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PREDICT

SPILLOVER

A new tool for ranking the risk of viral spillover from animals to humans

It is estimated that there are more than 500,000 undiscovered viruses in animals with the potential to spillover into people¹. Of this large pool, how do we determine which viruses pose the greatest threat to humans? The PREDICT Project of the U.S. Agency for International Development (USAID) Emerging Pandemic Threats Program has identified more than a thousand known and novel viruses in wildlife at high-risk disease

transmission interfaces around the world. The project has rapidly expanded our knowledge of viral threats but also has raised questions about the risk these viruses pose to humans. To address this problem, the PREDICT team has developed a new tool to systematically evaluate wildlife viruses in terms of their zoonotic (transmission from animals to humans) and pandemic potential using a scientifically informed process.

The Value of Expert Opinion

Host

- Intimacy of interaction: wild animals - humans
- Host plasticity: orders
- Frequency of interaction: wild animals - humans
- Number of primary interfaces
- Frequency of interaction: domestic animals - humans
- Intimacy of interaction: domestic animals - humans
- Host plasticity: species
- Genetic relatedness of host - humans
- Geography: host
- Sample diversity
- Habitat breadth
- Conservation status
- Diet breadth

Environment

- Human population density
- Deforestation
- Agricultural change
- Urbanization
- Livestock density
- Land use

Virus

- Transmission: animal - human
- Viral infectivity: humans
- Transmission: human - human
- Virus epidemicity
- Virus transmission mode
- Viral infectivity: terrestrial animals
- Proportion viral family: infect humans
- Proportion viral family: known human pathogens
- Geography: virus
- Virus genome
- Duration of infection: humans
- Proportion viral family: infect terrestrial animals
- Proportion viral family: infect >1 host
- Severity of the disease in humans
- Viral infectivity: birds
- Virus segmentation
- Virulence: terrestrial mammals
- Virus envelope
- Proportion viral family: infect birds
- Viral infectivity: other animals
- Virulence: birds
- Proportion viral family: infect other animals
- Virulence: other animals

Figure 1: A List of host, virus and environmental risk factors included in SpillOver: Viral Risk Ranking, scaled color (yellow-orange-red) according to expert opinion of risk contribution (none to high) to viral spillover from animals to humans.

A number of ecological and behavioral characteristics may influence zoonotic transmission potential and the ability of a virus to spread and cause disease in humans. Using knowledge gained through extensive literature review and research in the field, we identified 42 host, virus, and environmental risk factors thought to be important

for a virus to be able to transmit and spread in humans (Fig 1). However, the risk factors do not contribute equally. Using an unbiased approach, the PREDICT team conducted a risk assessment survey of 66 international experts in the fields of virology, epidemiology, ecology, molecular biology, public health, veterinary and human

medicine, and One Health. Each participant ranked risk factors identified as important contributors to viral spillover from no risk to high risk. By soliciting expert opinion, we identified the top perceived contributors

to spillover risk including virus transmission abilities, and frequent/intimate interactions between humans and animals (Fig. 1).

Development of SpillOver: Viral Risk Ranking Tool

SPILLOVER

VIRAL RISK RANKING



Figure 2: Components of the SpillOver: Viral Risk Ranking website tool

The PREDICT team is creating an interactive website application, called SpillOver: Viral Risk Ranking (Fig. 2). The tool uses a risk ranking framework to produce a detailed spillover risk report for each virus by combining expert opinion, records of virus detection, and external data sources for the 42 risk factors. The SpillOver Virus Report details the relative risk of host, viral, and environmental factors that contribute to a virus' overall Spillover Risk Score. The simple design of SpillOver Ranking Comparison page allows non-technical users and policy makers, as well as the general public to compare and explore the relative public health risk of viruses belonging to families of concern to human health and the opportunity to filter viruses on a selection of key attributes, including country and animal species. As viral discovery efforts continue to expand our understanding of potential pathogens which exist in nature, the SpillOver Rank Your Virus tool provides an adaptive platform to collate and rank new and existing viruses and to improve our assessment of their risks, with the ultimate aim of forecasting and preventing future disease outbreaks.

