



Research and development to improve preparedness for Nipah virus epidemics

Peter Horby

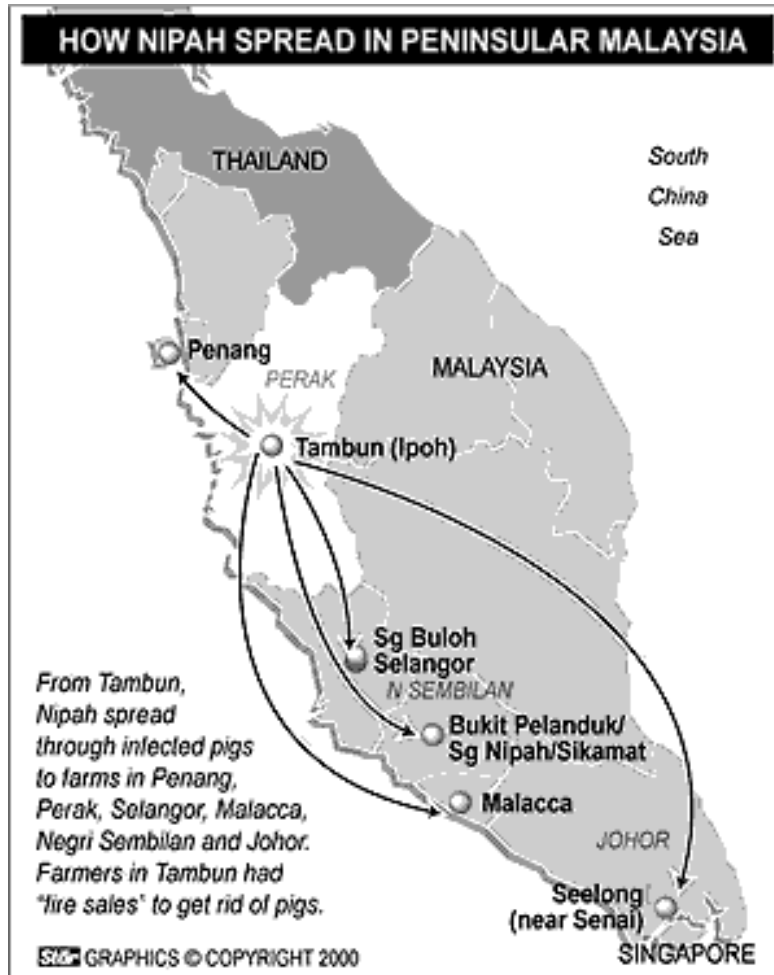
Director, Pandemic Sciences Institute

NMRC Awards Ceremony and Research Symposium, May 23-24 2024, Singapore.

Why worry about Nipah?



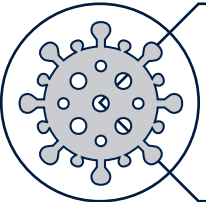
Nipah virus origins and spread



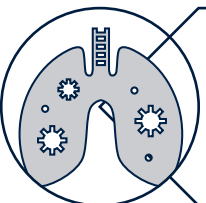
Chua *et al.* J infect., 2001

- Original outbreak in Malaysia and Singapore (1998-1999)
- 288 human cases of acute encephalitis
 - 109 deaths
 - CFR: 39%
- Novel paramyxovirus isolated from a patient in Sungai Nipah village
 - Same family as measles virus
 - But Nipah is a zoonoses, whereas measles is only found in humans
- Since that time, there have been outbreaks in five countries
- There are two predominant strains: NiV-Malaysia (NiV-M) and NiV-Bangladesh (NiV-B)
- Human cases in Malaysia, Singapore, Philippines, Bangladesh, India

Nipah Virus Disease: Symptoms and Pathology

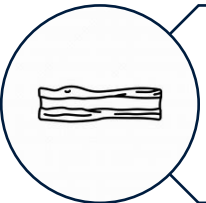


Virus commonly identified in lung and kidney



Respiratory presentation:

