# Targeting surveillance in healthy versus diseased wild mammals for zoonotic virus discovery

How to find the next zoonotic virus

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## Abstract

We analyzed a database of mammal-virus associations to ask whether zoonotic disease surveillance targeting diseased animals is the best strategy to identify potentially zoonotic pathogens.

## Introduction

Bats and rodents can harbor viruses that are potentially harmful to humans. Nearly two-thirds of emerging infectious diseases (Eidson, et al. 2001) that affect humans are zoonotic, and three-quarters of these originate in wildlife, making surveillance of wildlife for novel pathogens part of a logical strategy to prevent future zoonotic EIDs.

## Methods

We focused our analysis on mammalian hosts and viruses as they are more likely to be associated with human EIDs than any other host-pathogen type (Cleaveland, Laurenson and Taylor 2001, Woolhouse and Gowtage-Sequeria 2005). See supporting Methods for more.

<data.xlsx>

Dataset 1 Database of all human emerging viruses previously identified as originating in wildlife. Data from: (Morse 1993).

## Results

Figure 1. License: [CC0-1.0](http://creativecommons.org/publicdomain/zero/1.0/legalcode). Data from: **Error! Reference source not found.**; (Jones, et al. 2008). (A) The proportion of hosts symptomatic by mammal order are given with standard error bars, calculated assuming binomial error structure. The total number of each host order or virus family included in the database is given above each bar. Note, all host orders and virus families in the database are included here, but analyses are limited to those host orders or virus families with at least three entries in the database. (B) The proportion of virus families for which hosts are reported symptomatic are given with standard error bars, calculated assuming binomial error structure. The total number of each host order or virus family included in the database is given above each bar. Note, all host orders and virus families in the database are included here, but analyses are limited to those host orders or virus families with at least three entries in the database.

Our search of 605 mammal-virus associations investigated yielded explicit information on host health in 52% of the 312 mammal-virus pairs. Of these, approximately 28% of infected wildlife hosts were reported to present with visible disease (n = 88) and 72% (n = 224) were reported without evidence of visible disease. The proportion of hosts that were symptomatic differed across host order and virus family Figure 1.

Hosts infected with filoviruses were marginally more likely to be visibly diseased (Table 1).

Table 1 Logistic regression analysis with bias reduction of whether a host presents with disease for 234 mammal–virus pairs from 5 taxonomic orders of mammals and 10 taxonomic families of viruses. The subset of data used was selected by using a cutoff of at least 3 records in the database to avoid making inference about host orders or virus families, for which we had very little information.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Predictor | Coefficient | SE | Test statistic (Z) | p-value | OR | 95% CI |
| Bunyaviridae | -1.74 | 0.64 | -2.71 | 0.01 | 0.18 | (0.05, 0.62) |
| Filoviridae | 3.26 | 1.83 | 1.78 | 0.08 | 26.07 | (0.72, 944.49) |
| Herpesviridae | 0.10 | 0.65 | 0.16 | 0.87 | 1.11 | (0.31, 3.94) |
| Paramyxoviridae | 3.43 | 1.42 | 2.41 | 0.02 | 30.95 | (1.90, 503.52) |
| Picornaviridae | 1.12 | 0.76 | 1.48 | 0.14 | 3.08 | (0.69, 13.68) |
| Poxviridae | 2.29 | 0.81 | 2.82 | <0.001 | 9.90 | (2.01, 48.72) |
| Reoviridae | 2.13 | 1.05 | 2.02 | 0.04 | 8.39 | (1.07, 66.12) |
| Rhabdoviridae | 9.20 | 2.39 | 3.85 | <0.001 | NA | NA |
| Togaviridae | -0.36 | 0.63 | -0.58 | 0.56 | 0.70 | (0.20, 2.38) |

Species in the order Chiroptera have a lower probability of visible disease than in other orders (Figure 2), though **all Chiroptera infected with non-rabies rhabdoviruses have a high probability of visible disease**.

