Supplementary Material

Parameterization of the Durations of Phases of Foot-And-Mouth Disease in Cattle

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Supplementary Table S1: Details of the experiments included in this study, conducted at the USDA ARS Plum Island Animal Disease Center during 2011-2016 to accomplish various objectives related to the pathogenesis of the foot-and-mouth disease in cattle.

Studies	Virus strains	Exposure routes	Number of cattle	Inoculation dose	Contact challenge time points
(Pacheco et al., 2016b)	O/SKR/2010	Intra-dermal lingual inoculation	2	10^5.3 PFU	NA
		Cattle to cattle contact	4	NA	24 hpi*
		Pig to cattle contact	4		48 hpi
(Pacheco et al., 2016a)	A24 Cruzeiro	Pig to cattle contact	8	NA	48 hpi
		Intradermal lingual inoculation	2	10^4 TCID50	NA
		Intra-nasopharyngeal inoculation	5	10^5 BTID50	
			2	10^7 TCID50	
		Cattle to cattle contact	2	NA	

	Asia1 Shamir	Intra-dermal lingual inoculation	2	10^4 TCID50	NA
		Intra-nasopharyngeal inoculation	2	10^6 BTID50	
			2	10^7 BTID50	
		Cattle to cattle contact	2	NA	24 hpi
		Pig to cattle contact	4	NA	48 hpi
	O1 Manisa	Intra-nasopharyngeal inoculation	3	10^6 BTID50	
		Pig to cattle contact	4	NA	48 hpi
(Stenfeldt et al., 2016)	A24 Cruzeiro	Intra-nasopharyngeal inoculation	20	10^5 BTID50	NA
			2	10^6 BTID50	
(Stenfeldt et al., 2015)	A24 Cruzeiro	Intra-nasopharyngeal inoculation	10	10^5 BTID50	NA
(Stenfeldt et al., 2018b)	A24 Cruzeiro	Pig to cattle contact	10	NA	48 hpi
(Stenfeldt et al., 2018a)	O1Campos	Aerosol inoculation	8	10^7 PFU	
(Pacheco et al., 2013)	O1Campos	Aerosol inoculation	3	10^7 PFU	

*****hpi – hour post inoculation

Supplementary Table S2: Descriptive statistics for the incubation phase, latent phase, subclinical infectious phase, clinical infectious phase and total infectious phase duration due to FMD virus strains and serotypes from non-censored cattle. n is the number of cattle in each of the category.

Serotypes	Strains	Threshold-defined approach		Non-threshold approach	
		n	Mean, median 25^{th},75^{th} percentile)	n	Mean, median (25^{th},75^{th} percentile)
Incubation phase					
Pan-serotype	All	88	3.5, 3 (3, 4)	89	3.6, 3 (3, 4)
O	All	22	3, 3 (2, 3)	22	3, 3 (2, 3)
	O/SKR/2010	10	3, 3 (2, 3)	10	3, 3 (2, 3)
	O1Manisa	5	2.6, 2 (2, 2)	5	2.6, 2 (2, 2)
	O1Campos	7	3.3, 3 (3, 3.5)	7	3.3, 3 (3, 3.5)
Asia1	Asia1 Shamir	12	3.2, 3 (2, 4)	12	3.2, 3 (2, 4)
A	A24 Cruzeiro	54	3.8, 4 (3, 4.8)	55	3.9, 3.8 (3, 4)
Latent phase					

