Bovine tuberculosis in Michigan: the role of of elk in the bovine Tuberculosis transmission

D.J. O'Brien, M.K. Cosgrove, T. P. Stuber, A. Schooley, J. Crispell, S. Church, Y.T., Grohn, S. Robbe-Austerman, R.R. Kao

Bovine Tuberculosis Mini-Symposium

8 June 2017

Liliana Salvador

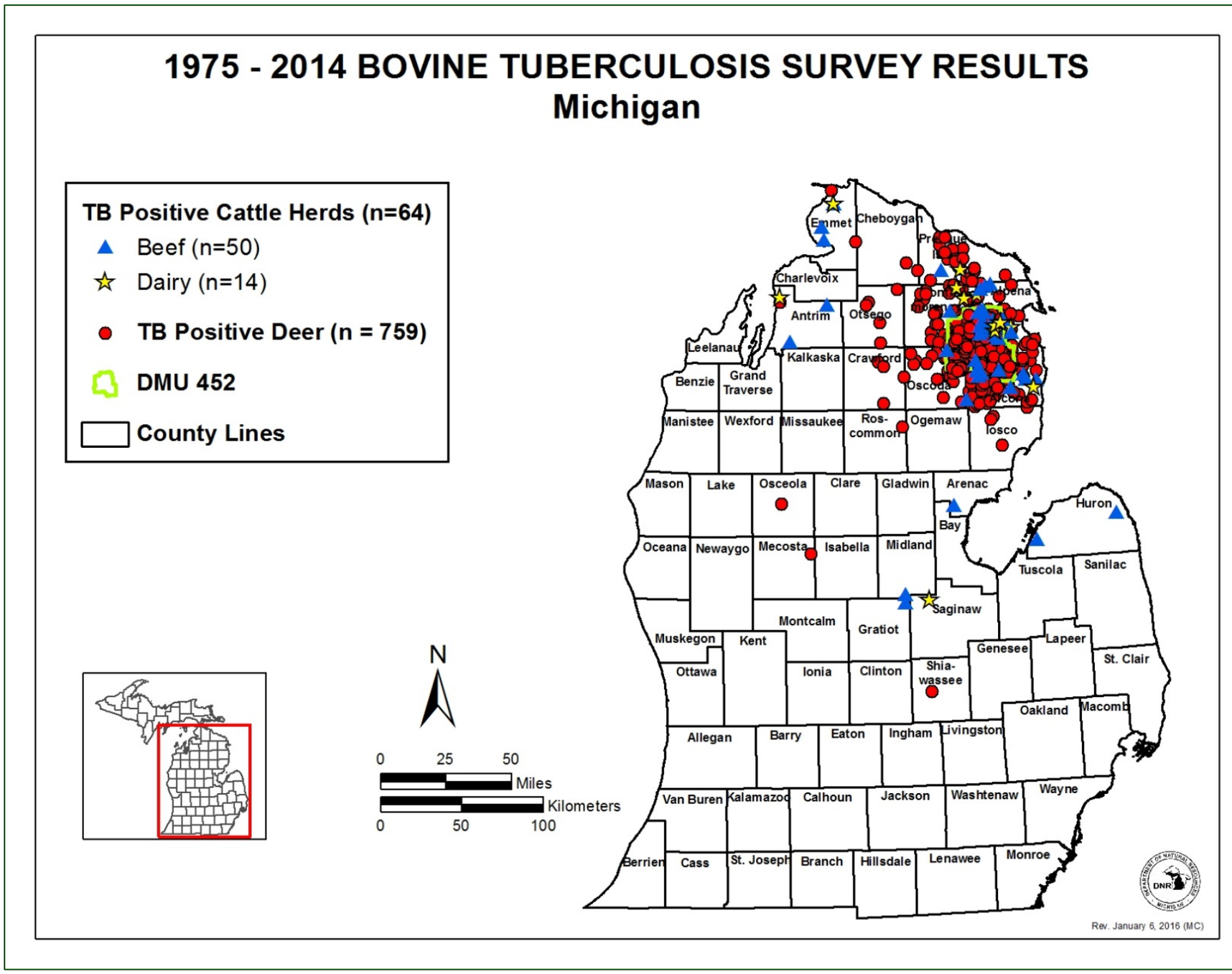
University of Glasgow

Cattle farms surrounded by deer habitat

University of Glasgow

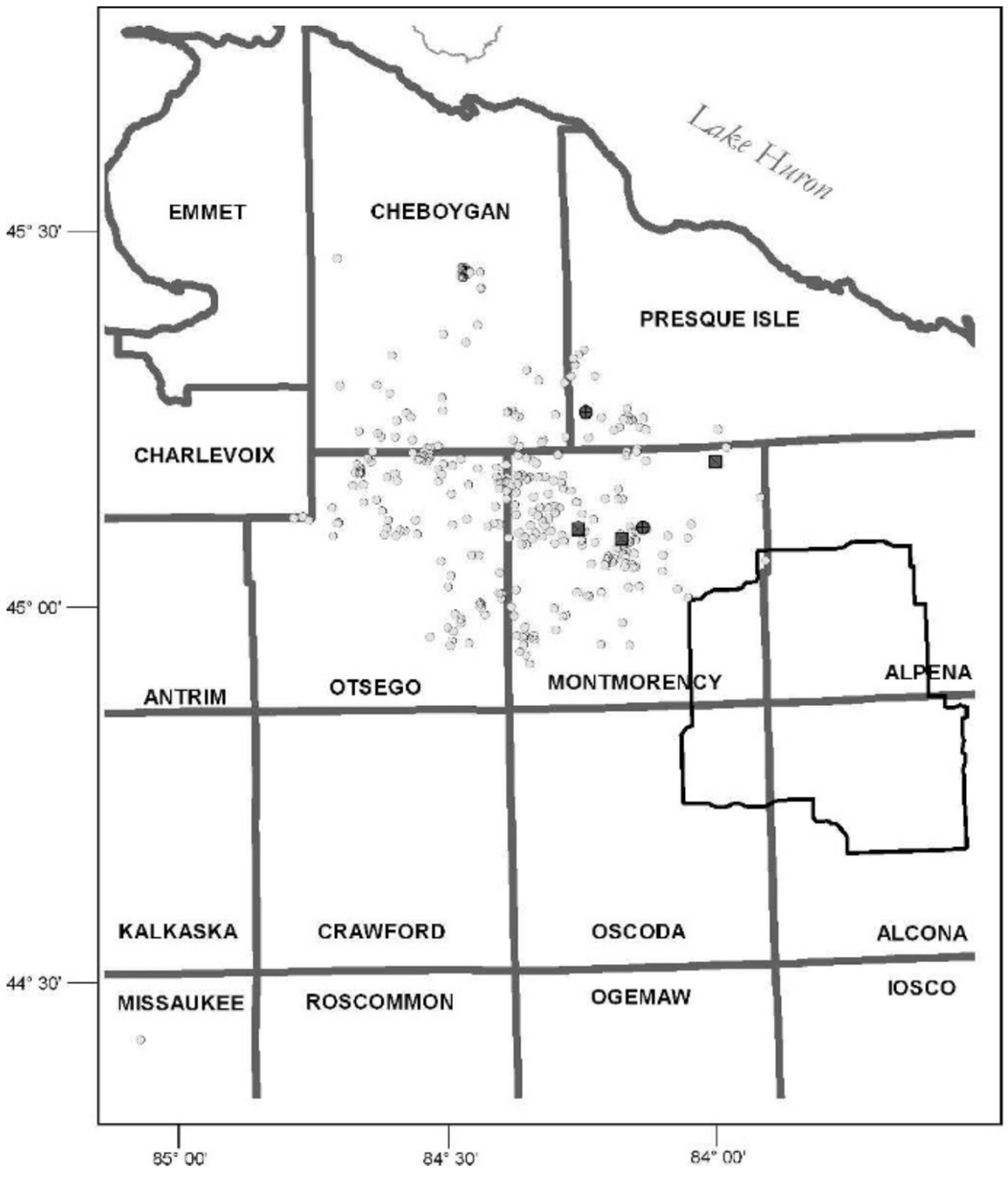
Cattle farms surrounded by deer habitat

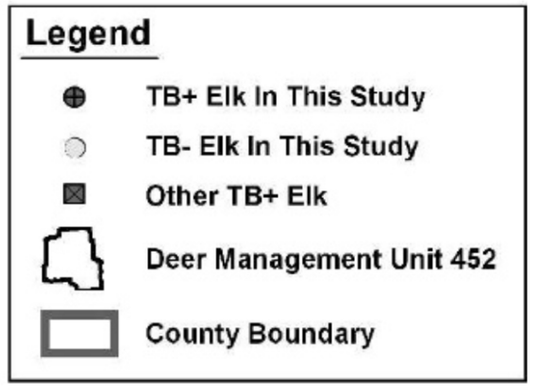
Bovine TB cases in deer



Population size in last 10 years: 1.7-2 million animals

Bovine TB cases in elk

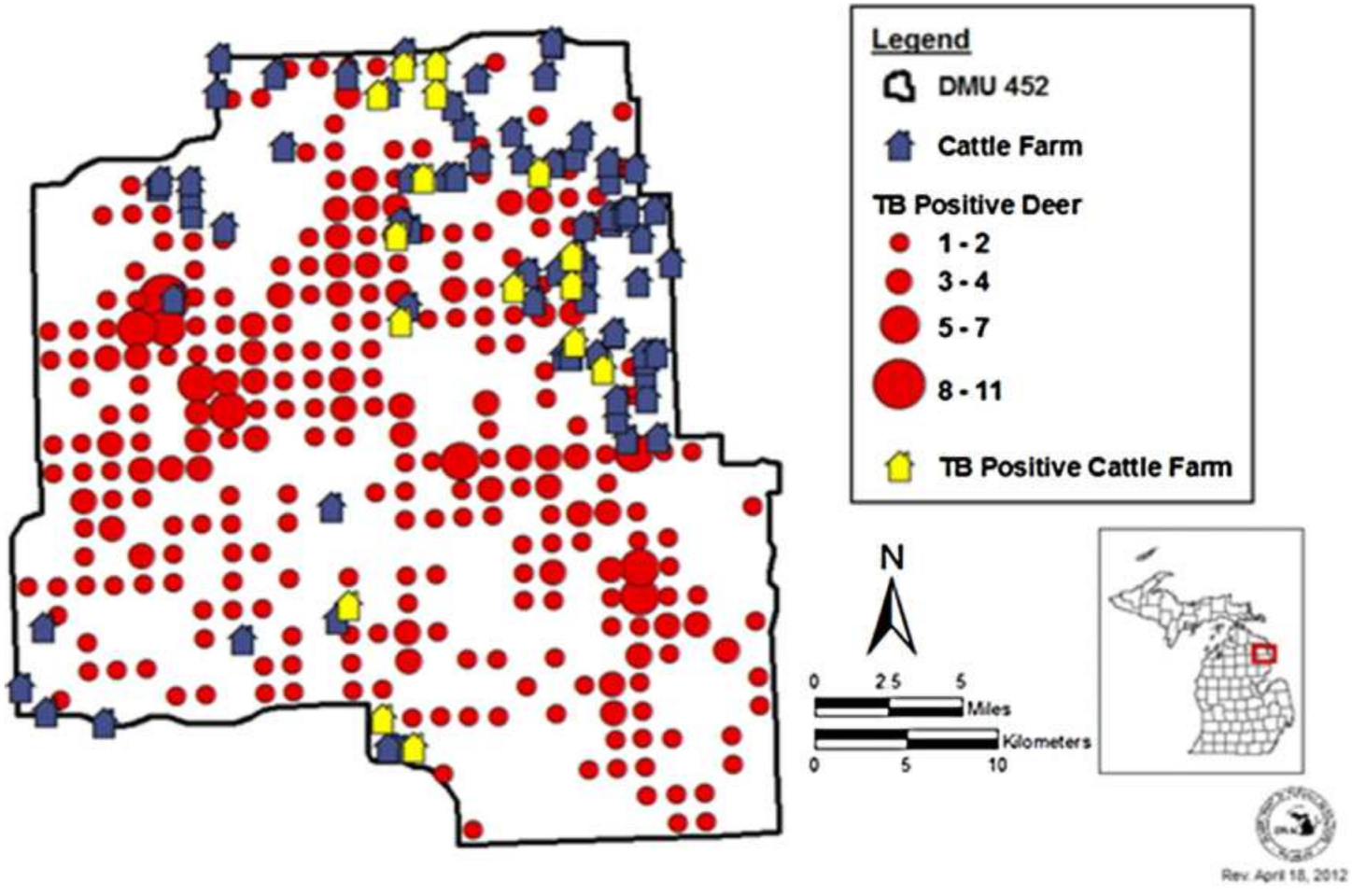




O'BRIEN, Daniel J., et al. *Journal of Wildlife Diseases*, 2008, vol. 44, no 4, p. 802-810.

