January 2014

Modeling The Zoonotic Transmission Dynamics Of Nipah Virus: Implications For Outbreak Control And Model-Guided Fieldwork

Natasha Wenzel
Yale University, natasha.wenzel@gmail.edu

YALE SCHOOL OF PUBLIC HEALTH

Modeling the Zoonotic Transmission Dynamics of Nipah Virus: Implications for Outbreak Control and Model-Guided Fieldwork

A THESIS

SUBMITTED IN FULFILLMENT OF REQUIREMENTS

For the degree

MASTERS OF PUBLIC HEALTH

Department of Epidemiology of Microbial Diseases

By

Natasha S. Wenzel

NEW HAVEN, CONNECTICUT

May 2014

ACKNOWLEDGEMENTS

Thank you to the Yale School of Public Health and the members of the Stolwijk Fellowship Committee for their funding in the pursuit of education.

My continuing gratitude to Dr. Alison Galvani, Dr. James Childs, Dr. Jeffrey Townsend, and Dr. David Durham for their advice, support, and encouragement.

Many thanks to Dr. David Haymann, Dr. Virginia Pitzer, Dr. Katie Atkins, and Dr. Steven Luby for their thoughtful ideas and critique.

Table of Contents

ABSTRACT

Modeling the Zoonotic Transmission Dynamics of Nipah Virus:
Implications for Outbreak Control and Model-Guided Fieldwork

Natasha Wenzel

Nipah virus is considered a biosafety level-4 pathogen that is endemic to bats of the genus *Pteropus*. Infection in humans presents clinically as febrile encephalitis with an extremely high case-fatality rate (78.2%). Outbreaks of Nipah virus infection have occurred in Bangladesh and India almost annually since 2001, most recently in January 2013. To elucidate Nipah virus persistence at the endemic host and human population level we developed a Susceptible-Exposed-Infectious-Recovered dynamic model and parameterized it from published epidemiological case data and serological bats surveys on the Nipah Virus-Bangladesh variant. We conducted a Markov Chain Monte Carlo simulation to estimate the unknown parameters for bat-to-bat, bat-to-human, human-to-human, and corpse-to-human transmission routes. We present the first estimates of the four disease transmission rates and reproductive numbers of Nipah virus in the human and bat population. Our results indicate that at population equilibrium 1.77 bats per day will have an active infection,, additionally 93.0% of human infections are the result of zoonotic transmission, but only 5.27% of these primary cases transmit disease to other humans, which may indicate the presence of super-spreaders. This work draws conclusions about enzootic viral maintenance of Nipah in the bat population as well as epizootic outbreaks in human hosts to better inform model- guided fieldwork and public health interventions in Bangladesh.

1 Introduction

In September 1998 an outbreak of a novel *Paramyxovirus* among swine farmers and abattoir workers in Malaysia and Singapore resulted in 265 severe febrile encephalitis cases.[1] Investigators isolated a novel zoonotic pathogen from the secretions of flying foxes of the genus *Pteropus* and named it "Nipah" virus (NiV) after the town in Malaysia where the virus was isolated.[2] Recent retrospective epidemiological work and mathematical modeling of the 1998 Malaysian Nipah outbreak suggest that the epidemic was the result of two viral spillover events from the flying fox wildlife reservoir into the commercial swine population.[3] Since 1999 no human cases of Nipah virus have been reported in Malaysia, but outbreaks of NiV infection have occurred in Bangladesh and India almost annually since 2001; the most recent outbreak occurred in January 2013.[4, 5] While NiV-M (Malaysia) and NiV-B (Bangladesh) are structurally similar, there are slight differences in clinical presentation and a significantly higher case-fatality rate (78.2%) in Bangladesh.[6] NiV-B has documented human-to-human, corpse-to-human, and nosocomial virus transmission.[7]

In order to explain the nearly seasonal re-emergence of NiV-B in the last decade, we determine the transmission intensities of the disease system. Initially we describe essential biology for *Pteropus Giganteus* and NiV-B that we collected from published reviews, outbreak investigations, and ecological surveys, which were used to develop the subsequent mathematical model representing NiV-B dynamics. Thereafter we examine the implications of our model results including how the pathogen is maintained at a population level in the reservoir host, reproductive ratio estimates for the virus in humans and flying foxes, and implications for surveillance and control. Last we use a sensitivity analysis on all dynamic model parameters to identify key biological features of the reservoir host and pathogen that facilitate transmission in the bat and human population. This model will aid in the prediction and prevention of Nipah virus infection, as well as inform fieldwork and public health interventions in the Bangladesh and India.

1.1 Nipah Virus and Flying Fox Biology

As with the emergence of any new infectious disease in humans, the emergence of Nipah requires exposure to the pathogen, successful infection of the hosts, and sufficient transmission between hosts to raise the basic reproductive number R above 1.[8] The phylogenetic diversity of viral strains isolated from case samples suggests each of the outbreaks in Bangladesh was the result of a separate, distinct zoonotic disease transmission to the human population.[9] The phylogenetic distance of NiV from other pathogens in the *Paramyxoviridae* family suggests that Henipaviruses are ancient viruses with a long evolutionary association with their flying fox hosts.[10] Seroepidemiological surveillance of *Pteropus giganteus*, the sole Pteropid flying fox species in India and Bangladesh that meets the criteria for a wildlife reservoir species, demonstrated widespread evidence of NiV-B seroprevalence.

Pteropus giganteus is a frugivorous colonial species, which is common in tropical regions of Southeast Asia. They aggregate in trees in permanent year round colonies of 100 or more, and engage in a multi-partner mating strategy.[11] Tropical frugivorous flying foxes, like *Pteropus giganteus*, start reproducing at the onset of the rainy season, during which fruit abundance increases.[12] The species has low natural mortality, an annual reproductive event, and delayed onset of sexual maturity.[13,14] Pteropid bats with acute Nipah viral infection display few clinical symptoms in laboratory tests.[15, 16] Transmission of maternal antibodies has been observed in captive flying foxes, though it is unclear whether transfer occurs transplacentally or via the mammary glands.[17] The foraging biology of flying foxes also has important implications for virus transmission. In order to ensure a constant food supply, flying foxes frequently migrate over large habitat areas. To avoid carrying unnecessary weight when flying, fruits are first chewed to extract nutrients while partially digested pulp and seeds are expectorated with a coating of saliva.

Retrospective epidemiological studies suggest that the main routes for human infection include direct or indirect contact with flying fox secretions, such as urine or saliva, in roosting areas or in contaminated foodstuffs.[18] Ingestion of raw date palm sap has been repeatedly implicated as an infection source in Bangladesh.[19] Palm sap is usually processed at high temperature to produce traditional sweeteners, however the fresh juice is also drunk raw as a delicacy.[20, 21] Sap harvesting occurs from mid-October through mid-March, which overlaps with the flying fox birth season and the seasonal outbreaks of NiV-B. [22] The process of date palm tapping leaves the tapping spiles open to the air. Infrared cameras placed in orchards overnight confirm that *Pteropus giganteus* often feeds at tapping sites, which can lead to cross-contamination.[23]

2 Methods

2.1 Model Description

We developed a compartmental Susceptible-Exposed-Infectious-Recovered (SEIR) model, with four different terms representing endemic flying fox-to-flying fox (β_{BB}), zoonotic flying fox-to-human (β_{BH}), direct human-to-human (β_{HH}), and post-mortem corpse-to-human (β_{F}) (Figure 1, Equation 1.2-3). We explicitly assume that no amplifier species are present and that NiV-B infection is occurring via one of these pathways.

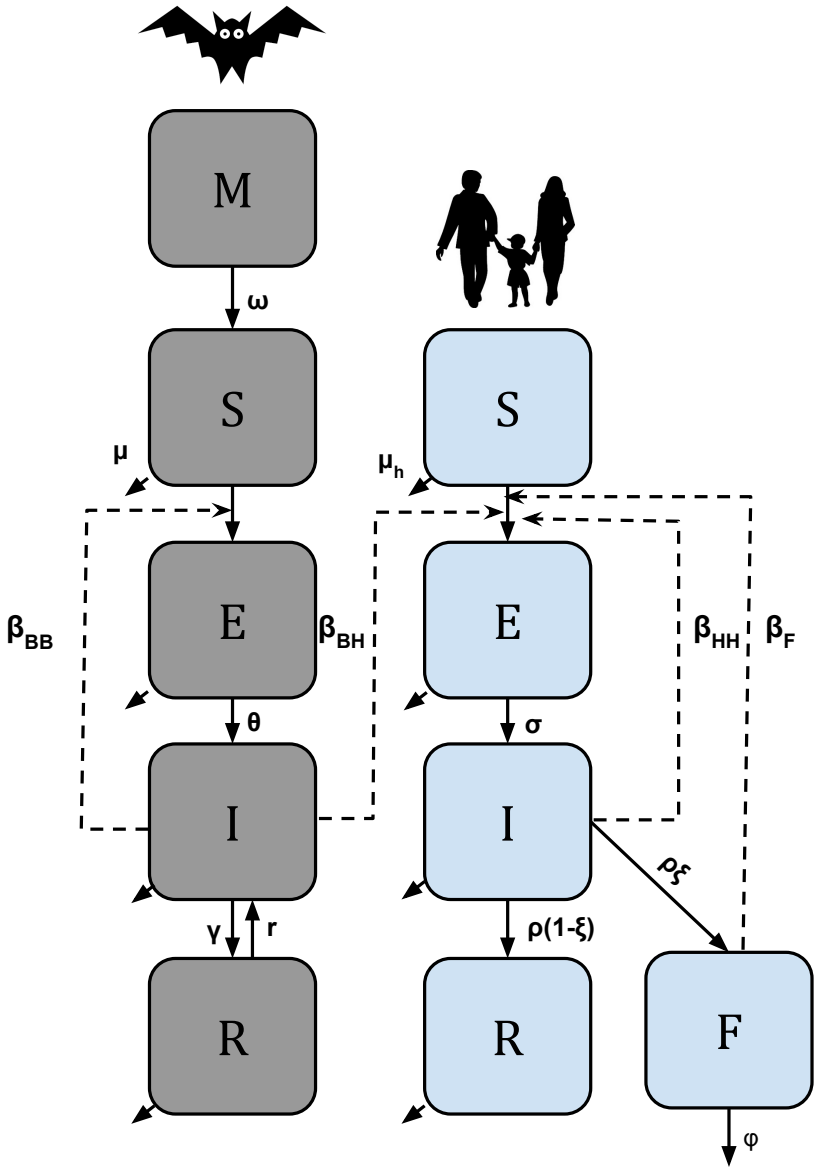


Fig. 1. The Compartmental Model of Transmission Dynamics. MSEIR represents endemic transmission in the flying fox population while SEIR-F represent direct and post-mortem transmission in humans. Spillover occurs when infectious flying foxes contact susceptible humans ($\boldsymbol{\beta_{BH}}$). Note dotted lines do not represent model flows.

The main pathway for human transmission is thought to be respiratory secretions, which necessitates close contact with infected case patients.[24,25] Direct transmission events usually occur in households, especially among family caregivers, rather than transmission to random individuals.[26, 27] Similarly a case-control study of the Faridpur cases in 2010 identified 2 family members who had ritually bathed the corpse of a NiV-infected patient and subsequently became infected.[28] According to Muslim funeral practices family members usually prepare the body for burial.[29] In this region, funeral preparation and burial occur very soon after death; in our model, the burial rate (φ) was set at 1 day. Thus in both direct and post-mortem transmission, a limited number of persons would come into contact with an infected case-patient's body, thus β_F and

β_{HH} are frequency dependent.

