**Supporting information**

**Estimating model parameters to understand endemic dynamics of FMDVs in African buffalo, using empirical data from cohort and experimental studies.**

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**S1 Duration of maternal antibodies against FMDV in African buffalo**

***S1.1 Data***

Data on antibody titres against three serotypes of foot-and-mouth disease virus (FMDV) (SAT-1, SAT-2 and SAT-3) from sequential captures of African buffalo calves were used to compute the age at which antibody titres declined below a threshold level assumed to be indicative of protection (log10 1.7). Specifically, the data were used to determine the age of each calf at the last capture where its titre was above the threshold for protection (assumed to be zero if there were no titres above the threshold) and the age of each calf at the first capture where its antibody titre was below the threshold for protection. Maternal immunity was assumed to wane at some point in this interval (Figure S1). Only those calves for which the dam was known to have a protective titre at the time of the calf’s birth were included in the analysis (25 calves for SAT-1, 36 for SAT-2 and 20 for SAT-3).

***S1.2 Statistical methods***

The duration of maternal immunity was assumed to follow a gamma distribution. The likelihood for the distribution parameters (mean and shape parameter) is given by,



where *a*0 is the age at which the last protective titre was observed, *a*1 is the age at which the first non-protective titre was observed for each calf (see Figure S1) and *f* is the probability density function for the gamma distribution parameterised as,



where *k*>0 is the shape parameter, *µ*>0 is the mean and Γ(*k*) is a gamma function. (Note that this parameterisation for the gamma distribution, , is used for all analyses in the study.)

Two possibilities for the distribution parameters were considered. In the first, the parameters were assumed to be common to all serotypes, while in the second they were assumed to differ amongst the serotypes. In the second model, the parameters for each serotype were assumed to be drawn from higher-level gamma distributions (i.e. there is hierarchical structure in the parameters). Data from duration of maternal antibodies from an earlier experiment (Bengis et al. 1986) were used to construct a mildly informative prior for the mean duration (exponential with mean 0.5 years). Non-informative priors (exponential with mean 100) were assumed for all other parameters.

Samples from the joint posterior distribution were generated using an adaptive Metropolis scheme (Haario et al. 2001), modified so that the scaling factor was tuned during burn-in to ensure an acceptance rate of between 20% and 40% for more efficient sampling of the target distribution (Andrieu & Thoms 2008). Convergence of the scheme was assessed visually and by examining various criteria provided in the coda package (Plummer et al. 2006) in R (R Core Team 2016).

The two possibilities for the distribution parameters (i.e. common to serotypes or different amongst serotypes) were compared using the deviance information criterion (DIC) (Spiegelhalter et al. 2002).

***S1.3 Results***

There was some evidence for differences in the duration of maternal antibodies amongst the three serotypes (DIC=217.3 for the model in which parameters differed amongst serotypes compared with DIC=217.6 for the model in which they were common). The posterior medians for the mean duration of maternal antibodies was 0.28 years, 0.43 years and 0.35 years for SAT-1, 2 and 3, respectively (Table S1).

**S2 Transmission parameters for African buffalo acutely infected with FMDV**

***S2.1 Data***

In the transmission experiments four African buffalo were inoculated with one of three strains of foot-and-mouth disease virus (FMDV). One strain each was selected from the three Southern African Territories (SAT) serotypes of FMDV, so that the strains are denoted SAT-1, SAT-2 or SAT-3 hereafter. After two days, four naïve in-contact buffalo were introduced to the pen containing the inoculated animals and allowed to mix. Blood samples were taken from all buffalo in a pen at approximately 2-3 day intervals for detection of FMDV RNA by qPCR.

***S2.2 Parameter estimation***

The transmission experiments were modelled using either *SIR* (susceptible (i.e. uninfected)-infected (and infectious)-recovered) or *SEIR* (susceptible-exposed (i.e. infected but not yet infectious)-infectious-recovered) models (Keeling & Rohani 2008). In both models a buffalo was assumed to be infectious if FMDV RNA was detected in its blood.

