

**Transmission network reconstruction for foot-and-mouth disease outbreaks incorporating farm-level covariates (Supplementary Materials)**

Simon M. Firestone<sup>1\*</sup>, Yoko Hayama<sup>2</sup>, Max S. Y. Lau<sup>3</sup>, Takehisa Yamamoto<sup>2</sup>, Tatsuya Nishi<sup>4</sup>, Richard A. Bradhurst<sup>5</sup>, Haydar Demirhan<sup>6</sup>, Mark A. Stevenson<sup>1</sup>, Toshiyuki Tsutsui<sup>2</sup>

<sup>1</sup> Melbourne Veterinary School, Faculty of Veterinary and Agricultural Sciences, The University of Melbourne, Parkville, VIC 3010, Australia

<sup>2</sup> Viral Disease and Epidemiology Research Division, National Institute of Animal Health, National Agriculture Research Organization, Tsukuba, Ibaraki 305-0856, Japan

<sup>3</sup> Department of Biostatistics and Bioinformatics, Rollins School of Public Health, Emory University, Atlanta, Georgia, United States of America

<sup>4</sup> Exotic Disease Research Station, National Institute of Animal Health, National Agriculture and Food Research Organization, Kodaira, Tokyo, 187-0022, Japan

<sup>5</sup> Centre of Excellence for Biosecurity Risk Assessment, The University of Melbourne, Parkville, VIC 3010, Australia

<sup>6</sup> Mathematical Sciences Discipline, School of Science, RMIT University, Melbourne, VIC 3000, Australia

\* Corresponding author: [simon.firestone@unimelb.edu.au](mailto:simon.firestone@unimelb.edu.au)

## S1 Simulated outbreak datasets: data and parameterisation

All simulated datasets are available here: <https://doi.org/10.26188/5cf5e3af414a8>

In accordance with data-sharing agreements for AADIS and the Miyazaki 2010 FMD outbreak dataset, random noise has been added to the coordinates of the farms in the datasets made publicly available.

### Sellke threshold simulated FMD outbreaks in Japan (runs J1–J3)

Run	J1	J2	J3	Reference/comment
<i>n</i>	100	200	400	Assumed outbreak size
<i>n</i> (infected)	80	166	200	Testing variety of scenarios
<i>nt</i>	7667	7667	7667	Genome length (nucleotides)
<i>t_max</i>	100	100	100	Maximum length of outbreak (days)
$\alpha$	4.00E-05	4.00E-05	5.00E-06	Adjusted to scale background transmission
$\beta$	0.085	0.09	6.00E-04	Adjusted to scale $\beta_{ij}$ and n(infected)
$\mu_1$	2.00E-05	1.50E-05	3.00E-05	Cottam et al (2008)
$\mu_2$	2.00E-06	1.00E-06	5.00E-06	Cottam et al (2008) & Juleff et al (2013)
<i>a</i>	8	8	8	Alexandersen et al (2003) & Haydon et al (2003)
<i>b</i>	0.5	0.5	0.5	
<i>c</i>	15	12	21	Little prior information
$\kappa$ (power law)	1.7	1	2	Bouma et al (2003)
<i>p</i>	0.1	0.1	0.2	Little prior information
$\phi_{pigs}$	20	4	10	Alexandersen et al (2003)
$\phi_{other}$	3	3	1	
$\rho_{pigs}$	0.1	0.1	0.5	
$\rho_{other}$	0.5	0.5	0.1	
<i>v</i>	0.1	0.1	0.8	
$\tau$	0.03	0.03	0.01	
Proportion of cattle farms	0.33	0.6	0.5	
Proportion of pig farms	0.33	0.1	0.3	
Proportion of other farms	0.33	0.4	0.2	
Herd size, median (range)	279 (8, 7862)	288 (11, 5130)	277 (6, 10186)	

### **AADIS simulated FMD outbreaks in Australia (runs A1–A3)**

In brief, they included n=98, 100 and 298 infected premises, respectively, and were constructed using the Australian Animal Disease Spread (AADIS) hybrid model's baseline configuration, with movement restrictions and a stamping out only policy (i.e., no vaccination), each seeded on a large pig farm in central Victoria, Australia (Bradhurst et al., 2015). Molecular sequence evolution was forwards simulated from a most recent common ancestor at the seed premises, designated with the 7667 nucleotide whole genome consensus sequence (O/JPN/2010-6/1S) sampled from the first farm presumed to be infected in the 2010 outbreak of foot-and-mouth disease in Miyazaki Prefecture of Japan (Nishi et al., 2017). Phylogenies were simulated with VirusTreeSimulator and SeqGen version 1.3.3 (Rambaut and Grass, 1997), parameterised based on empirical observations from the 2001 outbreak of FMD in the UK (Cottam et al., 2006, Cottam et al., 2008) and 2010 outbreak in Japan (Nishi et al., 2017).

### **References**

- Bradhurst, R. A., S. E. Roche, I. J. East, P. Kwan and M. G. Garner, 2015: A hybrid modeling approach to simulating foot-and-mouth disease outbreaks in Australian livestock. *Frontiers in Environmental Science*, 3, 17.
- Cottam, E. M., D. T. Haydon, D. J. Paton, J. Gloster, J. W. Wilesmith, N. P. Ferris, G. H. Hutchings and D. P. King, 2006: Molecular epidemiology of the foot-and-mouth disease virus outbreak in the United Kingdom in 2001. *J. Virol.*, 80, 11274-11282.
- Cottam, E. M., G. Thébaud, J. Wadsworth, J. Gloster, L. Mansley, D. J. Paton, D. P. King and D. T. Haydon, 2008: Integrating genetic and epidemiological data to determine transmission pathways of foot-and-mouth disease virus. *Proc. R. Soc. Lond. B Biol. Sci.*, 275, 887-895.
- Nishi, T., M. Yamada, K. Fukai, N. Shimada, K. Morioka, K. Yoshida, K. Sakamoto, T. Kanno and M. Yamakawa, 2017: Genome variability of foot-and-mouth disease virus during the short period of the 2010 epidemic in Japan. *Vet Microbiol.*, 199, 62-67.
- Rambaut, A. and N. C. Grass, 1997: Seq-Gen: an application for the Monte Carlo simulation of DNA sequence evolution along phylogenetic trees. *Bioinformatics*, 13, 235-238.