In India and Bangladesh palm tapping is a very well developed cottage industry. Regardless of population size, the number of sap-producing palms is relatively fixed, [30] and the number of people who may come into contact with NiV inoculum via date palm sap would be relatively constant; thus flying-fox-to-human transmission (β_{BH}) would also be frequency dependent. Documented contamination of date palm tapping sites by flying foxes and the concurrence of the NiV index cases with the date palm sap harvesting season suggest that palm sap is a major transmission pathway for this zoonosis. However, case-patients with NiV infection who do not recall ingesting date palm foodstuffs or having contact with infected people or animals are frequently identified.[31, 32]

In this model we do not explicitly assume any zoonotic transmission mechanism; we are primarily concerned with estimating the transmission intensity. We use Bayesian methods to obtain an estimate of transmission intensities based on prior parameters distributions; thus no explicit zoonotic transmission mechanism is defined.

$$\frac{dS_H}{dt} = \Lambda_H - \frac{S_H}{S_H + E_H + I_H + R_H} \quad [\beta_{BH} I_B + \beta_{HH} I_H + \beta_F F_H] - \mu_H S_H$$

$$\frac{dE_H}{dt} = \frac{S_H}{S_H + E_H + I_H + R_H} [\beta_{BH} I_B + \beta_{HH} I_H + \beta_F F_H] - \mu_H E_H - \sigma_H E_H$$

$$\frac{dI_H}{dt} = \sigma_H E_H - \mu_H I_H - \rho_H I_H \qquad (1.1)$$

$$\frac{dF_H}{dt} = \rho_H \xi I_H - \varphi F_H$$

$$\frac{dR_H}{dt} = \rho_H (1 - \xi) I_H - \mu_H R_H$$

The main transmission pathway for Nipah virus in the flying fox reservoir host is through urine or saliva, which necessitates close contact. Mutual grooming and use of urine as a grooming product may also facilitate horizontal transmission of NiV.[33] Thousands of animals can populate the roosts of flying foxes and the surrounding air can contain a mist of urine particles contributing to aerosolized infection. [34] Given the high contact rate of flying foxes within a colony structure we assumed the flying-fox-to-flying fox transmission term (β_{BB}) to be density dependent. Population growth was included in the model by adapting the density-dependent population growth equation:

$$N_{t+1} = b(1 - \frac{N_t}{K}) N_t - \mu_B N_t) \qquad (1.2)$$

where K is the carrying capacity at equilibrium, b is the birth rate average, and μ_B is the basal death rate.

We assume recovered flying foxes confer maternal immunity to newborns and pups, which wanes over the course of 270-420 days.[35] As only recovered flying-foxes can convey maternal immunity the number of females in the R compartment directly contribute to the number of newborns with maternal antibodies. Births from the S, E, or I compartment flow directly into the Susceptible compartment; thus Susceptibles can be explicitly stated as a combination of immunologically naïve births from S, E, I and of those juvenile flying foxes whose maternal immunity to NiV-B has waned at a rate ϖ.

$$\frac{dB_B}{dt} = R_B\left(1 - \frac{B_B + S_B + E_B + I_B + R_B}{k}\right) - \varpi B_B - \mu_B B_B$$

$$\frac{dS_B}{dt} = (S_B + E_B + I_B)\left(1 - \frac{B_B + S_B + E_B + I_B + R_B}{k}\right) - \beta_{BB} S_B I_B + \varpi B_B - \mu_B S_B$$

$$\frac{dE_B}{dt} = \beta_{BB} S_B I_B - \mu_B E_B - \theta_B E_B \qquad (1.3)$$

$$\frac{dI_B}{dt} = \theta_B E_B - \mu_B I_B - \gamma_B I_B + rR_B$$

$$\frac{dR_B}{dt} = \gamma_B I_B - \mu_B R_B - rR_B$$

The model also included a parameter, r, to explore viral recrudescence, the spontaneous recurrence of an infectious disease after it has been quiescent. This disease process has been proposed in the literature as an explanation for pathogen persistence within the flying fox population, particularly in individuals who are immunocompromised.[36, 37] Recrudescence was included in our model as movement from the recovered class (R_B) back to the infectious class (I_B) at a rate, r (Equation 1.3).

2.2 Parameters

Human epidemiological parameters such as case fatality, incubation period, and infectious period were collated from a summary of case reports from 2001-2007 by Luby et al.,[38] and subsequent outbreak investigation reports from the International Centre for Diarrheal Disease Research, Bangladesh (ICDDR,B).[39, 40, 41] (Table S1)

2.3 Deriving the Log-Likelihood Equation

To derive a log-likelihood expression for our model we combined serological surveillance data and epidemiological case data (Table S1) to estimate the human basic reproductive number ($R_{0\ humans}$), flying fox basic reproductive number (R_{0Bats}), equilibrium number of flying foxes with acute infection, and the likelihood of specific transmission events:

$$ln\,\mathcal{L}(Total) = ln\mathcal{L}(\mathcal{F}) + ln\mathcal{L}(\mathcal{U}) + ln\mathcal{L}(\mathcal{I}_{Bats}) + \ln\mathcal{L}\,(R_{0\,Bats}) + \ln\mathcal{L}(R_{0\,humans}) \quad (2.1)$$

2.3.1 Deriving a Log-Likelihood Equation for the Flying Fox Reproductive Number

An equation for $R_{0\,Bats}$ was derived for using the Next Generation matrix method[42] such that:

$$R_{0\,Bats} = \frac{K\beta_{BB}(1-\mu_B)\sigma_B}{(\gamma_B+\mu_B)(\sigma_B+\mu_B)} \quad (2.2)$$

Parameter estimates from Table S1 combined with equation 2.2 allowed for numerical estimation of $R_{0\,Bats}$. We used the age-dependent nature of the probability of being susceptible, as represented by being seronegative, to generate a log-likelihood value for every estimate of $R_{0\,Bats}$.[43]

$$\ln\mathcal{L}(a_i,\ b_i,\ \mu_{bats}\ ;\ \widehat{R_{0\,Bats}}) =$$

$$\prod_{i=1}^{n}\exp(-a_i\mu_{bats}(R_{0\,Bats}-1))\prod_{i=1}^{m}[1-\exp(-b_i\mu_{bats}(R_{0\,Bats}-1))] \quad (2.3)$$

where n is the number of flying foxes who are seronegative at ages a_1, a_2 …a_n and m the number of individuals who are seropositive at ages b_1, b_2...b_m with surveyed newborns and pups omitted. Field seroprevalence surveys for flying foxes include two age classes, juveniles—defined as animals displaying no secondary sexual characteristics—and adults. For equation 2.3 we considered the average juvenile age to be 1.125 years and the average adult age at 15.75 years old.[44] This log-likelihood value for $R_{0\,Bats}$ is added into the likelihood expression $\mathcal{L}(\text{Total})$ to determine the total likelihood of each set of sampled parameters.

2.3.2 Deriving a Log-Likelihood Equation for the Human Reproductive Number

Similarly an expression for $R_{0\,humans}$ was derived using the Next Generation matrix method:

$$R_{0\,humans} = \frac{\sigma_H(\beta_{HH}+\beta_F\rho_H\xi)}{(\rho_H+\mu_H)(\sigma_H+\mu_H)} \quad (2.4)$$

We assume the number of secondary cases produced by an infected individual follows a Poisson distribution, with rate $R_{0\,humans}$. To calculate $\ln\mathcal{L}(R_{0\,humans})$, let X_0 represent the total number of cases produced by the initial N_0 cases, such that $X_0 \sim N_0$ * Poisson($R_{0humans}$). A review of human Nipah virus cases from 2001-2007[45] observed a total of 29 secondary infections (X_0) produced by 60 initial Nipah case-patients (N_0). Using the value from equation 2.4, a log-likelihood function for the value of $R_{0\,humans}$ would be:

$$\ln\mathcal{L}\left(X_0, N_0; \widehat{R_{0\,humans}}\right) = -N_0 * R_{0\,humans} + \sum_{i=1}^{N_0} X_0 \ln\left(R_{0\,humans}\right) - \sum_{i=1}^{N_0} \ln\left(X_0!\right) \quad (2.5)$$

2.3.3 Deriving Log-Likelihood Equations for Transmission Events

The model calculates the proportion of new cases that can be attributed to contact with a deceased case-patient as:

$$\mathcal{F} = \frac{\beta_F F_H}{\beta_{BH} I_B + \beta_{HH} I_H + \beta_F F_H} \quad (2.6)$$

For Nipah outbreaks $\mathcal{F}$ follows a beta distribution $\mathcal{F} \sim \text{Beta}(\alpha, \beta)$, which is reliant on shape-parameter α, the number of infections attributable to post-mortem transmission, and shape-parameter β, the number of infections from other transmission sources. Using the value from equation 2.6, the beta log-likelihood function for $\mathcal{F}$ would be:

$$\ln\mathcal{L}(\alpha, \beta; \hat{\mathcal{F}}) = \sum_{i=1}^{N} \ln\Gamma(\alpha+\beta) - [\ln\Gamma(\alpha) + \ln\Gamma(\beta)] + (\alpha-1)\ln(\mathcal{F}) + (\beta-1)\ln(1-\mathcal{F}) \quad (2.7)$$

where Γ( ) denotes the gamma function. Two case-patients from the 2010 Faridpur and 2011 Rangpur outbreaks could be attributed to contact with deceased NiV-B patients (α).[46] The remaining 44 infected cases from these outbreaks were derived from zoonotic or direct transmission (β). Case data from outbreaks that occurred before 2010 were not included in this calculation as post-mortem transmission was not confirmed as a route of infection until 2010.[47]

In our model the proportion of primary human cases that do not contribute to the direct transmission force of infection is given by the term $\mathcal{U}$. Cases which do not contribute to direct transmission leave the I_H class via natural death (μ_H), case recovery or case-fatality (ρ_H). The formula for the proportion, $\mathcal{U}$, was calculated in the following manner:

$$\mathcal{U} = \frac{I_H\rho_H + I_H\mu_H}{I_H\rho_H + I_H\mu_H + \left(\frac{I_H\beta_{HH}S_H}{S_H+E_H+I_H+R_H}\right)} = \frac{\cancel{I_H}(\rho_H+\mu_H)}{\cancel{I_H}\left[\rho_H+\mu_H+\left(\frac{\beta_{HH}S_H}{S_H+E_H+I_H+R_H}\right)\right]} = \frac{\rho_H+\mu_H}{\rho_H+\mu_H+\left(\frac{\beta_{HH}S_H}{S_H+E_H+I_H+R_H}\right)} \quad (2.8)$$

A review of human Nipah outbreaks from 2001-2007 noted 60 primary human cases attributed to zoonosis.[48] These primary cases displayed heterogeneity in transmission; five produced secondary infections via direct transmission while the remaining 55 primary cases did not. It is unclear whether these transmission differences are the result of host-heterogeneities such as immune status or contact patterns. As in equation 2.7 we let shape parameter α be the number of primary cases that did not transmit to a secondary case, and β be the number of cases who transmitted infection. Using the value from equation 2.8, the log-likelihood function for $\ln\mathcal{L}(\mathcal{U})$ follows a beta distribution, $\mathcal{U} \sim$ Beta(55, 5):

$$\ln\mathcal{L}(\alpha, \beta; \hat{\mathcal{U}}) = \sum_{i=1}^{N} \ln\Gamma(\alpha+\beta) - [\ln\Gamma(\alpha) + \ln\Gamma(\beta)] + (\alpha-1)\ln(\mathcal{U}) + (\beta-1)\ln(1-\mathcal{U}) \quad (2.9)$$

To derive a likelihood function for the proportion of infectious flying foxes at population equilibrium, $\mathcal{I}_{Bats}$, we sourced data from a longitudinal study of acute NiV infection in *Pteropus Lylei*.[49] Of 1936 samples partial NiV-B sequences were obtained from 19 flying foxes. The model calculates $\mathcal{I}_{Bats}$ as the fraction of infectious flying foxes over the total population:

$$\mathcal{I}_{Bats} = \frac{I_B + R_B(\frac{r}{r+\mu_B})}{B_B + S_B + E_B + I_B + R_B} \tag{3.0}$$

Note equation 3.0 includes flying foxes that revert to the infectious class via disease recrudesence. As with the previous transmission events the fraction of flying foxes with acute NiV-B infection can be fitted to a beta distribution, yielding $\mathcal{I}_{Bats} \sim \text{Beta}(19, 1917)$ and the following beta log-likelihood:

$$\ln\mathcal{L}(\alpha, \beta; \widehat{\mathcal{I}_{Bats}}) = \sum_{i=1}^{N} \ln\Gamma(\alpha+\beta) - [\ln\Gamma(\alpha) + \ln\Gamma(\beta)] + (\alpha-1)\ln(\mathcal{I}_{Bats}) + (\beta-1)\ln(1-\mathcal{I}_{Bats}) \tag{3.1}$$

For every parameter set, we algebraically calculate the equilibrium values of equations 1.1 and 1.3 to obtain a corresponding log-likelihood value from equations 2.3, 2.5, 2.7, 2.9, 3.1. To estimate unknown transmission and recrudescence intensities the Markov Chain Monte Carlo (MCMC) algorithm with Metropolis-Hastings sampling was used to determine the parameter space that maximized the sum of log-likelihoods, $L(Total)$ (Equation 2.1). Conjugate prior distributions for parameters were obtained for the literature and used to fit the model (Table S2). Uniform priors for the flying fox-to-flying fox (β_{BB}), flying fox-to-human (β_{BH}), human-to-human (β_{HH}), and corpse-to-human (β_F) transmission rates, and the recrudescent rate (r), were used as no data existed to inform their prior distributions.