The force of infection for a buffalo is given by,



where *s* is the strain used in the transmission experiment (i.e. SAT-1, SAT-2 or SAT-3), *I*(*t*) and *N*(*t*) are the number of infectious buffalo and total number of buffalo in the pen at time *t*, respectively, and *βs* is the strain-specific transmission rate. Where included, the latent period (i.e. the time from infection to becoming infectious) for each buffalo was assumed to be drawn from a gamma distribution with strain-specific mean and shape parameter Finally, the duration of the infectious period was assumed to follow a gamma distribution with strain-specific mean and shape parameter  The basic reproduction number for strain *s* can be computed as,



Parameters (transmission rates, latent and infectious period parameters) were estimated in a Bayesian framework, including a data augmentation step, such that the unobserved infection times and partially-observed latent and infectious periods are included in the analysis as nuisance parameters (Hu et al. 2017).

The likelihood for the data, *L*, can be split into two components, one relating to the inoculated buffalo, *LI*, and one related to the in-contact buffalo, *LC*, so that,



where **φ** is a vector of model parameters and  **E**={*Ej*} and **I**={*Ij*} are vectors of infection times, latent periods and infectious periods, respectively. The likelihood for the *SIR* model is identical except that terms related to the latent periods do not need to be included.

Inoculated buffalo were assumed to be infected at *t*=0 and all were positive at the first observation time after inoculation (*t*=2). Accordingly, no inferences were drawn about the latent period for inoculated buffalo. However, the resulting uncertainty in the infectious period was incorporated in the likelihood by assuming the latent period could be between zero and two days, so that,



where *sj* is the strain with which animal *j* was inoculated, *fI* is the probability density function (PDF) for the gamma-distributed infectious periods.

The likelihood for the in-contact buffalo is given by,



The first term in the likelihood, , is the probability that buffalo *j* becomes infected at time  (conditional on not having been infected previously; *t*0 is the time at which the in-contact buffalo were put in the pen). The second term corresponds to the gamma-distributed latent period for buffalo *j*, *Ej* (with PDF, *fE*). The third term corresponds to the gamma-distributed infectious period for buffalo *j* (with PDF, *fI*, and cumulative density function (CDF), *FI*), where *cj* is a variable indicating whether (*cj*=1) or not (*cj*=0) animal *j* was still viral RNA-positive at the final observation time.

The infection times, latent periods and infectious periods for the animals were constrained so that they were consistent with the virus isolation data. In the case of the *SIR* model, the appropriate constraints are,



while for the *SEIR* model, they are,



where *LN*, *FP*, *LP* and *FN* denote the last negative, first positive, last positive and first negative blood sample, respectively.

The results for all strains were analysed together, considering several possibilities for variation amongst strains in the transmission rate and latent and infectious period parameters (Table S2). Where they varied amongst strains, the parameters for each strain were assumed to be drawn from higher-level exponential distributions (i.e. there is hierarchical structure in the parameters). In this case,



where *μ*p is the mean for the hierarchical distribution for parameter p (=*β*, *kE*, *μE*, *kI* or *μI*). In total, ten models were fitted to the data: four *SIR* models and six *SEIR* models (Table S2).

Mildly-informative priors were constructed for the latent and infectious period parameters based on data for the acute phase of infection for the buffalo (Maree et al. 2016). Specifically, an exponential prior with mean 1 was used for the shape parameter for the latent period, a gamma prior with mean 2 and shape 2 was used for the mean latent period, an exponential prior with mean 1 was used for the shape parameter for the infectious period, a gamma prior with mean 6 and shape 2 was used for the mean latent period. For the transmission parameter, a gamma prior with mean 1.85 and shape 1.39 was constructed (see appendix) based on the outcome of previous transmission experiments (Gainaru et al. 1986; Vosloo et al. 1996). When between-strain variation (i.e. hierarchical structure) was included for a parameter, the hyperprior for the parameter mean (*μ*p) was the same as the prior for that parameter without hierarchical structure.

Samples from the joint posterior distribution were generated using an adaptive Metropolis scheme (Haario et al. 2001), modified so that the scaling factor was tuned during burn-in to ensure an acceptance rate of between 20% and 40% for more efficient sampling of the target distribution (Andrieu & Thoms 2008). Two chains of 10,000,000 iterations were run, with the preceding 10,000,000 iterations discarded to allow for burn-in of the chain. The chains were then thinned (taking every 1000th sample) to reduce autocorrelation amongst the samples. Convergence of the scheme was assessed visually and by examining the Gelman-Rubin statistic provided in the coda package (Plummer et al. 2006) in R (R Core Team 2018).

