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

TVMDL 3rd Annual BRD Conference

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Abell, K., M. Theurer, R. Larson, B. White, and M. Apley. 2017. A mixed treatment comparison meta-analysis of metaphylaxis treatments for bovine respiratory disease in beef cattle. *J. Anim. Sci.* 95: 1-10.

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Introduction

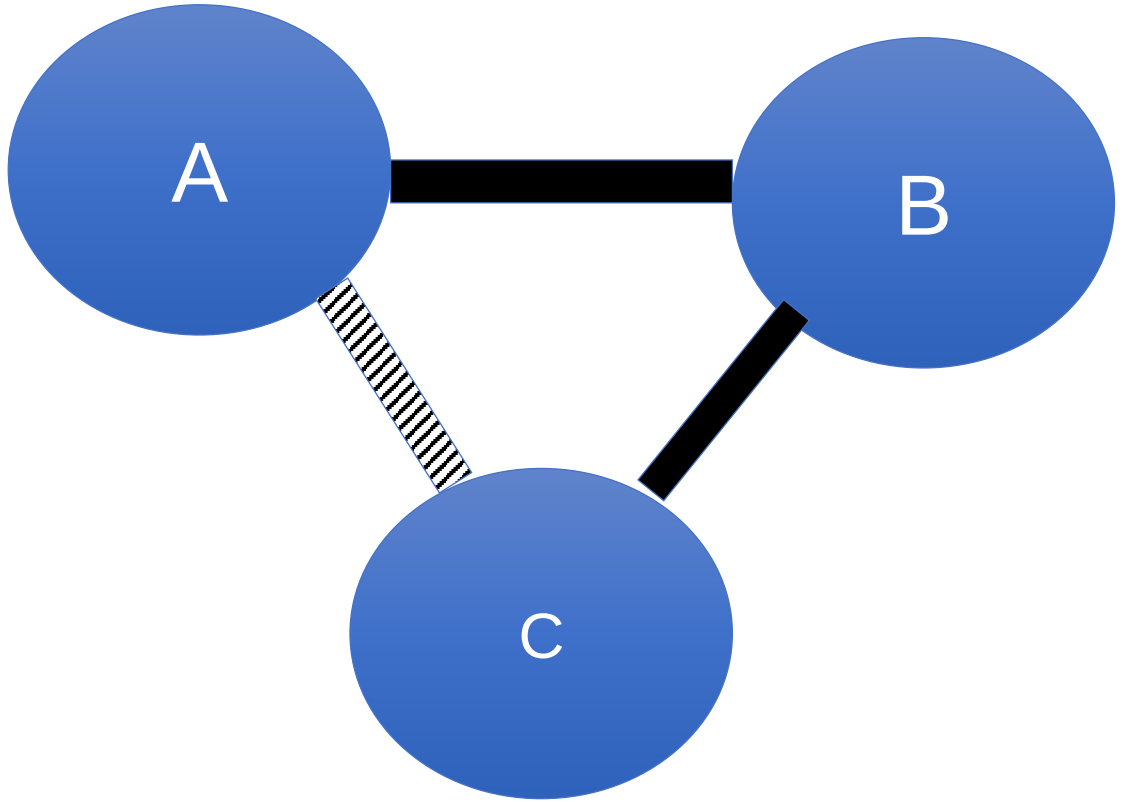
- Metaphylaxis
  - Prevent BRD in arriving feedlot cattle
  - Multiple antimicrobials used
  - Multiple clinical trials
  - How big is the effect of metaphylaxis?
- Meta-analysis and systematic reviews of available literature has been performed

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.