Pan-serotype	All	99	1.2, 1 (1, 1)	101	1.1, 1 (1, 1)
O	All	26	1.4, 1 (1, 2)	28	1.1, 1 (1, 1)
	O/SKR/2010	10	1.4, 1 (1, 1)	10	1.6, 2 (1, 2)
	O1Manisa	7	1.6, 2 (1, 2)	7	1.6, 2 (1, 2)
	O1Campos	9	1, 1 (1, 1)	11	1.1, 1 (1, 1)
Asia1	Asia1 Shamir	12	1.3, 1 (1, 2)	12	1.2, 1 (1, 1)
A	A24 Cruzeiro	61	1, 1 (1, 1)	61	1.1, 1 (1, 1)
Subclinical infectious phase					
Pan-serotype	All	90	2.4, 2 (1, 3)	91	2.5, 2 (1.5, 3)
O	All	22	1.7, 2 (1, 2)	23	1.9, 2 (1, 2)
	O/SKR/2010	10	1.6, 1 (1, 2)	10	2.1, 2 (1, 2)
	O1Manisa	5	1, 1 (0, 1)	6	1.2, 1 (0.3, 1.8)
	O1Campos	7	2.3, 2 (2, 2.5)	7	2.3, 2 (2, 2.5)
Asia1	Asia1 Shamir	12	1.8, 2 (1, 2.3)	12	2, 2 (1, 3)
A	A24 Cruzeiro	56	2.8, 3 (2, 3.3)	56	2.8, 3 (2, 4)
Clinical infectious phase					
Pan-serotype	All	42	7.1, 7 (5.3, 9)	40	8.6, 9 (6, 11)
O	All	14	6.6, 7 (4.3, 9)	13	8.5, 8 (6, 10)
	O/SKR/2010	9	5.8, 5 (4, 9)	8	8.3, 7 (5.8, 9.8)
	O1Manisa	2	7, 7 (7, 7)	2	6.5, 6.5 (6.3, 6.8)
	O1Campos	3	9, 10 (8.5, 10)	3	10.3, 10 (10,
Asia1	Asia1 Shamir	4	5.8, 6.5 (5.3, 7)	3	6, 6 (5.5, 6.5)
A	A24 Cruzeiro	24	7.5, 7 (6, 9.3)	24	9.4, 9.5 (6.8, 13)
Total infectious phase					
Pan-serotype	All	43	9.2, 9 (7, 12)	41	11.1, 11 (8, 13)
O	All	14	7.9, 7 (5.3, 10.5)	13	10.2, 11 (7, 13)
	O/SKR/2010	9	6.9, 6 (5, 9)	8	10, 9.5 (6.8, 11.8)
	O1Manisa	2	7, 7 (7, 7)	2	6.5, 6.5 (6.8,
	O1Campos	3	11.7, 13 (11, 13)	3	13, 13 (13, 13)
Asia1	Asia1 Shamir	4	7.8, 8.5 (7.3, 9)	3	8.3, 9 (8, 9)
A	A24 Cruzeiro	25	10.2, 9 (8, 13)	25	12, 13 (9, 16)

Supplementary Table S3: Descriptive statistics for the incubation phase, latent phase, subclinical infectious phase, clinical infectious phase and total infectious phase durations due to exposure methods from non-censored cattle. n is the number of cattle in each of the category.

Exposure methods	Threshold-defined approach		Non-threshold approach	
	n	Mean, median 25^{th}, 75^{th} percentile)	n	Mean, median (25^{th}, 75^{th} percentile)
Incubation phase				
All	88	3.5, 3 (3, 4)	89	3.6, 3 (3, 4)
Cattle to cattle contact	8	4.5, 5 (2.7, 6)	8	4.5, 5 (2.7, 6)
Pig to cattle contact	29	3.4, 3 (2, 4)	29	3.4, 3 (2, 4)
Intra-dermal lingual inoculation	6	1.5, 1.5 (1, 2)	6	1.5, 1.5 (1, 2)
Simulated natural inoculation	45	3.6, 3 (3, 4)	46	3.7, 3.5 (3, 4)
Latent phase				
All	99	1.2, 1 (1, 1)	101	1.1, 1 (1, 1)
Cattle to cattle contact	8	1.5, 1.5 (1, 2)	8	1.5, 1.5 (1, 2)
Pig to cattle contact	30	1, 1 (1, 1)	30	1.1, 1 (1, 1)
Intra-dermal lingual inoculation	6	1.2, 1 (1, 1)	6	1, 1 (1, 1)
Simulated natural inoculation	55	1.1, 1(1, 1)	57	1.1, 1 (1, 1)
Subclinical infectious phase				
All	90	2.4, 2 (1, 3)	91	2.5, 2 (1.5, 3)
Cattle to cattle contact	8	3, 3 (1.7, 4)	8	3, 3 (1.7, 4)
Pig to cattle contact	30	2.3, 2 (1, 3)	30	2.4, 2.5 (1, 3)
Intra-dermal lingual inoculation	6	0.3, 0 (0, 0)	6	0.7, 1 (0.25, 1)
Simulated natural inoculation	46	2.6, 2.5 (2, 3)	47	2.6, 2 (2, 3)
Clinical infectious phase				
All	42	7.1, 7 (5.3, 9)	40	8.6, 9 (6, 11)
Cattle to cattle contact	3	4.3, 5 (4, 5)	3	5, 5 (4.5, 5.5)
Pig to cattle contact	12	7.1, 7 (6, 9)	12	8.6, 8 (7, 9.2)
Intra-dermal lingual inoculation	3	5, 4 (4, 5.5)	1	6
Simulated natural inoculation	24	7.6, 7 (6, 10)	24	9.5, 10 (6, 13)
Total infectious phase				
All	43	9.2, 9 (7, 12)	41	11.1, 11 (8, 13)