The most commonly used measure of model comparison, the deviance information criterion (DIC) (Spiegelhalter et al. 2002) is not uniquely defined for data augmentation models (Celeux et al. 2006), such as the one used in this analysis. In addition, DIC uses point estimates rather than the full posterior distribution (Gelman et al. 2014). Accordingly, the different models were compared using leave-one-out (LOO) cross-validation methods (Gelman et al. 2014; Vehtari et al. 2017). For computational efficiency, approximate LOO was implemented using Pareto-smoothed importance sampling (PSIS) from the MCMC chains as described in Vehtari et al. (2017). In the PSIS-LOO approach, we compute -2×expected log pointwise predictive density (elpd) for a model as a measure of its predictive accuracy. (Here, multiplication by -2 puts it on the conventional scale of deviance.)

***S2.3 Results***

The *SIR* model with the lowest elpd is that in which all parameters vary amongst strains (model 4; Table S2). The model with the lowest elpd is the *SEIR* model in which all parameters vary amongst strains (Δelpd>4 for models 1-8; Table S2). However, the change in elpd compared with the *SEIR* model in which all parameters except the transmission rate differ amongst strains (model 9) is small (Δelpd=0.6; Table S1).

The marginal posterior distributions for the best-fit *SIR* and *SEIR* models (models 4 and 10, respectively) are shown in Figure S2 and summarised in Table S3. In both models the highest transmission rate (and also basic reproduction number) was that for SAT-1 and the lowest for SAT-3, with SAT-2 in between (Figure S2; Table S3). For the *SEIR* model, the mean latent period was highest for SAT-3 and lowest for SAT-1, with SAT-2 in between, while for the mean infectious period the order was reversed (Figure S2; Table S3).

The inferred transmission dynamics are shown in Figure S3 for the best-fit *SIR* and *SEIR* models (models 4 and 10, respectively). For SAT-1, there is little difference between the *SIR* and *SEIR* models, though the infection times for the in-contact buffalo are slightly earlier in the *SEIR* compared with the *SIR* model. However, in both cases, all four in-contact buffalo were most likely infected by the inoculated animals. For SAT-2, the infection times for the in-contact buffalo are earlier in the *SEIR* compared with the *SIR* model, markedly so for three of the animals. Moreover, in the *SEIR* model the in-contact buffalo are most likely infected by the inoculated animals, whereas in the *SIR* model, three of the in-contact buffalo could have been infected by an in-contact animal. Finally, for SAT-3, the transmission dynamics are quite different between the *SIR* and *SEIR* models. For the *SIR* model, there is a clear pattern of who infects whom: two in-contact buffalo are infected by the inoculated animals, these then infect the third in-contact buffalo, which subsequently infects the fourth in-contact animal. Although this pattern remains consistent with the infection times inferred using the *SEIR* model, other patterns are possible. This includes three of the in-contact buffalo being infected by the inoculated animals, one of which infects the fourth in-contact animal, as well as all four in-contact buffalo being infected by the inoculated animals.

**S3 Transmission rates for FMDV carrier African buffalo**

***S3.1 Data***

In the carrier transmission experiments, each pen held twelve (group one) or eleven (group two) African buffalo. Six were carriers persistently infected with one strain of FMDV (denoted SAT-1, SAT-2 or SAT-3, which is also the serotype of strain), with two carriers for each strain; the remaining animals were naïve in-contact buffalo. Animals were sampled (tonsil swabs) repeatedly during the experiment and a positive result (by PCR) for an in-contact buffalo was assumed to indicate transmission had occurred. The results are summarised in Table S4 and were analysed independently for each serotype, with carriers infected with other serotypes treated as in-contact animals.

For experiments where transmission of the strain occurred, results were analysed up to the first time point at which transmission was observed to have occurred (i.e. an in-contact buffalo had a positive PCR result). For experiments where transmission of the strain did not occur, results were analysed up to the last time point when samples for both carriers of the serotype were positive. In both cases this simplified the analysis by allowing us to assume the force of infection was constant during the study period.

***S3.2 Parameter estimation***

The likelihood for each transmission experiment is given by



where *nU* and *nI* are the number of uninfected and infected in-contact buffalo at the end of the study period, respectively,



are the probabilities an in-contact buffalo remains uninfected or becomes infected during the study period, respectively, *λ*(*τ*) is the force of infection on day *τ* of the experiment, *t*0 is the time of last sampling at which all in-contact buffalo were PCR-negative and *t*1 is the time of first sampling at which in-contact buffalo were PCR-positive. The term in the likelihood, , relating to infection of in-contact buffalo allows for the fact not all in-contact buffalo may have been infected by carriers (i.e. once the first in-contact buffalo became infected, it could transmit to other in-contact animals). Here, the force of infection is given by



where *I* and *N* are the number of infectious (carrier) buffalo and total number of buffalo in the pen, respectively, and *β* is the transmission rate. In this case, the likelihood for those groups in which transmission occurred can be rewritten as,



while for those groups in which transmission did not occur it can be rewritten as,



Finally, the likelihood was constructed by multiplying the appropriate likelihoods for groups 1 and 2 and strains SAT-1, SAT-2 and SAT-3.