- 14% non-productive cough
- 6% of chest X-rays show mild focal abnormalities

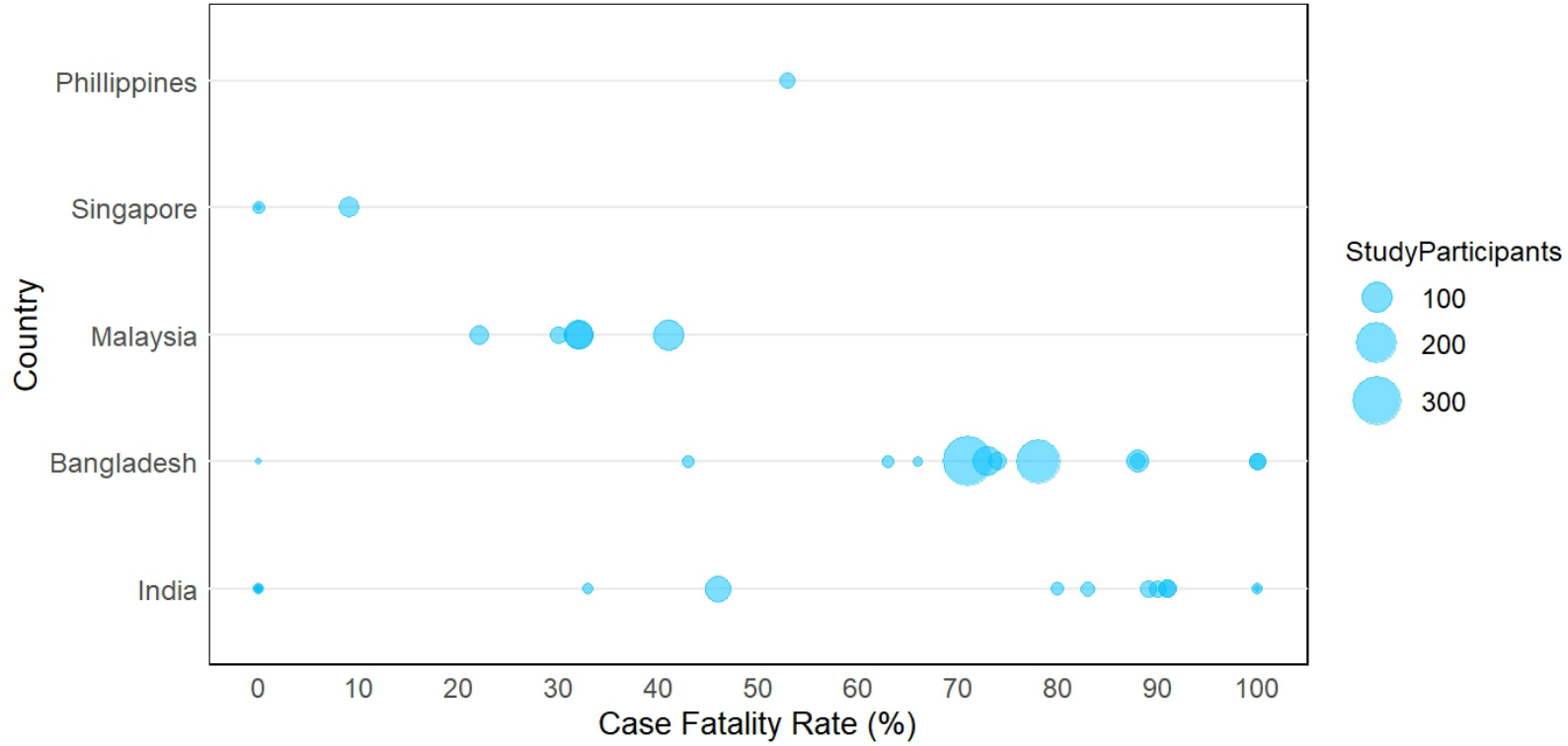


