An on-farm algorithm to guide selective dry cow therapy

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Blan ket Dry Cow Therapy (BDCT)

5 Point Plan

1. Treat and record clinical mastitis cases

2. Post milking teat disinfection

3. **Dry cow therapy**

4. Cull chronic cases

5. Milking machine maintenance
The High Incidence Rate of Clinical Mastitis in the weeks following calving is due in large part to Infection during the dry period.

Green et al. JDS 2002;85(10):2589–99
Blanket Dry Cow Therapy is not prudent use for all dairies

73-95% of cultures at dry off return “Negative” results
(44% 1985)

The national average for bulk tank SCC in 2014 was 193,000 cells/mL
(295,000 in 1997)

11.1% of overall test days were over 400,000 cells/mL in 2016
(27.2% in 1995)

There are several ways to mitigate the high incidence rate, but most producers elect to treat with antimicrobials.

93% of cows were treated with intramammary antimicrobials at dry off

NAHMS-USDA 2014
Policy

Economics

Antimicrobial Resistance

Residues

More harm?
Selective Dry Cow Therapy (SDCT)

Identifying and treating ONLY cows/quarters that currently have or are at risk for infections

Which cows/quarters to treat?

**NEEDS**: accurate, quick, cheap

Currently available tools for identifying cows:

- Cowside
- Culture
- On-farm records
Cameron et al., 2015

$n = 729; 16$ farms

Mastitis in last 90 days?

- Yes:
  - Treat with Abx and sealant

- No:
  - CMT ≥2
    - Yes:
      - Treat with Abx and sealant
    - No:
      - Low Risk Group
        - Treat with Abx and sealant

Last Test SCC ≥200k

- Yes:
  - Treat with Abx and sealant

- No:
  - Petrifilm growth?
    - Yes (SDCT):
      - Treat with Abx and sealant
    - No (BDCT):
      - Sealant only

21% Abx reduction
Cameron et al. 2015, results

- SDCT = BDCT for:
  - Milk production for 200 days in milk
  - Somatic cell count for 200 days in milk
  - % quarters infected at freshening
Selective Dry Cow Therapy (SDCT)

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- Culture
- On-farm records
Quarter-level Culture

- Pilot study (Patel, Godden et al. 2017)
- 56 Minnesota cows
- No initial screening: Cows Randomized to Blanket (BDCT) or Selective (SDCT)
Quarter-level Culture

Sample individual quarters for On-farm culture (OFC) to identify quarters likely to be infected *

1-2 days before dry off

Bacterial Growth

Antibiotic plus Teat sealant in these quarters

No Bacterial Growth

Teat sealant only in these quarters

Day of dry off

* Note: OFC or other test to identify infection at the quarter level

(Patel et al., 2018)
# Quarter-level culture to drive SDCT

## Results (Patel et al., 2018)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Odds ratio of SDCT:BDCT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMI at dry off</td>
<td>1.2</td>
<td>0.51</td>
</tr>
<tr>
<td>Cure</td>
<td>0.6</td>
<td>0.53</td>
</tr>
<tr>
<td>New IMI at calving</td>
<td>0.91</td>
<td>0.76</td>
</tr>
</tbody>
</table>

- Abx reduction: 48%
- Cost savings $2.62/cow
Selective Dry Cow Therapy (SDCT)

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Which cows/quarters to treat?

**NEEDS:** accurate, quick, cheap

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- Culture
- On-farm records
Rajala-Schultz et al., 2011

“Low-risk” cows:

- <200,000 SCC last 3 months
- No mastitis in first 90 DIM
- If mastitis, had to have SCC<100,000 for entire lact.
- Randomized to be treated/not and compared
Rajala-Schultz et al., 2011

“Low-risk” cows:

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- No mastitis in first 90 DIM
- If mastitis, had to have SCC<100,000 for entire lact.
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= no differences in milk (kg)
= differences in SCC (↑ in SCC of 16%)
Rajala-Schultz et al., 2011

“Low-risk” cows:
- <200,000 SCC last 3 months
- No mastitis in first 90 DIM
- If mastitis, had to have SCC<100,000 for entire lact.
- Randomized to be treated/not and compared

= no differences in milk (kg)
= differences in SCC (↑ in SCC of 16%)
→ 1 farm the driver of increase
→ ¾ farms had BTSCC of >250,000
→ No teat sealants
Selective Dry Cow Therapy (SDCT)

Identifying and treating ONLY cows/quarters that currently have or are at risk for infections

Which cows/quarters to treat?