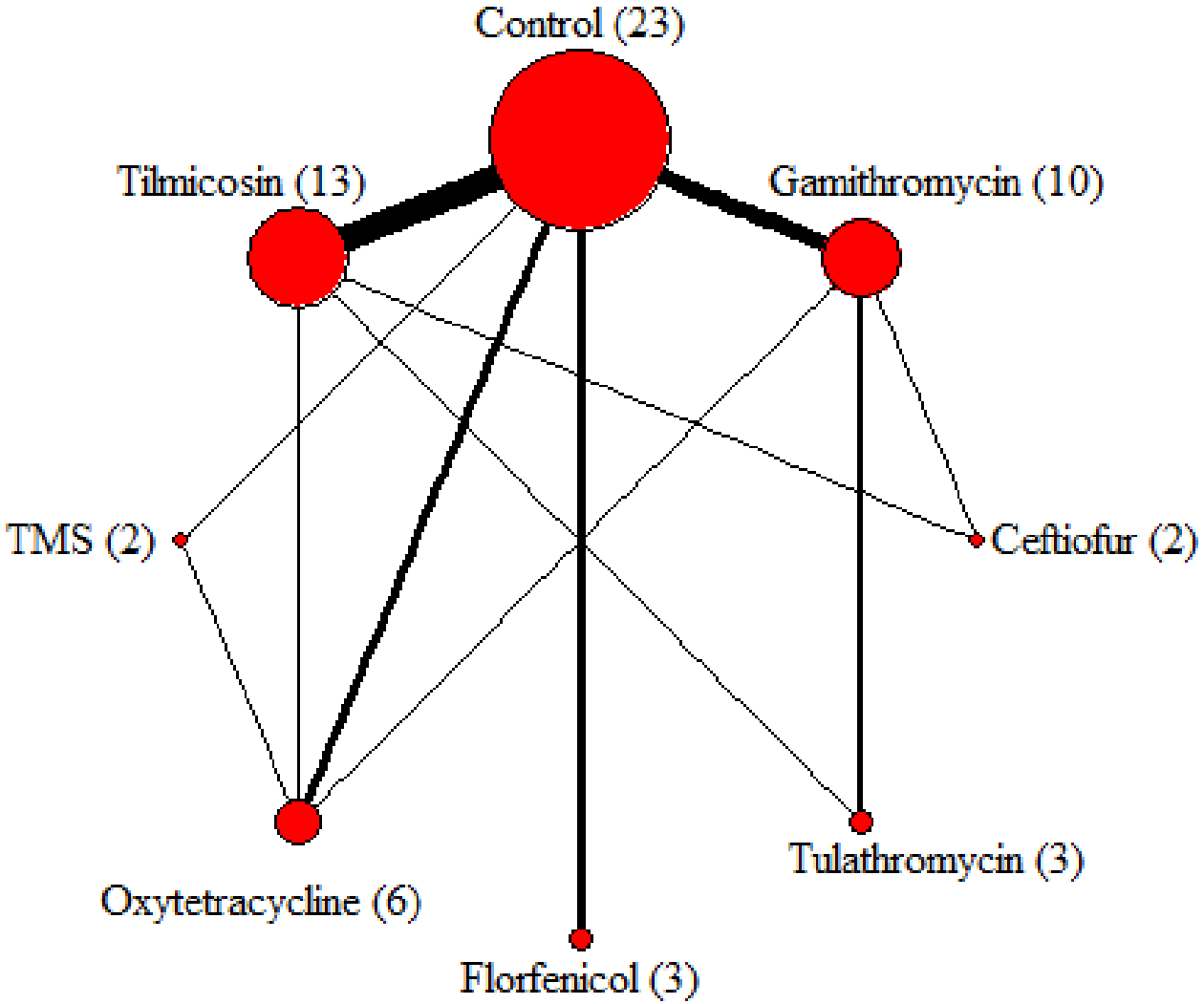
Data extraction

- 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