## Supplementary Materials, S2

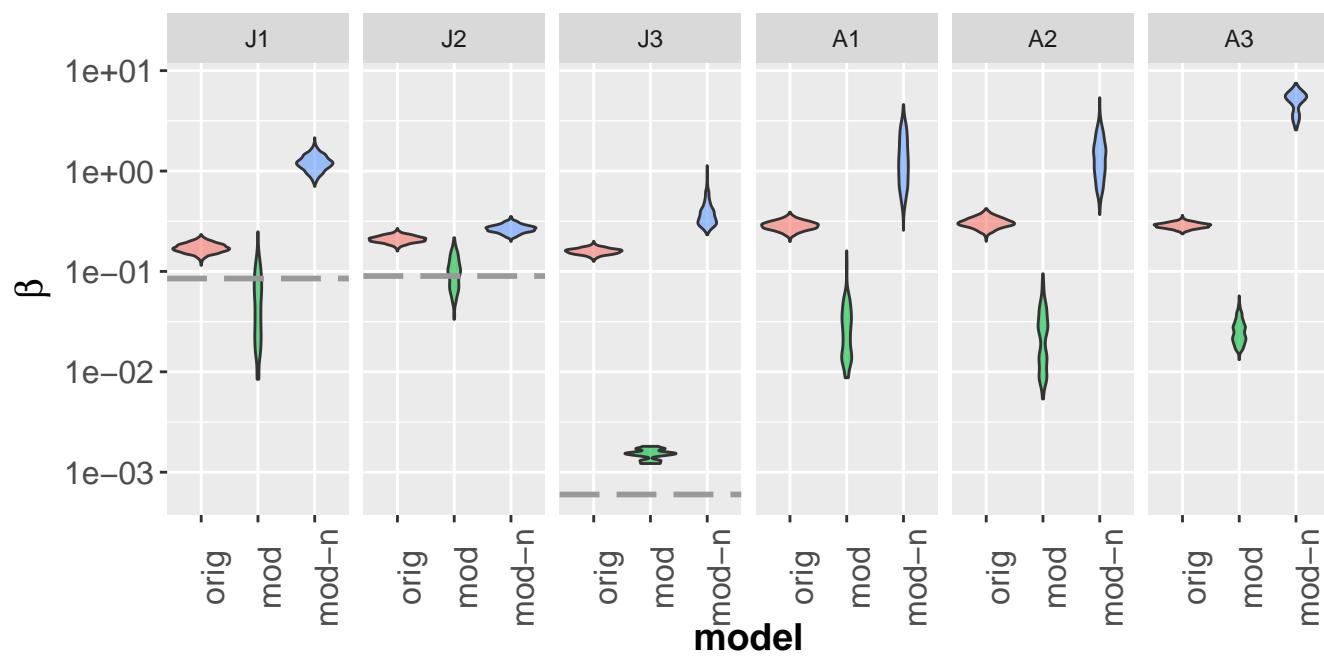
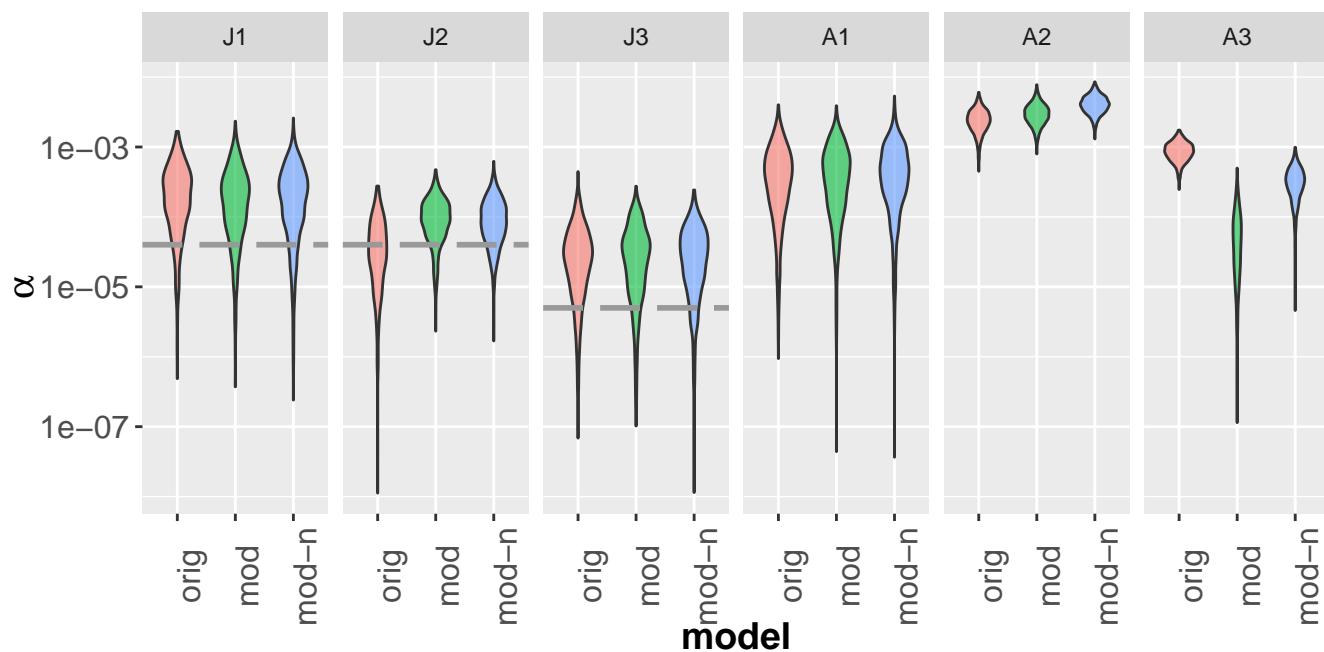
**Table S2: Comparison of the accuracy of inferences of Lau's joint Bayesian inference of the transmission network and two modified models, for six simulated outbreaks of foot-and-mouth disease in Japan and Australia, detailed by run.**