Two possibilities for the transmission rates were considered. In the first, the rates were assumed to be common to all strains, while in the second they were assumed to differ amongst the strains. In the second model, the rates for each strain were assumed to be drawn from a higher-level exponential distribution (i.e. there is hierarchical structure in the parameters). An exponential prior with mean 1 was assumed for the (mean) transmission rate, based on that estimated for acutely-infected buffalo (Table S3). Non-informative priors (exponential with a mean 100) were used for other parameters.

Samples from the joint posterior distribution were generated using an adaptive Metropolis scheme (Haario et al. 2001), modified so that the scaling factor was tuned during burn-in to ensure an acceptance rate of between 20% and 40% for more efficient sampling of the target distribution (Andrieu & Thoms 2008). Convergence of the scheme was assessed visually and by examining various criteria provided in the coda package (Plummer et al. 2006) in R (R Core Team 2018).

The two possibilities for the transmission rates (i.e. common to serotypes or different amongst serotypes) were compared using the deviance information criterion (DIC) (Spiegelhalter et al. 2002).

***S3.3 Results***

The model in which the transmission rates differed amongst strains resulted in a significantly better fit compared to that in which the transmission rate was common (DIC=16.8 for differing rates compared with DIC=19.8 for a common rate). The transmission rates for each strain are presented in Table S5. The estimate was highest for SAT-1 and lowest for SAT-2, with SAT-3 intermediate.

**S4 Duration of FMDV carrier status in African buffalo**

***S4.1 Data***

Data on virus isolation from tonsil swabs taken from eight African buffalo experimentally infected with three serotypes of foot-and-mouth disease virus (FMDV) (SAT-1, SAT-2 and SAT-3) were used to estimate the duration of carrier status (Maree et al. 2016). Specifically, the data were used to determine the time post infection of the last positive sample for infectious FMDV and the first subsequent negative sample (Table S6). This assumes that the last positive sample was genuinely the last positive sample, but, because detection of FMDV was intermittent in all the buffalo, this may not be the case. Only buffalo which were confirmed carriers for the serotype (i.e. positive sample at 28 or more days post infection) were included in the analysis (seven for SAT-1, four for SAT-2 and five for SAT-3).

***S4.2 Statistical methods***

The duration of carrier status was assumed to follow a gamma distribution. The likelihood for the distribution parameters (mean *μ* and shape parameter *k*) is given by,



where *tp* is the time of the last positive sample, *tn* is the time of the first subsequent negative sample for the *j*th buffalo, *cj* is a variable indicating whether there was (*cj*=0) or was not (*cj*=1) a first negative sample (i.e. whether or not the observation for the animal is right-censored) and *f* is the probability density function for the gamma distribution and *sj* is the serotype with which the *j*th buffalo was infected.

Four possibilities for the distribution parameters were considered: (i) mean and shape parameter common to all serotypes; (ii) mean differs amongst serotypes and shape parameter common; (iii) mean common and shape parameter differs amongst serotypes; and (iv) mean and shape parameter differ amongst serotypes. Where they varied amongst serotypes, the parameters for each serotype were assumed to be drawn from higher-level gamma distributions (i.e. there is hierarchical structure in the parameters).

An informative prior was constructed for the mean duration of carrier status using data on the duration of carrier status in experimentally-infected African buffalo (Table S6) extracted from the published literature (Dawe et al. 1994; Vosloo et al. 1996). Fitting an exponential distribution to these data by maximum likelihood yielded an estimate for the distribution (or hierarchical) mean of 307. Non-informative priors (exponential with mean 100) were assumed for all remaining parameters.

Samples from the joint posterior distribution were generated using an adaptive Metropolis scheme (Haario et al. 2001), modified so that the scaling factor was tuned during burn-in to ensure an acceptance rate of between 20% and 40% for more efficient sampling of the target distribution (Andrieu & Thoms 2008). For each serotype, two chains of 200,000 iterations were run, with the preceding 100,000 iterations discarded to allow for burn-in of the chain. Chains were subsequently thinned (by taking every 20th sample) to reduce autocorrelation amongst the samples. Convergence of the scheme was assessed visually and by examining various criteria provided in the coda package (Plummer et al. 2006) in R (R Core Team 2018).

