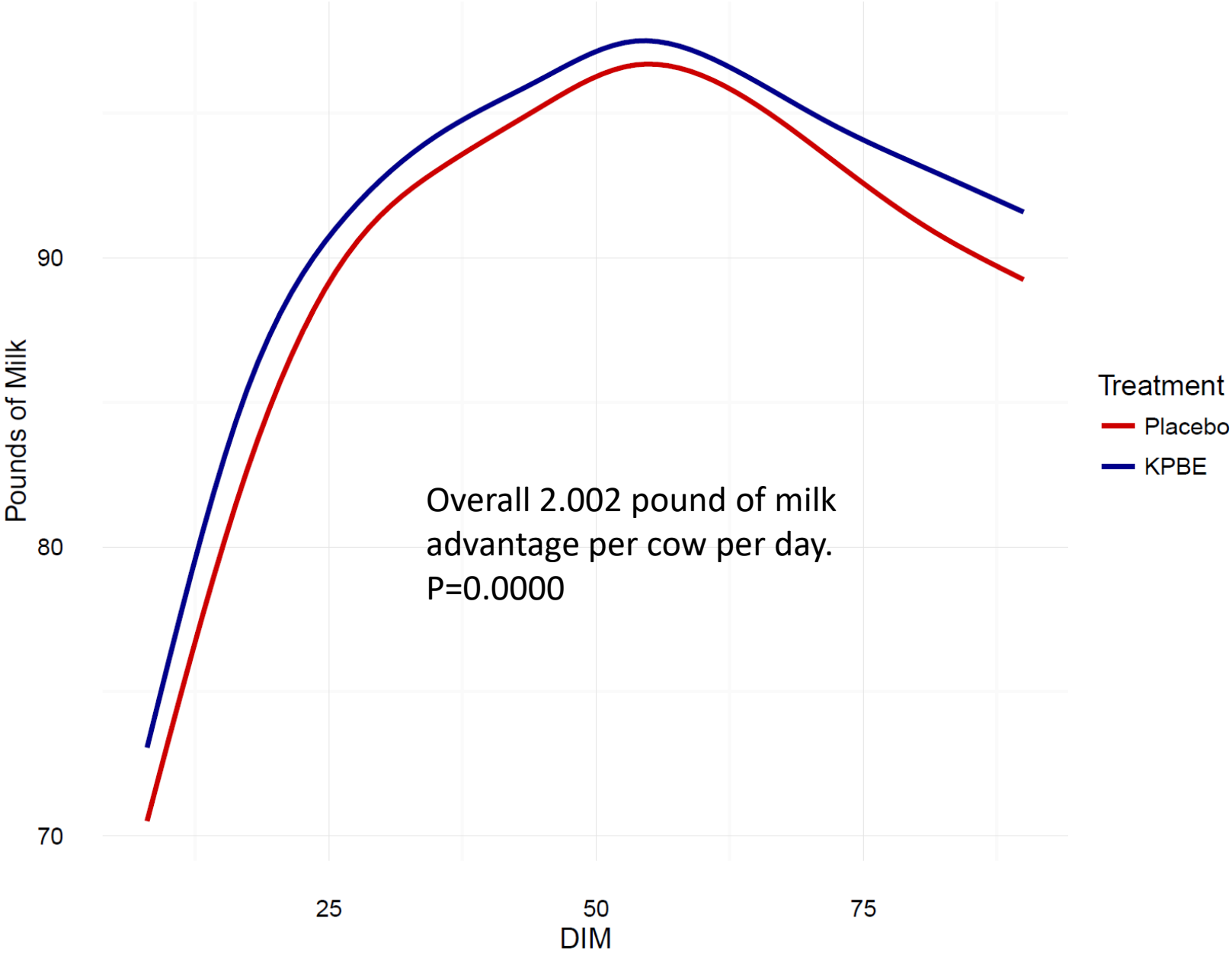
KPBE: 2 cows were culled or died before end of lactation from Klebsiella mastitis