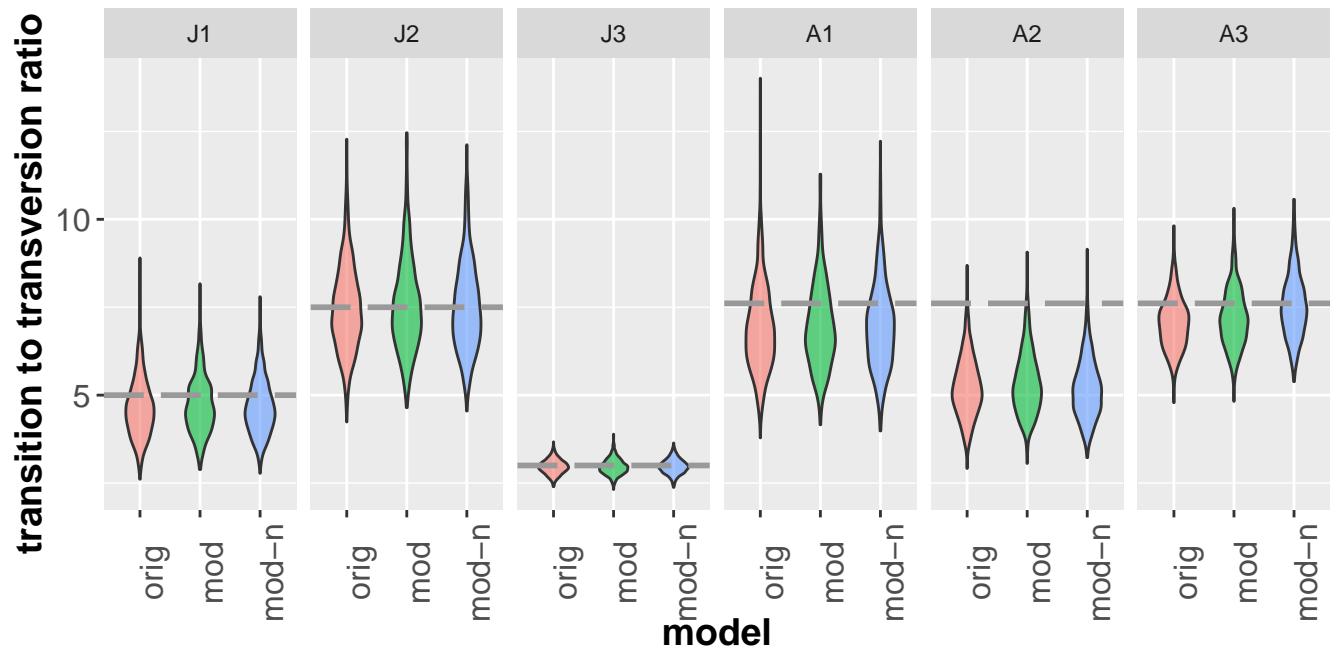
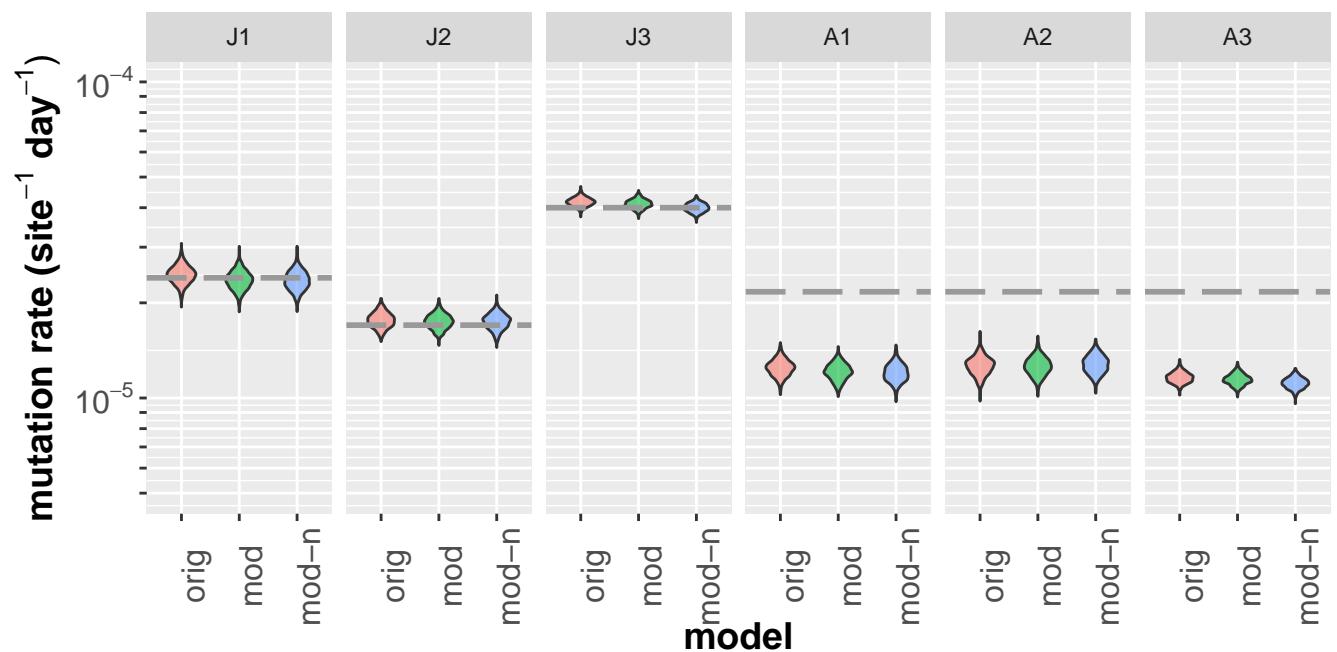
Run <sup>a</sup>	Model <sup>b</sup>	Accuracy <sup>c</sup>		
		Overall (%)	>50% support (%)	>80% support (%)
J1	original	80/100 (80)	78/88 (89)	62/66 (94)
	extended	85/100 (85)	83/92 (90)	76/79 (96)
	extended (norm)	84/100 (84)	82/91 (90)	77/81 (95)
J2	original	159/200 (80)	149/167 (89)	126/129 (98)
	extended	170/200 (85)	158/174 (91)	134/138 (97)
	extended (norm)	167/200 (84)	156/173 (90)	135/142 (95)
J3	original	357/400 (89)	334/348 (96)	287/289 (99)
	extended	376/400 (94)	357/367 (97)	326/327 (99)
	extended (norm)	372/400 (93)	359/370 (97)	331/332 (99)
A1	original	77/98 (79)	71/83 (86)	54/60 (90)
	extended	83/98 (85)	81/88 (92)	63/69 (91)
	extended (norm)	84/98 (86)	80/88 (91)	56/59 (95)
A2	original	74/100 (74)	70/93 (75)	48/57 (84)
	extended	77/100 (77)	74/92 (80)	53/56 (95)
	extended (norm)	75/100 (75)	74/98 (76)	57/67 (85)
A3	original	222/298 (75)	206/248 (83)	152/169 (90)
	extended	227/298 (76)	217/252 (86)	164/173 (95)
	extended (norm)	226/298 (76)	215/254 (85)	162/171 (95)