2.4 Sensitivity Analysis

We conducted a sensitivity analysis of the complete model to determine which model outputs were most affected by parameter variation. Sensitivity analysis assists in identifying parameter and output uncertainty as well as areas for further study. The Sobol method[50] is a robust method for conducting parameter sensitivity analysis because it is independent from model structure, captures the effect of individual parameters as well as parameter interactions on output, and provides a quantitative measure ($\mathbb{S}_i$) of the contribution of each parameter to uncertainty. Given a model of a relationship between output and parameters $y=f(X)=f(x_1, x_2, \ldots, x_k)$ Sobol's first order index is:

$$\mathbb{S}_i = \frac{V[E(y|x_i)]}{V(y)} \tag{3.2}$$

where $\mathbb{S}_i$=1 indicates that f(X) depends solely on x_i and $\mathbb{S}_i$=0 indicates f(X) has no relationship with x_i.[51] MCMC techniques were used to determine $V[E(y|x_i)]$, the partial variance. V(y), the variance of the output, y, was calculated from the posterior distributions of the MCMC.

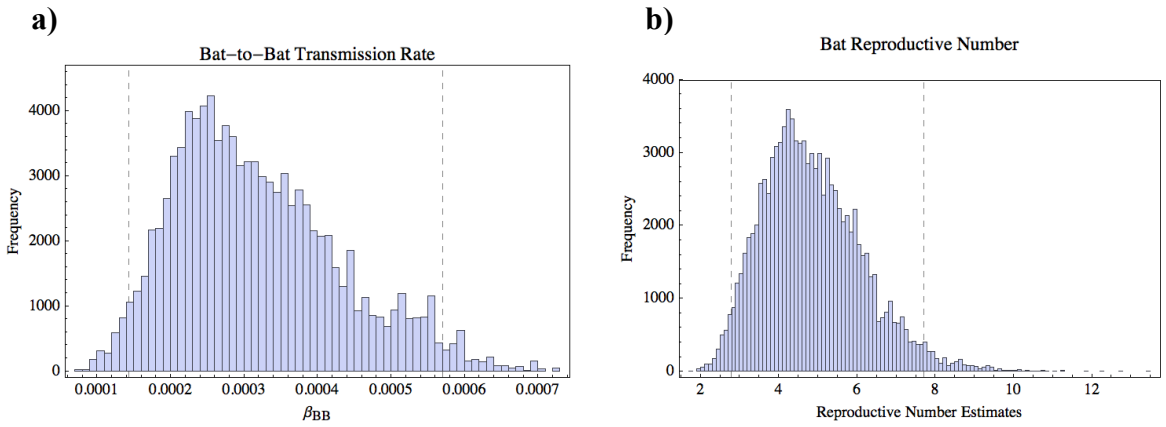
3 Results

Our results quantify several key epidemiological parameters and transmission rates between the Nipah virus wildlife reservoir, *Pteropus Giganteus*, and spillover infection to human hosts. Median estimates and 95% credible regions for the four transmission rate parameters are given in Table 3.1 for comparison purposes.

Table 3.1 *Transmission Rate and Recrudesence results of the MCMC*

PARAMETER	DESCRIPTION	MEDIAN	95% CREDIBLE REGION	
β_{BB}	Endemic Transmission	$3.00*10^{-4}$	$1.44*10^{-4}$	$5.71*10^{-4}$
β_{BH}	Zoonosis Transmission	$7.35*10^{-2}$	$7.0*10^{-2}$	$8.14*10^{-2}$
β_{HH}	Direct Transmission	$8.62*10^{-2}$	$7.38*10^{-2}$	$9.89*10^{-2}$
β_F	Post-Mortem Transmission	0.13	$2.99*10^{-2}$	0.283
r	Recrudesence	$1.86*10^{-6}$	$7.15*10^{-7}$	$3.129*10^{-6}$

3.1 Enzootic Transmission



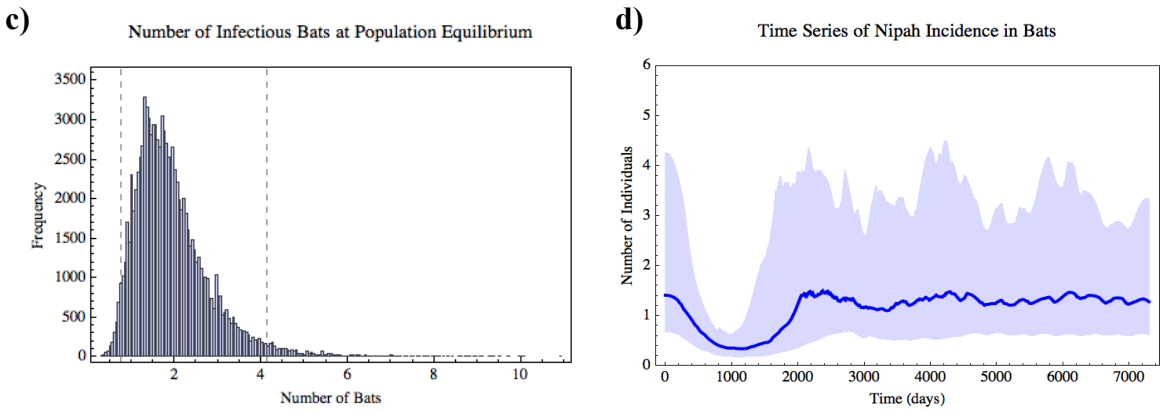


Fig. 2. a) Histogram of Transmission Rate estimates for Enzootic Transmission. This posterior distribution is a measure of the uncertainty in parameter β_{BB} as estimated by the MCMC. **b) Histogram of Reproductive Number Estimates for Enzootic Transmission.** This posterior distribution is the result of the $R_{0\ Bats}$ estimates calculated by equations 2.2-3**. c) Number of Infectious flying foxes per day.** This is a posterior distribution is a measure of $I_{B,}$ the number of flying foxes shedding live virus per day, in a simulated colony of 1000 individuals at population equilibrium. **d) Nipah Incidence in the Bat Population Over Time.** Simulated time series of the Nipah virus incidence in the bat population over 20 years.

To explore factors that drive pathogen maintenance and explain the seasonal patterns of Nipah infection in flying foxes, field data and MCMC analysis were used to generate a posterior distribution of the enzootic transmission rate (β_{BB}) (Figure 2a). Our results estimated the median flying fox-to-flying fox transmission intensity at $3.00*10^{-4}$ (95% Credible Region [CR], $1.44*10^{-4}$--$5.71*10^{-4}$), which is the rate at which susceptible flying foxes become infected with NiV-B via enzootic transmission per day. The model estimated the basic reproductive number ($R_{0\ Bats}$) for Nipah enzootic transmission at 4.70 (95% Credible Region [CR], 2.79-7.72) in a completely susceptible population (Figure 2b). No current published value for enzootic Nipah virus exists to validate our findings for $R_{0\ Bats}$.

Our model made quantitative predictions about the serological status and number of infectious flying foxes that fit independent, empirical field data on bats of the genus *Pteropus.* Serological studies of Nipah virus antibodies in free-ranging Pteropoid bat colonies have found seroprevalence to be as high as 54%.[52, 53] The model generated a seroprevalence estimate of 74.18% (95% CR, 60.30%--83.07%) calculated as $\frac{R_B}{N}$. Viral isolation and molecular studies of wild flying foxes suggest incidence of acute NIV infection to be less than 1%.[54, 55] Using the likelihood function for $\mathcal{I}_{Bats}$ (Equation 3.1) the incidence of acute NiV infection was calculated as 1.00% (95% CR, 0.65%--1.47%). As depicted in Figure 2b, the number of infectious flying foxes per day is 1.77 (95% CR, 0.78—4.15). Using the transmission rate results of the MCMC to solve differential equation 1.3 and including a seasonal forcing term (Equation S1.1) to simulate the flying fox birth season we generated Figure 2d, the number of flying foxes with acute infection over 20 years. Our results suggest low Nipah disease incidence in the flying fox population with a majority of individuals recovered.

3.2 Zoonotic Transmission

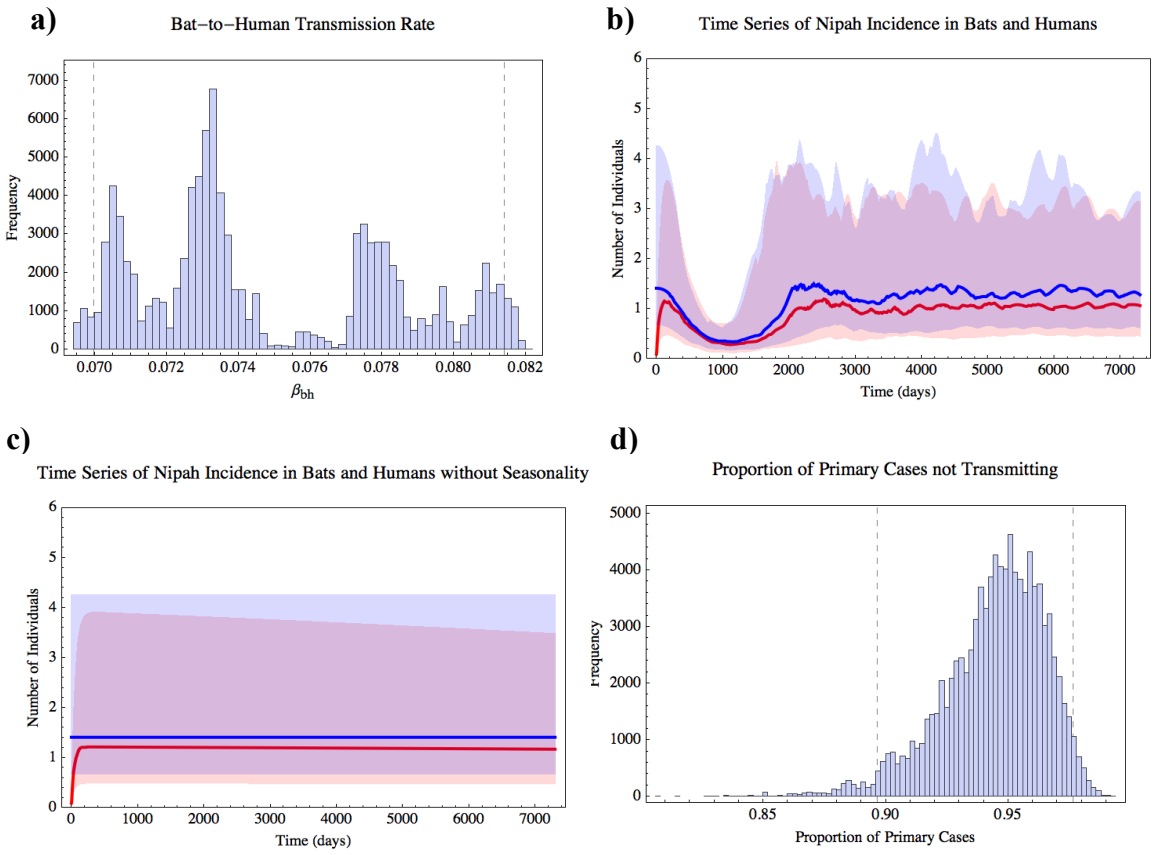


Fig. 3. a) Histogram of Transmission Rate estimates for Zoonotic Transmission. This posterior distribution is a measure of the uncertainty in parameter $\boldsymbol{\beta_{BH}}$ as estimated by the MCMC **b) Time Series of Nipah Incidence in the Bat and Human Population with Seasonality.** A simulated time series of Bat (Blue) and Human (Red) Nipah incidence over a period of 20 years displaying a temporal-lag relationship. **c) Time Series of Nipah Incidence in the Bat and Human Population without Seasonality.** A simulated time series of Bat (Blue) and Human (Red) Nipah incidence over a period of 20 years without including the seasonal forcing term. **d) Histogram of the Proportion of Primary Case-Patients not Transmitting Disease.** This posterior distribution is the result of $\boldsymbol{\ln\mathcal{L}(\alpha, \beta; \hat{u})}$ log-likelihood function described in section 2.3.3.