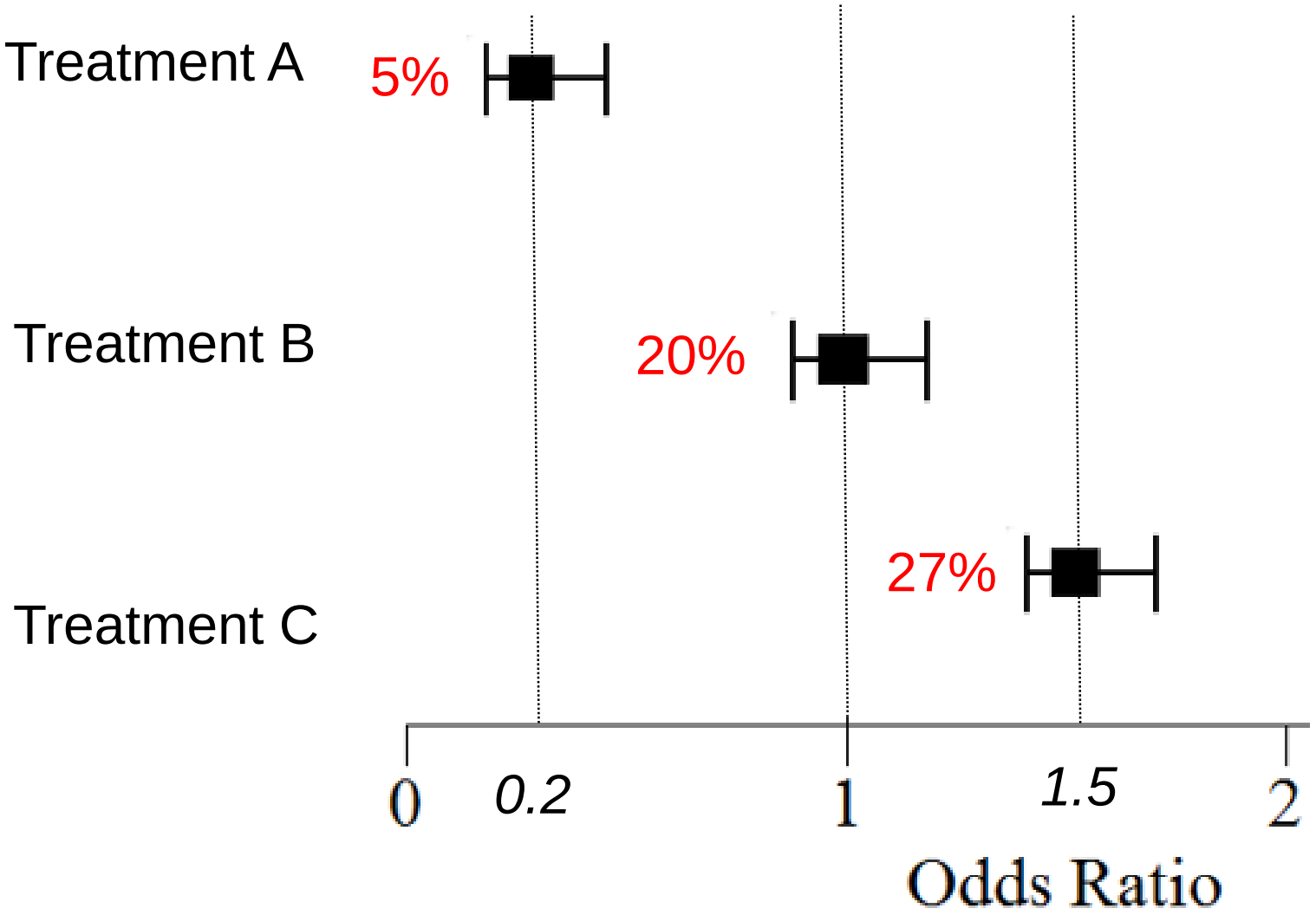
Model

- 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)