The four possibilities for the distribution parameters (i.e. whether the mean or shape parameter are common to serotypes or different amongst serotypes) were compared using the deviance information criterion (DIC) (Spiegelhalter et al. 2002).

***S4.3 Results***

The best-fit model (as judged by the DIC) was one in which the mean duration in carrier status varied amongst serotypes, but where the shape parameter was common to all serotypes (mean and shape common: DIC=76.3; mean differs, shape common: DIC=73.1; mean common, shape differs: DIC=76.2; mean and shape differ: DIC=73.3). The mean duration of carrier status was longest for SAT-1 (243 days) and shorter for SAT-2 (180 days) and SAT-3 (174 days), though there is considerable uncertainty in these estimates (Table S7).

**S5 Probability of an African buffalo becoming a FMDV carrier**

***S5.1 Data***

Following the acute transmission experiments (see section S2.1), some of the needle inoculated and contact-challenged African buffalo became foot-and-mouth disease virus (FMDV) carriers (i.e. FMDV could be isolated from the animal at more than 30 days post infection) (Table S8). In another experiment, eight buffalo were inoculated with same three strains of FMDV (Maree et al. 2016) and several of these became carriers for the strains with which they were inoculated (Table S8).

***S5.2 Statistical analysis***

The data for each strain were analysed using a binomial likelihood with a beta prior distribution for the probability of becoming a carrier. Because these are conjugate distributions (Gelman et al. 2004), the posterior distribution is also a beta distribution with parameters *α*+*C* and *β*+(*N*-*C*), where *α* and *β* are the parameters for the prior distribution and *C* and *N* are the number of carrier buffalo and the total number of acutely-infected buffalo, respectively. A beta distribution with parameters *α*=1 and *β*=1 (i.e. Uniform(0,1) distribution) was used as the prior for all three strains.

***S5.3 Results***

The probability of becoming a carrier (posterior median) for SAT-1 was 0.90 (95% credible interval (CI): 0.70-0.98; posterior: Beta(15,2)), for SAT-2 was 0.44 (95% CI: 0.23-0.67; posterior: Beta(8,10)) and for SAT-3 it was 0.67 (95% CI: 0.44-0.86; posterior: Beta(12,6)).

**References**

Andrieu, C. & Thoms, J. 2008 A tutorial on adaptive MCMC. *Stat. Comput.* **18**, 343-373.

Bengis, R.G., Thomson, G.R., Hedger, R.S., de Vos, V. & Pini, A. 1986 Foot-and-mouth disease and the African buffalo (*Syncerus caffer*). 1. Carriers as a source of infection for cattle. *Ondesterpoort J. Vet. Res.* **53**, 69-73.

Celeux, G., Forbes, F., Robert, C.P. & Titterington, D.M. 2006 Deviance information criteria for missing data models. *Bayesian Analysis* **1**, 651-674.

Dawe, P.S., Sorensen, K., Ferris, N.P., Barnett, I.T.P., Armstrong, R.M. & Knowles, N.J. 1994 Experimental transmission of foot-and-mouth disease virus from carrier African buffalo (*Syncerus caffer*) to cattle in Zimbabwe. *Vet. Record* **134**, 211-215.

Gainaru, M.D., Thomson, G.R., Bengis, R.G., Esterhuysen, J.J., Bruce, W. & Pini, A. 1986 Foot-and-mouth disease and the African buffalo (*Syncerus caffer*). II. Virus excretion and transmission during acute infection. *Ondesterpoort J. Vet. Research* **53**, 75-85.

Gelman, A., Hwang, J. & Vehtari, A. 2014 Understanding predictive information criteria for Bayesian models. *Stat. Comput.* **24**, 997-1016.

Gelman, A., Carlin, J.B., Stern, H.S. & Rubin, D.B. 2004 *Bayesian data analysis (2nd edition)*. Boca Raton, Florida, U.S.A.: Chapman Hall/CRC.

Haario, H., Saksman, E. & Tamminen, J. 2001 An adaptive Metropolis algorithm. *Bernoulli* **7**, 223-242.

Hu, B., Gonzales, J.L. & Gubbins, S. 2017 Bayesian inference of epidemiological parameters from transmission experiments. *Sci. Reports* **7**, 16774.