Population size in last 10 years: 800-1500 animals

Bovine TB cases in deer and cattle farms



- Total farms: 52 140, average farm size: 191 acres
- 46 cattle herds infected (2005-11): affects cattle trade due to movement restrictions
- Usually single infections, risk of infection is low but constant (3-4 breakdowns/year)
- BTB eradication program: cost of US$200 million during 1994-2010 in Michigan alone

Mammal Review
Volume 45, Issue 3, pages 160-175, 30 JUN 2015 DOI: 10.1111/mam.12042
http://onlinelibrary.wiley.com/doi/10.1111/mam.12042/full#mam12042-fig-0001

O'BRIEN, Daniel J., et al. *Journal of Wildlife Diseases*, 2008, vol. 44, no 4, p. 802-810.

Cross-species transmission parameters

How much and how often?

β

γ

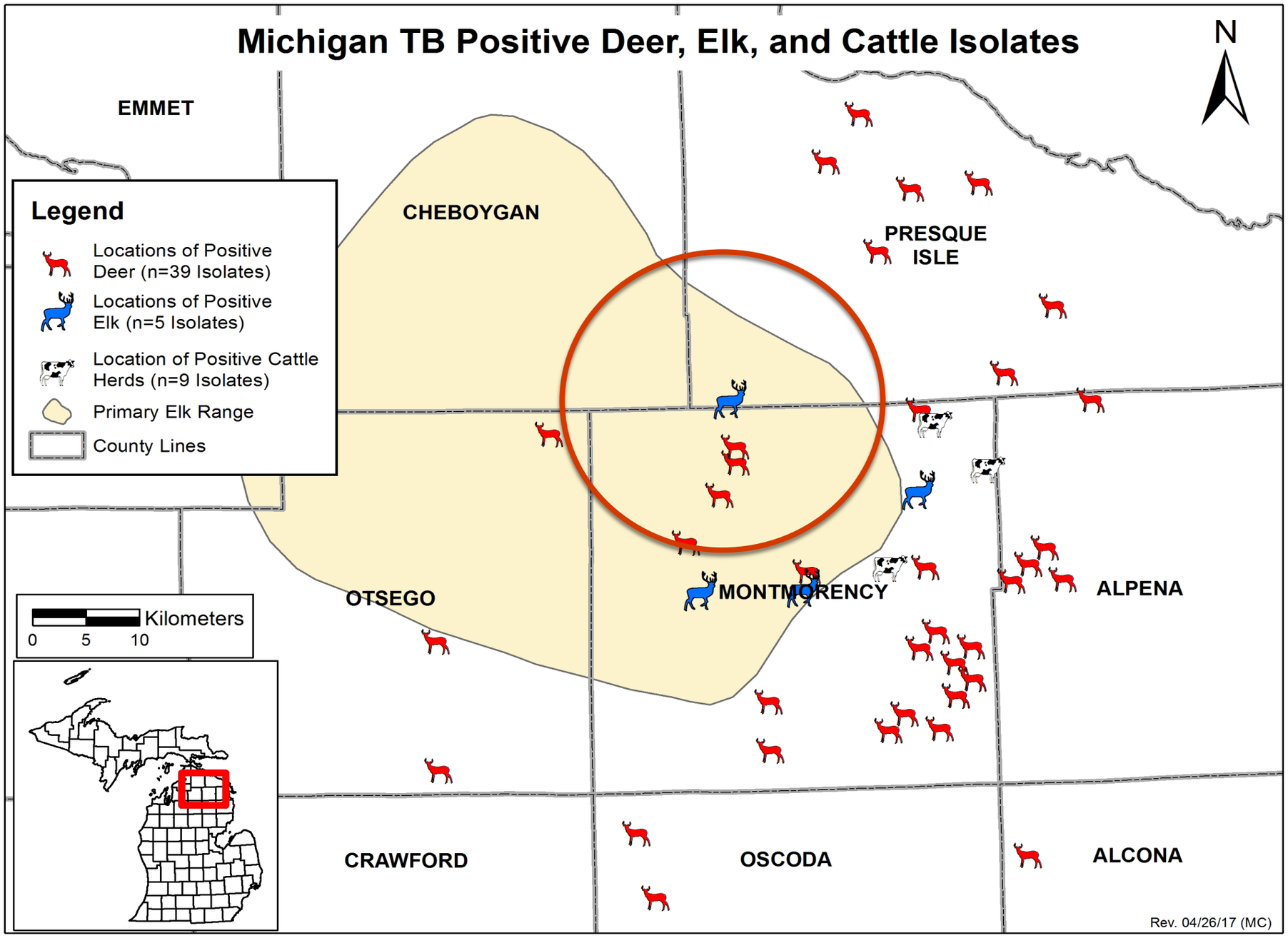
α

Is $\beta = \gamma = \alpha$?