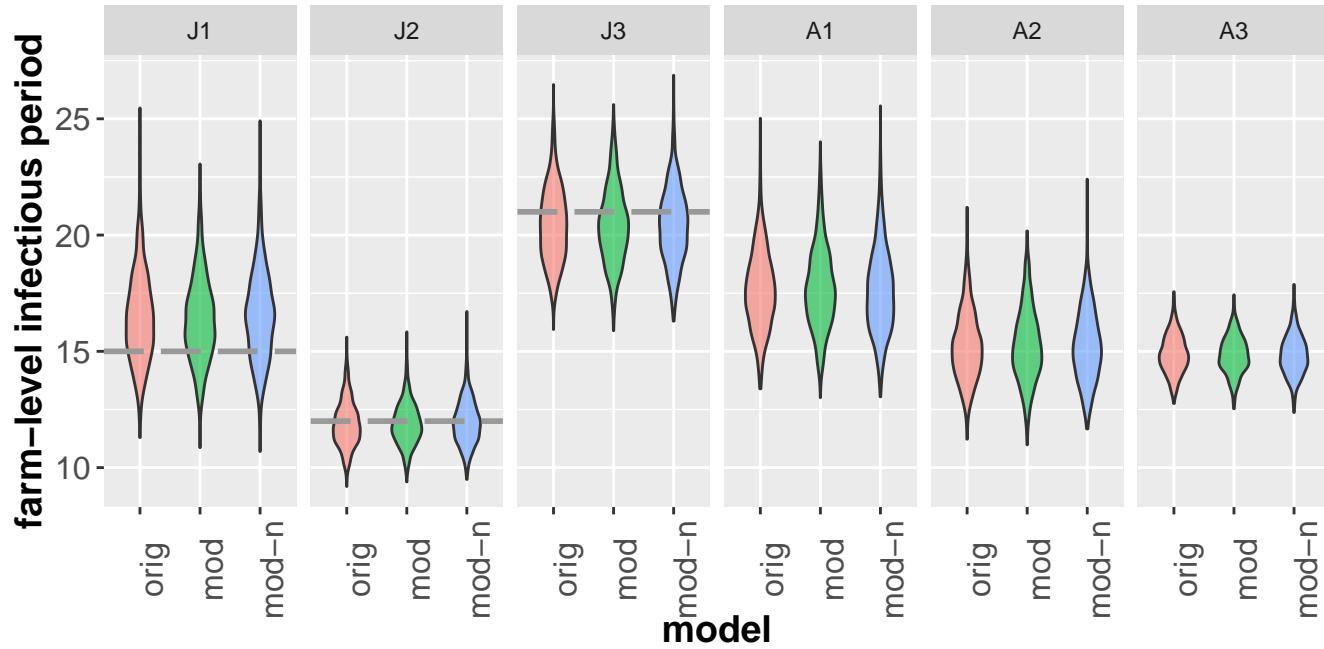
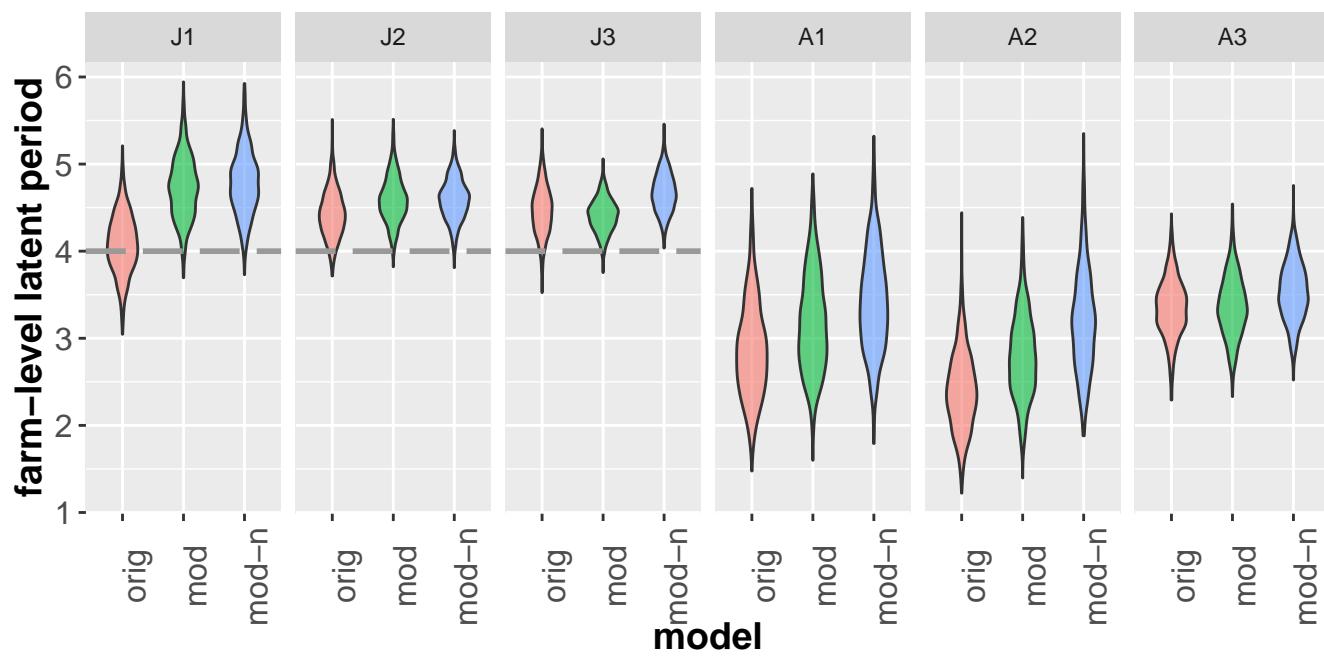
norm = normalised; IP = infected premises. <sup>a</sup> Runs J1, J2 and J3 were FMD outbreaks in Miyazaki Prefecture of Japan simulated in the same framework as the Extended model. Runs A1, A2, A3 were FMD outbreaks in south-eastern Australia simulated in using the Australian Animal Disease Simulation (AADIS) model (Bradhurst et al., 2015). <sup>b</sup> The original model is as described in (Lau et al., 2015, Firestone et al., provisionally accepted for publication). The extended model incorporated additional terms for farm level transmissibility and susceptibility based on farm type and number of animals. The extended (norm) model incorporated the same terms, with normalisation by mean transmissibility and susceptibility of all farms. <sup>c</sup> Accuracy was defined as the proportion of IPs for which the model-predicted most likely source (highest likelihood or most posterior support) was the true source. The denominator for accuracy at >50% and >80% support includes only those IPs for which the model-predicted most likely source attained that level of likelihood or posterior support.