Keeling, M.J. & Rohani, P. 2008 *Modelling infectious diseases in humans and animals*. Princeton, New Jersey, U.S.A.: Princeton University Press.

Maree, F., de Klerk-Lorist, L.-M., Gubbins, S., Zhang, F., Seago, J., Perez-Martin, E., Reid, E., Scott, K., van Schalkwyk, L., Bengis, R., Charleston, B. & Juleff, N. 2016 Differential persistence of foot-and-mouth disease virus in African buffalo is related to viral virulence. *J. Virol.* **90**, 5132-5140.

Plummer, M., Best, N., Cowles, K. & Vines, K. 2006 CODA: Convergence Diagnosis and Output Analysis for MCMC. *R News* **6**, 7-11.

R Core Team 2018 R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. (<http://www.R-project.org/>).

Spiegelhalter, D.J., Best, N.G., Carlin, B.P. & van der Linde, A. 2002 Bayesian measures of model complexity and fit (with discussion). *J. R. Stat. Soc. B* **64**, 583-639.

Vehtari, A., Gelman, A. & Gabry, J. 2017 Practical Bayesian model evaluation using leave-one-out cross-validation and WAIC. *Stat. Comput.* **27**, 1413-1432.

Vosloo, W., Bastos, A.D., Kirkbride, E., Esterhuysen, J.J., Janse van Rensburg, D., Bengis, R.G., Keet, D.W. & Thomson, G.R. 1996 Persistent infection of African buffalo (*Syncerus caffer*) with SAT-type foot-and-mouth disease viruses: rate of fixation of mutations, antigenic change and interspecies transmission. *J. Gen. Virol.* **77**, 1457-1467.

**Appendix Constructing the prior distribution for the acute transmission rate**

Two previous experiments have considered transmission of FMDV from acutely-infected African buffalo (Gainaru et al. 1986; Vosloo et al. 1996). For each experiment we extracted the number of inoculated buffalo, the number of in-contact buffalo, the number of these which became infected and the duration of the challenge (i.e. the time from when the in-contact animals were introduced to the inoculated ones until virus was first isolated from an in-contact animal) (see Table A1). The likelihood for the data can be written as,



where *I* is the number of inoculated buffalo, *t*C is the duration of challenge, *nU* the number of in-contact buffalo that remain uninfected at the end of the challenge period, *nI* is the number of in-contact buffalo that become infected during the challenge period and *N* is the total number of buffalo in the *j*th experiment (Table A.1). The posterior distribution for the transmission rate, *p*(*β*), is given by,



where *π*(*β*) is the prior distribution for the transmission rate (we used a non-informative exponential prior with mean 100). Rather than use the full posterior, , as the prior for our analysis, we constructed a less informative prior by using a gamma distribution parameterised so that its median and interquartile range coincided with the median and 95% credible interval of the posterior, . In this case, the mean is 1.85 and the shape is 1.39.

**Table A1.** Outcome of transmission experiments for FMDV in acutely-infected buffalo.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Gainaru et al. (1986) |  |  | Vosloo et al. (1996) |
| serotype\* | SAT-1 | SAT-2 | SAT-2 | SAT-2 |
| number of challenge buffalo | 2 | 2 | 2 | 2 |
| number of in-contact buffalo |  |  |  |  |
| infected | 4 | 4 | 4 | 1 |
| total | 4 | 4 | 4 | 2 |
| duration of challenge (days) | 4 | 4 | 4 | 7 |

\* note: these are not the same strains as used in the present study

**Table S1.** Mean and shape parameters for the gamma-distributed duration of maternal antibodies against FMDV in African buffalo.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| serotype | mean | | shape | |
| estimate† | 95% CI‡ | estimate† | 95% CI‡ |
| *model 1* |  |  |  |  |
| all | 0.37 | (0.29, 0.46) | 1.19 | (0.75, 1.81) |
| *model 2* |  |  |  |  |
| SAT-1 | 0.28 | (0.18, 0.45) | 1.01 | (0.41, 1.68) |
| SAT-2 | 0.43 | (0.32, 0.60) | 1.35 | (0.77, 2.61) |
| SAT-3 | 0.35 | (0.23, 0.57) | 1.20 | (0.65, 2.01) |