University of Glasgow

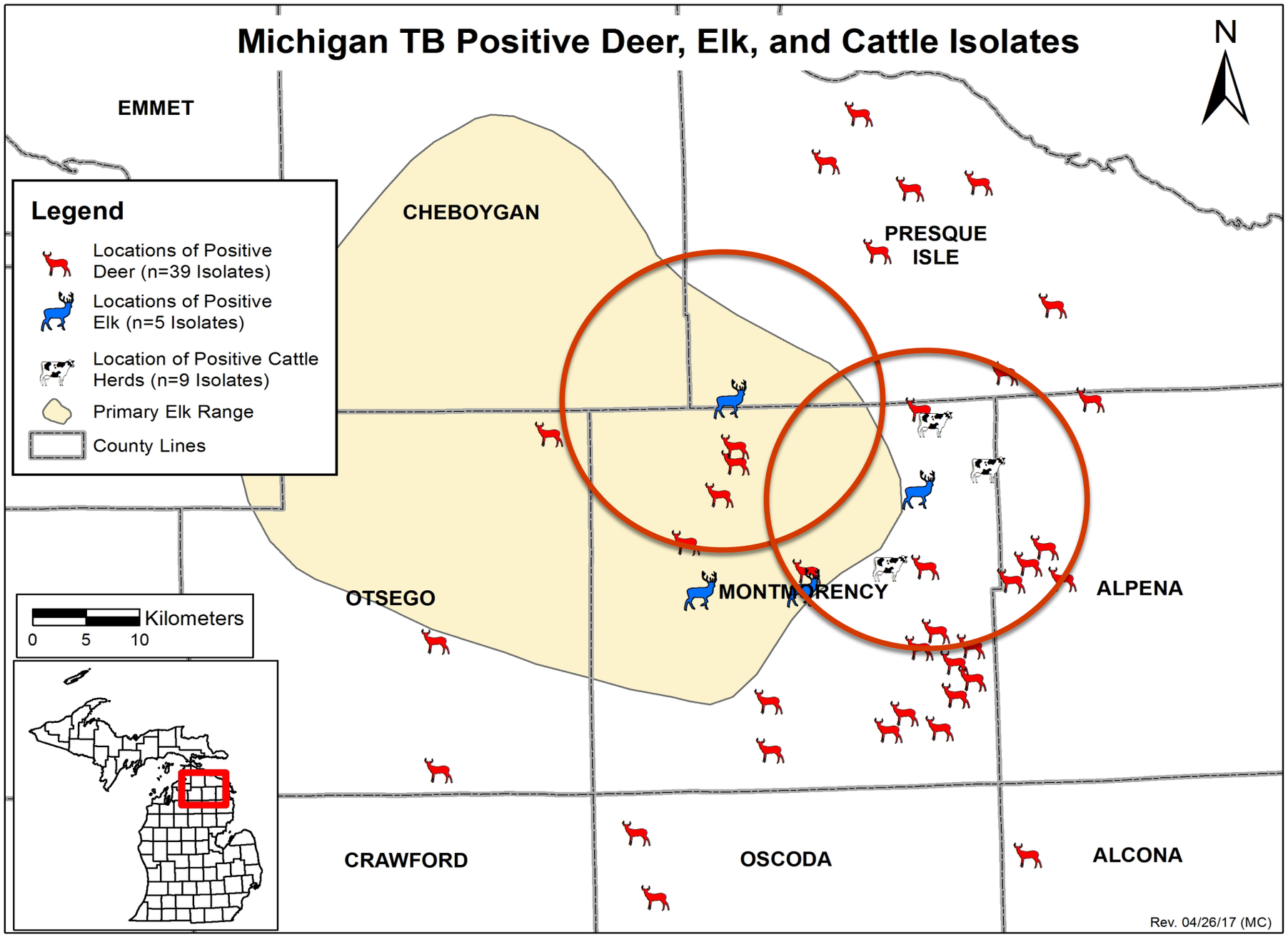
Understanding the role of elk in bTB transmission

Isolates spatial locations



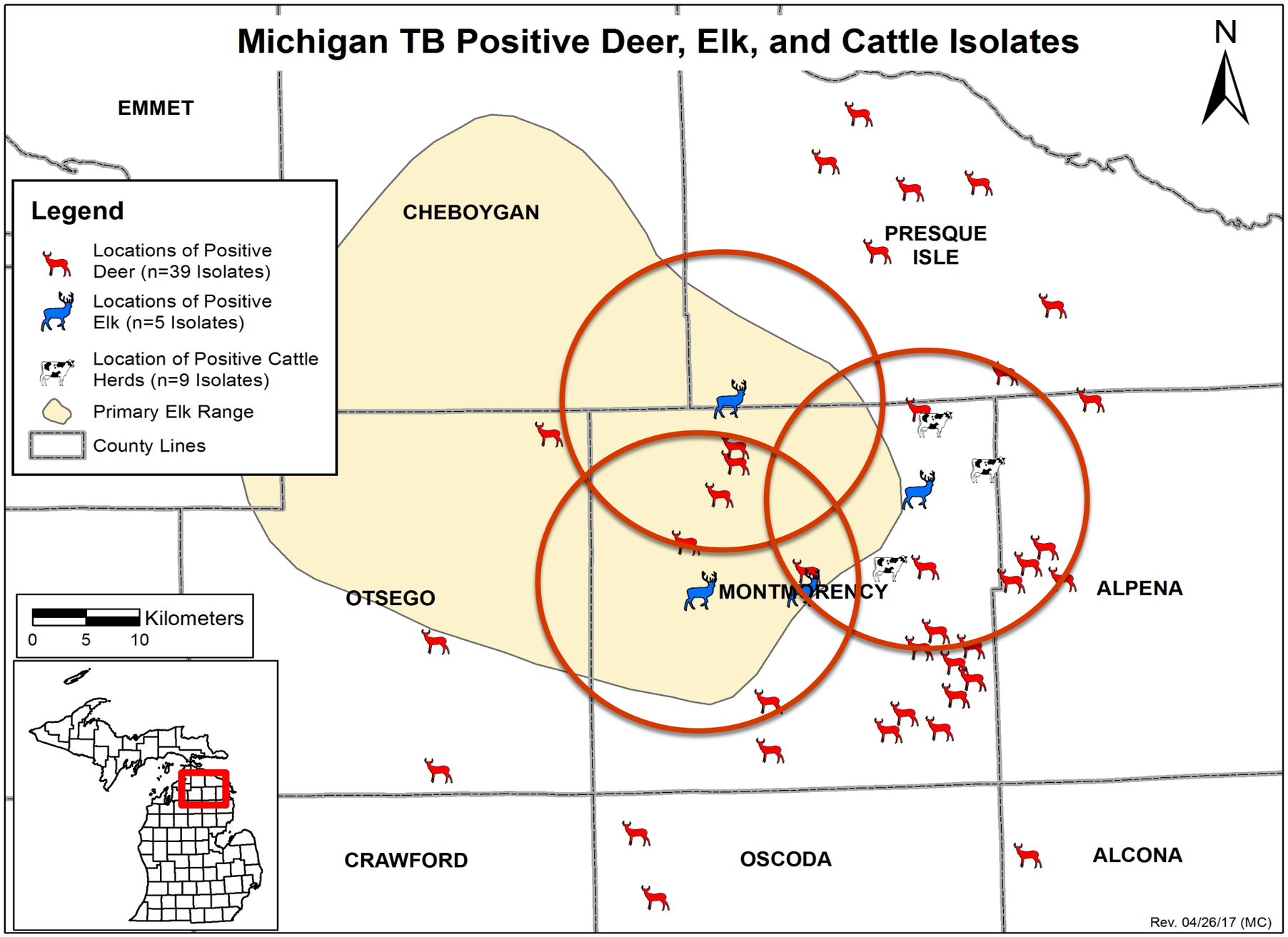
Understanding the role of elk in bTB transmission

Isolates spatial locations



Understanding the role of elk in bTB transmission

Isolates spatial locations



Bovine TB in Michigan: Data

- 53 field isolates from different counties in Michigan:
  5 elk; 9 cattle, 39 deer positive bTB isolates

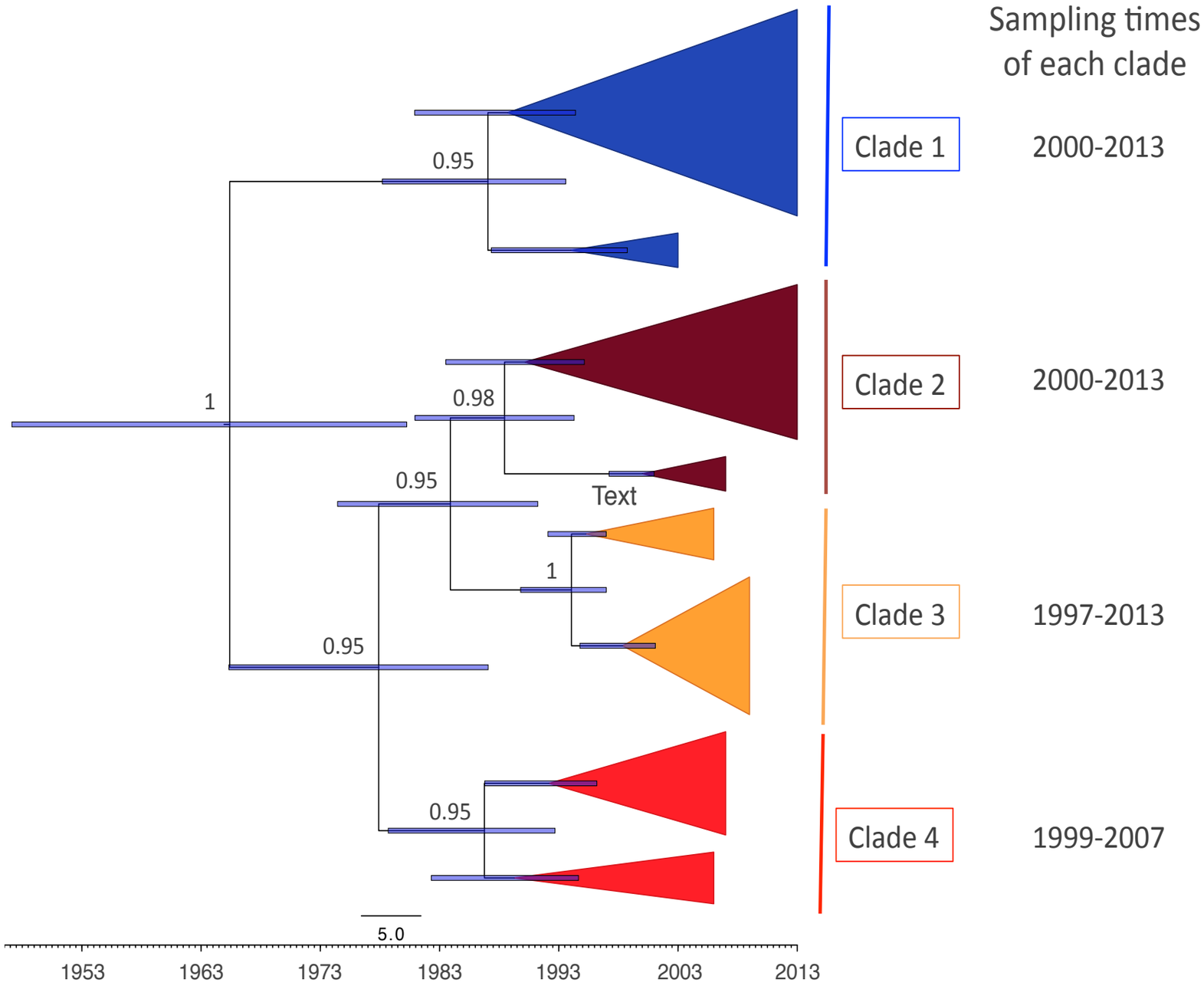
- Date range: 14 years (1999 to 2013)