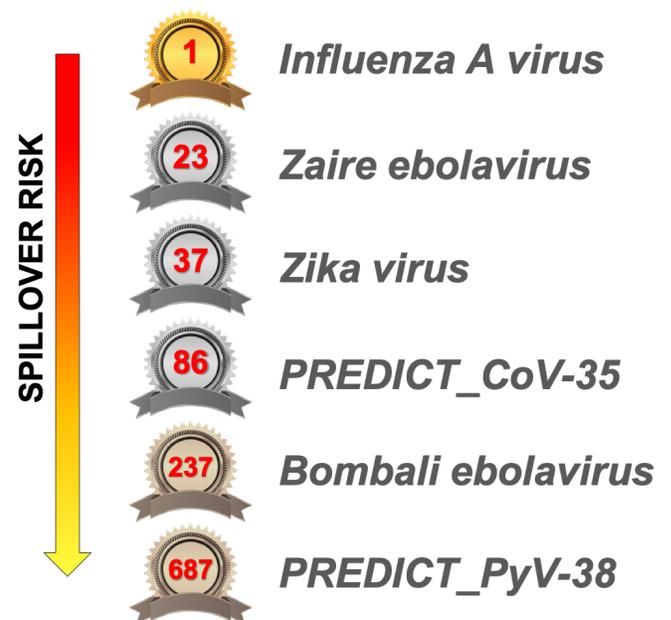


Figure 3: A selection of preliminary results from the SpillOver viral risk ranking assessment including the top ranked virus (*Influenza A virus*), viruses responsible for recent zoonotic outbreaks (*Zaire ebolavirus*, *Zika virus*) and novel viruses discovered during PREDICT (*PREDICT_CoV-35*, *Bombali ebolavirus*).

Creating Order Out of Chaos

SpillOver helps bring some rationality and management of risk when discovering new viruses. To date, SpillOver has ranked 687 viruses, including 79 known zoonotic viruses. The top 45 ranked viruses were all known zoonotic viruses that have had previously-documented spillover from animals to humans. Influenza A virus, a ubiquitous zoonotic virus causing frequent and severe disease in humans, was the highest ranked virus.

Of the 614 viruses detected in the first phase of PREDICT, 35 viruses were assigned higher spillover risk values than previously-known zoonotic viruses, such as Coronavirus PREDICT_CoV-35. PREDICT_CoV-

35 provisionally ranks in position 86 out of 687. This virus has been found in bats in Cambodia, Cameroon, Democratic Republic of the Congo, and Viet Nam at high-risk disease transmission interfaces including hunting and human dwellings.

The PREDICT-discovered Bombali ebolavirus detected in bats living inside houses in Sierra Leone did not rank as highly. However, given the short timeframe since its identification, it is likely that we do not know the full host and geographic range of Bombali ebolavirus and more information as it is discovered could change risk estimations.

A Major Step Towards Predicting Viral Spillover

Combining multiple sources and analytics, the simple design of SpillOver requires only a few pieces of readily available information to produce a comparative risk report and addresses calls for an infrastructure to interpret global infectious disease data. All future viral detections from PREDICT and related projects will be reported on this system, and we encourage collaborative participation from external viral discovery efforts.

By creating SpillOver, PREDICT has developed a globally accessible springboard to prompt scientists and policy makers to move towards solutions in the pandemic era. The innovative design is fully customizable for future

developments, including updating new and existing risk factors and incorporation of newly-developed and updated data sets. By creating a starting point, we attempt to address the burden of uncertainty created by viral discoveries which can be used to identify specific viruses to target for further investigation (for example, further genome characterization, cell line infection studies, and animal models) that will better inform our understanding of spillover risk. Together, this information can lead to public health interventions prior to a zoonotic outbreak, instead of the costly, in both the economic and societal sense, reactionary response the world has used to date.

Reference:

Carroll D, Daszak P, Wolfe ND, et al. The Global Virome Project. *Science* 2018;359:872-4.