Many pathogens can infect and cause disease in a "dead-end" host that is not part of the normal transmission dynamics.[56] To improve our understanding of zoonotic transmission events that drive seasonal recurrence of Nipah virus outbreaks in humans, epidemiological data and MCMC analysis were used to generate a posterior distribution of the transmission rate (β_{BH}) between flying foxes and humans (Figure 3a). Our results estimated the median flying fox-to-human transmission intensity at $7.35*10^{-2}$ (95% CR, $7.0*10^{-2}$ - $8.14*10^{-2}$), which is the rate at which susceptible humans become infected with NiV-B via zoonotic infection per day.

Using the transmission rate results of the MCMC to solve differential equations 1.2-1.3 and including a seasonal forcing term (Equation S1.1) to simulate the flying fox birth season we estimated a time series of the number of human Nipah infections over 20 years. Figure 3b and 3c

demonstrates the relationship between NiV incidence in the flying fox population and in the human population including and excluding the seasonal forcing term respectively. The time series that includes seasonality displays a temporal lag between flying fox disease incidence and human infections (Figure 3b). Excluding the seasonal forcing term obscures this time lag relationship as demonstrated in Figure 3c.

For infection in a novel host pathogen optimization is based entirely on maximizing between-host transmission. In our model the number of primary case-patients that do not contribute to the direct transmission force of infection ($\beta_{HH} S_H I_H$) is an important measure not only for disease prevention, but also of viral adaptation in a new host. Using the log-likelihood equation $\ln\mathcal{L}(\alpha, \beta; \hat{u})$ and epidemiological data from previous NiV outbreaks, an estimate of primary case-patients who do not transmit could be made (Figure 3d). We found that 94.73% (95% CR, 89.70% - 97.70%) Nipah case-patients who were exposed via zoonosis do not contribute to the human-to-human force of infection, which indicates that on average a minority of primary cases are responsible for secondary disease transmission.

3.3 Direct Transmission

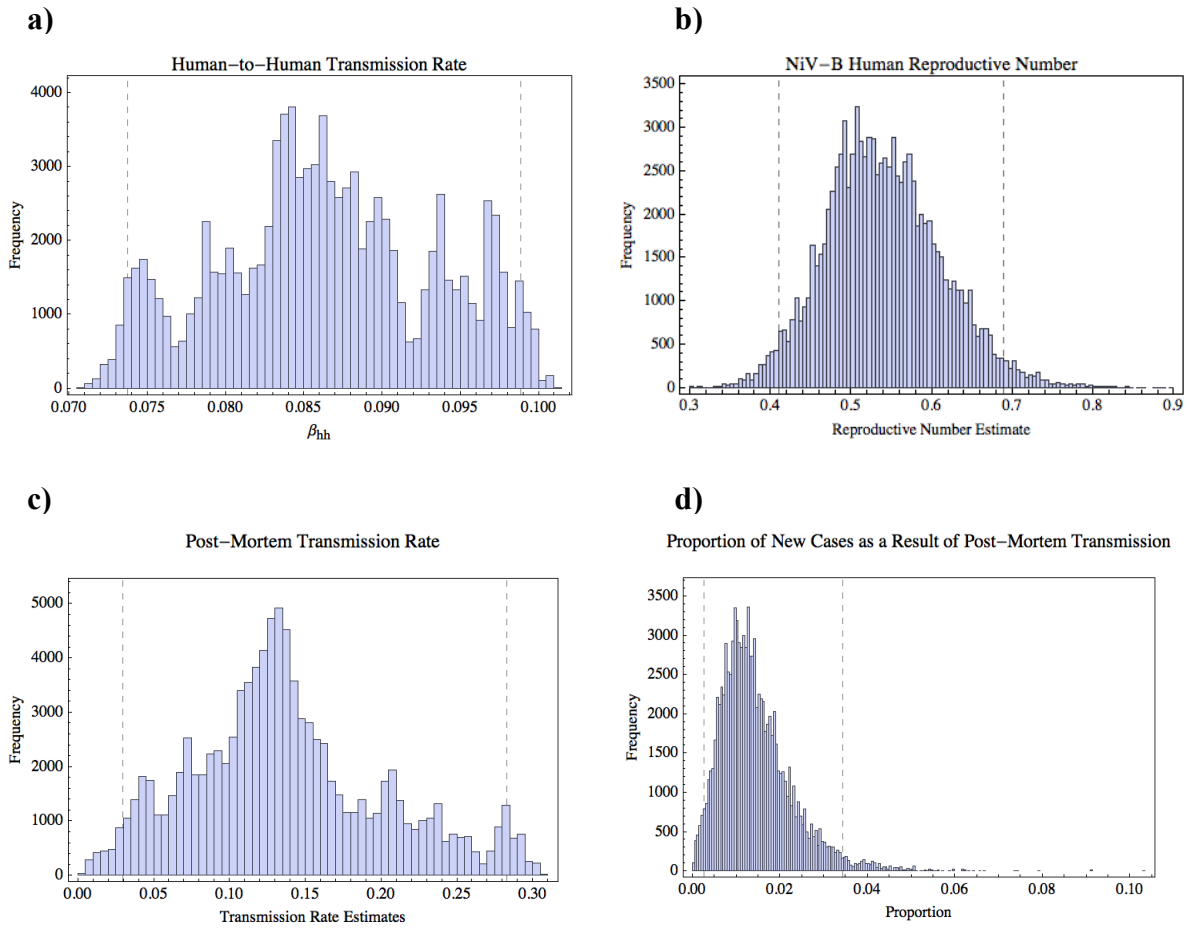


Fig. 4. a) Histogram of Transmission Rate estimates for Direct Transmission. This posterior distribution is a measure of the uncertainty in parameter β_{HH} as estimated by the MCMC. **b) Histogram of Reproductive Number Estimates for Direct Transmission.** This posterior distribution is the result of $\ln\mathcal{L}(X_0, N_0; \widehat{R_{0\,humans}})$ log-likelihood calculated by equation 2.5. **c) Histogram of Transmission Rate estimates for Post-Mortem Transmission.** This posterior distribution is a measure of the uncertainty in parameter β_F as estimated by the MCMC. **d) Proportion of New Cases that Result from Post-Mortem Transmission.** Of all new human infections, $\mathcal{F}$ is the proportion that are due to disease transmission from a deceased case-patient as defined in equation 2.6.

To establish in a new host population, a pathogen must have both successful infection of new hosts and sufficient transmission between hosts to raise the basic reproductive number R_0 in this host above 1. Determining human epidemiological parameters such the direct transmission rate and $R_{0\,Human}$ informs disease prevention and control measures. Our results estimate the median direct transmission intensity at $8.61*10^{-2}$ (95% CR, $7.38*10^{-2}$ - $9.89*10^{-2}$) (Figure 4a), which is the rate at which susceptible humans become infected via NiV-B infection from another human per day. From our model the median R_{0Human} for direct transmission was 0.536 (95% CR, 0.410 – 0.689) (Figure 4b), which corroborates our prior distribution, the only published estimate of $R_{0\,Human}$ at 0.48.[57] Our model analysis suggests R_{0Human} is less than 1; therefore NiV-B is not capable of establishing endemic transmission in the human population at this time.

Nipah virus has been demonstrated as capable of transmitting post-mortem, usually during funeral preparation by a friend or family member.[58] Since this discovery in the 2010 Faridpur outbreak, post-mortem hygiene interventions and personal protective equipment have been used to handle infected remains. Using case data prior to the interventions for post-mortem transmission, and beta log-likelihood techniques $\ln\mathcal{L}(\alpha, \beta; \hat{\mathcal{F}})$ we estimated the unknown transmission rate for post-mortem infection and the proportion of total NiV-B cases that occur from post-mortem contact. Results from the MCMC analysis were used to generate a posterior distribution of the transmission rate (β_F) between deceased and live hosts (Figure 4c). The median post-mortem transmission rate was estimated to be 0.13 (95% CR, 2.99*10-2—0.283), the rate at which susceptible humans become infected via contact from a deceased case-patient. Although the post-mortem transmission rate is higher than both the direct and zoonotic transmission rate, the proportion of total NiV-B case-patients that result from this transmission type is 1.29% (95% CR, 0.27 – 3.45%) (Figure 4d). This low percentage is likely because a limited number of family members undertake funeral preparations and because burial usually occurs approximately 1 day after death.

3.5 Recrudescence

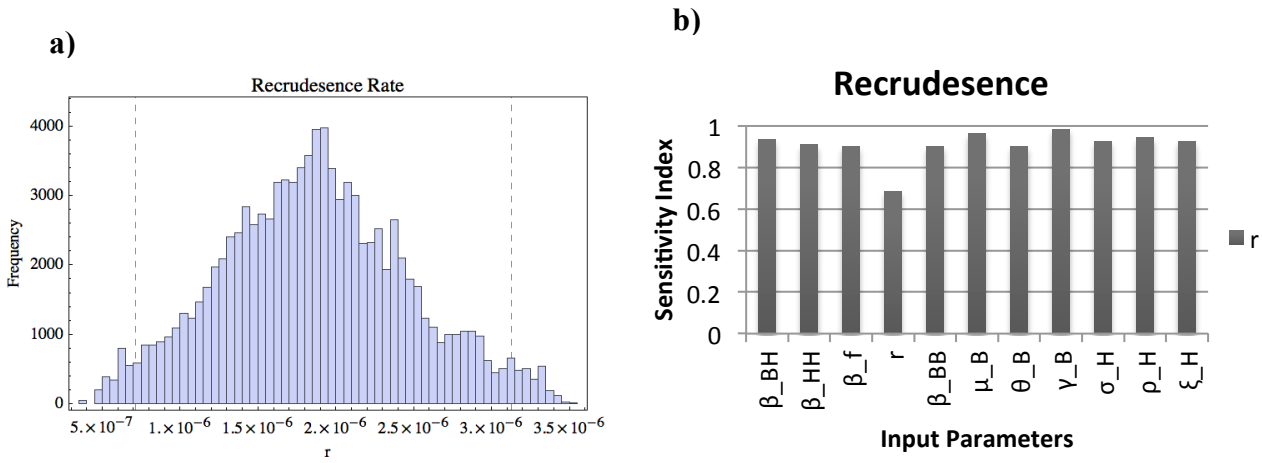


Fig. 5. a) Histogram of Recrudesence Rate Parameter Value Estimates. This posterior distribution is a measure of the uncertainty in parameter r as estimated by the MCMC. **b) Sensitivity Index for Recrudescence Parameter r.** Analysis determining how sensitive model output, r, is to input parameters.

