A mixed treatment comparison meta-analysis of metaphylaxis treatments for BRD

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Kaitlynn M. Abell, DVM, PhD
kaitlynn@precisionanimalsolutions.com


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Introduction

• Metaphylaxis
  • Prevent BRD in arriving feedlot cattle
  • Multiple antimicrobials used
  • Multiple clinical trials
  • How big is the effect of metaphylaxis?

• Meta-analysis and systematic reviews of available literature has been performed
Typical Meta-analysis

- Pairwise comparison between treatments
- Direct randomized controlled trial evidence
- Assumes: Similarity and Consistency
But...

1. No direct evidence exists
2. Insufficient direct evidence
3. More than 2 treatments
MTC Meta-analysis

• Assess indirect comparisons between treatments where an actual clinical trial was not performed

• Combines direct and indirect evidence to provide more precise and accurate effect estimates

• Also assumes similarity and consistency between trials
Objective

• Evaluate the effect of parenterally administered metaphylactic treatments approved for feeder and stocker calves on morbidity and mortality due to BRD using a MTC meta-analysis.

• These results should aid in the understanding of the effect of metaphylactic treatment options on clinically important BRD outcomes.
Literature search

• Conducted in April 2016
• Randomized controlled trials
• Metaphylaxis was the only treatment variable
• Initial search revealed 3,753 papers
• Final analysis included 33 studies with a total of 42 trials.
Data extraction

• Trial data extracted separately
• Trial arm was a different treatment for each trial
  • Treatment A, B, and C = 3 trials arms
• Data included
  • Interventions for each trial arm
  • Number of animals enrolled in each trial arm
  • Event occurrence for each trial arm
Event Occurrence

• Cumulative incidence
  • Morbidity d1 to ≤ 60
  • Morbidity d1 to closeout
  • Mortality d1 to closeout
  • Retreatment d1 to closeout
Network – Morbidity d1 to ≤ 60
Model

• Bayesian hierarchical approach – combines data with prior information
• Inferences about a parameter (mean) are based on a prior distribution of the parameter and the data
  • unlike frequentist models where we get p values, and confidence intervals
• Use simulation to get results
  • Markov Chain Monte Carlo (MCMC) methods (WinBugs)
Morbidity $d_1$ to $\leq 60$ days

- Outcome is time dependent, time to event occurrence has an exponential distribution
- Output: Posterior means for odds ratios with 95% CrI
Forest plot application

Treatment A
5%

Treatment B
20%

Treatment C
27%

Odds Ratio
Event Occurrence

• Cumulative incidence
  • Morbidity d1 to ≤ 60
  • Morbidity d1 to closeout
  • Mortality d1 to closeout
  • Retreatment d1 to closeout
Morbidity d1 to closeout
Mortality d1 to closeout
Retreatment Morbidity d1 to closeout

• Assumes all trials occur within the same time period
• Further days at risk would not affect differences between events
Forest Plot – **Morbidity** d1 to closeout

- Tulathromycin
- Tildipirosin
- Gamithromycin
- Ceftiofur
- Tilmicosin
- Oxytetracycline
- TMS

Odds Ratio

0  1  2
Forest Plot – Mortality d1 to closeout

Antimicrobial

- Tulathromycin
- Tilmicosin
- Ceftiofur
- Tildipirosin
- TMS
- Oxytetracycline
- Gamithromycin

Odds Ratio
Forest Plot – Retreat *morbidity d1* to closeout

Antimicrobial:
- Tulathromycin
- Ceftiofur
- Gamithromycin
- Tilmicosin
- Oxytetracycline
- Tildipirosin

Odds Ratio
Conclusion

• Accurately identified differences between metaphylactic treatments related to morbidity, retreatment, and mortality.
• Provide guidance to predict expected outcomes after treatment.
• Metaphylactic treatment options offer different effects on morbidity and mortality odds in feeder and stocker cattle.
Performance analysis

• The initial screening of the literature revealed 170 publications
• A total of 11 trials meeting all inclusion criteria

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADG</td>
<td>8</td>
</tr>
<tr>
<td>DMI</td>
<td>6</td>
</tr>
<tr>
<td>F:G</td>
<td>7</td>
</tr>
<tr>
<td>HCW</td>
<td>4</td>
</tr>
<tr>
<td>QG Choice or Better</td>
<td>6</td>
</tr>
<tr>
<td>YG 1-2</td>
<td>6</td>
</tr>
</tbody>
</table>
Conclusion

• Estimates were not robust enough to determine differences among antimicrobials for ADG, DMI, F:G, HCW, quality grade choice or better, or yield grade 1-2.

• Small number of trials included in the analysis
Questions

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