- Extract and sequence DNA from all isolates using Illumina sequencing

- Bioinformatic pipeline to align sequences with BWA, and to identify consensus SNPs with GATK (698 sites)

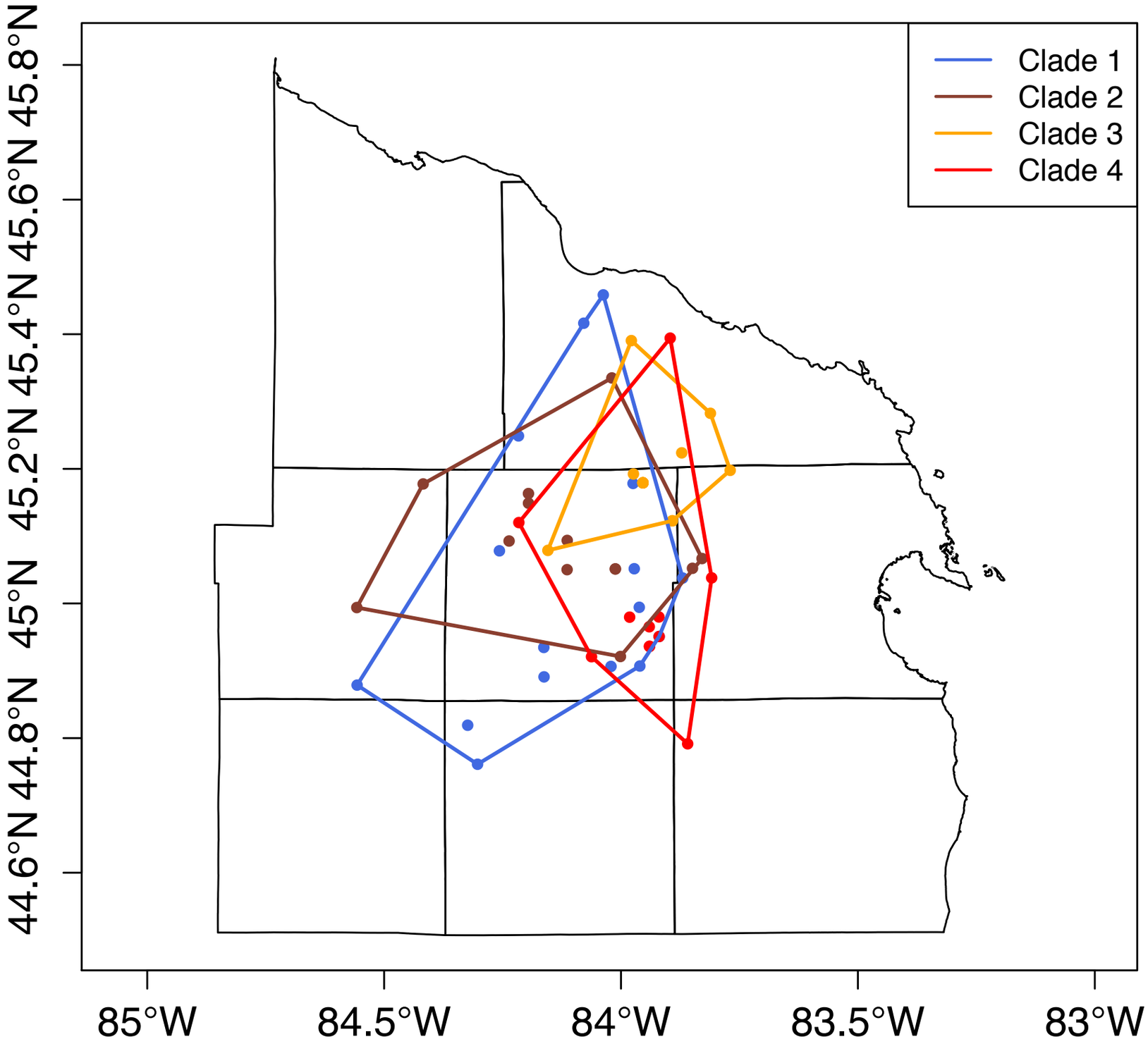
Understanding the role of elk in bTB transmission

Time-calibrated phylogeny

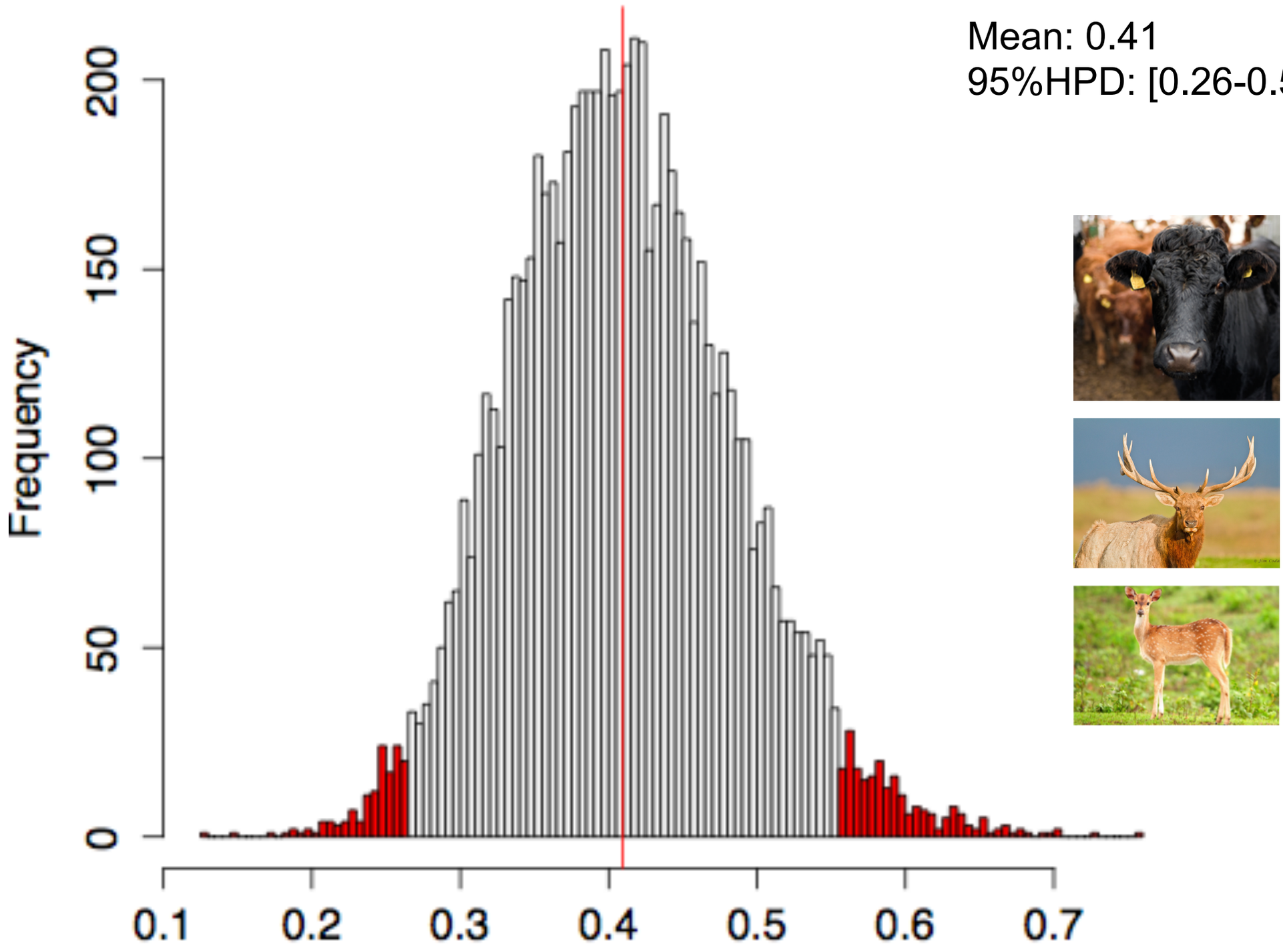


Substitution model: HKY (supported by *jmodeltest*), strick molecular clock, constant population size