Recrudescence is defined as the recurrence of symptoms in a host whose blood stream infection has previously been at such a low level as not to be clinically demonstrable. Recovered individuals who undergo stress such nutritional deficits or pregnancy may become immunocompromised.[59] NiV-B recrudescence has previously been theorized as an explanatory mechanism for disease maintenance in flying foxes. The only confirmed case of recrudescence occurred in captive flying foxes;[60] thus there is no data to fit a prior distribution. Recrudescence was included in our model as movement from the recovered class back to the infectious class at a rate r. Our results approximate the median recrudescence rate at $1.86*10^{-6}$ (95% CR, $7.15*10^{-7}$ — $3.129*10^{-6}$) per day (Figure 5a). Figure 5b displays Sobol's first order sensitivity index for the output, r, to the input parameters, indicating that r is very sensitive to a number of input parameters in the flying fox and human disease system. The high degree of sensitivity to each of the input parameters is likely because so few data exist to inform the model, and the small order of magnitude of the value itself.

3.6 Sensitivity Analysis

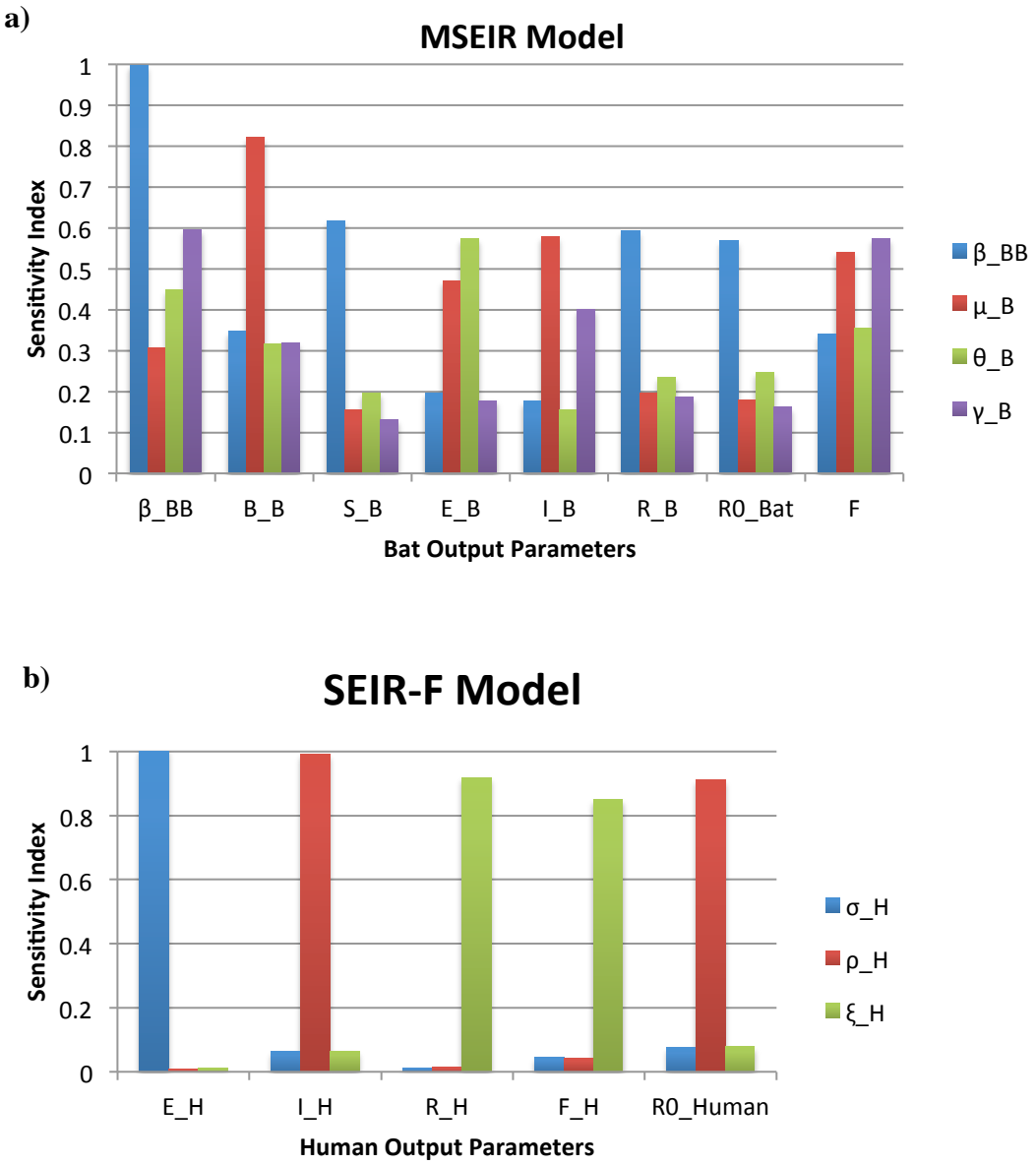


Fig. 5. a) Sensitivity Index for Bat Output Parameters. Analysis determining how sensitive model output was to changes in the input parameters. The y-axis represents the Sobol's sensitive index where $\mathbb{S}_i=1$ indicates that f(X) depends solely on x_i and $\mathbb{S}_i=0$ indicates f(X) has no relationship with x_i. **b) Sensitivity Index for Human Output Parameters.** Only output parameters with a sensitivity value >0.5 are included.

Sensitivity analysis on the MSEIR and SEIR-F combined model for the effect of individual parameter values on output demonstrated four general outcomes: (i) the number of exposed and infectious flying foxes is strongly affected by the natural mortality rate, μ_B (ii) the number of susceptible and recovered flying foxes are strongly influenced by the enzootic transmission rate, β_{BB} (iii) in the human population the proportion of individuals who recover or die from infection is strongly affected by the case-fatality rate and (iv) in general, many output parameters were very sensitive to the "outflow rate", which is the duration an individual spent in

the compartment. In particular human infections were strongly affected by $\rho_{H,}$ the duration of infectiousness. Surprisingly $\mathcal{F}$, the proportion of new human cases that result from post-mortem transmission, was moderately sensitive to the input parameter γ_B , the infectious period for bats. This result is likely due to the formula for $\mathcal{F}$ (Equation 2.6) where the number of infectious bats, I_B, is a component of the denominator.

4 Discussion

4.1 Implications for Outbreak Control and Disease Prevention

Diseases emerge in association with changes in the nature and intensity of human interactions with a wildlife reservoir host or pathogen by increasing the likelihood that contact occurs between a pathogen and a naive host population. **[61]** Shifts in ecological opportunities also pose evolutionary challenges that can facilitate pathogen adaptation. Here we have used a compartmental SEIR model to get quantitative estimates of the key parameters in the recent emergence of a novel deadly virus in South Asia.

Luby et al. made an arithmetic estimate of Nipah virus R_0 in humans based on a summary of cases from 2001-2007.[62] The estimate made by Luby et al. (0.48) and from our model (0.54) for $R_{0\ Human}$ reflect the average value of those primary case-patients who do not transmit and those who do. Our results from $\ln\mathcal{L}(\alpha, \beta; \hat{u})$ demonstrate that 94.72%, (95% CR, 89.70%--97.70%) of flying fox-to-human cases do not generate secondary cases; thus of these zoonosis derived case-patients 0.053 is the proportion who generate secondary cases. In studies of avian influenza, Ferguson et al. developed an alternative method to calculate $R_{0\ Human}$ from avian-to-human contact:[63]

$$R_{Transmission} = \frac{p_c}{1-p_c}$$

where p_c is the proportion of flying fox-to-human cases generating at least 1 secondary case. Using this metric an alternative estimate for $R_{0\ Human}$ is 0.056, which *does not* reflect an averaged value across all zoonotic case patients. During Nipah outbreaks primary cases that do transmit have established transmission chains upwards of five individuals. As with other zoonotic diseases like SARS, this transmission pattern may be indicative of super-spreaders. Lloyd-Smith et al. defines super-spreaders as those who transmit more infection than is predicted by a homogenous 'null model'.[64] Small et al. super-spreaders occur in small-world or scale-free networks, implying that super-spreaders are not a result of variable infectiousness but a characteristic of individuals who have more opportunities to infect other hosts.[65] For disease surveillance purposes $R_{Transmission}$ can act as a general prediction of cluster size during an outbreak. Should the number of cases generated by an individual exceed the amount predicted by $R_{Transmission}$ anomalous behavior may be occurring that is conducive to disease transmission. We did not calculate a $R_{effective}$ for the reservoir population as the assumption of equation 2.3 is that the disease has reached equilibrium within the bat population such that $R_{effective}$ =1.

4.1.1 Pathogen Virulence

Calisher et al. proposed in their 2006 paper that based on the phylogenetic distance of NiV from other pathogens in the *Paramyxoviridae* family, NiV have had long evolutionary co-existence with their flying fox hosts. According to virulence evolution theory, infected hosts evolve to reduce the damage pathogens cause in order to maximize their fitness. Virulence in the novel human host does not represent the equilibrium for pathogen fitness; consequently rapid pathogen evolution can take place to adapt to the new host.

In our study the increased post-mortem transmission rate may not indicate simply contact pattern differences, but an adaptive virulence event whereby the increased transmission rate is indicative of increased virulence in a novel host. NiV-B is able to transmit post-mortem, in other species novel host death through increased virulence can be an effective tradeoff to maximize transmission. [66] This rate increase may be due to increased viral load in the inoculum during the disease progression to fatality; many virulent disease strains manifest severe symptoms and increased infectivity prior to death. Despite this high rate, the proportion of new Nipah cases that can be attributed to post-mortem exposure source was estimated at a low 1.29%. Post-mortem transmission relies on a very specific contact exchange, which is rare relative to the number of direct human contacts and spillover transmission mechanisms that are possible in daily life. Host switches are facilitated by frequent contact between the novel and reservoir host, especially when they begin to share resources such as food or space.[67] Although Nipah infection has yet to reach optimal virulence in humans as demonstrated by the flying fox population, there is the possibility it may do so if zoonotic host-switching continues to occur in the future.

4.2 Implications for Model Guided Fieldwork

Our estimates of the flying-fox-to-flying fox transmission rate and $R_{0\ Bat}$ demonstrate the high infectivity of NiV-B within the reservoir population; however our results also demonstrate that in a colony of 1000 bats at population equilibrium, on average, 1.8 flying foxes per day shed live virus. In a population of 1000 the model generates ~1% of bats with acute infection which is problematic for field research seeking to establish disease reservoirs through genome homology. At endemic equilibrium the flying fox population is comprised of both susceptible individuals and those with acquired immunity. The ratio of susceptible and recovered flying foxes maintains herd immunity and pathogen persistence in a process known as “epidemic enhancement”. [68] Population level changes such as birth pulses, migration, and die-offs can upset this ratio and cause outbreaks in reservoir and incidental hosts. Field research should target known population disruptions if we wish to further out understanding on enzootic disease. Our model assumes the flying fox population is at equilibrium, which accounts for births and deaths but omits seasonal immigration and emigration. Despite this limitation our model results for flying fox incidence of

Nipah virus and population seroprevalence were well validated against independent empirical field data.

Our MCMC analysis suggests recrudescence in the flying fox population is non-zero, and occurs in the population at some low rate; however its effect on the flying fox transmission rate is unclear. Flying fox population output parameters including I_B, the infectious class, were largely insensitive to recrudescence. It has been theorized that recrudescence may be a result of immunosuppression from the stresses of reproduction or age. The results of field seroprevalence studies on *Pteropus Vampyrus* and *P. hypomelanus* bats noted elevated NiV-antibody levels in adult bats that were pregnant and lactating. To meet the energy demands of reproduction increased food intake and changes in foraging behavior through pregnancy and the lactation period have been observed in lab studies of bats.[69] In a study of free ranging little brown bats (*Myotis Lucifugus*) costs of reproduction remained low during pregnancy, but lactation increased energy demands by 50% in comparison to pregnant animals.[70] This includes the direct cost of production of the young and milk supply, maternal care, flight during pregnancy.[71] When we included a seasonal forcing term (Equation S1.1) to emulate the flying fox birth-cycle the temporal lag relationship between Nipah incidence in the bat and human population was evident (Figure 3b). If additional enzootic transmission were occurring during this time because of recrudescence it may partially explain the seasonal outbreak of NiV-B in Bangladesh. However more research into the immunosuppressive aspect of flying fox pregnancy and lactation is needed before any clear relationship can be determined.