**NEEDS:** accurate, quick, cheap

Currently available tools for identifying cows:

- Cowside
- Culture
- On-farm records
Study Question:

Does using on-farm records to identify and treat only “high risk” cows result in negative outcomes for those cows that are not treated (“low risk” cows)?
Computer Algorithm

- Last month’s SCC ≤ 200k
- Avg SCC last 3 months ≤200k
- ≤1 case of clinical mastitis
- No current symptoms of clinical mastitis
- No mastitis in the last 30 days

=LOW RISK
Study Design

Cows Due To Dry (1800/yr)

Run Algorithm

Low Risk

Randomize

Intramammary antibiotics And Sealant (ABXTS)

Sealant Only (TS)

High Risk

Intramammary antibiotics And Sealant

64% cows = low risk
Several outcomes were assessed

1. Bacteriological Cure
Several outcomes were assessed

1. Dry
2. New Infection Risk
Several outcomes were assessed

Dry

0-7DIM

Calving

30 DIM

First Test

3 & 4. First test milk production and linear score (LS)
Several outcomes were assessed

5 & 6. Risk of survival and clinical mastitis up to 30 DIM
Statistics: Models

SAS version 9.4

Covariates Explored
- Dry period length
- LS at last test
- Milk at last test
- Days in milk at data/sample retrieval
- Parity
- Previous mastitis event (yes, no)
- Organism present at fresh or dry

Bivariate Analysis
Covariates vs. Outcome
- $\chi^2$
- t-tests
- analysis of variance
- Interactions
- PROC FREQ, TTEST, ANOVA
Regression analysis

- Continuous variables: generalized linear regression models (PROC MIXED)

- Binary outcomes:
  binomial logistic regression (PROC LOGISTIC)

Model Building

- Terms/interactions $P \leq 0.2$ in bivariate analysis offered into model

- Backwards stepwise removal of explanatory variables until all terms included have $P \leq 0.1$

- Treatment forced

Statistics: Models

SAS version 9.4
Results
There were similar numbers of cows and quarters in each treatment group

<table>
<thead>
<tr>
<th></th>
<th>ABXTS</th>
<th>TS</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cows</td>
<td>304</td>
<td>307</td>
<td>611</td>
</tr>
<tr>
<td>Quarters</td>
<td>1040</td>
<td>1058</td>
<td>2098</td>
</tr>
<tr>
<td>Percentage</td>
<td>50%</td>
<td>50%</td>
<td></td>
</tr>
</tbody>
</table>
### Pre “treatment” quarter-level culture results at dry-off

<table>
<thead>
<tr>
<th></th>
<th>Treatment Group</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TS (n = 1204)</td>
<td>ABXTS (n = 1183)</td>
<td>P-value</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>n</strong></td>
<td><strong>%</strong></td>
<td><strong>n</strong></td>
<td><strong>%</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>1086</td>
<td>90.2</td>
<td>1064</td>
<td>90.0</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>Coagulase negative <em>Staphylococcus</em> spp.</td>
<td>59</td>
<td>4.9</td>
<td>78</td>
<td>6.6</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Mixed Growth</td>
<td>22</td>
<td>1.8</td>
<td>20</td>
<td>1.7</td>
<td>0.88</td>
<td></td>
</tr>
<tr>
<td><em>Corynebacterium</em> spp.</td>
<td>24</td>
<td>2.0</td>
<td>12</td>
<td>1.0</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td><em>Lactococcus</em> spp.</td>
<td>5</td>
<td>0.4</td>
<td>4</td>
<td>0.3</td>
<td>&gt; 99.99</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus</em> spp.</td>
<td>2</td>
<td>0.2</td>
<td>1</td>
<td>0.1</td>
<td>&gt; 99.99</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>0.5</td>
<td>4</td>
<td>0.3</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>Total intramammary infections</td>
<td>114</td>
<td>9.5</td>
<td>115</td>
<td>9.7</td>
<td>0.84</td>
<td></td>
</tr>
</tbody>
</table>

**Algorithm Performance:**

- Positive Predictive Value = 71%
- Negative Predictive Value = 70%

**High Risk Quarters**

- Negative 69.4%
- CNS 13.9%
- Mixed Culture 4.9%
- Lactococcus 6.3%
- Coryne. spp 2.5%
- Contamination 0.7%
- Strep spp/dys 1.4%
- Other 0.7%

*n = 553*
Models
1. Does not treating low risk quarters at dry off lead to...