Diffuse vasculitis



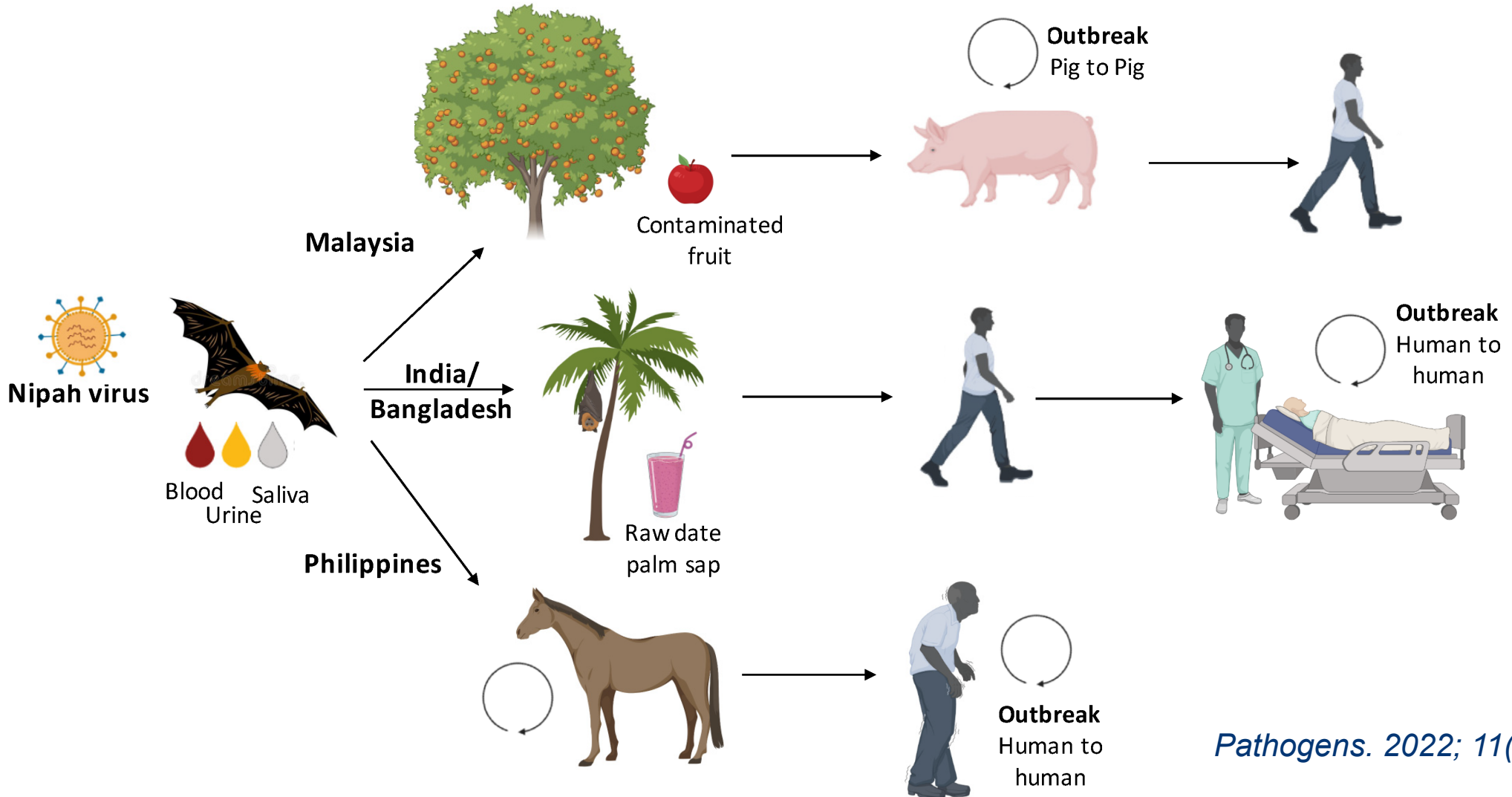
The brain is the most severely affected organ - tropism to the brainstem