Spatial distribution of clades



Molecular rate of evolution

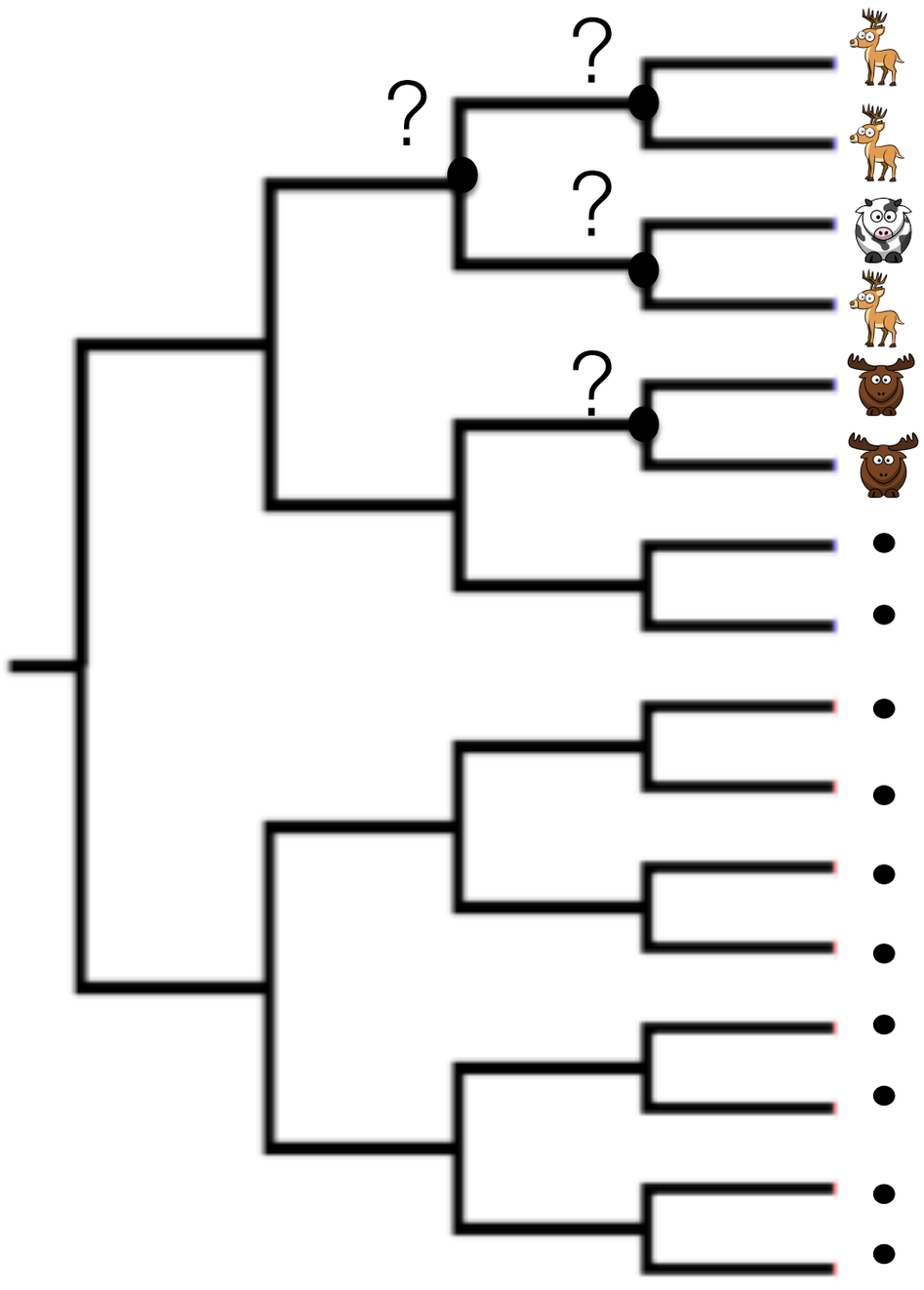


Mean: 0.41
95%HPD: [0.26-0.55]

Mean clock rate - other studies

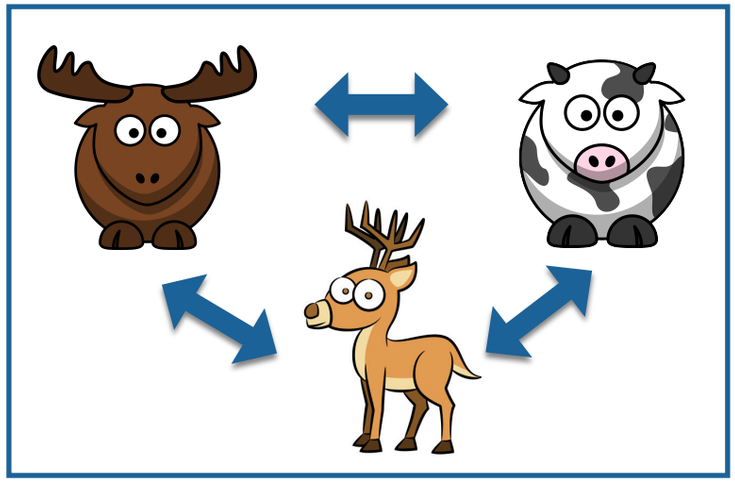
Source	Bacteria species	mean clock rate/ genome/year
Walker *et. al.* 2013	*M.Tuberculosis*	0.50 [0.30-0.70]
Bryant *et al.* 2013	*M. Tuberculosis*	0.30 [0.16-0.80]
Biek *et al.* 2012	*M. bovis*	0.15 [0.04-0.26]
Trewby *et al.* 2015	*M. bovis*	0.20 [0.10-0.30]
Crisp *et al. 2017*	*M. bovis*	0.59 [0.30-0.95]
Current study	*M. bovis*	0.41 [0.26-0.55]

Discrete Trait Analysis (DTA)



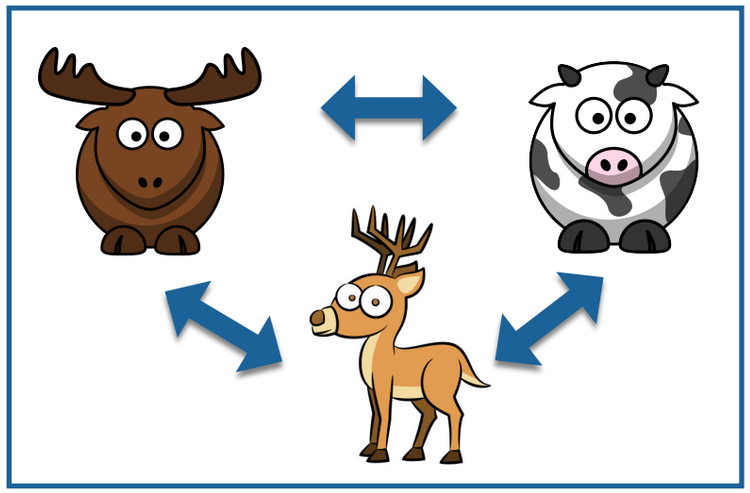
- Infer host state probabilities for internal nodes

- Estimate probability transition rate between hosts

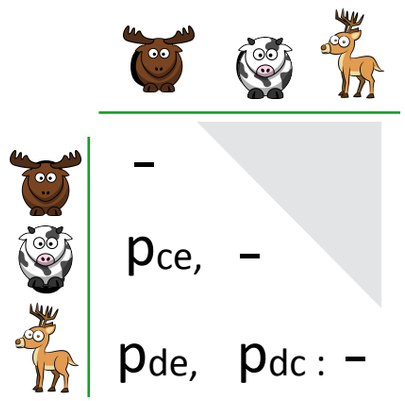


Drummond & Rambaut, BEAST - Bayesian evolutionary analysis by sampling trees, 2007
Bouckaert et al. 2014 - BEAST2 - A software platform for bayesian evolutionary analyses, 2014

Discrete Trait Analysis (DTA)



Transition rate matrix (M):



