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Evidence for pathogen-pathogen associations in East African Zebu cattle

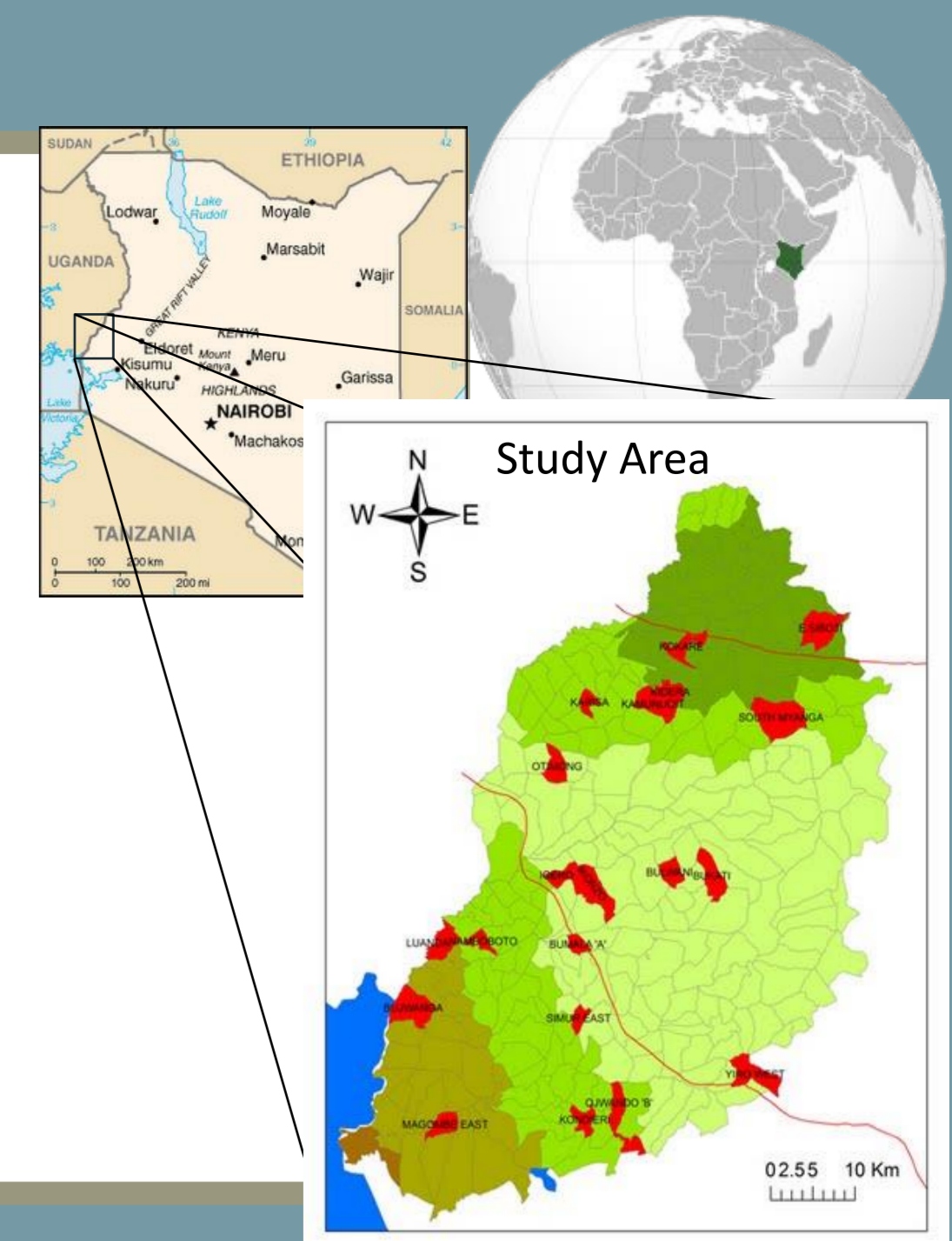
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Background:

- Associations between pathogens may be important determinants of dynamics of infections, but comprehensive data on full pathogen burdens are rare. Little is about whether such associations are generally positive or negative, and about the time scale on which they operate.
- We use the unique longitudinal study, called the **Infectious Diseases in East Africa Livestock (IDEAL) Project**¹ to track the fine-scale dynamics of coinfection by multiple pathogen species to determine:
 - The nature of concurrent associations and of lagged effects, both over short and relatively longer term.
 - The extent to which such associations are driven by other characteristics of either the calf or its environment.