Decreased **bacteriological cure** over the dry period?
YES! Risk of cure is higher for the antimicrobial treated quarters

Logistic regression model for bacteriological cure n=171

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>SE</th>
<th>P-value</th>
<th>Odds Ratio</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>6.25</td>
<td>1.30</td>
<td>&lt;0.0001</td>
<td>0.55</td>
<td>0.32-0.96</td>
</tr>
<tr>
<td>Treatment group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TS</td>
<td>-1.12</td>
<td>0.55</td>
<td>0.04</td>
<td>0.32</td>
<td>0.11-0.96</td>
</tr>
<tr>
<td>Referent</td>
<td></td>
<td></td>
<td></td>
<td>0.10</td>
<td>0.01-0.80</td>
</tr>
<tr>
<td>Organism cultured at dry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS</td>
<td>-2.33</td>
<td>1.05</td>
<td>0.03</td>
<td>0.10</td>
<td>0.01-0.80</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days in milk at fresh sample</td>
<td>-0.52</td>
<td>0.16</td>
<td>0.002</td>
<td>0.52</td>
<td>0.32-0.96</td>
</tr>
</tbody>
</table>
Bacteriological Cure

$n=171$

$P = 0.04$

93.2% 97.8%

Percent Cure

TS
ABXTS
20 samples did not cure: 95% were Coagulase-negative Staph (CNS)

<table>
<thead>
<tr>
<th>Non-cures: Fresh Culture</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TS</td>
</tr>
<tr>
<td>No Growth</td>
<td>0</td>
</tr>
<tr>
<td>Coagulase-negative Staph (CNS)</td>
<td>13</td>
</tr>
<tr>
<td>Strep dysgalactiae</td>
<td>1</td>
</tr>
<tr>
<td>Strep uberis</td>
<td>0</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>0</td>
</tr>
<tr>
<td>Lactococcus</td>
<td>0</td>
</tr>
</tbody>
</table>
2. Does not treating low risk quarters at dry off lead to...

Increased **new infection** risk over the dry period?
Bacteriological Cure

n=171

$P = 0.04$

93.2% 97.8%

New Infection

$P = 0.17$

11.2% 8.8%
3. Does not treating low risk cows at dry off lead to...

Differences in \textbf{LS} at first test?
Bacteriological Cure

- **TS**
  - 93.2% with a *P* value of 0.04
  - Percent Cure 93.2%

- **ABXTS**
  - 97.8% with a *P* value of 0.04
  - Percent Cure 97.8%

New Infection

- Percent New Infections
  - **TS**: 11.2%
  - **ABXTS**: 8.8%
  - *P* = 0.17

Linear Score at First Test

- Linear Score
  - **TS**: 2.7
  - **ABXTS**: 2.5
  - *P* = 0.10
Milk production within the first 30 days fresh
Milk yield over the first 30 days was similar between groups

- ABXTS
- TS

<table>
<thead>
<tr>
<th></th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Effect</td>
<td>0.2</td>
</tr>
<tr>
<td>Time Effect</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Treatment* Time Interaction</td>
<td>0.4</td>
</tr>
</tbody>
</table>
5. Does not treating low risk quarters at dry off lead to... Increased **culling and mastitis** within the first 30 days fresh?
## Culling and Mastitis

<table>
<thead>
<tr>
<th></th>
<th>ABXTS</th>
<th>TS</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died/culled &lt;30 DIM</td>
<td>18</td>
<td>15</td>
<td>0.6</td>
</tr>
<tr>
<td>Mastitis &lt;30 DIM</td>
<td>9</td>
<td>5</td>
<td>0.33</td>
</tr>
<tr>
<td>Total Cows with data</td>
<td>304</td>
<td>307</td>
<td></td>
</tr>
</tbody>
</table>

~$7,000 per 1000 cows
Conclusions

❖ The impact of CNS needs to be further investigated

❖ Similar algorithms at appropriate dairies can produce economic returns and promote aspects of public health

❖ The proposed algorithm reduced antimicrobial use by 64% without adversely affecting production and clinical health outcomes
Use of a culture-independent on-farm algorithm to guide the use of selective dry-cow antibiotic therapy

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*Department of Population Medicine and Diagnostic Sciences, College of Veterinary Medicine, and
†Pro-Dairy, Department of Animal Science, Cornell University, Ithaca, NY 14853
‡Valley Agricultural Software, King Ferry, NY 13081
Applications:

- Additional Farms
- Alter sensitivity?
- Comparison to other SDCT programs
Current Project
Primary Objective

Null Hypothesis:

Blanket = Culture = Algorithm
2nd Objective

Blanket = Culture = Algorithm
3rd Objective:

Blanket

Untreated

Before Dry-off

After Freshening
4th Objective

Identifying and treating ONLY cows/quarters that currently have or are at risk for infections

Which cows/quarters to treat?