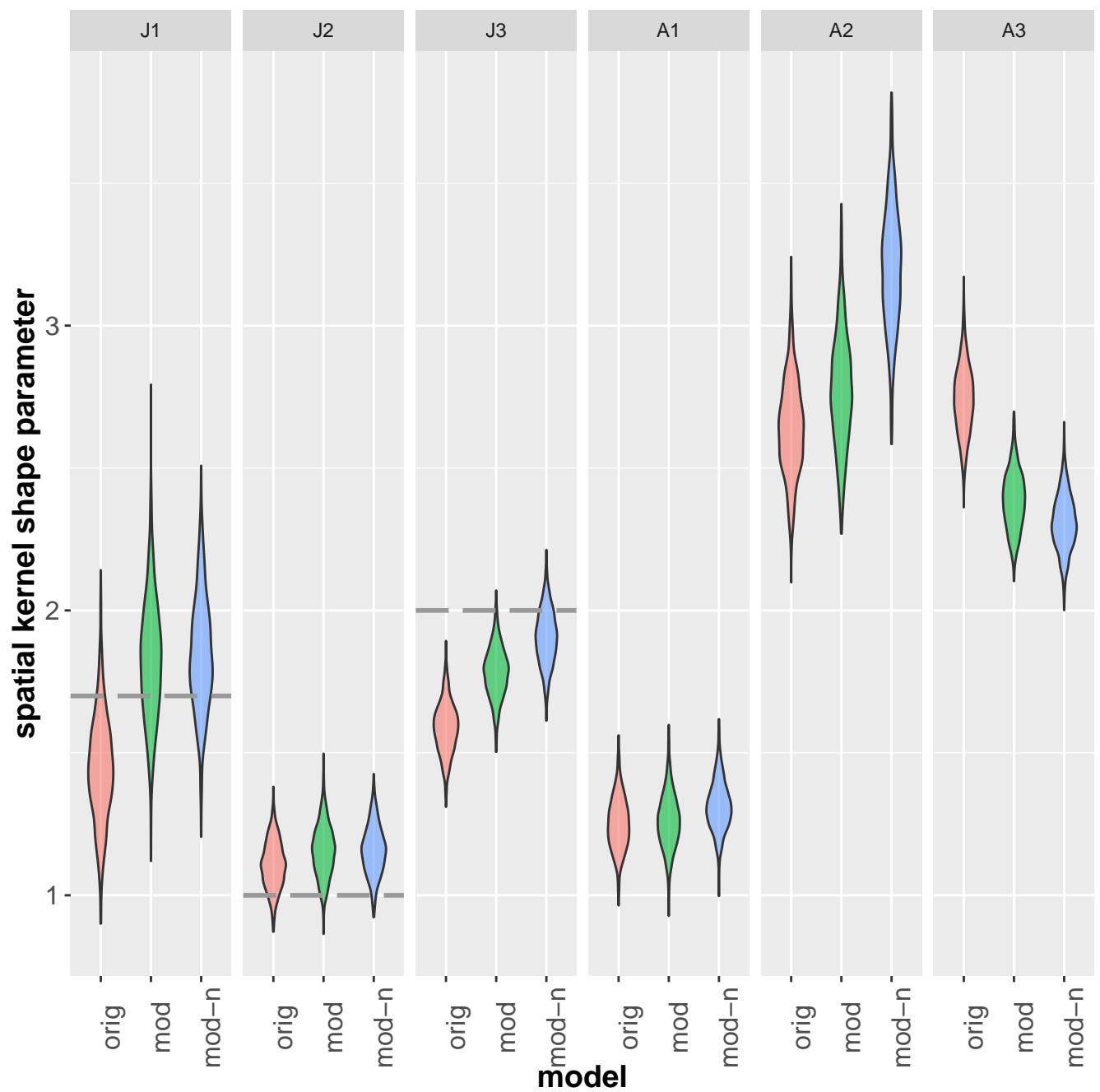
## References

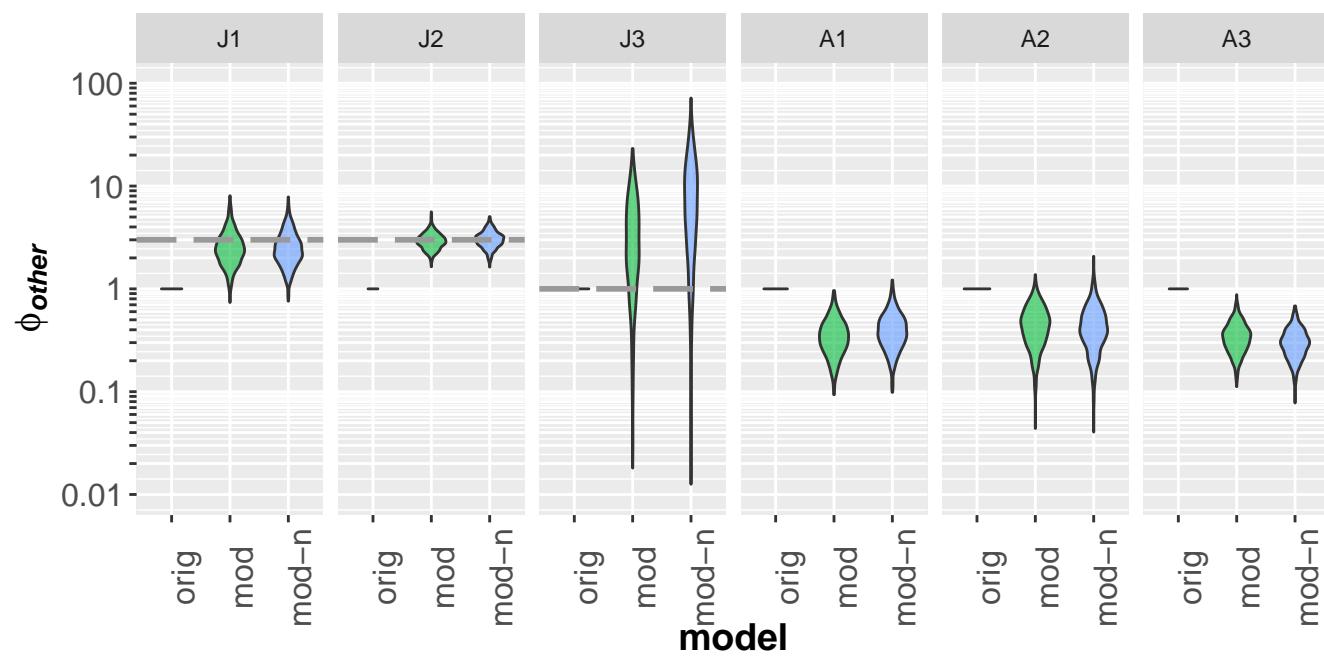
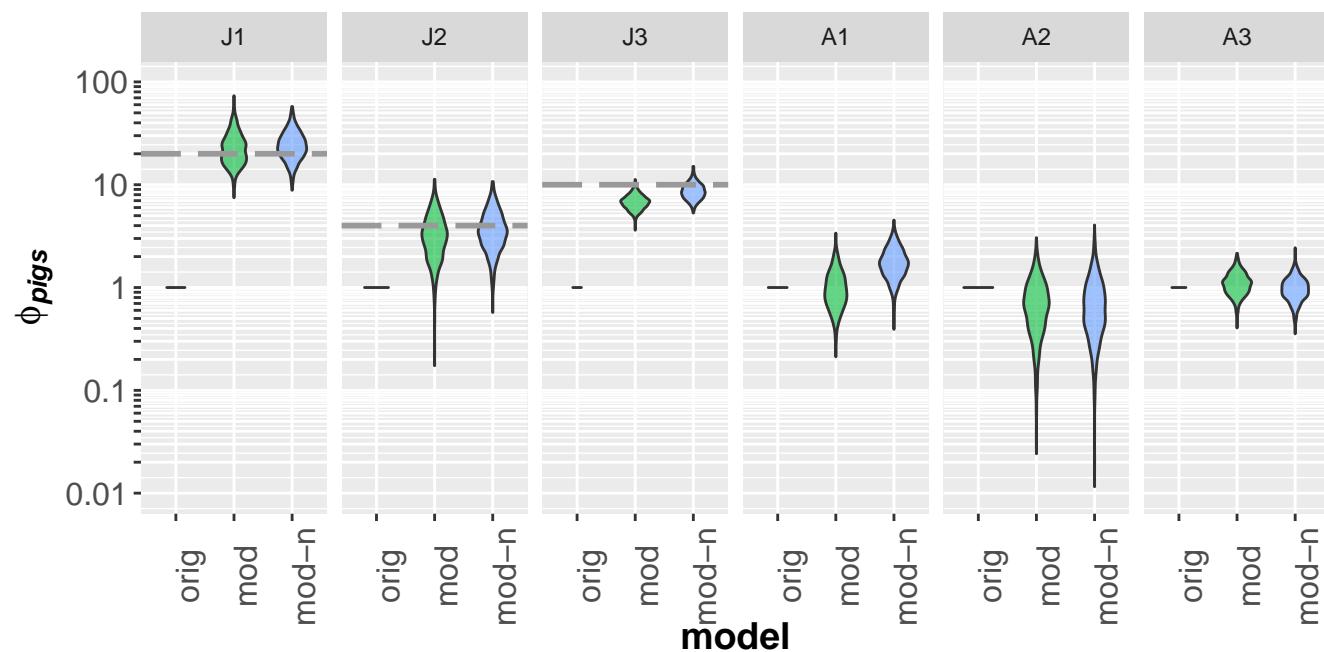
- Bradhurst, R. A., S. E. Roche, I. J. East, P. Kwan and M. G. Garner, 2015: A hybrid modeling approach to simulating foot-and-mouth disease outbreaks in Australian livestock. *Frontiers in Environmental Science*, 3, 17.
- Firestone, S. M., Y. Hayama, R. A. Bradhurst, T. Yamamoto, T. Tsutsui and M. A. Stevenson, provisionally accepted for publication: Reconstructing outbreaks: a methods comparison of transmission network models. *Sci. Rep.*
- Lau, M. S., G. Marion, G. Streftaris and G. Gibson, 2015: A systematic Bayesian integration of epidemiological and genetic data. *PLoS Comput. Biol.*, 11, e1004633.