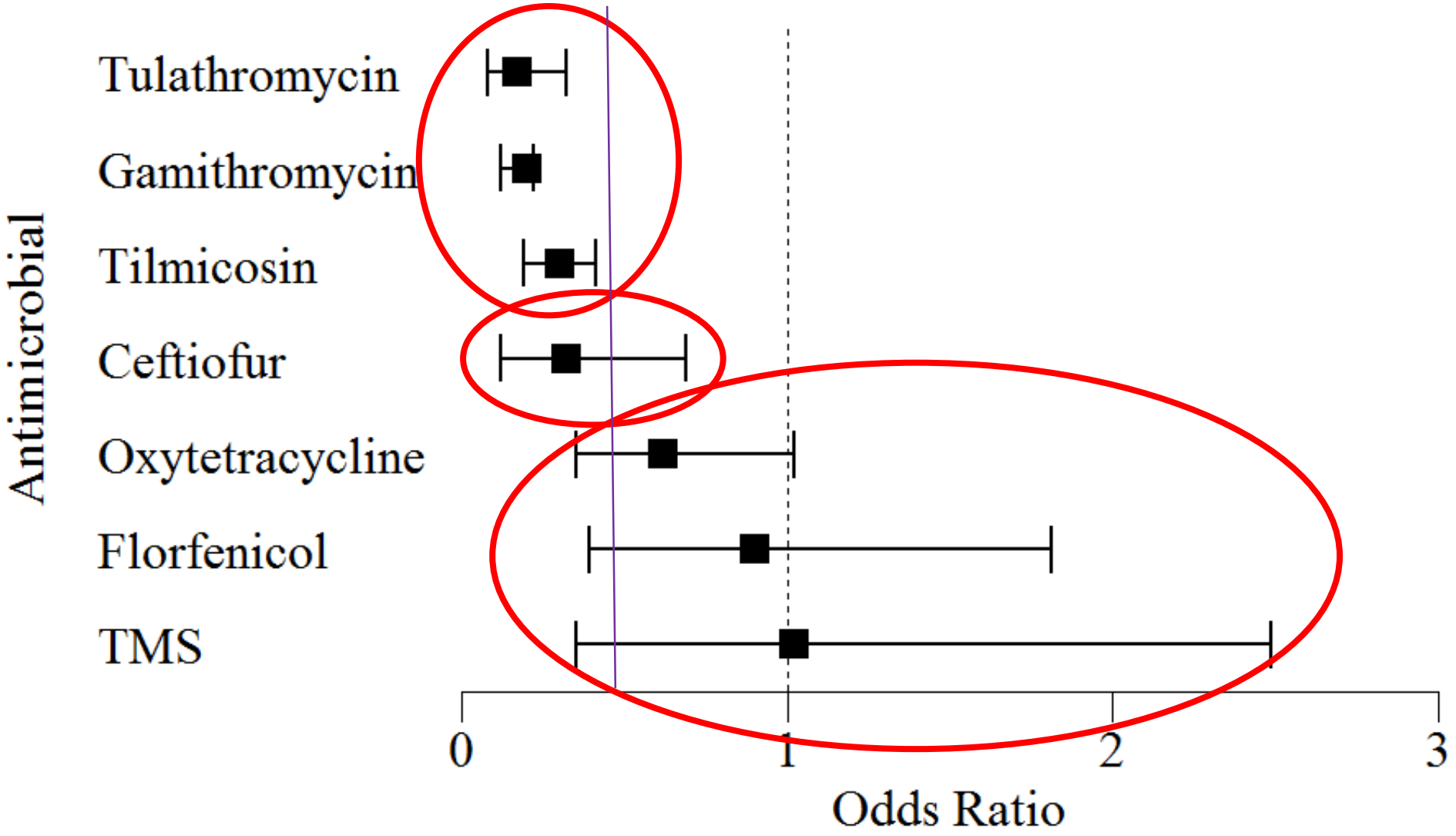
Morbidity d1 to ≤ 60 days

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

Forest plot application



Forest Plot – Morbidity d1 to ≤ 60