**NEEDS:** accurate, quick, cheap

Currently available tools for identifying cows:

Cowside
Take Home Messages

❖ SDCT – Economically beneficial option vs blanket therapy in many studies (the right herds)
  – no appreciable negative outcomes
  – multiple ways of applying

❖ Lots more exploring to do!
Treat a dry cow as a Princess

No stress

Proper BCS

Balanced ration

Healthy udder

Perfect hygiene

Adapted from Lely
Acknowledgments

- Funding
  - Engaged Cornell
  - NY Farm Viability Institute
  - Academic Venture Fund

- Farm management and employees

- QMPS Staff and Veterinarians

- Sampling and support
  - Monique Obsharski
  - Anne Hesse
  - Wolfgang Heuwieser
  - Rachel Murphy
  - Germán Granados
  - Anja Sipka
  - Valeria Alanis
## Economics of Algorithm

<table>
<thead>
<tr>
<th>% Cows Treated</th>
<th>$6.87</th>
<th>$6</th>
<th>$7</th>
<th>$8</th>
<th>$9</th>
<th>$10</th>
<th>$11</th>
<th>$12</th>
<th>$13</th>
<th>$14</th>
<th>$15</th>
<th>$16</th>
<th>$17</th>
<th>$18</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>$5.66</td>
<td>$6.46</td>
<td>$7.26</td>
<td>$8.06</td>
<td>$8.86</td>
<td>$9.66</td>
<td>$10.46</td>
<td>$11.26</td>
<td>$12.06</td>
<td>$12.86</td>
<td>$13.66</td>
<td>$14.46</td>
<td>$15.26</td>
<td></td>
</tr>
<tr>
<td>30%</td>
<td>$4.95</td>
<td>$5.65</td>
<td>$6.35</td>
<td>$7.05</td>
<td>$7.75</td>
<td>$8.45</td>
<td>$9.15</td>
<td>$9.85</td>
<td>$10.55</td>
<td>$11.25</td>
<td>$11.95</td>
<td>$12.65</td>
<td>$13.35</td>
<td></td>
</tr>
<tr>
<td>40%</td>
<td>$4.24</td>
<td>$4.84</td>
<td>$5.44</td>
<td>$6.04</td>
<td>$6.64</td>
<td>$7.24</td>
<td>$7.84</td>
<td>$8.44</td>
<td>$9.04</td>
<td>$9.64</td>
<td>$10.24</td>
<td>$10.84</td>
<td>$11.44</td>
<td></td>
</tr>
<tr>
<td>50%</td>
<td>$3.53</td>
<td>$4.03</td>
<td>$4.53</td>
<td>$5.03</td>
<td>$5.53</td>
<td>$6.03</td>
<td>$6.53</td>
<td>$7.03</td>
<td>$7.53</td>
<td>$8.03</td>
<td>$8.53</td>
<td>$9.03</td>
<td>$9.53</td>
<td></td>
</tr>
<tr>
<td>60%</td>
<td>$2.83</td>
<td>$3.23</td>
<td>$3.63</td>
<td>$4.03</td>
<td>$4.43</td>
<td>$4.83</td>
<td>$5.23</td>
<td>$5.63</td>
<td>$6.03</td>
<td>$6.43</td>
<td>$6.83</td>
<td>$7.23</td>
<td>$7.63</td>
<td></td>
</tr>
<tr>
<td>70%</td>
<td>$2.12</td>
<td>$2.42</td>
<td>$2.72</td>
<td>$3.02</td>
<td>$3.32</td>
<td>$3.62</td>
<td>$3.92</td>
<td>$4.22</td>
<td>$4.52</td>
<td>$4.82</td>
<td>$5.12</td>
<td>$5.42</td>
<td>$5.72</td>
<td></td>
</tr>
<tr>
<td>80%</td>
<td>$1.41</td>
<td>$1.61</td>
<td>$1.81</td>
<td>$2.01</td>
<td>$2.21</td>
<td>$2.41</td>
<td>$2.61</td>
<td>$2.81</td>
<td>$3.01</td>
<td>$3.21</td>
<td>$3.41</td>
<td>$3.61</td>
<td>$3.81</td>
<td></td>
</tr>
<tr>
<td>90%</td>
<td>$0.71</td>
<td>$0.81</td>
<td>$0.91</td>
<td>$1.01</td>
<td>$1.11</td>
<td>$1.21</td>
<td>$1.31</td>
<td>$1.41</td>
<td>$1.51</td>
<td>$1.61</td>
<td>$1.71</td>
<td>$1.81</td>
<td>$1.91</td>
<td></td>
</tr>
<tr>
<td>100%</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
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<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
<td></td>
</tr>
</tbody>
</table>
Do we want to kill Staph spp (CNS) with Abx?

Figure 3. The actual average daily milk yield in the first 285 DIM of 85 dairy heifers that were not infected (●), infected with CNS (▲), or infected with a major pathogen (■) in early lactation.

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† Department of Production Animal Health, Faculty of Veterinary Medicine, University of Calgary