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Meta-analysis of the transmission of Mycobacterium avium subsp. paratuberculosis in experimentally infected sheep to inform mathematical modelling

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Purpose:
A state-transition model was developed to evaluate the economic effects of interventions for on-farm control of paratuberculosis in sheep. The model required pathways and parameters describing within-host progression of Mycobacterium avium subsp. paratuberculosis (MAP). Because the pathophysiology of the progression of ovine paratuberculosis is complex and still poorly understood the objective of this work was to systematically evaluate findings from published infection experiments to identify suitable model parameter estimates for our model

Methods:
Twenty experimental and natural infection studies with MAP were subjected to systematic review and meta-analysis. The state-transition model was parameterized by the results of the meta-analysis.

Results:
We identified two possible pathways following infection with MAP in sheep and the rates at which sheep entered and stayed in latent and shedding states. Age at infection and MAP inoculum doses had significant effects on the fate of infected sheep ($p<0.05$) with higher MAP doses decreasing the time to onset of fecal shedding while higher age at infection decreased the odds of progressing to clinical paratuberculosis.

Conclusions:
Meta-analysis of natural or experimental infection studies of sheep with paratuberculosis can improve the current understanding of the pathophysiology of MAP infection and contribute towards building biologically relevant mathematical models for this disease.

Relevance:
This study provided a robust framework for mathematical modeling of ovine paratuberculosis.