Methods:

- 548 shorthorn zebu calves in West Kenya were screened every five weeks for the first year of life and the sequence of infections monitored
- 455 survived until 51 weeks of age
- Generalised linear mixed models was built to answer the following question:

Aim 1: Is infection with pathogen A at the present time point (T₀) associated with infection with pathogen B at the present time point (T₀) or at a previous time point (T_x) or other pathogens (pathogen C etc.) at the present and multiple time points?
- Potential environmental confounders were added into the model to evaluate the extent to which pathogen-pathogen associations are driven by characteristics of the calf or its environment (Aim 2).

Descriptive Results:

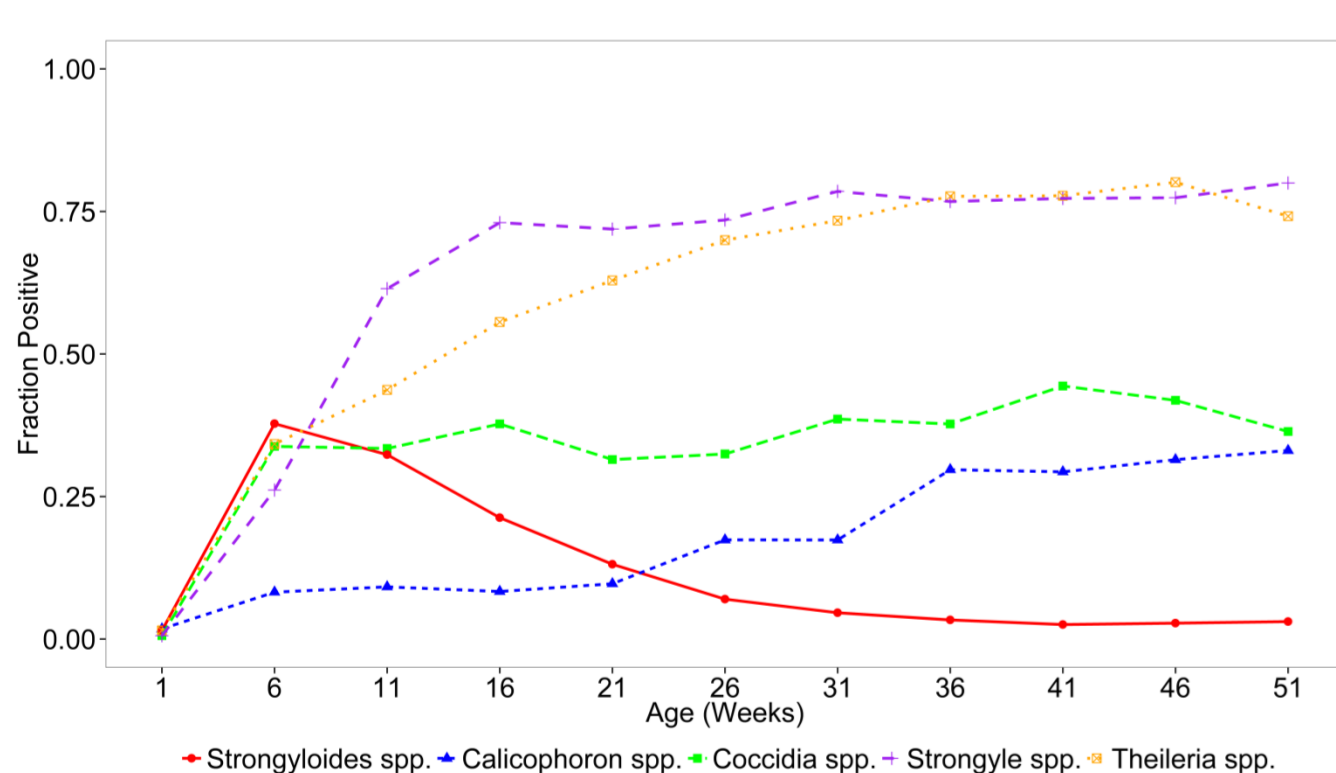


Figure 1: Fraction of calves infected with the pathogen at each age

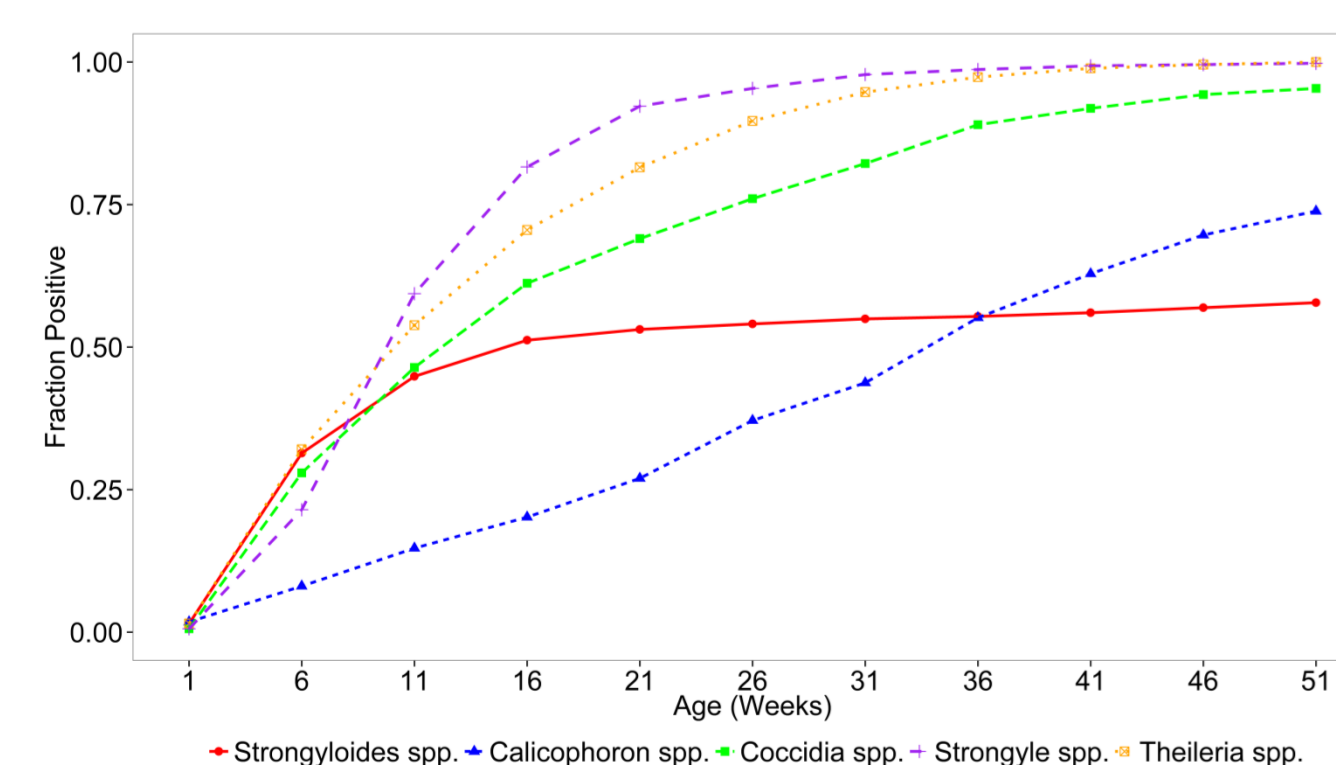


Figure 2: Cumulative fraction of calves ever infected by the pathogen up until the age stated