The enzootic transmission rate (β_{BB}) and natural mortality rate (μ_B) were the most important parameters driving flying fox population and pathogen maintenance. Changes in the enzootic transmission rate (β_{BB}) strongly affect the number of susceptible and recovered flying foxes. Higher transmission rates lead to a higher force of transmission and ultimately more recovered bats with few susceptibles, while low transmission rates decrease the force of transmission allowing a high number of susceptibles and few recovered. Changes in the natural mortality rate (μ_B) affects population viability. The restricted annual reproductive rate of the *Pteropus* species means that populations take a relatively long time to recover from losses.[72] In other bat species such as big brown bats, natural mortality rate varies by season and often threatens the viability of bat populations.[73] In terms of pathogen maintenance the natural mortality rate also has an effect as fewer incubating or infectious bats could lead to pathogen extinction. This phenomenon is demonstrated in Figure 5a in that output parameters E_H and I_H are strongly affected by μ_B. Little data exists on the natural mortality rate in bat colonies. Although *Pteropous Giganteus* has few natural predators, lifespan and age-estimates are collected from captive specimens only.[74] As natural mortality rate (μ_B) has been implicated as one of the most important parameters driving flying fox population and pathogen maintenance it warrants further field research. Fieldwork should focus not only on natural mortality, but additional mortality due to anthropogenic disturbances such as hunting or deforestation.

5 Conclusions

This research increases our understanding of pathogen dynamics in a disease reservoir host, incidental human host, and their interaction. Our results indicate that Nipah virus infection in the reservoir host, *Pteropus Giganteus*, is enzootic at low levels with a periodic epidemic pattern in flying foxes, likely a result of seasonal birth cycles. Our analysis suggests recrudescence in the flying fox population occurs in the population at a low rate; however the sensitivity analysis indicated bat parameters, including I_B, the infectious class, were largely insensitive to the recrudescence. Sensitivity analysis of our model output parameters indicates the natural mortality rate of bats (μ_B) should be the focus of further field study as it strongly affects population viability and pathogen maintenance. In the context of public health, Nipah virus infection is unable to sustain human-to-human transmission chains with $R_{0\ Human}$ below 1. From our analysis, only 5.28% of zoonotic case-patients generate secondary cases. An alternate $R_{0\ Human}$ estimate was calculated, given as $R_{Transmission}$, which was much lower than the estimate generated by the log-likelihood function $\ln\mathcal{L}(X_0, N_0; \widehat{R_{0\ humans}})$. This difference between the two reproductive number estimates, 0.54 and 0.06, suggests that super-spreaders have likely occurred in past Nipah outbreaks. Additionally we estimated four transmission rates using the Markov Chain Monte Carlo algorithm, which can now be used to reference and to parameterize future mathematical models of Nipah virus when more data are available for validation. This simple model design may also be useful for modification and application to other zoonotic pathogens in order to study both reservoir host and human population disease dynamics.

Supplementary Information

Table S1: Field Data from Literature with References

Parameter	*Definition*	*Estimated Range*	*Reference*
$1/\theta_{Bats}$	Incubation period for Bats	4-9 days	Plowright et al., Halprin et al. 2011:949,
μ_{Bats}	Mortality Rate of Bats	1/30 years	Plowright et al. (2011), Silbernagel, E., (2005)
$1/\gamma_{Bats}$	Infectious Period for Bats	12,18 days	Middleton et al. 2007, Halpin et al. 2011
$1/\varpi\omega$	Period of Maternal Immunity	270-420 days	Sohayati et al. (2011)
b	Bat Birth Rate	0.00136986	An annual rate birth for all sexually mature female flying foxes.
k	Area Carrying Capacity	1250 bats	Derived from equation 1.2
$1/\sigma_{Humans}$	Incubation Period for Humans	6-11, 8-13, 8-12 days	Luby et al. (2009), Homaira et al. (2010), Sazzad et al. (2013)
μ_{Humans}	Mortality Rate of Humans	1/(69.2 years)	United Nations Development Program
$1/\rho_{Humans}$	Infectious Period for Humans	4-7, 4-8 days	Homaira et al. (2010), Sazzad et al. (2013)
ξ	Case Fatality Rate	0.776 deaths per case	Luby et al. (2009), Homaira et al. (2010), Lo et al. (2012), Field et al. (2011)
φ	Burial Rate	1 $days^{-1}$	

Table S2: Prior Distributions for fitting Markov Chain Monte Carlo Algorithm

Parameters	**Definition**	**Distribution**	**Rate**
θ_{Bats}	Incubation period for Bats	Gamma (10.2426, 61.725)	0.110-0.250 $days^{-1}$
μ_{Bats}	Mortality Rate of Bats	Gamma (2.0, 10950.0)	0.1 $years^{-1}$
γ_{Bats}	Infectious Period for Bats	Gamma (12.5, 180)	0.056-0.0833 $days^{-1}$
ϖ	Period of Maternal Immunity	Gamma (59.8376, 20310.1)	0.0024-0.0037 $days^{-1}$
σ_{Humans}	Rate of progression from latency	Gamma (21.1565, 196.088)	0.091-0.167 $days^{-1}$
μ_{Humans}	Mortality Rate of Humans	NA	0.014 $years^{-1}$
ρ_{Humans}	Rate of recovery from infectiousness	Gamma (16.0087, 87.6362)	0.143-0.250 $days^{-1}$
ξ	Case Fatality Rate	Beta(207, 57)	0.776 deaths per case

Equation S1.1

NiV-B outbreaks in Bangladesh occur between December and May, which coincides with the flying fox birth season. To account for seasonal changes to flying fox social grouping in response to reproduction and birth events a temporal window was defined within which the birth rate is positive and proportional to a cosine wave, and outside this window, from June to the end

of November, the number of new births was equal to zero:

$$\text{Seasonality(t)}=\begin{cases} 0 & if\ 150 < Mod[t,365] < 326 \\ \left[\frac{365*b}{180}\right]\left[1-cos\left[2\pi\left(\frac{Mod[t-326,\ 365]}{365/2}\right)\right]\right] & if\ Mod[t,365] < 150 \text{ or } Mod[t,365] > 326 \end{cases}$$

where time t is measured in days, and b is the birth rate. A modulus operator was included to replicate the window when the model was run over 365 days.

[1] Hs, V. P., Hossain, M. J., Parashar, U. D., Ali, M. M., Ksiazek, T. G., Kuzmin, I., Niezgoda, M., ... Breiman, R. F.(January 01, 2004). Nipah virus encephalitis reemergence, Bangladesh. Emerging Infectious Diseases, 10, 12, 2082-7.
[2] Siva SR, Chong HT, Tan CT (2009). "Ten year clinical and serological outcomes of Nipah virus infection". Neurology Asia 14: 53–58.
[3] Daszak, P., Zambrana-Torrelio, C., Bogich, T. L., Fernandez, M., Epstein, J. H., Murray, K. A., & Hamilton, H. (January 01, 2013). Interdisciplinary approaches to understanding disease emergence: the past, present, and future drivers of Nipah virus emergence. Proceedings of the National Academy of Sciences of the United States of America, 110, 3681-8.
[4] Hsu, V. P., Hossain, M. J., Parashar, U. D., Ali, M. M., Ksiazek, T. G., Kuzmin, I., Niezgoda, M., ... Breiman, R. F. (January 01, 2004). Nipah virus encephalitis reemergence, Bangladesh. Emerging Infectious Diseases, 10, 12, 2082-7.
[5] Luby, Stephen P., Hossain, M. Jahangir, Gurley, Emily S., Ahmed, Be-Nazir, Banu, Shakila, Khan, Salah Uddin, Homaira, Nusrat, ... Rahman, Mahmudur. (n.d.). Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007. Centers for Disease Control and Prevention.
[6] Ksiazek, T. G., Rota, P. A., & Rollin, P. E. (January 01, 2011). A review of Nipah and Hendra viruses with an historical aside. Virus Research, 162, 1, 173-183.
[7] Gurley, E. S., Montgomery, J. M., Hossain, M. J., Bell, M., Azad, A. K., Islam, M. R., Molla, M. A., ... Breiman, R. F. (January 01, 2007). Person-to-person transmission of Nipah virus in a Bangladeshi community. Emerging Infectious Diseases, 13, 7, 1031-7.
[8] Lloyd-Smith, J. O., George, D., Pepin, K. M., Pitzer, V. E., Pulliam, J. R., Dobson, A. P., Hudson, P. J., ... Grenfell, B. T. (January 01, 2009). Epidemic dynamics at the human-animal interface. *Science (new York, N.y.), 326,* 5958, 1362-7.
[9] Luby, Stephen P., Hossain, M. Jahangir, Gurley, Emily S., Ahmed, Be-Nazir, Banu, Shakila, Khan, Salah Uddin, Homaira, Nusrat, ... Rahman, Mahmudur. (n.d.). Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007. Centers for Disease Control and Prevention.
[10] Calisher, C. H., Childs, J. E., Field, H. E., Holmes, K. V., & Schountz, T. (January 01, 2006). Bats: Important Reservoir Hosts of Emerging Viruses. Clinical Microbiology Reviews, 19, 3, 531-545.
[11] Crichton, E. G., & Krutzsch, P. H. (2000). Reproductive biology of bats. San Diego, Calif: Academic Press.
[12] Crichton, E. G., & Krutzsch, P. H. (2000). Reproductive biology of bats. San Diego, Calif: Academic Press.
[13] Crichton, E. G., & Krutzsch, P. H. (2000). Reproductive biology of bats. San Diego, Calif: Academic Press.
[14] Wang, L.-F., Walker, P. J., & Poon, L. L. M. (December 01, 2011). Mass extinctions, biodiversity and mitochondrial function: Are bats 'special' as reservoirs for emerging viruses?. Current Opinion in Virology, 1, 6, 649-657.
[15] Epstein, J. H., Quan, P. L., Briese, T., Street, C., Jabado, O., Conlan, S., Ali, K. S., ... Lipkin, W. I. (January 01, 2010). Identification of GBV-D, a novel GB-like flavivirus from old world frugivorous bats (Pteropus giganteus) in Bangladesh. Plos Pathogens, 6.
[16] Epstein, Jonathan H., Prakash, Vibhu, Smith, Craig S., Daszak, Peter, McLaughlin, Amanda B., Meehan, Greer, Field, Hume E., ... Cunningham, Andrew A. (n.d.). Henipavirus Infection in Fruit Bats (Pteropus giganteus), India. Centers for Disease Control and Prevention.
[17] Epstein, J. H., Baker, M. L., Zambrana-Torrelio, C., Middleton, D., Barr, J. A., DuBovi, E., Boyd, V., ... Markotter, W. (June 27, 2013). Duration of Maternal Antibodies against Canine Distemper Virus and Hendra Virus in Pteropid Bats. *Plos One, 8,* 6.)
[18] Ksiazek, T. G., Rota, P. A., & Rollin, P. E. (January 01, 2011). A review of Nipah and Hendra viruses with an historical aside. Virus Research, 162, 1, 173-183.
[19] Luby, S. P., Rahman, M., Hossain, M. J., Blum, L. S., Husain, M. M., Gurley, E., Khan, R., ... Ksiazek, T. G. (January 01, 2006). Foodborne transmission of Nipah virus, Bangladesh. *Emerging Infectious Diseases, 12,* 12, 1888-94.
[20] Luby S. P., Gurley E. S., Hossain M. J. 2009 Transmission of human infection with Nipah virus. Clin. Infect. Dis. **49**, 1743–1748.(**doi:10.1086/647951**)
[21] Chowdhury, M. S. H., Halim, Md. A., Muhammed, N., Haque, F., & Koike, M.; yUfVPpkh. (2009). *Traditional utilization of wild date palm (Phoenix sylvestris Roxb) in rural Bangladesh: An approach to sustainable biodiversity management*. Springer.