Goh K J et al. NEJM, 2000



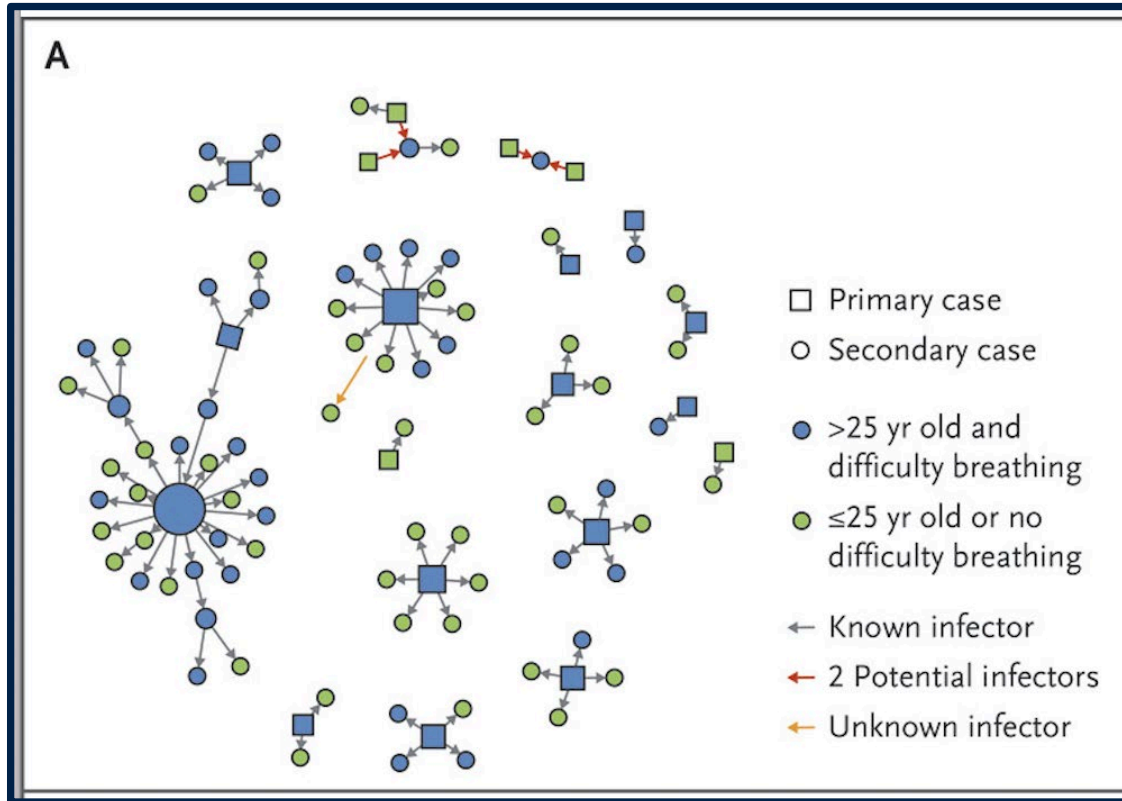
Average CFR 60%
Dr Z Hassan, 2024

Transmission of Nipah Virus

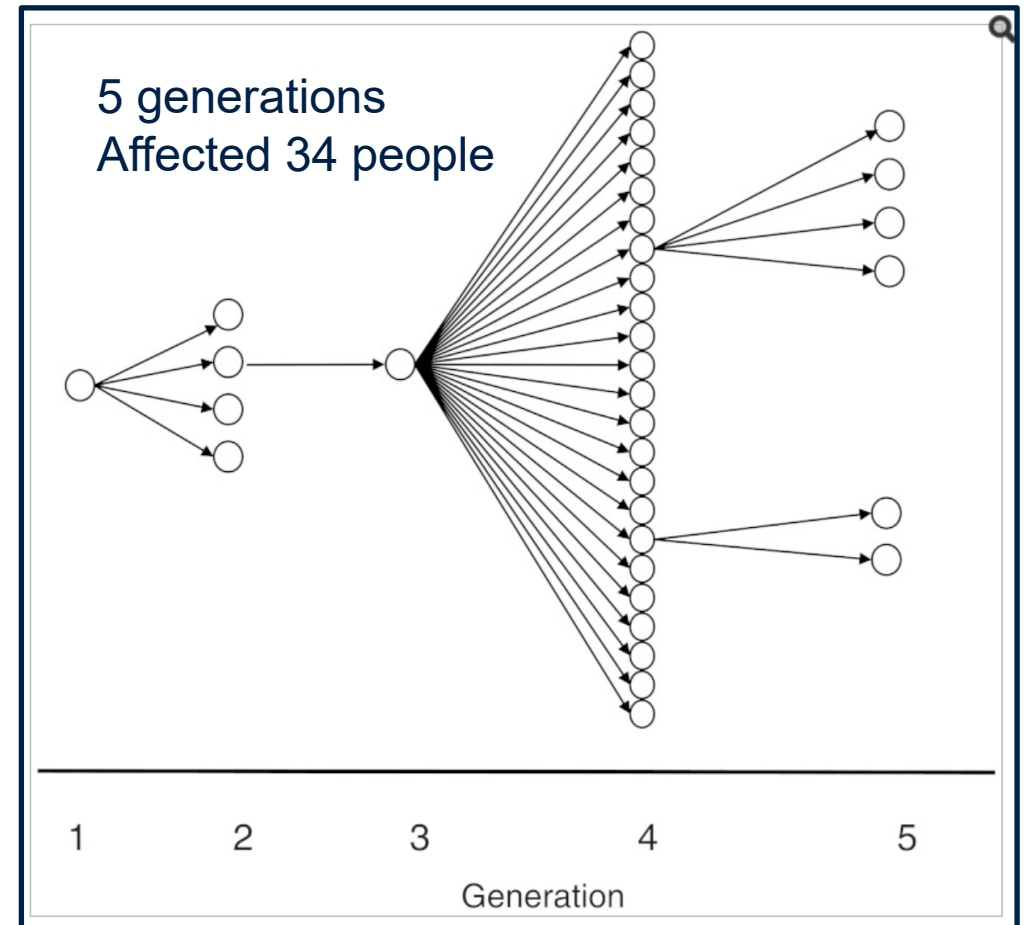


Pathogens. 2022; 11(12):1419.