Cattle to cattle contact	3	5.6, 6 (5, 6.5)	3	6.3, 6 (5.5, 7)
Pig to cattle contact	13	8.5, 8 (7, 9)	13	10.2, 9 (8, 11)
Intra-dermal lingual inoculation	3	5.6, 5 (4.5, 6.5)	1	7
Simulated natural inoculation	24	10.4, 9.5 (8, 13)	24	12.4, 13 (9, 16)

Supplementary Table S4. The distribution fit for the FMD phase durations obtained from the animal-level data and best-fit AFT model data for threshold-defined approach. The animal-level data are from the non-censored animals only.

Serotypes	Animal-level data		Model-predicted data	
	Continuous	Discrete	Continuous	Discrete
1. Incubation period				
Pan-serotype	Weibull(2.3,3.2)	**Binomial(8,0.4)	Logistic(4.1,0.4)	Binomial(6,0.7)
O	Lognormal(3.3,1.2)	Binomial(9,0.3)	Logistic(3.5,0.4)	**Binomial(5,0.73)
Asia1	Normal(3.2,1.1)	**Binomial(5,0.6)	Logistic(3.4,0.5)	**Binomial(5,0.7)
A	Normal(3.8,1.4)	**Binomial(7,0.5)	Logistic(4.4,0.2)	Binomial(6,0.77)
2. Latent duration				
Pan-serotype	Pert(1,1,3.5)	Binomial(3,0.4)	Pert(1.2,1.2,2.4)	Binomial(2,0.7)
O	Logistic(1.2,0.3)	Binomial(3,0.5)	Pert(1.4,1.5,2.4)	Binomial(2, 0.96)
Asia1	Normal(1.3,0.5)	**Binomial(2, 0.7)	Normal(1.4, 0.2)	Binomial(2, 0.8)
A	Pert(1,1,3.3)	Binomial(3,0.4)	Pert(1.2,1.2,1.7)	Binomial(2, 0.5)
3. Subclinical infectious duration				
Pan-serotype	Weibull(2,3.2)	**Poisson(2.4)	Weibull(6.8,4.6)	Binomial(5,0.6)
O	Logistic(1.6,0.7)	**Poisson(1.7)	Logistic(2.4,0.25)	Binomial(3,0.7)
Asia1	**Normal(1.8,0.9)	Binomial(3,0.6)	Logistic(2,0.3)	Binomial(3,0.66)
A	Logistic(2.7,0.8)	**Poisson(2.8)	Logistic(3.4,0.16)	Binomial(5,0.7)
4. Clinical infectious duration				
Pan-serotype	Pert(2.4,6.2,15.1)	**Poisson(7.07)	Pert(3.7,9.7,10)	Binomial(10,0.86)
O	**Normal(6.6,2.5)	**Poisson(6.6)	Pert(2.7,8.9,9)	Binomial(9,0.9)
*Asia1	Constant(5.8)	Constant(5.8)	Pert(3.2,9.9,10)	Binomial(10,0.86)
A	Pert(3.6,6.3,16.4)	**Poisson(7.5)	Normal(9.1,0.6)	Binomial(10,0.9)
5. Total infectious duration				
Pan-serotype	Pert(3.1,8.2,19)	**Poisson(9.2)	Normal(11.4,1.1)	Binomial(13,0.9)
O	Pert(4,4,26.3)	**Poisson(7.9)	Pert(6.8,10.7,10.7)	**Binomial(11,0.9)
*Asia1	Constant(7.8)	Constant(7.8)	Pert(6.4,11.9,12)	**Binomial(12,0.9)
A	Pert(7,7,25.6)	Poisson(10.16)	Pert(9.2,12.5,12.5)	Binomial(13,0.96)