† posterior median

‡ credible interval

**Table S2.** Comparison of models for the transmission of foot-and-mouth disease virus strains in acutely-infected African buffalo.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| model | parameters† | | | | | -2×elpd‡ |
| *kE* | *μE* | *kI* | *μI* | *β* |
| *SIR* |  |  |  |  |  |  |
| 1 | - | - | C | C | C | 139.6 |
| 2 | - | - | C | C | V | 138.1 |
| 3 | - | - | V | V | C | 135.2 |
| 4 | - | - | V | V | V | 133.4 |
| *SEIR* |  |  |  |  |  |  |
| 5 | C | C | C | C | C | 138.5 |
| 6 | C | C | C | C | V | 134.1 |
| 7 | V | V | C | C | C | 130.2 |
| 8 | C | C | V | V | C | 135.4 |
| 9 | V | V | V | V | C | 126.7 |
| 10 | V | V | V | V | V | 126.1 |

† C: common to all strains; V: varies amongst strains

‡ elpd: expected log pointwise predictive density

**Table S3.** Transmission parameters for three strains of foot-and-mouth disease virus in acutely-infected African buffalo.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| parameter |  | SAT-1 | | SAT-2 | | SAT-3 | |
| estimate† | 95% CI‡ | estimate† | 95% CI‡ | estimate† | 95% CI‡ |
| *SIR* model |  |  |  |  |  |  |  |
| infectious period |  |  |  |  |  |  |  |
| shape parameter | *kI* | 14.7 | (4.3, 41.0) | 7.4 | (2.2, 21.0) | 14.7 | (4.0, 44.3) |
| mean (days) | *μI* | 6.3 | (5.1, 8.0) | 5.3 | (3.9, 7.1) | 5.1 | (4.0, 6.5) |
| transmission rate | *β* | 1.9 | (0.5, 7.4) | 0.8 | (0.3, 1.7) | 0.5 | (0.2, 1.2) |
| basic reproduction number | *R*0 | 12.1 | (3.2, 49.0) | 4.0 | (1.3, 9.7) | 2.7 | (0.9, 6.2) |
| *SEIR* model |  |  |  |  |  |  |  |
| latent period |  |  |  |  |  |  |  |
| shape parameter | *kE* | 1.2 | (0.1, 8.7) | 1.6 | (0.2, 9.2) | 1.6 | (0.2, 8.3) |
| mean (days) | *µE* | 0.5 | (0.02, 2.4) | 1.3 | (0.1, 3.5) | 2.8 | (0.5, 7.0) |
| infectious period |  |  |  |  |  |  |  |
| shape parameter | *kI* | 11.8 | (3.5, 33.5) | 8.7 | (2.4, 27.0) | 11.8 | (3.3, 35.3) |
| mean (days) | *μI* | 5.7 | (4.4, 7.4) | 4.6 | (3.5, 6.3) | 4.2 | (3.2, 5.8) |
| transmission rate | *β* | 2.8 | (0.8, 11.3) | 1.6 | (0.4, 9.0) | 1.2 | (0.3, 7.8) |
| basic reproduction number | *R*0 | 15.8 | (4.1, 65.6) | 7.5 | (1.9, 41.5) | 5.2 | (1.3, 34.1) |

† posterior median

‡ CI: credible interval

**Table S4.** Outcome of experiments on the transmission for foot-and-mouth disease virus from carrier African buffalo.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| strain | group | *N* | *nU* | *nI* | *t*0 | *t*1 |
| SAT-1 | 1 | 12 | 3 | 7 | 0 | 14 |
|  | 2 | 11 | 3 | 6 | 14 | 44 |
| SAT-2 | 1 | 12 | 10 | 0 | - | 14 |
|  | 2 | 11 | 9 | 0 | - | 104 |
| SAT-3 | 1 | 12 | 7 | 3 | 0 | 14 |
|  | 2 | 11 | 9 | 0 | - | 44 |

*N* - number of buffalo in group (i.e. carrier and in-contact); *nU* - number of uninfected in-contact buffalo at *t*1; *nI* - number of infected in-contact buffalo at *t*1; *t*0 - time of last sampling at which all in-contact buffalo were PCR-negative (if transmission occurred); *t*1 - time of first sampling at which in-contact buffalo were PCR-positive (if transmission occurred) or time of last sampling at which both carriers were positive (if transmission did not occur).