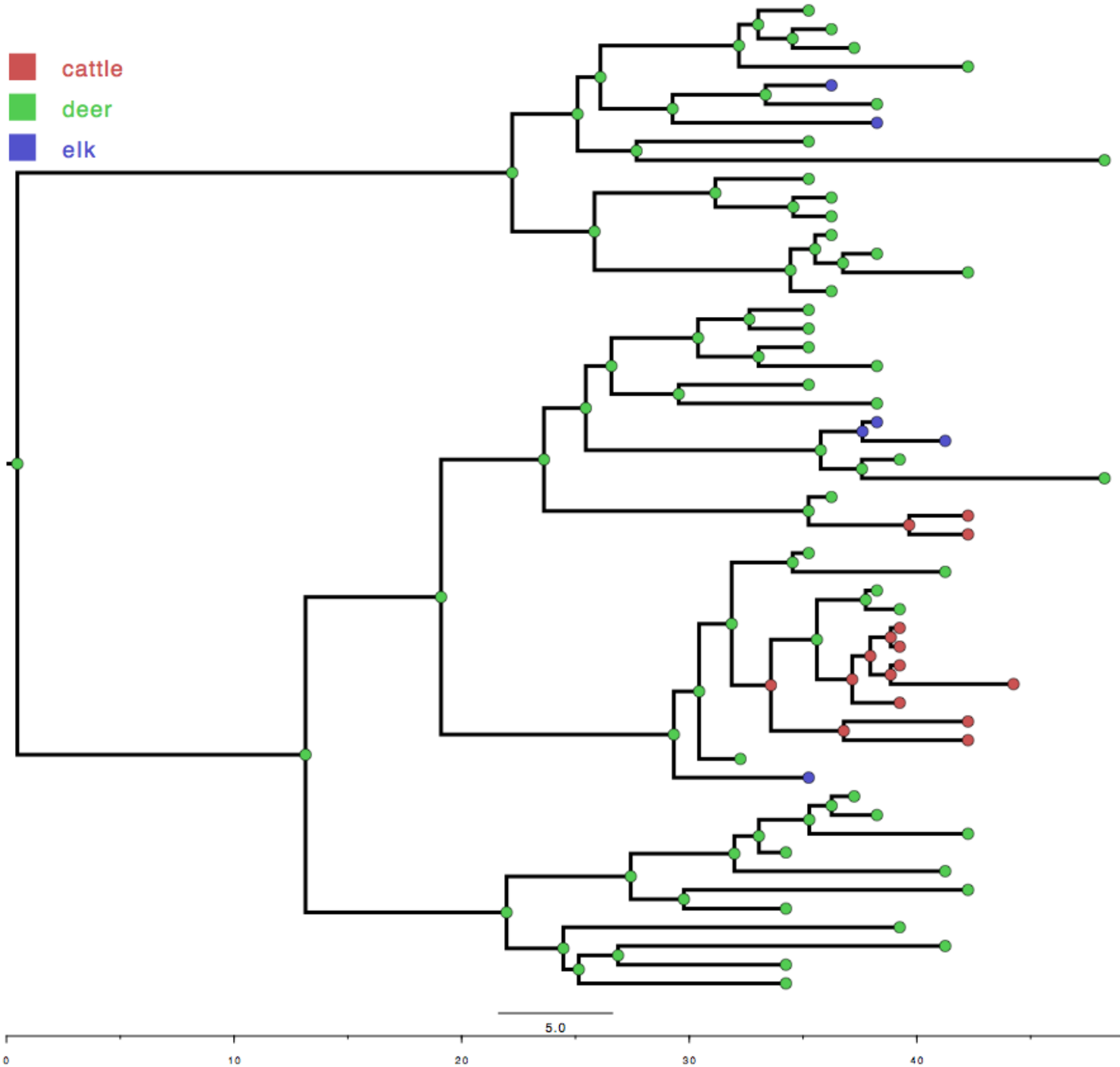
p_{ce}, p_{de}, p_{dc} : Probability of transition between different states

Probability of Ancestral state (x'), given branch length t and child state x

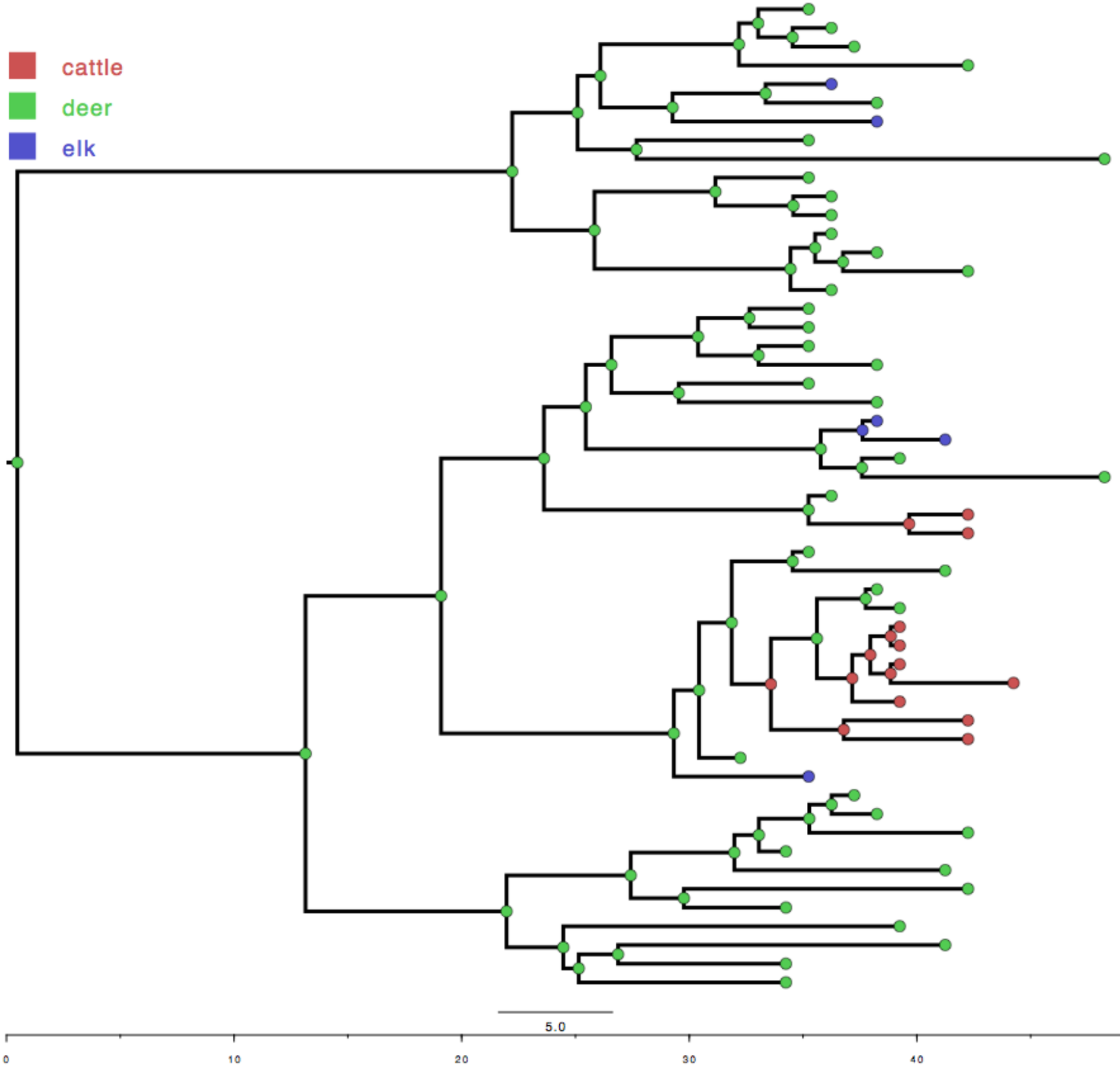
high prob: **strong support of direct migration between states**

Drummond & Rambaut, BEAST - Bayesian evolutionary analysis by sampling trees, 2007
Bouckaert et al. 2014 - BEAST2 - A software platform for bayesian evolutionary analyses, 2014