* The data were not sufficient in number to derive a distribution. Constant distribution represents the mean durations for the respective virus serotypes.

**Anderson-Darling or Chi Square test showed a good fit (p>0.05).

Supplementary Table S5. The distribution fit for the FMD phase durations obtained from the animal-level data and best-fit AFT model data for non-threshold approach to define infectiousness. The animal-level data are from the non-censored animals only.

Serotypes	Animal-level data		Model-predicted data	
	Continuous	Discrete	Continuous	Discrete
1. Incubation duration				
The distribution fit for threshold was the same as the non-threshold defined infectiousness (Table 4).				
2. Latent duration				
Pan-serotype	Pert(1,1,3.2)	Binomial(3,0.4)	Logistic(1.3,0.07)	Binomial(2,0.5)
O	Logistic(1.05,0.14)	Binomial(2,0.57)	Logistic(1.3,0.09)	Binomial(2,0.6)
Asia1	Normal(1.3,0.5)	Poisson(1.3)	Logistic(1.2,0.1)	Binomial(2,0.6)
A	Pert(1,1,3.3)	Binomial(3,0.4)	Logistic(1.3,0.04)	Binomial (2,0.5)
3. Subclinical infectious duration				
Pan-serotype	Weibull(2.2,3.2)	Binomial(12,0.2)	Logistic(3.1,0.4)	Binomial(5,0.5)
O	Logistic(1.8,0.6)	Poisson(1.9)	Logistic(2.4,0.2)	Binomial(3,0.7)
Asia1	Normal(2,0.85)	**Binomial(3,0.66)	Normal(2.6,0.9)	Binomial(3,0.8)
A	Normal(2.8,1.5)	**Poisson(2.8)	Normal(3.4, 0.4)	Binomial(5,0.6)
4. Clinical infectious duration				
Pan-serotype	**Normal(8.8,3.4)	**Poisson(8.8)	Logistic(11.3,0.7)	Binomial(15,0.74)
O	**Normal(8.5,3.3)	**Poisson(8.5)	Logistic(10.4,0.9)	Binomial(15,0.68)
*Asia1	*Constant(6)	*Constant(6)	Logistic(10.7,1.1)	Binomial(17,0.63)
A	**Normal(9.4,3.5)	Poisson(9.4)	Logistic(11.6,0.3)	Binomial(15,0.8)
5. Total infectious duration				
Pan-serotype	Pert(4.6,8.8,26.3)	**Poisson(11.1)	Logistic(13.9,0.7)	Binomial(15,0.9)
O	**Normal(10.2,3.4)	**Poisson(10.2)	Logistic(12.9,0.6)	Binomial(14,0.9)
*Asia1	*Constant(8.3)	*Constant(8.3)	Pert(6.8,13.8,13.8)	**Binomial(14, 0.9)
A	Pert(5.5,9.6,26.8)	**Poisson(11.96)	Logistic(14.7,0.4)	Binomial(15,0.97)

* The data were not sufficient in number to derive a distribution. Constant distribution represent the mean durations for the respective virus serotypes.

**Anderson-Darling or Chi Square test showed a good fit (p>0.05).

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