Person-to-person transmission

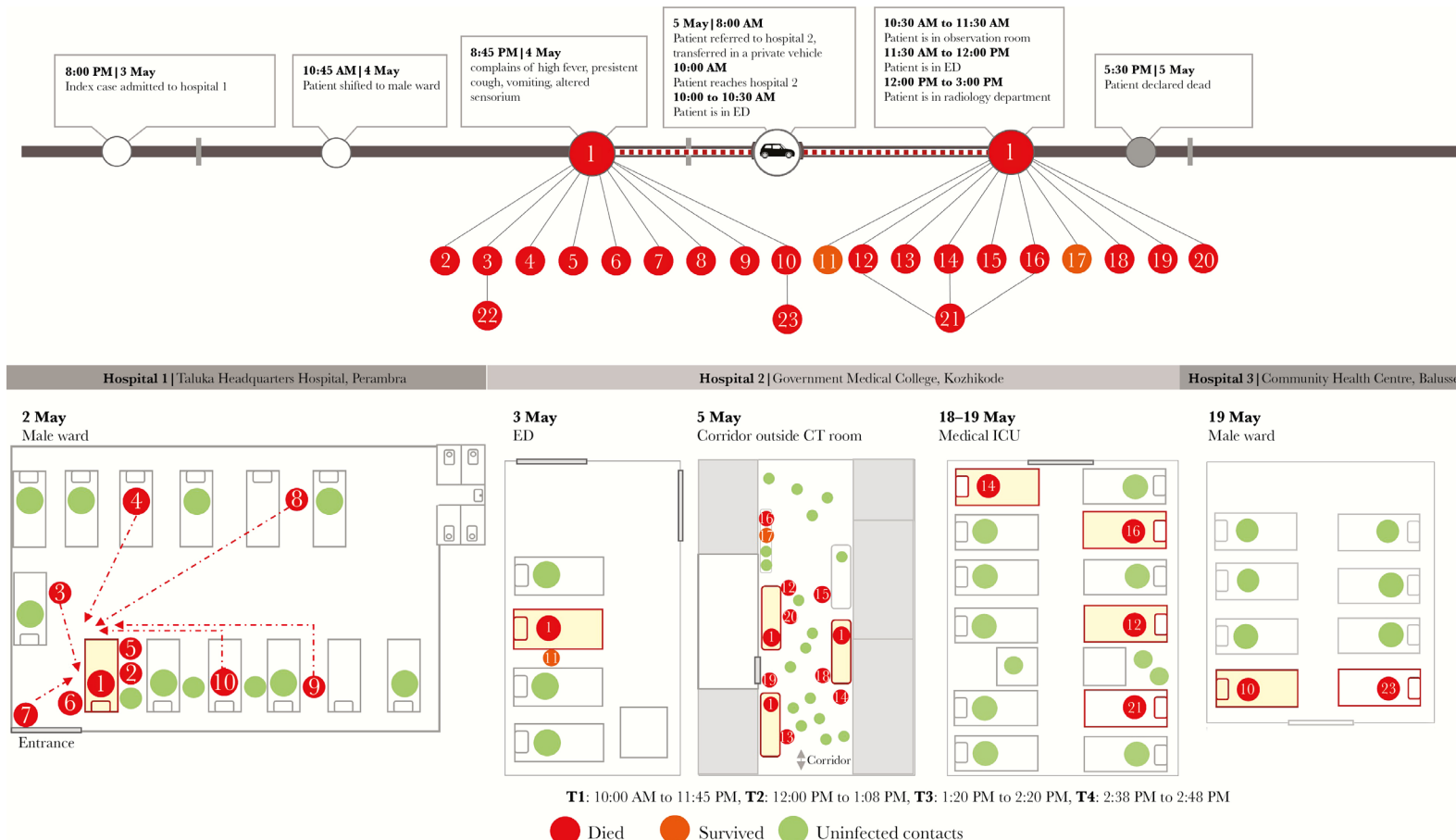


N Engl J Med 2019;380:1804-1814



Clinical Infectious Diseases, 49(11):1743-8.