**Table S5.** Estimates (posterior median and 95% credible interval (CI)) for transmission rates for different serotypes of foot-and-mouth disease virus from carrier African buffalo.

|  |  |  |
| --- | --- | --- |
| strain | median | 95% credible interval |
| SAT-1 | 0.028 | (0.005, 0.095) |
| SAT-2 | 0.003 | (0, 0.016) |
| SAT-3 | 0.012 | (0.002, 0.044) |

**Table S6.** Duration (in days post infection) of foot-and-mouth disease virus carrier state in African buffalo.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| reference | serotype | | | | | |
| SAT-1 | | SAT-2 | | SAT-3 | |
| *tlp*† | *tfn*‡ | *tlp* | *tfn* | *tlp* | *tfn* |
| Maree et al. 2016§ | 316 | 336 | 136 | 155 | 126 | 136 |
|  | >185 | - | >185 | - | >185 | - |
|  | >400 | - | nc¶ | nc | 95 | 109 |
|  | 200 | 214 | 35 | 80 | nc | nc |
|  | >185 | - | nc | nc | 109 | 126 |
|  | 168 | 185 | nc | nc | nc | nc |
|  | 214 | 231 | 35 | 80 | 35 | 80 |
| Dawe et al. 1994 | - | - | 126 | 154 | - | - |
|  | - | - | >188 | - | - | - |
| Vosloo et al. 1996 | - | - | 366 | 399 | - | - |
|  | - | - | nc | nc | - | - |

† *tlp* - time of last positive virus isolation (a > sign indicates the observation is right-censored)

‡ *tfn* - time of first subsequent negative virus isolation

¶ nc - not a carrier (i.e. no positive samples 28 days or more post infection)

§ animals were co-infected with all three serotypes

**Table S7.** Mean and shape parameters for the gamma-distributed duration of carrier status for FMDV in African buffalo.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| serotype | mean (days) | | shape† | |
| estimate‡ | 95% CI¶ | estimate‡ | 95% CI¶ |
| SAT-1 | 243 | (170, 370) |  |  |
| SAT-2 | 180 | (106, 316) | 3.2 | (1.3, 8.5) |
| SAT-3 | 174 | (104, 298) |  |  |

† common to all serotypes

‡ posterior median

¶ credible interval

**Table S8.** Number of African buffalo becoming carriers following infection with three strains of foot-and-mouth disease virus.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| study | strain | | | | | |
| SAT-1 | | SAT-2 | | SAT-3 | |
| C† | N‡ | C | N | C | N |
| present study |  |  |  |  |  |  |
| needle inoculated | 4 | 4 | 2 | 4 | 3 | 4 |
| contact challenged | 3 | 3 | 1 | 4 | 3 | 4 |
| Maree et al. 2016¶ | 7 | 8 | 4 | 8 | 5 | 8 |

† number of buffalo becoming carriers

‡ number of buffalo infected

¶ animals were co-infected with all three serotypes



**Figure S1.** Duration of maternal antibodies against foot-and-mouth disease virus in African buffalo. Each bar shows the time for which a calf was assumed to be protected (in blue) and the period in which maternal protection waned (in yellow).



**Figure S2.** Transmission parameters for three strains of foot-and-mouth disease virus (SAT-1, SAT-2 and SAT-3) in acutely-infected African buffalo: (*a*) shape parameter for the latent period (*kE*); (*b*) mean latent period (in days) (*μE*); (*c*) shape parameter for the infectious period (*kI*); (*d*) mean infectious period (in days) (*μI*); (*e*) transmission rate (per day) (*β*); and (*f*) basic reproduction number (*R*0). Each plot shows the marginal posterior density (shape), the posterior median (circle) and 25th and 75th percentiles (line) for the parameter. The colour of the shape indicates the FMDV strain and the model used: SAT-1, *SIR* model (blue), SAT-1, *SEIR* model (green), SAT-2, *SIR* model (red), SAT-2, *SEIR* model (magenta), SAT-3, *SIR* model (cyan) and SAT-3, *SEIR* model (yellow).



**Figure S3.** Inferred transmission dynamics for three strains of foot-and-mouth disease virus (SAT-1, SAT-2 and SAT-3) during acute infection in African buffalo. Results are shown for the best-fit *SIR* and *SEIR* models. Each panel shows a violin plot of the inferred infection times for each in-contact buffalo, with the red shape indicating the posterior density for the infection time and the black circle and line indicating the posterior median and posterior interquartile range for the infection times. The blue shapes show the inferred times at which each buffalo was infectious, with the width of each shape indicating the proportion of samples for which the buffalo was infectious at that time. An "I" denotes an inoculated buffalo and a "C" denotes an in-contact buffalo.