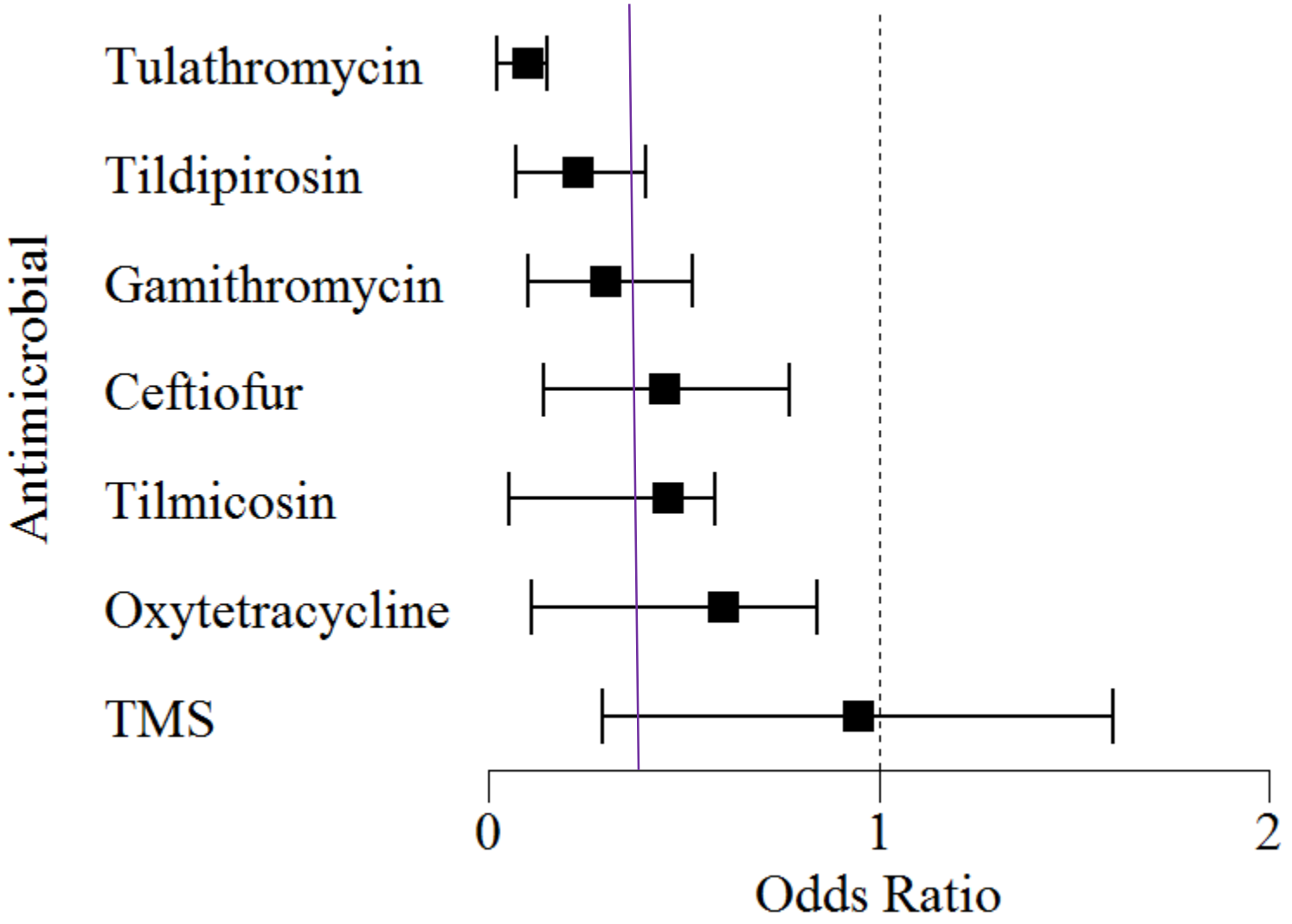
Event Occurrence

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

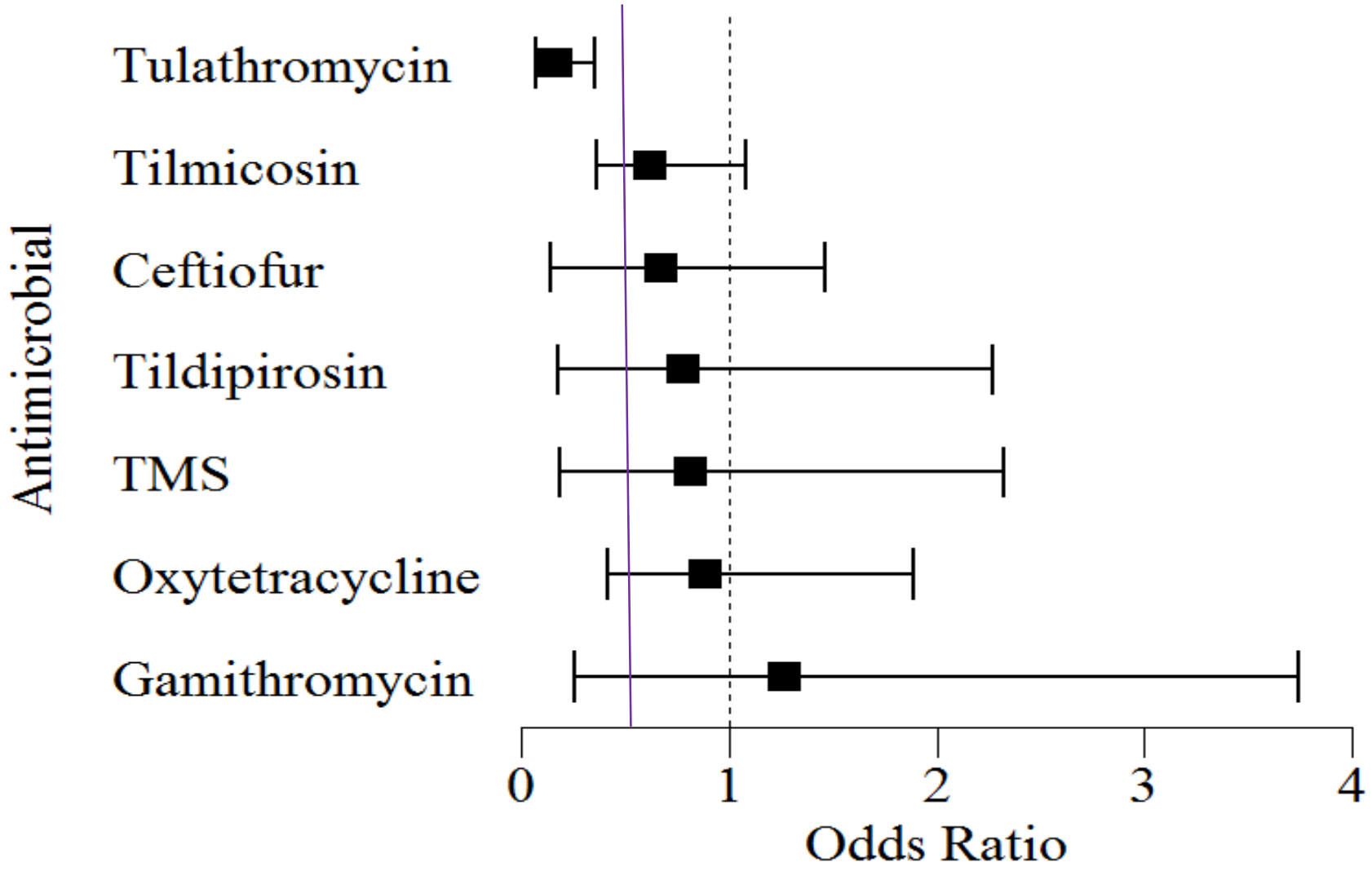
Morbidity d1 to closeout
Mortality d1 to closeout
Retreatment Morbidity d1 to closeout

- Assumes all trials occur within the same time period
- Further days at risk would not affect differences between events