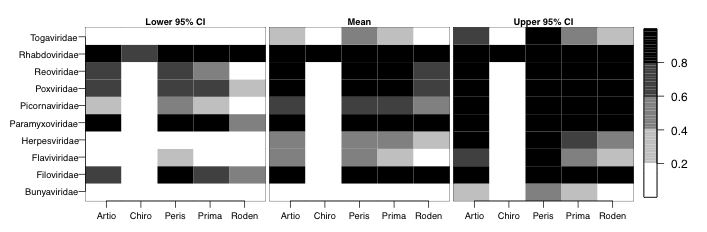
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Figure 2 The probability of being symptomatic based on a logistic regression analysis with bias reduction of whether or not a host presents with disease for 234 mammal-virus pairs from 5 orders of mammals and 10 families of viruses, including the lower 95% confidence interval (left), mean (center), and upper 95% confidence interval (right). Probabilities are based on the predicted values of the logistic regression and are given on a five-point gray scale from white (0.0 – 0.2) to black (0.8 - 1.0). Confidence values were calculated as the coefficient plus 1.96 times the standard error.

## Conclusions

Generally, we found that the probability of presenting with visible disease depends on the host and virus taxonomy, and the only host order for which a single strategy (in this case healthy animal surveillance) can be applied across nearly all virus families (excluding Rhabdoviridae) is for Chiroptera. Therefore, particularly for the case of novel virus detection, our results point to a mixed strategy of targeted syndromic and healthy animal surveillance across host and virus taxonomies.

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## Supporting Information

Previous analyses show that zoonotic disease emergence events and human pathogen species richness are spatially correlated with mammal and bird diversity (Jones, et al. 2008)[[2]](#endnote-1). However, these studies weight all species equally. In reality, the risk of zoonotic viral transmission, or spillover, likely varies among host species due to differences in underlying viral richness, opportunity for contact with humans, propensity to exhibit clinical signs that exacerbate viral shedding, other ecological, behavioral and life-history differences, and phylogenetic distance from humans. We hypothesize that the number of viruses a given mammal species shares with humans decreases with phylogenetic distance from humans and increases with opportunity for human contact. We used generalized additive models (GAMs) to identify and rank host-specific predictors (ecological, life history, taxonomic, and phylogenetic traits, and a control for research effort) of the number of total and zoonotic viruses in mammals.

### Methods

#### Database

To construct the mammal–virus association database we initially extracted all viruses listed as occurring in any mammal from the International Committee on Taxonomy of Viruses database (ICTVdb), and further individually went through each virus listed in the ICTV 8th edition master list and searched the literature for mammalian hosts.

<https://www.ncbi.nlm.nih.gov/nuccore/KJ501319>

Supporting Dataset 1 West Nile Virus genome Data from: Edison et al. (2001, Table 1).

# References

Cleaveland, S., M.K. Laurenson, and L.H. Taylor. "Diseases of Humans and Their Domestic Mammals: Pathogen Characteristics, Host Range and the Risk of Emergence." *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences* 356, no. 1411 (July 2001): 991-999.

Eidson, Millicent, et al. "Crow deaths as a sentinel surveillance system for West Nile virus in the northeastern United States, 1999." *Emerging Infectious Diseases* 7, no. 4 (August 2001): 615-620.

Jones, Kate E., et al. "Global Trends in Emerging Infectious Diseases." *Nature* 451, no. 7181 (2008): 990-993.

Morse, Stephen S. *Emerging Viruses.* illustrated edition. Edited by Stephen S. Morse. New York, NY: Oxford University Press, 1993.

Woolhouse, Mark E.J., and Sonya Gowtage-Sequeria. "Host range and emerging and reemerging pathogens." *Emerging Infectious Diseases* 11, no. 12 (2005): 1842-1847.

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2. See also other publications by Kate E. Jones. [↑](#endnote-ref-1)