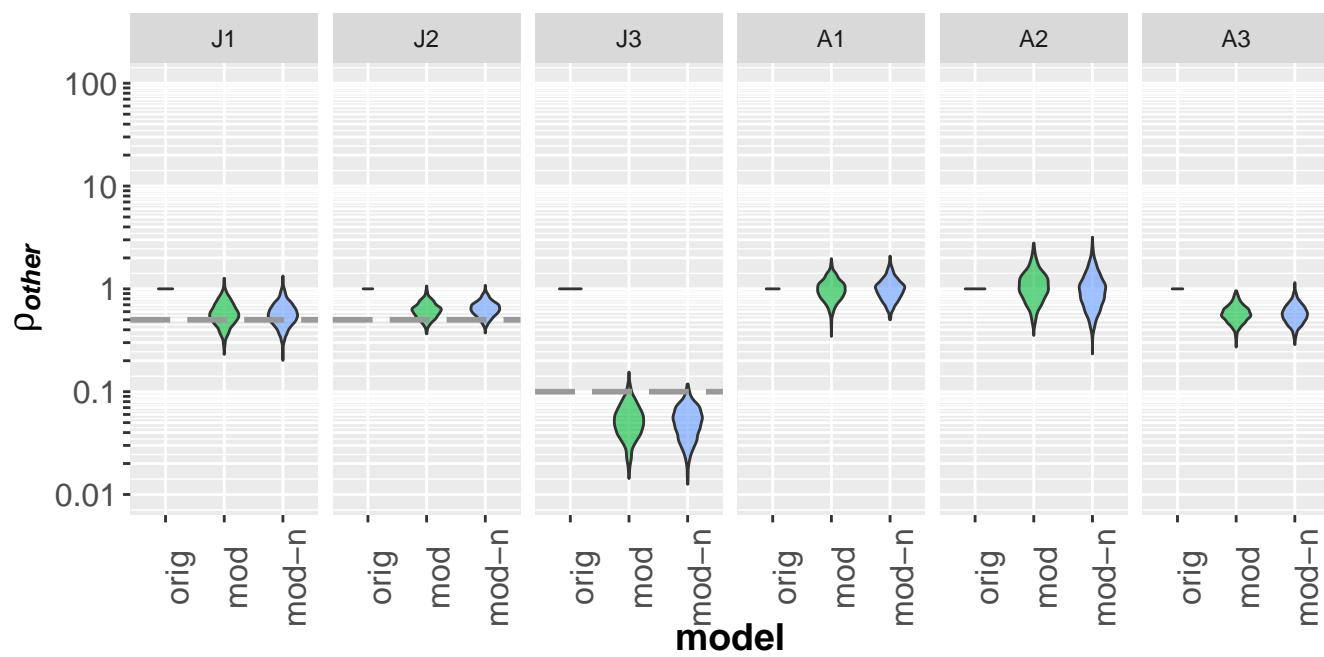
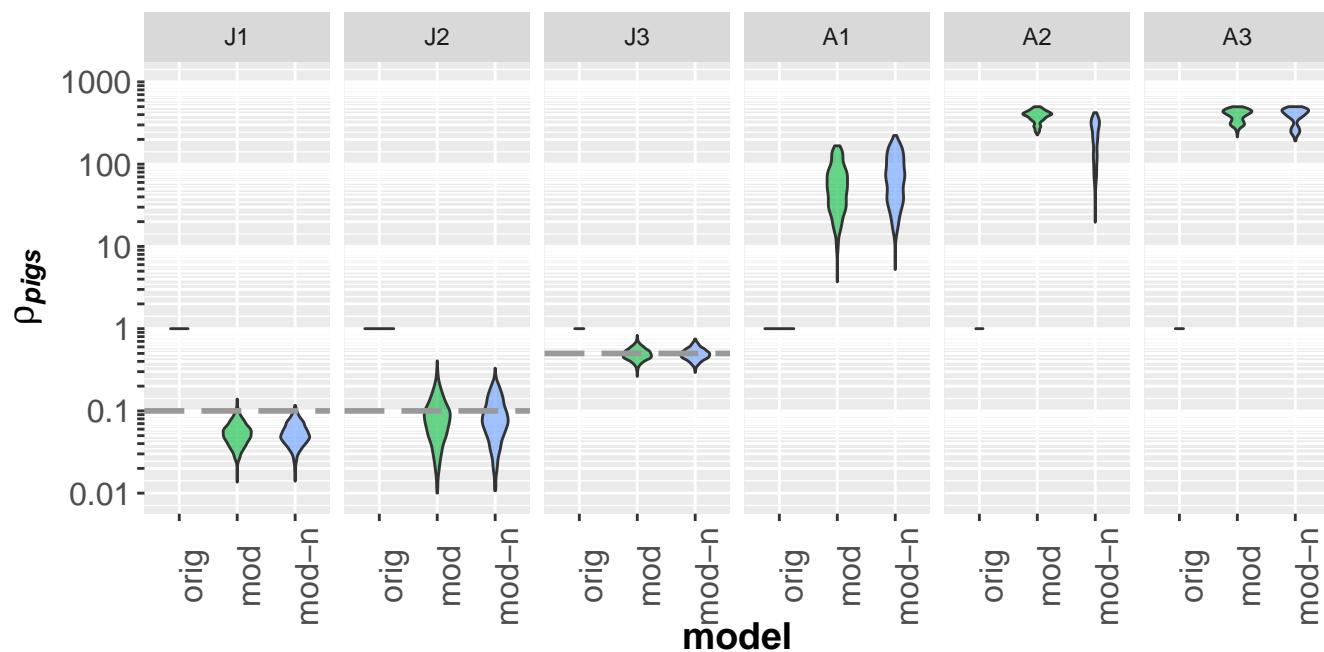