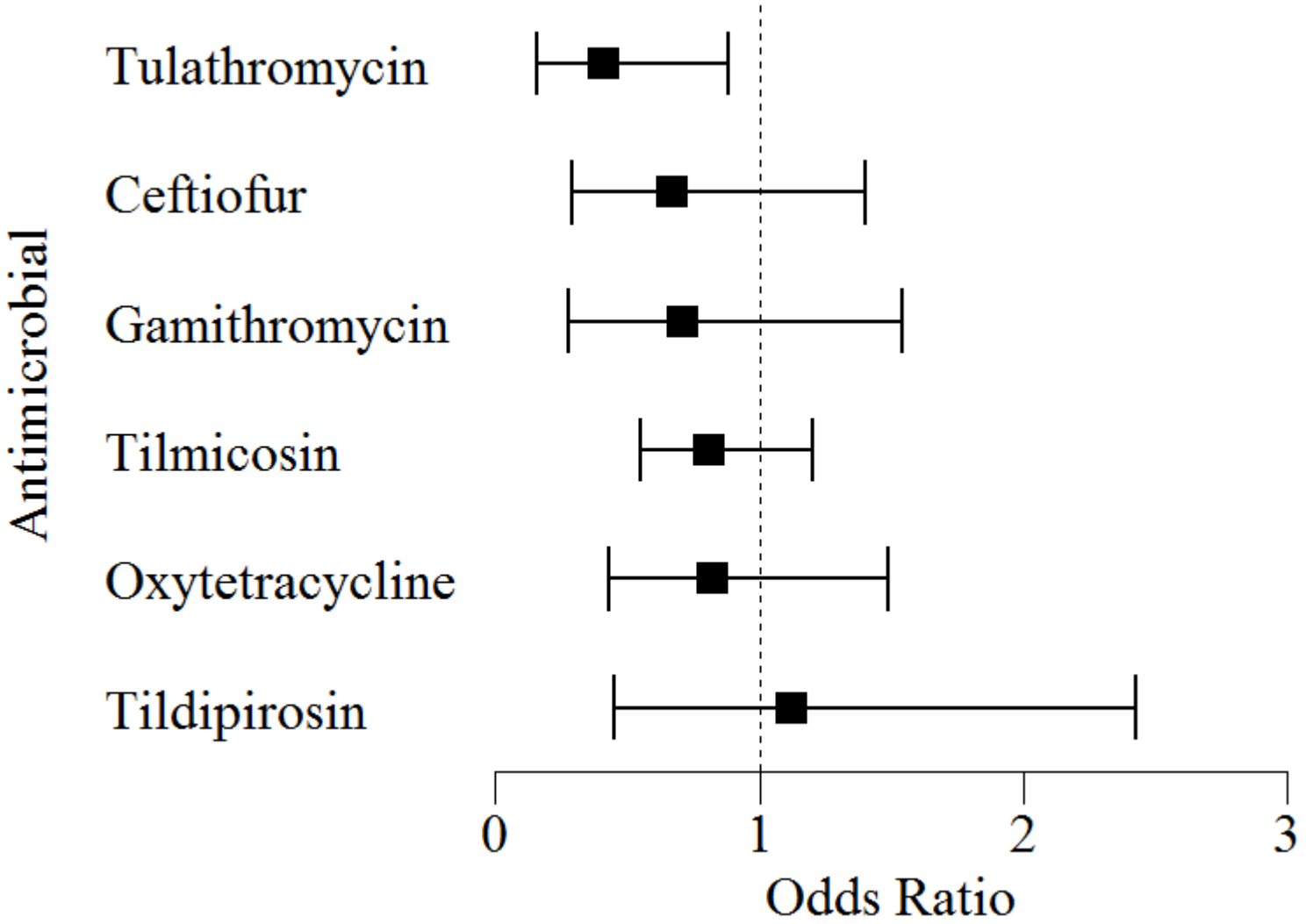
Forest Plot – Morbidity d1 to closeout



Forest Plot – Mortality d1 to closeout



Forest Plot – Retreat morbidity d1 to closeout



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

Outcome	Number of Trials
ADG	8
DMI	6
F:G	7
HCW	4
QG Choice or Better	6
YG 1-2	6

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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