Emerg Infect Dis. 2007 Jul;13(7):1031-7.

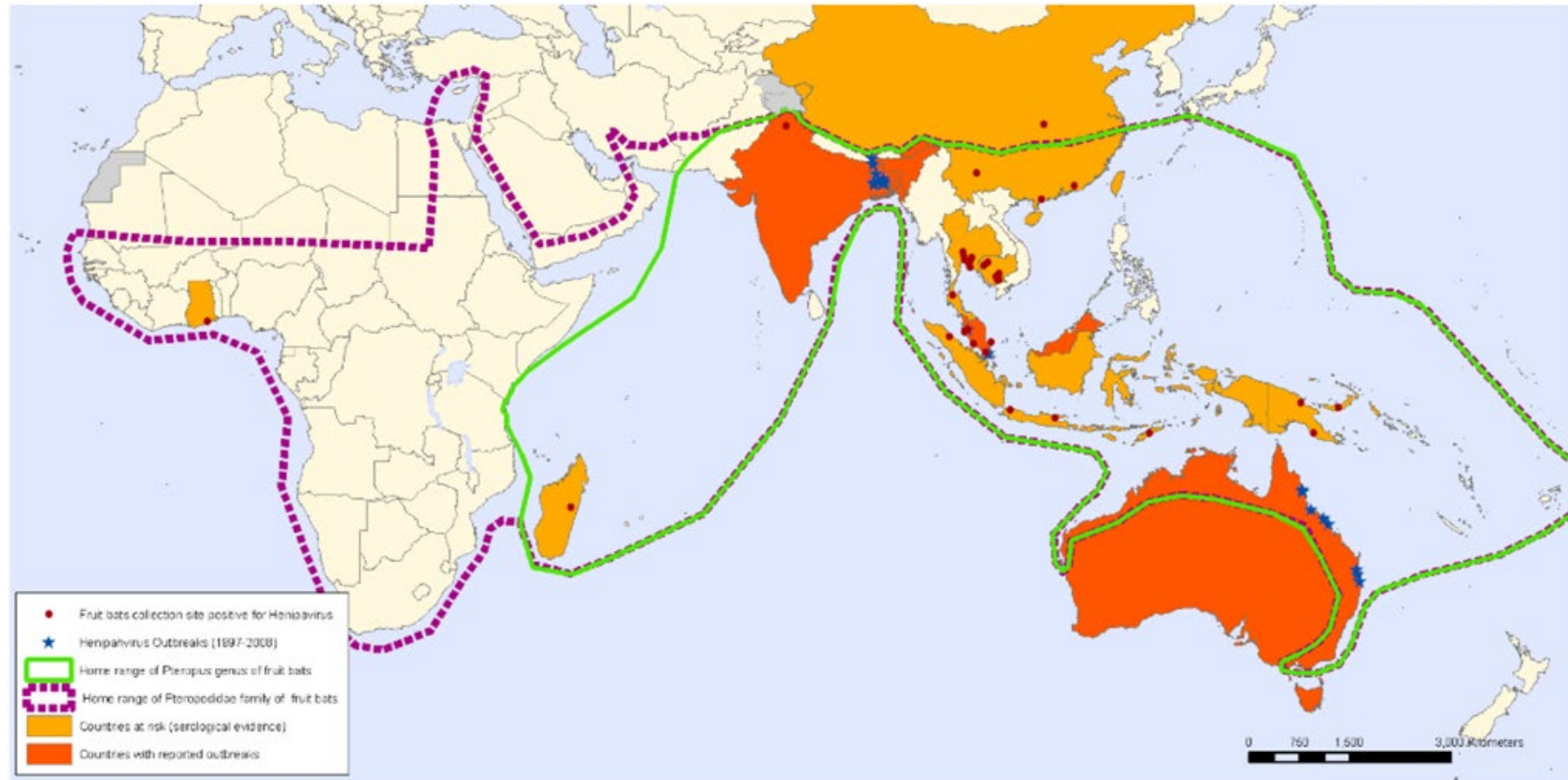
Nosocomial transmission Nipah virus disease in Kozhikode District, Kerala State, India, 2018