Ancestral host-state reconstruction



Ancestral host-state reconstruction

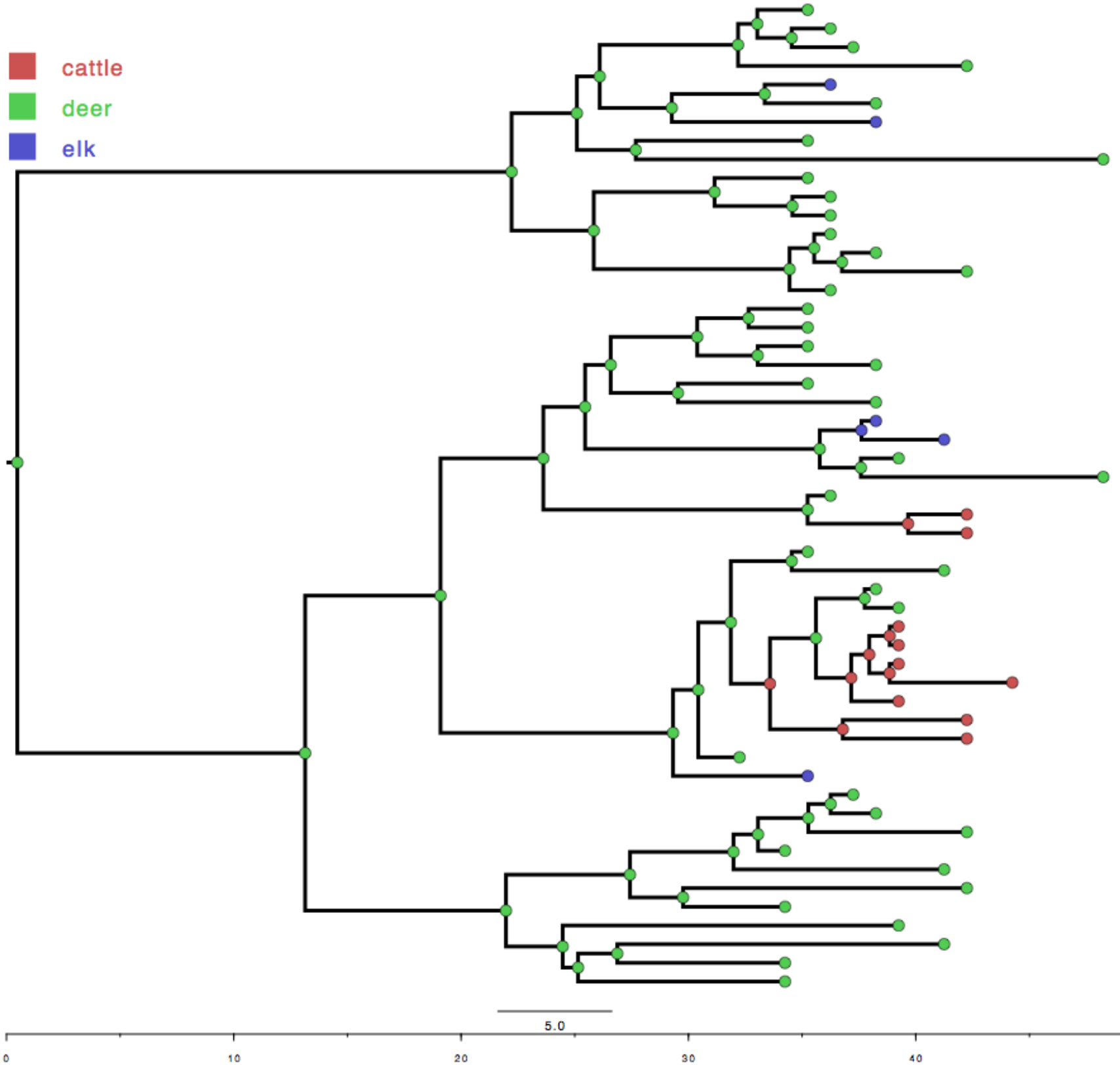


Clade 1

Deer

Elk

Ancestral host-state reconstruction



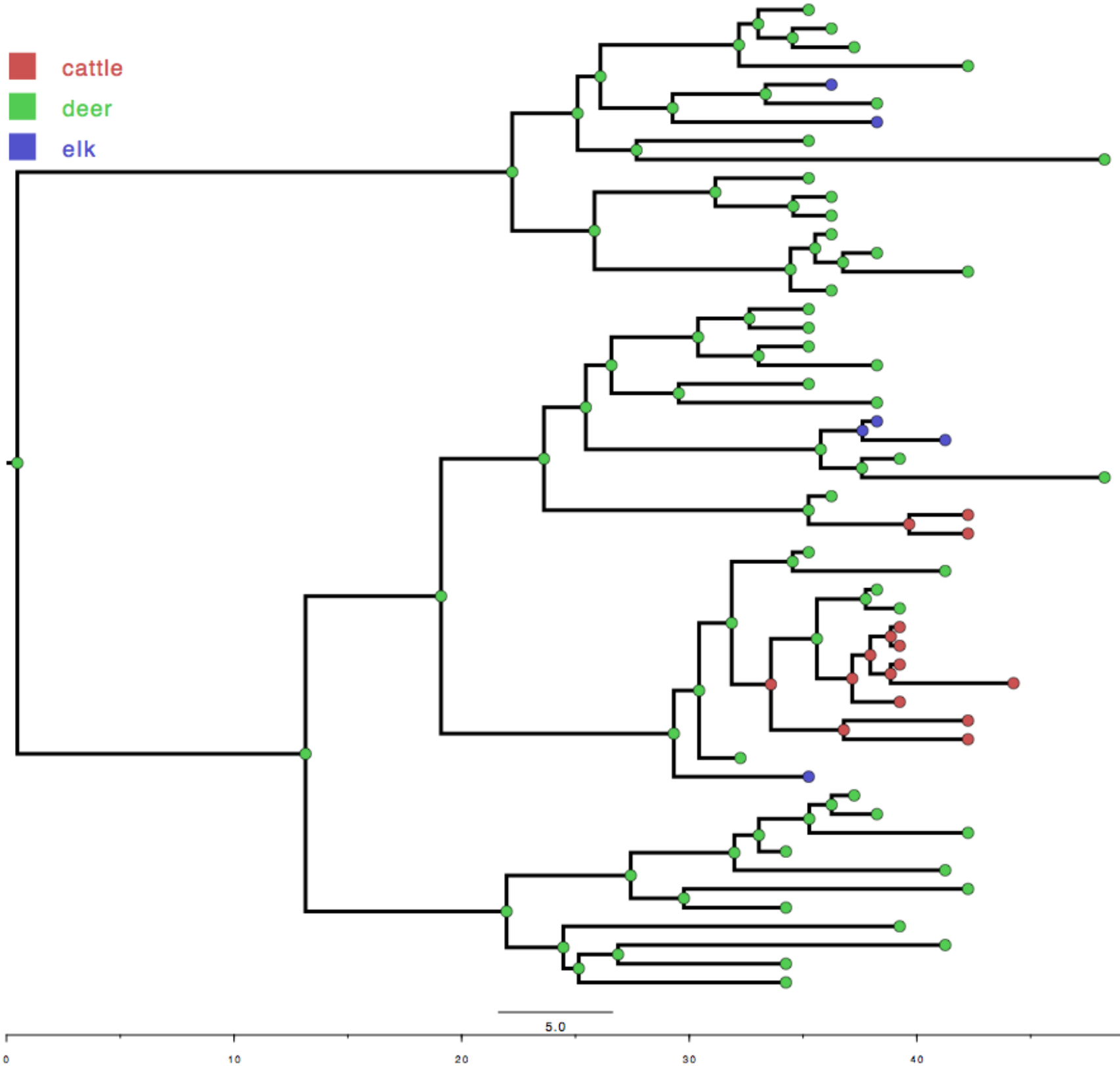
Clade 2

Cattle

Deer

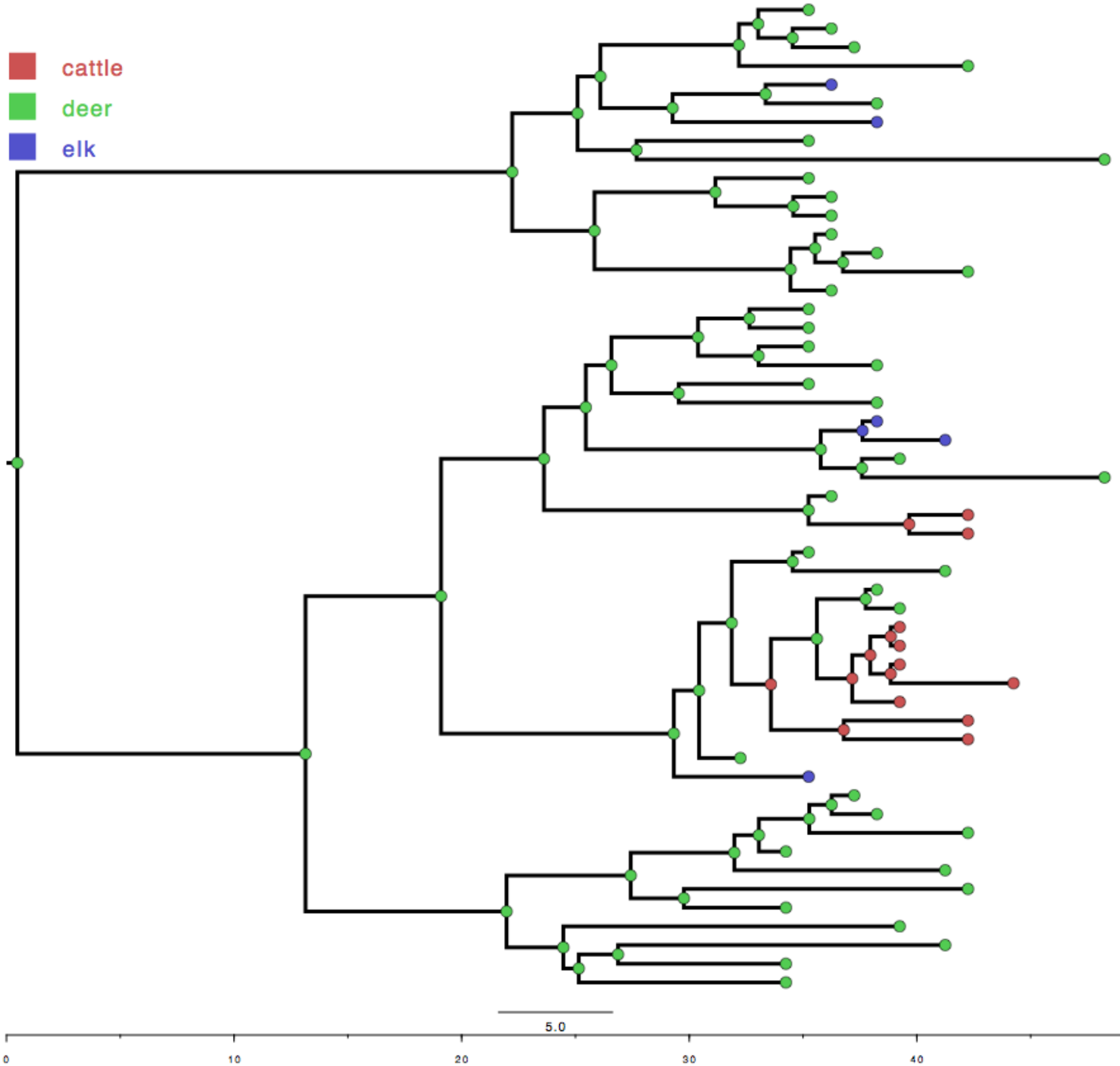
Elk

Ancestral host-state reconstruction



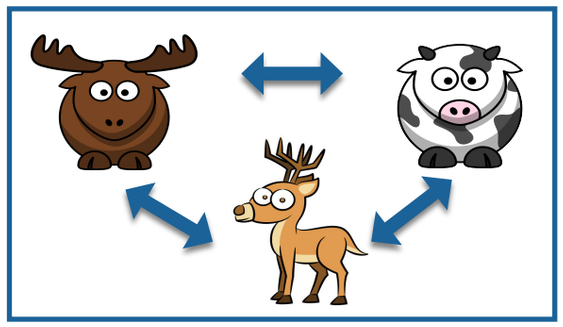
Clade 3
Cattle
Deer
Elk

Ancestral host-state reconstruction



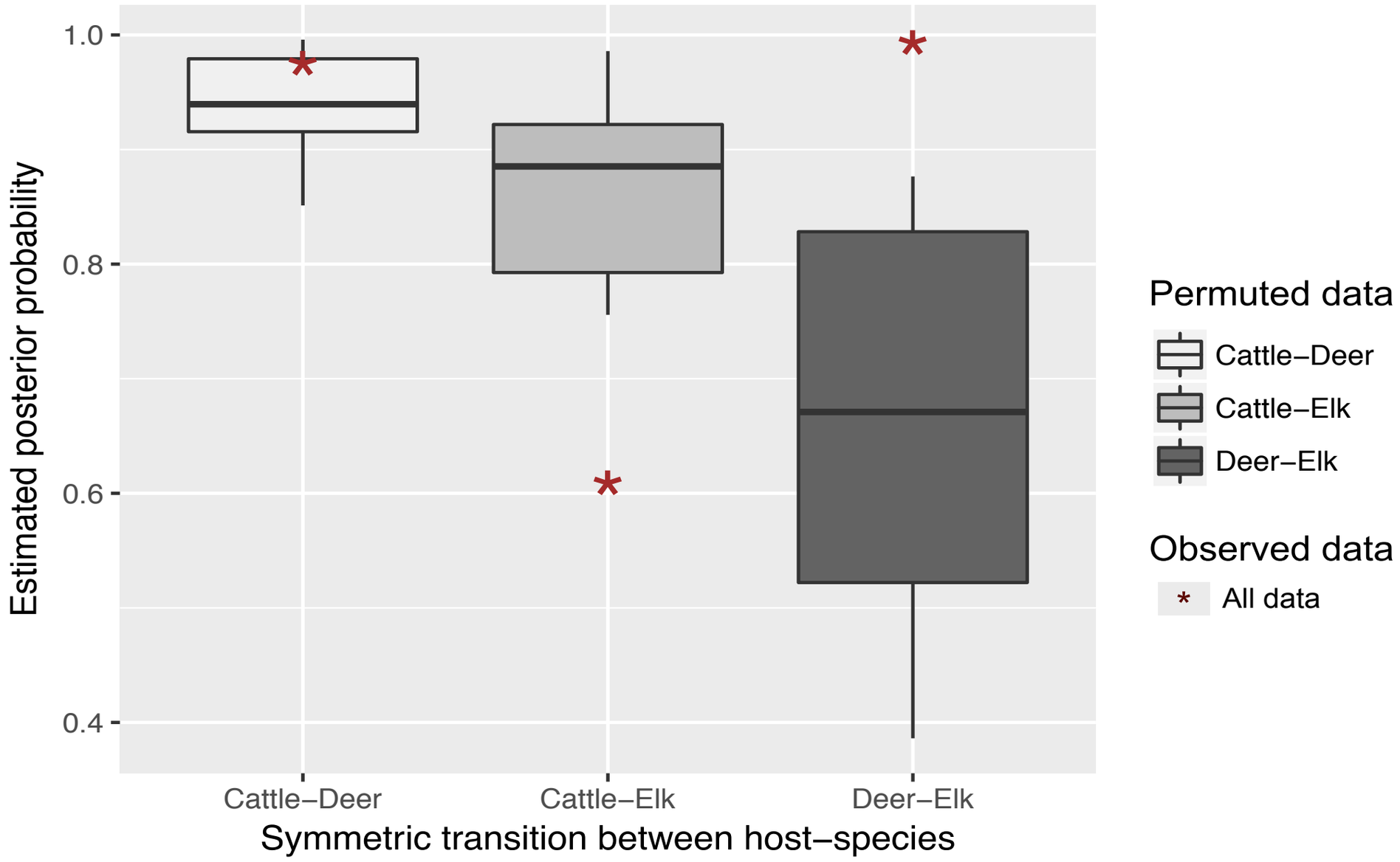
Clade 4
Deer

Pathogen transition between host-species

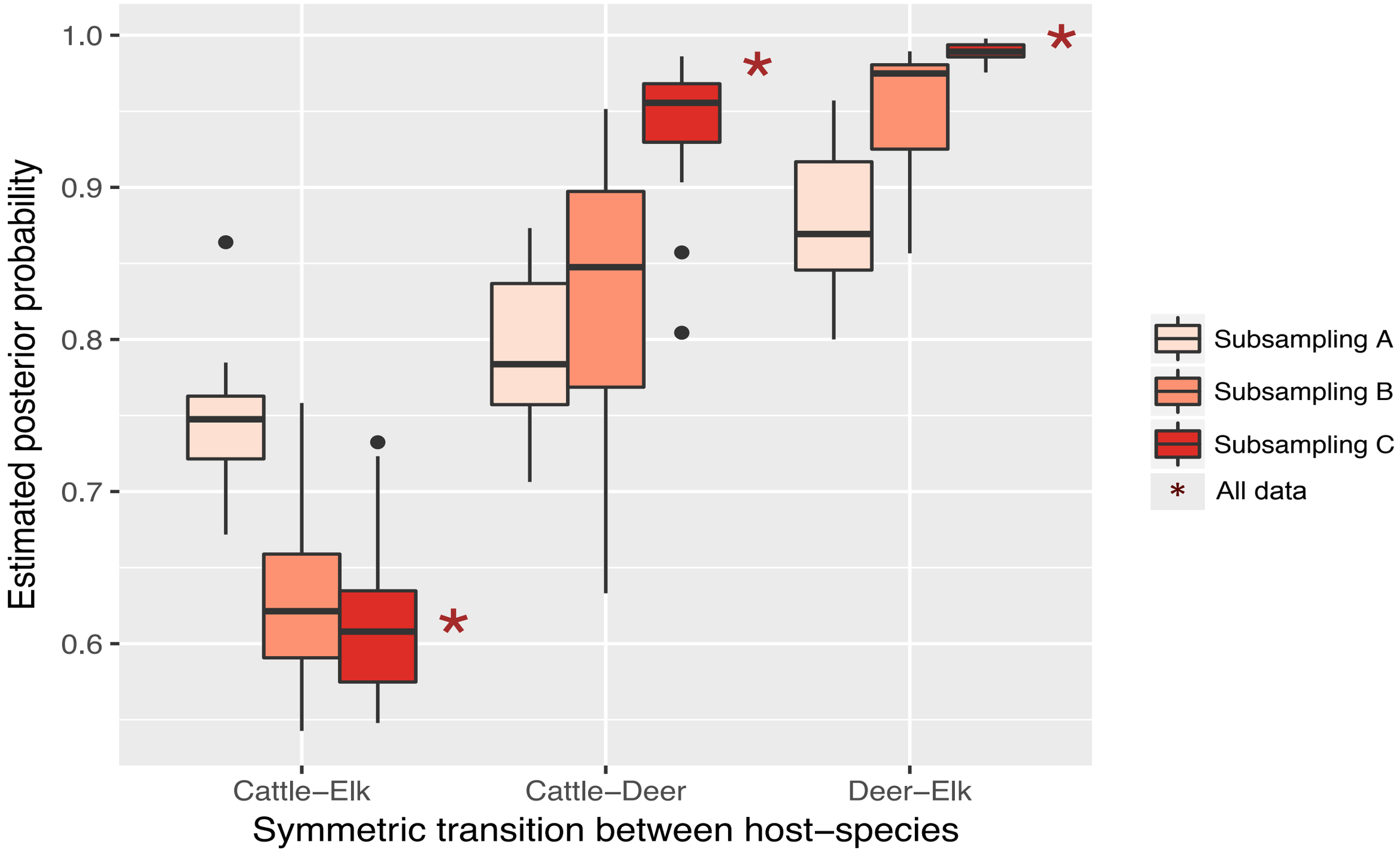


Host-species interaction	Estimated posterior probability of transition between host-species (symmetric)	Estimated absolute transition between host-species (event/genome/year)	Strength of support by Bayes' factor (BF > 3: well supported BF > 10: very strong support)
Cattle-Deer	**0.979**	**0.886**	**14.17** ✓
Cattle-Elk	0.617	0.897	0.49 X
Deer-Elk	**0.996**	**1.224**	**75.68** ✓

Sensitivity analysis 1: Host-species



Sensitivity analysis 2: sample size



Conclusions

- Four major clades with strong support that could not be distinguished from the others by sampling time, host-species, nor sampling area

Conclusions

- Mean estimated substitution rate consistent with other *M. tuberculosis* and *M. bovis* studies

Conclusions

- High possibility of intra-species transmission in the sampled elk, cattle and deer populations

Conclusions

- Strong support for inter-species transmission between deer and cattle, and deer and elk

Conclusions

- There is no support for transmission between cattle and elk

Elk in Michigan not a significant source of *M.bovis* infection and *M. bovis* infection most likely maintained by deer

Conclusions

Elk in Michigan not a significant source of *M.bovis* infection and *M. bovis* infection most likely maintained by deer

Many thanks for listening!

Liliana Salvador
liliana.salvador@glasgow.ac.uk
Boyd Orr Centre for Population and Ecosystem Health
IBAHCM, University of Glasgow