Results:

Aim 1:

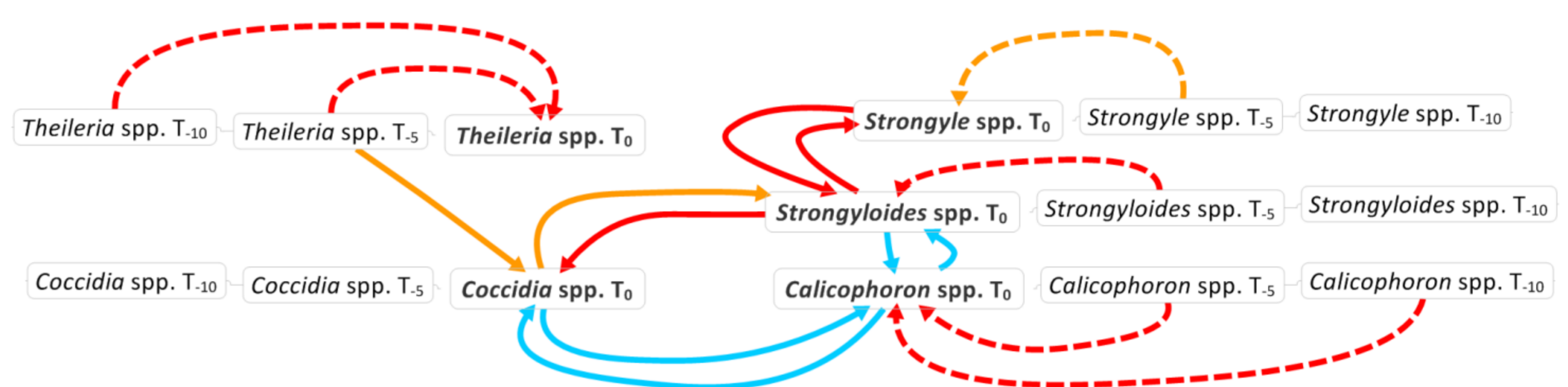


Figure 3: A schematic diagram showing the significant associations between pathogens identified from the analysis of pathogen presence at the current visit (T₀) or at previous time point, 5 or 10 weeks prior to the current visit (T₅ and T₁₀, respectively) **before** accounting for the characteristics of either the calf or its environment

- Positive associations (risk factors, OR >1): Significant at **P<0.01** and **P<0.001**
- Negative associations (protective factors, OR < 1): Significant at **P<0.01** and **P<0.001**
- Arrows: Explanatory variable → Response variable
 - Interspecific associations
 - - - Intraspecific associations

Aim 2:

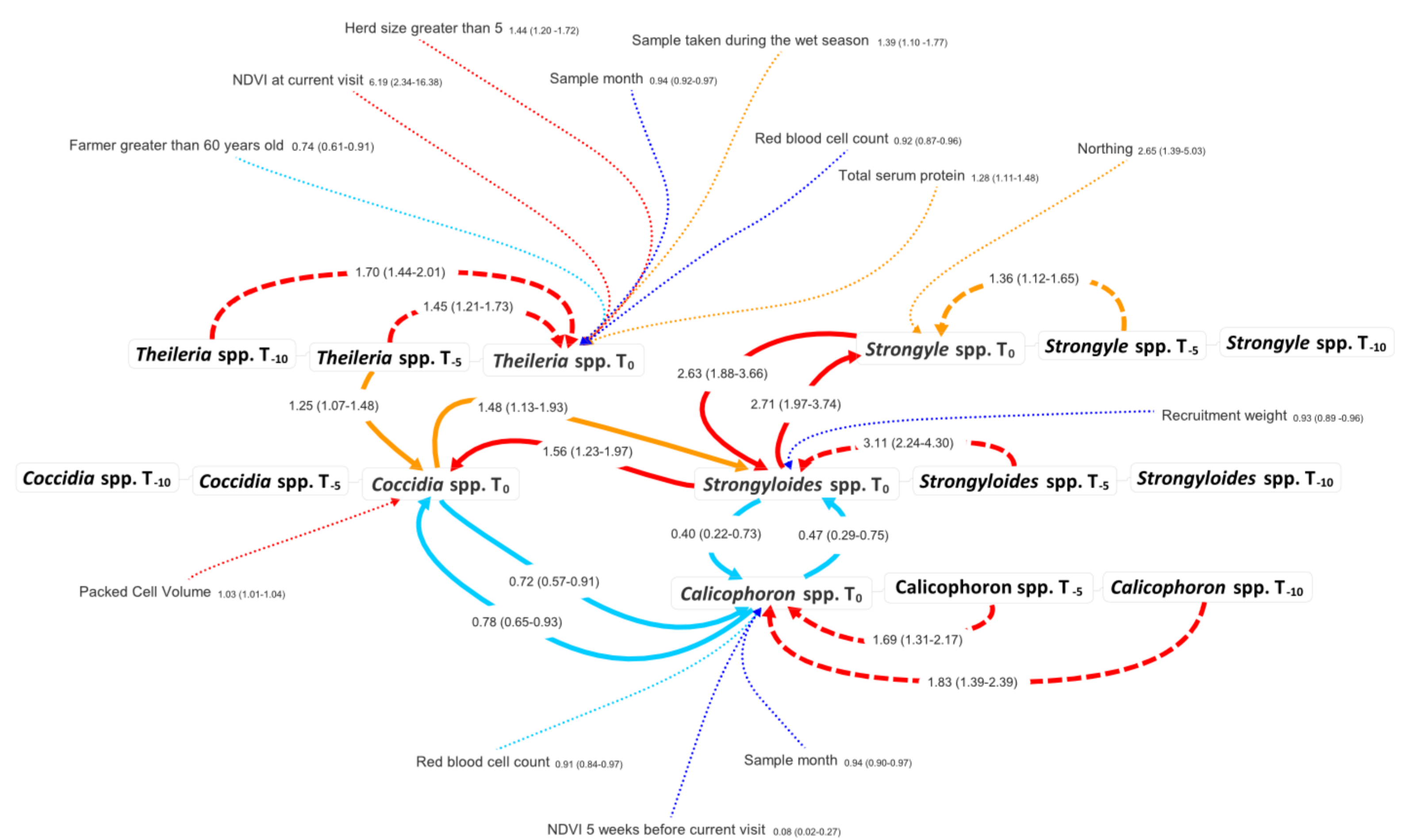


Figure 4: A schematic diagram showing the significant associations between pathogens identified from the analysis of pathogen presence at the current visit (T₀) or at previous time point, 5 or 10 weeks prior to the current visit (T₅ and T₁₀, respectively) **after** accounting for the characteristics of either the calf or its environment

- Positive associations (risk factors, OR > 1): Significant at **P<0.01** and **P<0.001**
- Negative associations (protective factors, OR <1): Significant at **P<0.01** and **P<0.001**
- Arrows: Explanatory variable → Response variable
 - Interspecific associations
 - - - Intraspecific associations
 - Characteristics of either the calf or its environment
- Numbers represent the odds ratio and are followed by the 95% confidence interval

Summary:

- 40% of associations between all possible pairwise combinations of pathogens were statistically significant.
- Both positive (55.6%) and negative (44.4%) associations between pathogens exist.
- Most associations occurred over short periods of time rather than long-term carry-over effects.
- The same associations between pathogens remained after accounting for environmental and calf variation.
- Concurrent or previous infection with the alternative pathogens is associated with a higher risk (or level of protection) for infection with the pathogen of interest than the characteristics of the calf or its environment