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


Bovine Tuberculosis Mini-Symposium

8 June 2017

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Cattle farms surrounded by deer habitat
Cattle farms surrounded by deer habitat
Bovine TB cases in deer

1975 - 2014 BOVINE TUBERCULOSIS SURVEY RESULTS
Michigan

- TB Positive Cattle Herds (n=64)
  - Beef (n=50)
  - Dairy (n=14)
- TB Positive Deer (n = 759)
- DMU 452
- County Lines

Population size in last 10 years: 1.7-2 million animals
Bovine TB cases in elk


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

Cross-species transmission parameters

How much and how often?

Is $\beta = \gamma = \alpha$?
Understanding the role of elk in bTB transmission

Isolates spatial locations
Understanding the role of elk in bTB transmission

Isolates spatial locations

Legend:
- Locations of Positive Deer (n=39 isolates)
- Locations of Positive Elk (n=5 isolates)
- Location of Positive Cattle Herds (n=9 isolates)
- Primary Elk Range
- County Lines

Michigan TB Positive Deer, Elk, and Cattle Isolates
Isolates spatial locations

Understanding the role of elk in bTB transmission
• 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

Sampling times of each clade

- **Clade 1**: 2000-2013
- **Clade 2**: 2000-2013
- **Clade 3**: 1997-2013
- **Clade 4**: 1999-2007

Substitution model: HKY (supported by jmodeltest), strict 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

<table>
<thead>
<tr>
<th>Source</th>
<th>Bacteria species</th>
<th>mean clock rate/genome/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Walker et. al. 2013</td>
<td><em>M. Tuberculosis</em></td>
<td>0.50 [0.30-0.70]</td>
</tr>
<tr>
<td>Bryant et al. 2013</td>
<td><em>M. Tuberculosis</em></td>
<td>0.30 [0.16-0.80]</td>
</tr>
<tr>
<td>Biek et al. 2012</td>
<td><em>M. bovis</em></td>
<td>0.15 [0.04-0.26]</td>
</tr>
<tr>
<td>Trewby et al. 2015</td>
<td><em>M. bovis</em></td>
<td>0.20 [0.10-0.30]</td>
</tr>
<tr>
<td>Crisp et al. 2017</td>
<td><em>M. bovis</em></td>
<td>0.59 [0.30-0.95]</td>
</tr>
<tr>
<td>Current study</td>
<td><em>M. bovis</em></td>
<td>0.41 [0.26-0.55]</td>
</tr>
</tbody>
</table>
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
Transition rate matrix (M):

\[
\begin{array}{ccc}
- & p_{ce} & - \\
p_{de} & - & p_{dc}
\end{array}
\]

- \(p_{ce}\), \(p_{de}\), \(p_{dc}\):
  - 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 4
Deer
### Pathogen transition between host-species

<table>
<thead>
<tr>
<th>Host-species interaction</th>
<th>Estimated posterior probability of transition between host-species (symmetric)</th>
<th>Estimated absolute transition between host-species (event/genome/year)</th>
<th>Strength of support by Bayes’ factor (BF &gt; 3: well supported; BF &gt; 10: very strong support)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle-Deer</td>
<td>0.979</td>
<td>0.886</td>
<td>14.17 (✓)</td>
</tr>
<tr>
<td>Cattle-Elk</td>
<td>0.617</td>
<td>0.897</td>
<td>0.49 (✗)</td>
</tr>
<tr>
<td>Deer-Elk</td>
<td>0.996</td>
<td>1.224</td>
<td>75.68 (✓)</td>
</tr>
</tbody>
</table>
Sensitivity analysis 1: Host-species

Symmetric transition between host–species

Estimated posterior probability

- Cattle–Deer
- Cattle–Elk
- Deer–Elk

Permutated data

Observed data

All data
Symmetric transition between host–species

Estimated posterior probability

Sensitivity analysis 2: sample size

- Subsampling A
- Subsampling B
- Subsampling C
- All data

Cattle–Elk
Cattle–Deer
Deer–Elk
Conclusions

- Four major clades with strong support that could not be distinguished from the others by sampling time, host-species, nor sampling area.
• 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
Strong support for inter-species transmission between deer and cattle, and deer and elk
Conclusions

- Four major clades with strong support that could not be distinguished from the others by sampling host-species, nor sampling area
- Mean estimated subtyping rate consistent with other *M. tuberculosis* and *M. bovis* studies
- High possibility of intra-species transmission in the sampled elk, caribou, and deer populations
- Strong support for inter-species transmission between deer and caribou, and deer and elk
- 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
Elk in Michigan not a significant source of *M. bovis* infection and *M. bovis* infection most likely maintained by deer
Many thanks for listening!

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