[22] Gurley, E. S., & Luby, S. P. (August 01, 2011). Nipah virus transmission in south Asia: Exploring the mysteries and addressing the problems. *Future Virology, 6,* 8, 897-900.
[23] Luby S. P., Gurley E. S., Hossain M. J. 2009 Transmission of human infection with Nipah virus. Clin. Infect. Dis. 49, 1743–1748.(doi:10.1086/647951)
[24] Sazzad, H. M., Hossain, M. J., Gurley, E. S., Ameen, K. M., Parveen, S., Islam, M. S., Faruque, L. I., ... Luby, S. P. (January 01, 2013). Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. *Emerging Infectious Diseases, 19,* 2, 210-7.
[25] Luby S. P., Gurley E. S., Hossain M. J. 2009 Transmission of human infection with Nipah virus. Clin. Infect. Dis. 49, 1743–1748.(doi:10.1086/647951)
[26] Gurley, E. S., Montgomery, J. M., Hossain, M. J., Bell, M., Azad, A. K., Islam, M. R., Molla, M. A., ... Breiman, R. F. (January 01, 2007). Person-to-person transmission of Nipah virus in a Bangladeshi community. Emerging Infectious Diseases, 13, 7, 1031-7.
[27] Gurley, E. S., & Luby, S. P. (August 01, 2011). Nipah virus transmission in south Asia: Exploring the mysteries and addressing the problems. *Future Virology, 6,* 8, 897-900.
[28] Sazzad, H. M., Hossain, M. J., Gurley, E. S., Ameen, K. M., Parveen, S., Islam, M. S., Faruque, L. I., ... Luby, S. P. (January 01, 2013). Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. *Emerging Infectious Diseases, 19,* 2, 210-7.
[29] Sazzad, H. M., Hossain, M. J., Gurley, E. S., Ameen, K. M., Parveen, S., Islam, M. S., Faruque, L. I., ... Luby, S. P. (January 01, 2013). Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. *Emerging Infectious Diseases, 19,* 2, 210-7.
[30] Chowdhury, M. S. H., Halim, Md. A., Muhammed, N., Haque, F., & Koike, M.; yUfVPpkh. (2009). *Traditional utilization of wild date palm (Phoenix sylvestris Roxb) in rural Bangladesh: An approach to sustainable biodiversity management*. Springer.
[31] Gurley, E. S., & Luby, S. P. (August 01, 2011). Nipah virus transmission in south Asia: Exploring the mysteries and addressing the problems. *Future Virology, 6,* 8, 897-900.
[32] Montgomery, J. M. (January 01, 2008). Risk Factors for Nipah Virus Encephalitis, Bangladesh. *Emerging Infectious Diseases, 14,* 10, 1526-1532.
[33] Middleton, D. J., Westbury, H. A., Morrissy, C. J., van, . H. B. M., Russell, G. M., Braun, M. A., & Hyatt, A. D. (January 01, 2002). Experimental Nipah virus infection in pigs and cats. *Journal of Comparative Pathology, 126*.
[34] Middleton, D. J., Westbury, H. A., Morrissy, C. J., van, . H. B. M., Russell, G. M., Braun, M. A., & Hyatt, A. D. (January 01, 2002). Experimental Nipah virus infection in pigs and cats. *Journal of Comparative Pathology, 126*.
[35] Sohayati, A. R., Hassan, L., Sharifah, S. H., Lazarus, K., Zaini, C. M., Epstein, J. H., Shamsyul, N. N., ... Henipavirus Ecology Research Group. (January 01, 2011). Evidence for Nipah virus recrudescence and serological patterns of captive Pteropus vampyrus. Epidemiology and Infection, 139, 10, 1570-9
[36] Hyatt, A. D., Daszak, P., Cunningham, A. A., Field, H., & Gould, A. R. (March 01, 2004). Henipaviruses: Gaps in the Knowledge of Emergence. *Ecohealth, 1,* 1, 25-38.
[37] Rahman, S. A., Hassan, L., Epstein, J. H., Mamat, Z. C., Yatim, A. M., Hassan, S. S., Field, H. E., ... Henipavirus Ecology Research Group. (January 01, 2013). Risk Factors for Nipah virus infection among pteropid bats, Peninsular Malaysia. *Emerging Infectious Diseases, 19,* 1, 51-60.
[38]Luby, Stephen P., Hossain, M. Jahangir, Gurley, Emily S., Ahmed, Be-Nazir, Banu, Shakila, Khan, Salah Uddin, Homaira, Nusrat, ... Rahman, Mahmudur. (2009). *Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007*. Centers for Disease Control and Prevention.
[39] Sazzad, H. M., Hossain, M. J., Gurley, E. S., Ameen, K. M., Parveen, S., Islam, M. S., Faruque, L. I., ... Luby, S. P. (January 01, 2013). Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. *Emerging Infectious Diseases, 19,* 2, 210-7.
[40] (June 2010). Nipah outbreak in Faridpur District, Bangladesh, 2010. ICDDR,B: Health and Science Bulletin, 8, 2,6-11.
[41] (March 2012). Nipah transmission from bats to humans associated with drinking traditional liquor (tari) in northern Bangladesh, 2011. ICDDR,B: Health and Science Bulletin, 10, 1, 16-20.
[42] Hefferman, J., R. Smith, and L. Wahl (2005). Perspectives on the basic reproduction ratio. Journal of the Royal Society Interface 2, 281–293.
[43] Keeling, M. J., & Rohani, P. (2008). *Modeling infectious diseases in humans and animals*. Princeton: Princeton University Press.

[44] Silbernagel, E. 2005. "Pteropus giganteus" (On-line), Animal Diversity Web. Accessed April 28, 2014 at http://animaldiversity.ummz.umich.edu/accounts/Pteropus_giganteus/
[45] Luby, Stephen P., Hossain, M. Jahangir, Gurley, Emily S., Ahmed, Be-Nazir, Banu, Shakila, Khan, Salah Uddin, Homaira, Nusrat, ... Rahman, Mahmudur. (2009). *Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007*. Centers for Disease Control and Prevention.
[46] Sazzad, H. M., Hossain, M. J., Gurley, E. S., Ameen, K. M., Parveen, S., Islam, M. S., Faruque, L. I., ... Luby, S. P. (January 01, 2013). Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. *Emerging Infectious Diseases, 19,* 2, 210-7.

[47] Sazzad, H. M., Hossain, M. J., Gurley, E. S., Ameen, K. M., Parveen, S., Islam, M. S., Faruque, L. I., ... Luby, S. P. (January 01, 2013). Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. *Emerging Infectious Diseases, 19,* 2, 210-7.
[48] Luby, Stephen P., Hossain, M. Jahangir, Gurley, Emily S., Ahmed, Be-Nazir, Banu, Shakila, Khan, Salah Uddin, Homaira, Nusrat, ... Rahman, Mahmudur. (2009). *Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007*. Centers for Disease Control and Prevention.
[49] Wacharapluesadee, S., Boongird, K., Wanghongsa, S., Ratanasetyuth, N., Supavonwong, P., Saengsen, D., Gongal, G. N., ... Hemachudha, T. (January 01, 2010). A longitudinal study of the prevalence of Nipah virus in Pteropus lylei bats in Thailand: evidence for seasonal preference in disease transmission. *Vector Borne and Zoonotic Diseases (larchmont, N.y.), 10,* 2, 183-90.
[50] Sobol IM. 1990 On sensitivity estimates fornonlinear mathematical models. Matematicheskoe Modelirovanie 2, 112–118. [In Russian].
[51] Wu, J., Dhingra, R., Remais, J. V., & Gambhir, M. (September 06, 2013). Sensitivity analysis of infectious disease models: Methods, advances and their application. Journal of the Royal Society Interface, 10, 86.)
[52] Epstein, Jonathan H., Prakash, Vibhu, Smith, Craig S., Daszak, Peter, McLaughlin, Amanda B., Meehan, Greer, Field, Hume E., ... Cunningham, Andrew A. (2008).*Henipavirus Infection in Fruit Bats (Pteropus giganteus), India*. Centers for Disease Control and Prevention.
[53] Epstein, J., Field, H., Luby, S., Pulliam, J., & Daszak, P. (January 01, 2006). Nipah virus: Impact, origins, and causes of emergence. *Current Infectious Disease Reports, 8,* 1, 59-65.
[54] Epstein, J., Field, H., Luby, S., Pulliam, J., & Daszak, P. (January 01, 2006). Nipah virus: Impact, origins, and causes of emergence. *Current Infectious Disease Reports, 8,* 1, 59-65.
[55] Epstein, J. H., Baker, M. L., Zambrana-Torrelio, C., Middleton, D., Barr, J. A., DuBovi, E., Boyd, V., ... Markotter, W. (June 27, 2013). Duration of Maternal Antibodies against Canine Distemper Virus and Hendra Virus in Pteropid Bats. *Plos One, 8,* 6.)
[56] Koella, J. C., & Stearns, S. C. (2008). *Evolution in health and disease*. Oxford: Oxford University Press. P(156-159)
[57] Luby, Stephen P., Hossain, M. Jahangir, Gurley, Emily S., Ahmed, Be-Nazir, Banu, Shakila, Khan, Salah Uddin, Homaira, Nusrat, ... Rahman, Mahmudur. (2009). *Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007*. Centers for Disease Control and Prevention.
[58] Sazzad, H. M., Hossain, M. J., Gurley, E. S., Ameen, K. M., Parveen, S., Islam, M. S., Faruque, L. I., ... Luby, S. P. (January 01, 2013). Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. *Emerging Infectious Diseases, 19,* 2, 210-7.
[59] Rahman, S. A., Hassan, L., Epstein, J. H., Mamat, Z. C., Yatim, A. M., Hassan, S. S., Field, H. E., ... Henipavirus Ecology Research Group. (January 01, 2013). Risk Factors for Nipah virus infection among pteropid bats, Peninsular Malaysia. *Emerging Infectious Diseases, 19,* 1, 51-60.
[60] Sohayati, A. R., Hassan, L., Sharifah, S. H., Lazarus, K., Zaini, C. M., Epstein, J. H., Shamsyul, N. N., ... Henipavirus Ecology Research Group. (January 01, 2011). Evidence for Nipah virus recrudescence and serological patterns of captive Pteropus vampyrus. Epidemiology and Infection, 139, 10, 1570-9
[61] Koella, J. C., & Stearns, S. C. (2008). *Evolution in health and disease*. Oxford: Oxford University Press. P(156-159)
[62] Luby, Stephen P., Hossain, M. Jahangir, Gurley, Emily S., Ahmed, Be-Nazir, Banu, Shakila, Khan, Salah Uddin, Homaira, Nusrat, ... Rahman, Mahmudur. (2009). *Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007*. Centers for Disease Control and Prevention.
[63] Ferguson, N. M., Fraser, C., Donnelly, C. A., Ghani, A. C., & Anderson, R. M. (January 01, 2004). Public health.