Average Daily Milk Production Per Cow from Cows Vaccinated with KPBE vs. Placebo

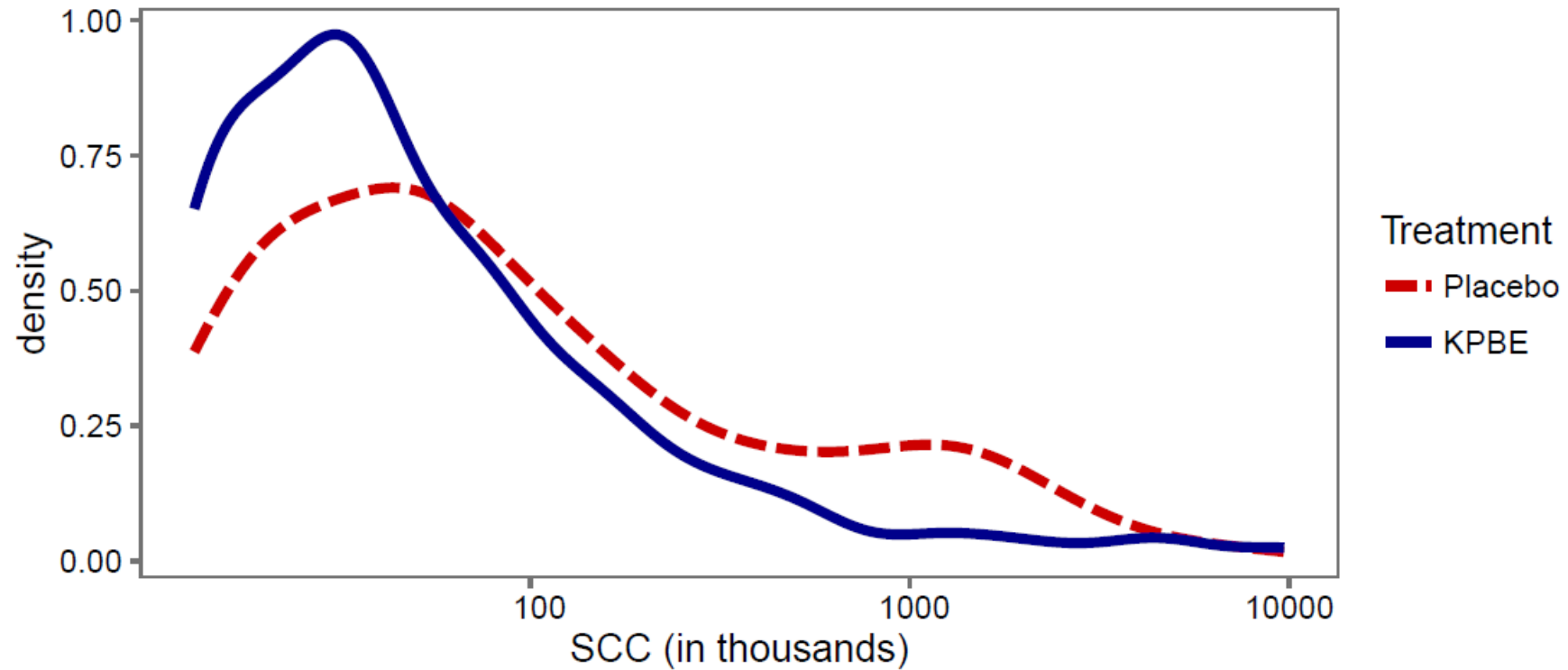


Overall 2.002 pound of milk advantage per cow per day. $P=0.0000$

Average Daily Milk Production Per Cow up to 90 Days In Milk

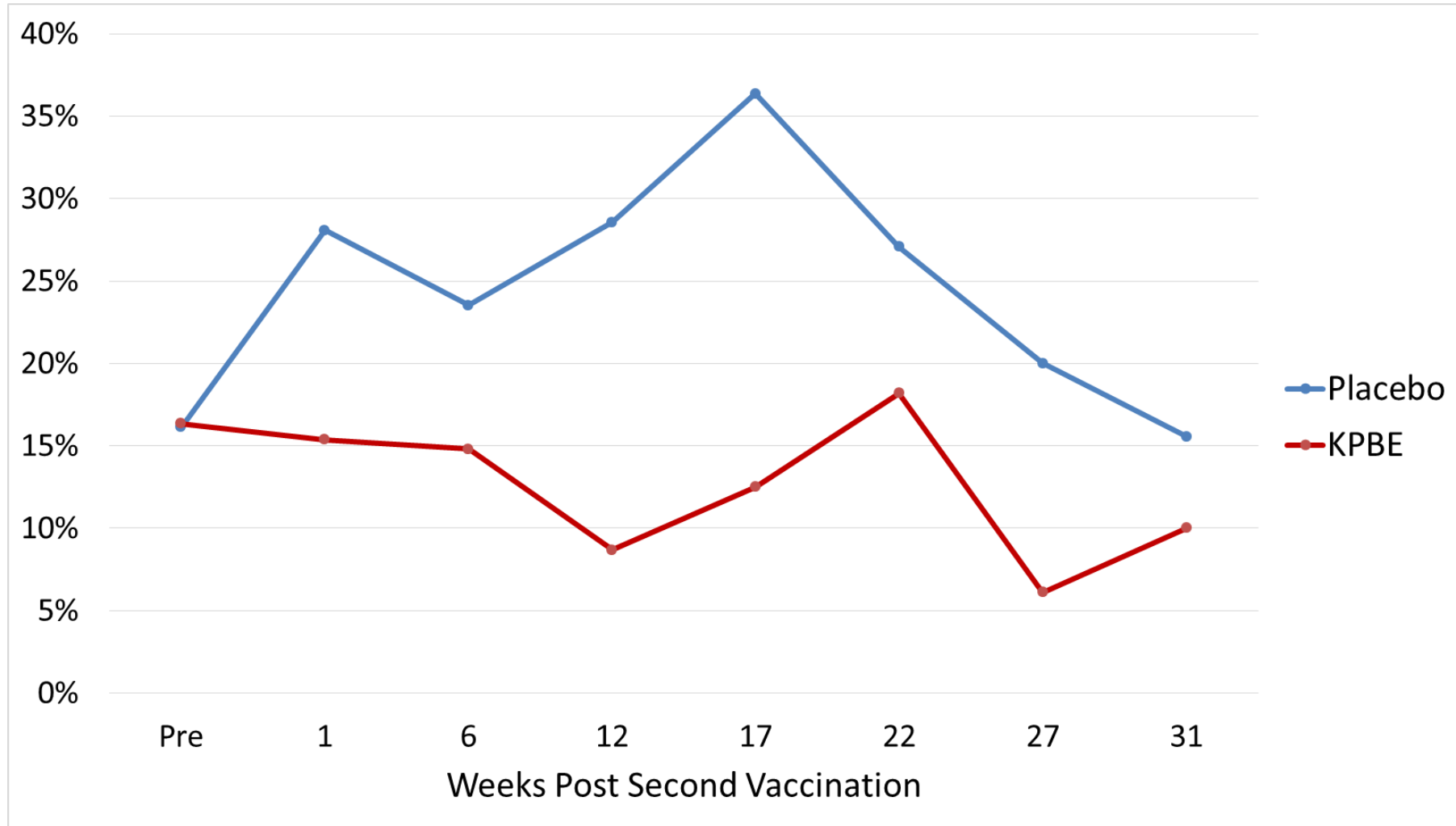


Distribution of Somatic Cell Counts For Cows 1-90 DIM



Controlling for other variables, treatment with KPBE reduces SCC scores on average 42%. $P=0.0000$

Percent of Cows 1-90 DIM Over 200,000 SCC



Categorical Analysis of Cows Over 200,000 SCC

	Below 200,000 cells/mL	More than 200,000 cells/mL	Sum
Placebo	194	66	260
KPBE	247	33	280
Sum	441	99	540