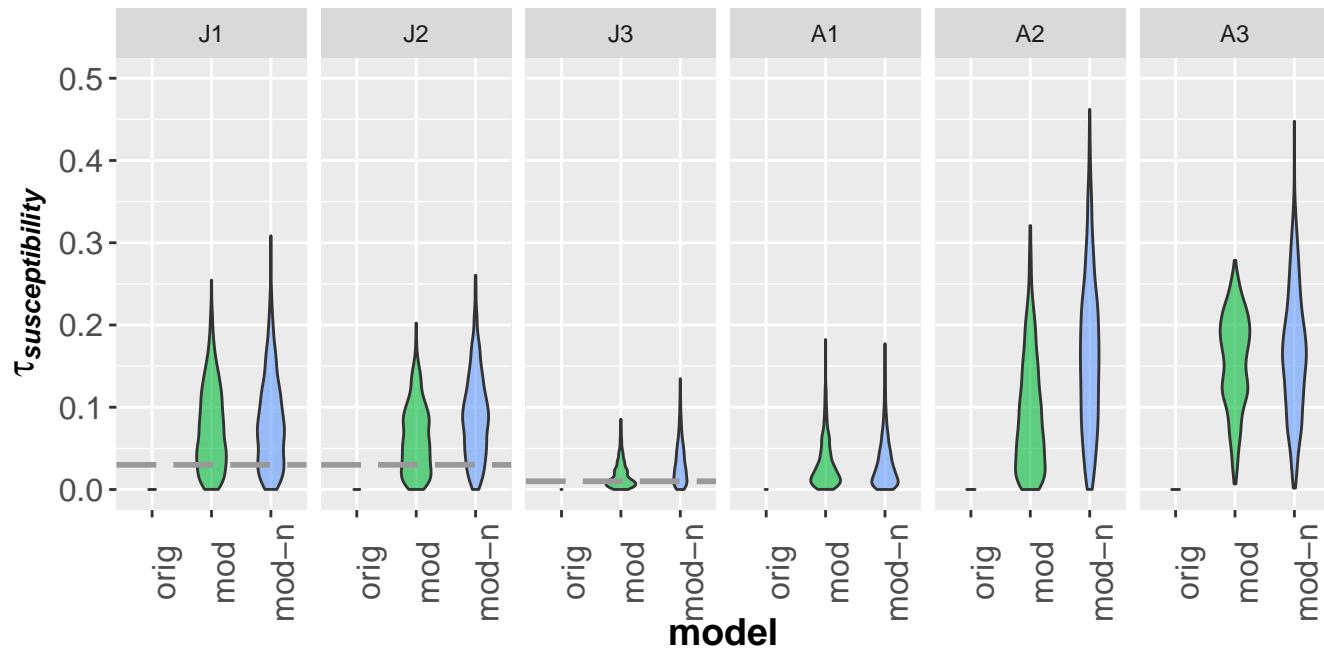
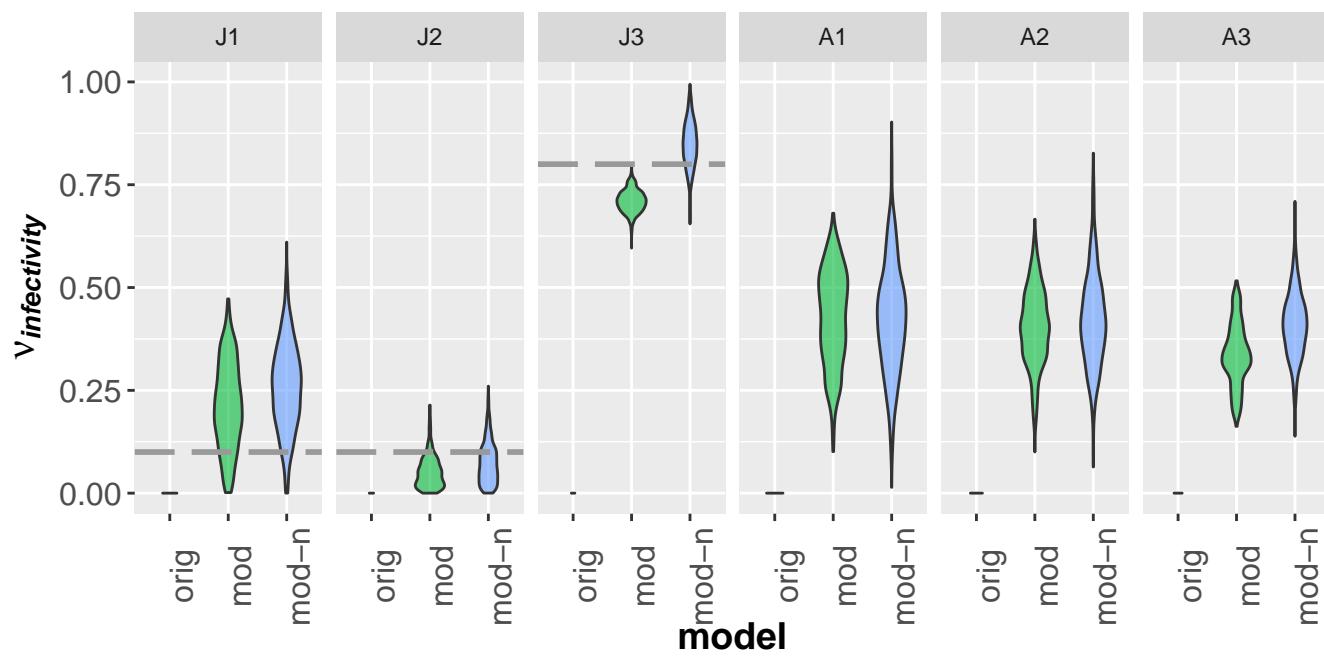