Public health risk from the avian H5N1 influenza epidemic.*Science (new York, N.y.), 304,* 5673, 968-9.
[64] Lloyd-Smith, J. O., Schreiber, S. J., Kopp, P. E., & Getz, W. M. (January 01, 2005). Superspreading and the effect of individual variation on disease emergence. *Nature, 438,*7066, 355-9.
[65] Small, M., Tse, C. K., & Walker, D. M. (March 15, 2006). Super-spreaders and the rate of transmission of the SARS virus. *Physica D: Nonlinear Phenomena, 215,* 2, 146-158.
[66] Pulkkinen, K., Suomalainen, L.-R., Read, A. F., Ebert, D., Rintamäki, P., & Valtonen, E. T. (n.d.). *Intensive fish farming and the evolution of pathogen virulence: the case of columnaris disease in Finland*. The Royal Society.
[67] Food and Agriculture Organisation of the United Nations. 2011. *Investigating the role of bats in emerging zoonoses: Balancing ecology, conservation and public health interests*. Edited by S.H. Newman, H.E. Field, C.E. de Jong and J.H. Epstein. FAO Animal Production and Health Manual No. 12. Rome.
[68] Pulliam, J. R., Dushoff, J. G., Levin, S. A., & Dobson, A. P. (January 01, 2007). Epidemic enhancement in partially immune populations. *Plos One, 2,* 1.)
[69] Crichton, E. G., & Krutzsch, P. H. (2000). *Reproductive biology of bats*. San Diego, Calif: Academic Press.
[70] Kurta, A., Bell, G.P., Nagy, K.A., Kunz, T.H. (1989) Energetics of Pregnancy and Lactation in Freeranging Little Brown Bats (*Myotis lucifugus*). Physiological Zoology, Vol. 62, pp. 804-818
[71] Kurta, A., Bell, G.P., Nagy, K.A., Kunz, T.H. (1989) Energetics of Pregnancy and Lactation in Freeranging Little Brown Bats (*Myotis lucifugus*). Physiological Zoology, Vol. 62, pp. 804-818
[72] Crichton, E. G., & Krutzsch, P. H. (2000). *Reproductive biology of bats*. San Diego, Calif: Academic Press.
[73] George, D. B., Webb, C. T., Farnsworth, M. L., O'Shea, T. J., Bowen, R. A., Smith, D. L., Stanley, T. R., ... Rupprecht, C. E. (January 01, 2011). Host and viral ecology determine bat rabies seasonality and maintenance. *Proceedings of the National Academy of Sciences of the United States of America, 108,* 25, 10208-13.
[74] Silbernagel, E. 2005. "Pteropus giganteus" (On-line), Animal Diversity Web. Accessed April 27, 2014 at http://animaldiversity.ummz.umich.edu/accounts/Pteropus_giganteus/

REFERENCE:

1. (June 2010). Nipah outbreak in Faridpur District, Bangladesh, 2010. ICDDR,B: Health and Science Bulletin, 8, 2,6-11.
2. (March 2012). Nipah transmission from bats to humans associated with drinking traditional liquor (tari) in northern Bangladesh, 2011. ICDDR,B: Health and Science Bulletin, 10, 1, 16-20.
3. Calisher, C. H., Childs, J. E., Field, H. E., Holmes, K. V., & Schountz, T. (January 01, 2006). Bats: Important Reservoir Hosts of Emerging Viruses. Clinical Microbiology Reviews, 19, 3, 531-545.
4. Chowdhury, M. S. H., Halim, Md. A., Muhammed, N., Haque, F., & Koike, M.; yUfVPpkh. (2009). Traditional utilization of wild date palm (Phoenix sylvestris Roxb) in rural Bangladesh: An approach to sustainable biodiversity management. Springer.
5. Crichton, E. G., & Krutzsch, P. H. (2000). Reproductive biology of bats. San Diego, Calif: Academic Press.
6. Daszak, P., Zambrana-Torrelio, C., Bogich, T. L., Fernandez, M., Epstein, J. H., Murray, K. A., & Hamilton, H. (January 01, 2013). Interdisciplinary approaches to understanding disease emergence: the past, present, and future drivers of Nipah virus emergence. Proceedings of the National Academy of Sciences of the United States of America, 110, 3681-8.
7. Epstein, J. H., Baker, M. L., Zambrana-Torrelio, C., Middleton, D., Barr, J. A., DuBovi, E., Boyd, V., ... Markotter, W. (June 27, 2013). Duration of Maternal Antibodies against Canine Distemper Virus and Hendra Virus in Pteropid Bats. Plos One, 8, 6.)
8. Epstein, J. H., Quan, P. L., Briese, T., Street, C., Jabado, O., Conlan, S., Ali, K. S., ... Lipkin, W. I. (January 01, 2010). Identification of GBV-D, a novel GB-like flavivirus from old world frugivorous bats (Pteropus giganteus) in Bangladesh. Plos Pathogens, 6.
9. Epstein, J., Field, H., Luby, S., Pulliam, J., & Daszak, P. (January 01, 2006). Nipah virus: Impact, origins, and causes of emergence. Current Infectious Disease Reports, 8, 1, 59-65.
10. Epstein, Jonathan H., Prakash, Vibhu, Smith, Craig S., Daszak, Peter, McLaughlin, Amanda B., Meehan, Greer, Field, Hume E., ... Cunningham, Andrew A. (n.d.). Henipavirus Infection in Fruit Bats (Pteropus giganteus), India. Centers for Disease Control and Prevention.
11. Ferguson, N. M., Fraser, C., Donnelly, C. A., Ghani, A. C., & Anderson, R. M. (January 01, 2004). Public health. Public health risk from the avian H5N1 influenza epidemic.Science (new York, N.y.), 304, 5673, 968-9.
12. Food and Agriculture Organisation of the United Nations. 2011. Investigating the role of bats in emerging zoonoses: Balancing ecology, conservation and public health interests. Edited by S.H. Newman, H.E. Field, C.E. de Jong and J.H. Epstein. FAO Animal Production and Health Manual No. 12. Rome.
13. George, D. B., Webb, C. T., Farnsworth, M. L., O'Shea, T. J., Bowen, R. A., Smith, D. L., Stanley, T. R., ... Rupprecht, C. E. (January 01, 2011). Host and viral ecology determine bat rabies seasonality and maintenance. Proceedings of the National Academy of Sciences of the United States of America, 108, 25, 10208-13.
14. Gurley, E. S., & Luby, S. P. (August 01, 2011). Nipah virus transmission in south Asia: Exploring the mysteries and addressing the problems. Future Virology, 6, 8, 897-900.
15. Gurley, E. S., Montgomery, J. M., Hossain, M. J., Bell, M., Azad, A. K., Islam, M. R., Molla, M. A., ... Breiman, R. F. (January 01, 2007). Person-to-person transmission of Nipah virus in a Bangladeshi community. Emerging Infectious Diseases, 13, 7, 1031-7.
16. Hefferman, J., R. Smith, and L. Wahl (2005). Perspectives on the basic reproduction ratio. Journal of the Royal Society Interface 2, 281–293.
17. Hsu, V. P., Hossain, M. J., Parashar, U. D., Ali, M. M., Ksiazek, T. G., Kuzmin, I., Niezgoda, M., ... Breiman, R. F. (January 01, 2004). Nipah virus encephalitis reemergence, Bangladesh. Emerging Infectious Diseases, 10, 12, 2082-7.
18. Hyatt, A. D., Daszak, P., Cunningham, A. A., Field, H., & Gould, A. R. (March 01, 2004). Henipaviruses: Gaps in the Knowledge of Emergence. Ecohealth, 1, 1, 25-38.
19. Keeling, M. J., & Rohani, P. (2008). Modeling infectious diseases in humans and animals. Princeton:

Princeton University Press.
20. Koella, J. C., & Stearns, S. C. (2008). Evolution in health and disease. Oxford: Oxford University Press. P(156-159)
21. Ksiazek, T. G., Rota, P. A., & Rollin, P. E. (January 01, 2011). A review of Nipah and Hendra viruses with an historical aside. Virus Research, 162, 1, 173-183.
22. Kurta, A., Bell, G.P., Nagy, K.A., Kunz, T.H. (1989) Energetics of Pregnancy and Lactation in Freeranging Little Brown Bats (Myotis lucifugus). Physiological Zoology, Vol. 62, pp. 804-818
23. Lloyd-Smith, J. O., George, D., Pepin, K. M., Pitzer, V. E., Pulliam, J. R., Dobson, A. P., Hudson, P. J., ... Grenfell, B. T. (January 01, 2009). Epidemic dynamics at the human-animal interface. Science (new York, N.y.), 326, 5958, 1362-7.
24. Lloyd-Smith, J. O., Schreiber, S. J., Kopp, P. E., & Getz, W. M. (January 01, 2005). Superspreading and the effect of individual variation on disease emergence. Nature, 438,7066, 355-9.
25. Luby, Stephen P., Hossain, M. Jahangir, Gurley, Emily S., Ahmed, Be-Nazir, Banu, Shakila, Khan, Salah Uddin, Homaira, Nusrat, ... Rahman, Mahmudur. (2009). Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007. Centers for Disease Control and Prevention.
26. Luby S. P., Gurley E. S., Hossain M. J. 2009 Transmission of human infection with Nipah virus. Clin. Infect. Dis. 49, 1743–1748.(doi:10.1086/647951)
27. Luby, S. P., Rahman, M., Hossain, M. J., Blum, L. S., Husain, M. M., Gurley, E., Khan, R., ... Ksiazek, T. G. (January 01, 2006). Foodborne transmission of Nipah virus, Bangladesh. Emerging Infectious Diseases, 12, 12, 1888-94.
28. Luby, Stephen P., Hossain, M. Jahangir, Gurley, Emily S., Ahmed, Be-Nazir, Banu, Shakila, Khan, Salah Uddin, Homaira, Nusrat, ... Rahman, Mahmudur. (n.d.). Recurrent Zoonotic Transmission of Nipah Virus into Humans, Bangladesh, 2001–2007. Centers for Disease Control and Prevention.
29. Middleton, D. J., Westbury, H. A., Morrissy, C. J., van, . H. B. M., Russell, G. M., Braun, M. A., & Hyatt, A. D. (January 01, 2002). Experimental Nipah virus infection in pigs and cats. Journal of Comparative Pathology, 126.
30. Montgomery, J. M. (January 01, 2008). Risk Factors for Nipah Virus Encephalitis, Bangladesh. Emerging Infectious Diseases, 14, 10, 1526-1532.
31. Pulkkinen, K., Suomalainen, L.-R., Read, A. F., Ebert, D., Rintamäki, P., & Valtonen, E. T. (n.d.). Intensive fish farming and the evolution of pathogen virulence: the case of columnaris disease in Finland. The Royal Society.
32. Pulliam, J. R., Dushoff, J. G., Levin, S. A., & Dobson, A. P. (January 01, 2007). Epidemic enhancement in partially immune populations. Plos One, 2, 1.)
33. Rahman, S. A., Hassan, L., Epstein, J. H., Mamat, Z. C., Yatim, A. M., Hassan, S. S., Field, H. E., ... Henipavirus Ecology Research Group. (January 01, 2013). Risk Factors for Nipah virus infection among pteropid bats, Peninsular Malaysia. Emerging Infectious Diseases, 19, 1, 51-60.
34. Sazzad, H. M., Hossain, M. J., Gurley, E. S., Ameen, K. M., Parveen, S., Islam, M. S., Faruque, L. I., ... Luby, S. P. (January 01, 2013). Nipah virus infection outbreak with nosocomial and corpse-to-human transmission, Bangladesh. Emerging Infectious Diseases, 19, 2, 210-7.
35. Silbernagel, E. 2005. "Pteropus giganteus" (On-line), Animal Diversity Web. Accessed April 28, 2014 at http://animaldiversity.ummz.umich.edu/accounts/Pteropus_giganteus/
36. Siva SR, Chong HT, Tan CT (2009). "Ten year clinical and serological outcomes of Nipah virus infection". Neurology Asia 14: 53–58.
37. Small, M., Tse, C. K., & Walker, D. M. (March 15, 2006). Super-spreaders and the rate of transmission of the SARS virus. Physica D: Nonlinear Phenomena, 215, 2, 146-158.
38. Sobol IM. 1990 On sensitivity estimates fornonlinear mathematical models. Matematicheskoe Modelirovanie 2, 112–118. [In Russian].
39. Sohayati, A. R., Hassan, L., Sharifah, S. H., Lazarus, K., Zaini, C. M., Epstein, J. H., Shamsyul, N. N., ... Henipavirus Ecology Research Group. (January 01, 2011). Evidence for Nipah virus recrudescence and serological patterns of captive Pteropus vampyrus. Epidemiology and Infection, 139, 10, 1570-9
40. Wacharapluesadee, S., Boongird, K., Wanghongsa, S., Ratanasetyuth, N., Supavonwong, P., Saengsen, D., Gongal, G. N., ... Hemachudha, T. (January 01, 2010). A longitudinal study of the prevalence of Nipah virus in Pteropus lylei bats in Thailand: evidence for seasonal preference in disease transmission. Vector

Borne and Zoonotic Diseases (larchmont, N.y.), 10, 2, 183-90.
41. Wang, L.-F., Walker, P. J., & Poon, L. L. M. (December 01, 2011). Mass extinctions, biodiversity and mitochondrial function: Are bats 'special' as reservoirs for emerging viruses?. Current Opinion in Virology, 1, 6, 649-657.
42. Wu, J., Dhingra, R., Remais, J. V., & Gambhir, M. (September 06, 2013). Sensitivity analysis of infectious disease models: Methods, advances and their application. Journal of the Royal Society Interface, 10, 86.)