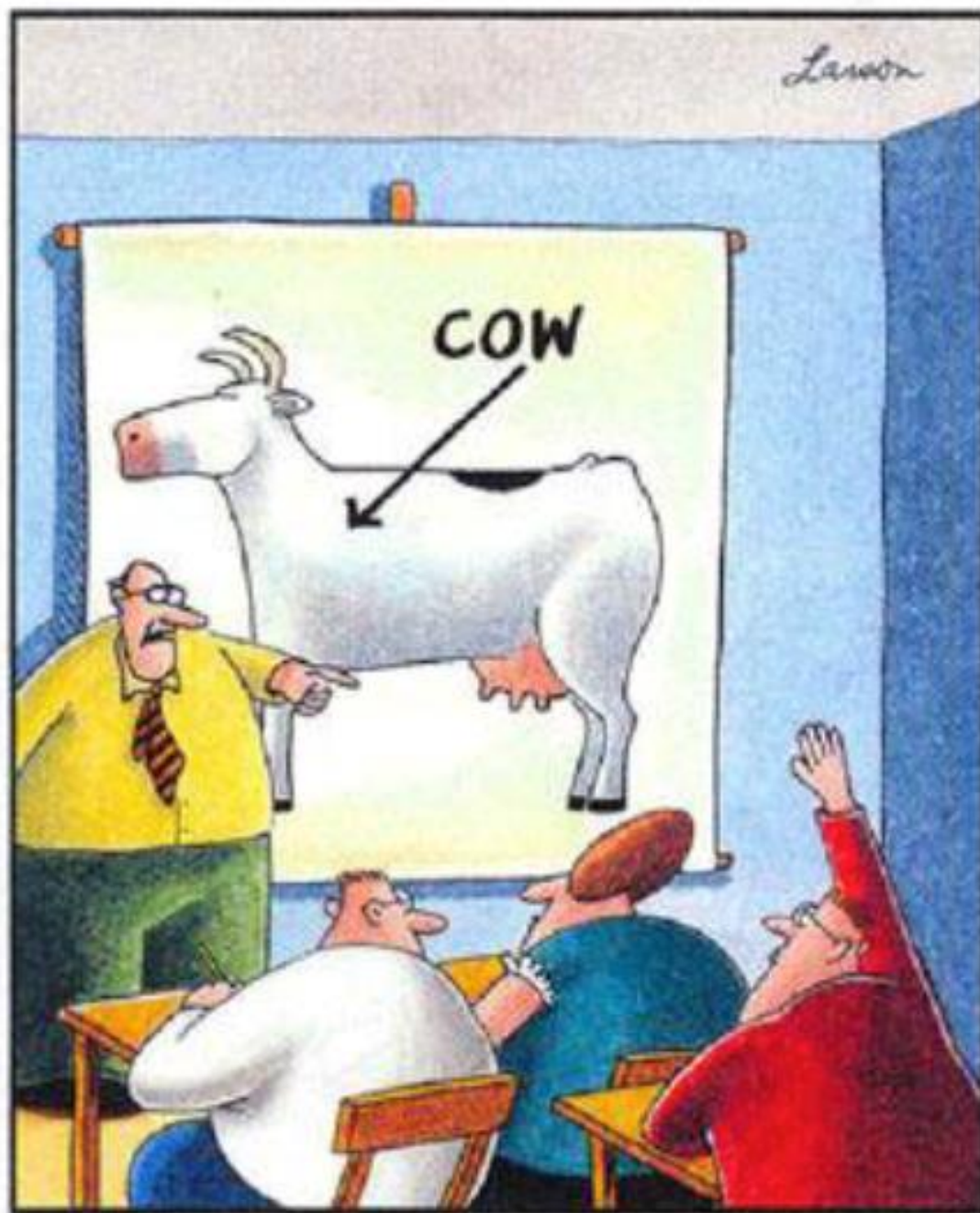
Prevented Fraction 0.5357. 95% CI:0.3196 to 0.6832. P=0.0000

Current Situation

- Vaccinated entire herd 2x:
 - April '16' - 1.85 lb/day milk drop (3 days before & 3 after)
 - May '16 – 2.39 lb/d milk drop
- May '14 – April '15 – 56% of cases sold/died.
- May 1 – Sept 1, 16 – 32% of cases sold/died.



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"Yes ... I believe there's a question in the back."