**S4 Nucleotide substitution model fit, FMD JPN 2010**

Model	Parameters	BIC	AICc	InL	I	G	TsTv	Freq A	Freq T	Freq C	Freq G
TN93+G	211	28855.92837	26413.74145	-12995.81381 n/a		0.130200216	9.076621971	0.25267511	0.207517529	0.282105132	0.25770223
TN93+G+I	212	28864.53158	26410.77085	-12993.32797	0.658211802	1.128512764	9.078792105	0.25267511	0.207517529	0.282105132	0.25770223
TN93+I	211	28874.867	26432.68008	-13005.28312	0.48313269 n/a		9.054655315	0.25267511	0.207517529	0.282105132	0.25770223
HKY+G	210	28884.22187	26453.60876	-13016.748 n/a		0.091456744	9.078205262	0.25267511	0.207517529	0.282105132	0.25770223
TN93	210	28886.71381	26456.1007	-13017.99397 n/a	n/a		9.039801569	0.25267511	0.207517529	0.282105132	0.25770223
HKY+G+I	211	28891.65401	26449.46709	-13013.67663	0.6945073	1.117198154	9.088293207	0.25267511	0.207517529	0.282105132	0.25770223
T92+G	208	28891.89381	26484.42833	-13034.15885 n/a		0.098889927	9.05254026	0.230096319	0.230096319	0.269903681	0.269903681
GTR+G	214	28895.57441	26418.66609	-12995.2745 n/a		0.130759886	7.514631099	0.25267511	0.207517529	0.282105132	0.25770223
T92+G+I	209	28899.50321	26480.46392	-13031.17612	0.688643473	1.117986426	9.056165217	0.230096319	0.230096319	0.269903681	0.269903681
GTR+G+I	215	28904.0168	26415.53469	-12992.70825	0.65793394	1.129782672	7.538650152	0.25267511	0.207517529	0.282105132	0.25770223
HKY+I	210	28906.01982	26475.40671	-13027.64698	0.48313269 n/a		9.049551648	0.25267511	0.207517529	0.282105132	0.25770223
GTR+I	214	28911.50824	26434.59991	-13003.24141	0.48313269 n/a		8.178632638	0.25267511	0.207517529	0.282105132	0.25770223
T92+I	208	28913.13531	26505.66983	-13044.7796	0.48313269 n/a		9.042822042	0.230096319	0.230096319	0.269903681	0.269903681
HKY	209	28918.7708	26499.73151	-13040.80991 n/a	n/a		9.03912873	0.25267511	0.207517529	0.282105132	0.25770223
T92	207	28925.68408	26529.79243	-13057.84143 n/a	n/a		9.03906144	0.230096319	0.230096319	0.269903681	0.269903681
GTR	213	28926.36894	26461.03442	-13017.45921 n/a	n/a		7.460939873	0.25267511	0.207517529	0.282105132	0.25770223
K2+G	207	28926.5078	26530.61616	-13058.25329 n/a		0.096171882	9.054583311	0.25	0.25	0.25	0.25
K2+G+I	208	28934.03521	26526.56974	-13055.22956	0.690861506	1.115134899	9.059015367	0.25	0.25	0.25	0.25
K2+I	207	28947.95835	26552.06671	-13068.97857	0.48313269 n/a		9.043104122	0.25	0.25	0.25	0.25
K2	206	28960.5753	26576.25749	-13082.07449 n/a	n/a		9.039041382	0.25	0.25	0.25	0.25
JC+G	206	29309.27585	26924.95803	-13256.42476 n/a		0.096748703	0.5	0.25	0.25	0.25	0.25
JC+G+I	207	29316.84345	26920.9518	-13253.42112	0.690282044	1.116562183	0.5	0.25	0.25	0.25	0.25
JC+I	206	29330.67429	26946.35648	-13267.12398	0.48313269 n/a		0.5	0.25	0.25	0.25	0.25
JC	205	29343.27176	26970.52778	-13280.21016 n/a	n/a		0.5	0.25	0.25	0.25	0.25

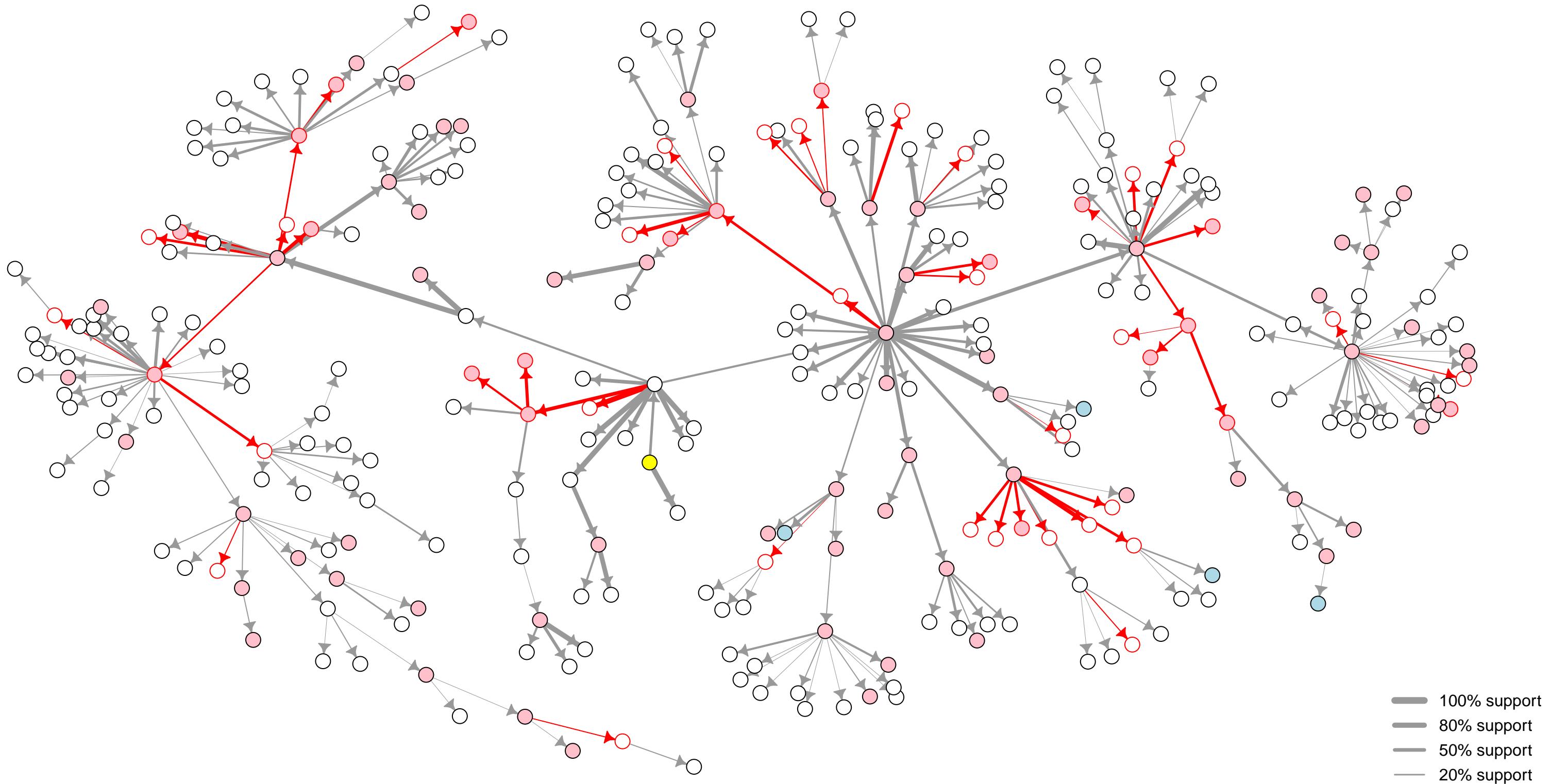
All positions containing gaps and missing data were eliminated. There were a total of 7559 positions in the final dataset. Evolutionary analyses were conducted in MEGA7<sup>1,2</sup>.

Abbreviations: Bayesian Information Criterion (BIC); Akaike Information Criterion corrected (AICc); Maximum negative log Likelihood value (InL); Proportion invariant (I); Discretised Gamma distribution shape parameter (G); Transition to transversion ratio (TsTv); Empirically estimated frequencies

References

1. Nei M. and Kumar S. (2000). Molecular Evolution and Phylogenetics. Oxford University Press, New York.
2. Kumar S., Stecher G., and Tamura K. (2016). MEGA7: Molecular Evolutionary Genetics Analysis version 7.0 for bigger datasets. Molecular Biology and Evolution 33:1870-1874.

Lau model (original) inferred transmission network in arbitrary space,  
differences from modified network in red.



Lau model (modified, normalised) inferred transmission network in arbitrary space,  
differences from modified network in red.