Disclaimer: All illustrations are for representational purpose only and not to scale

J Infect Dis. 2019 May 24;219(12):1867-1878.

Widespread geographic distribution of fruit bat reservoir



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Alert and Response Department
World Health Organization
Map Production: Public Health Information
and Geographic Information Systems (GIS)
World Health Organization

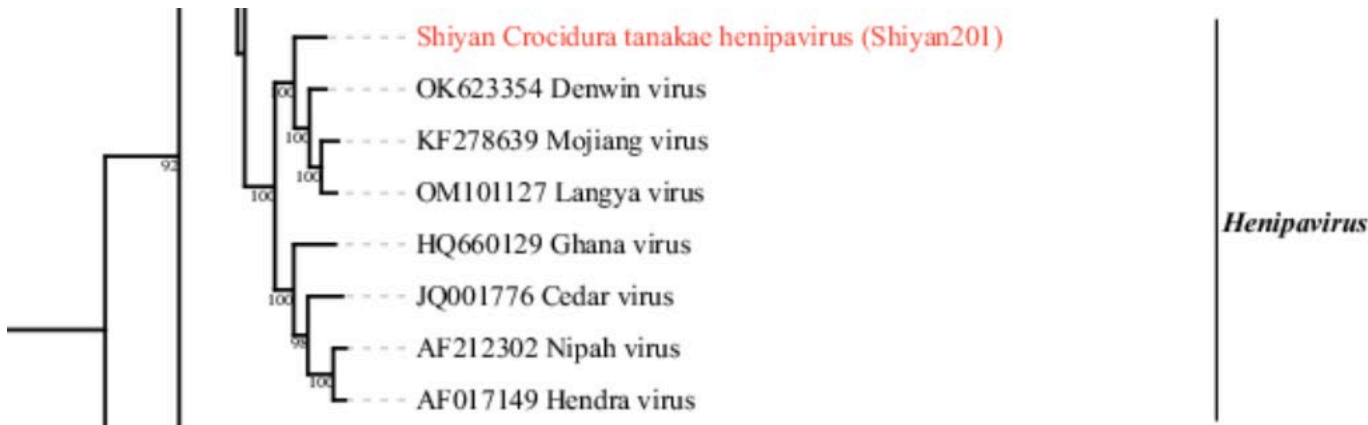
 **World Health Organization**
© WHO 2008. All rights reserved

Other Henipaviruses

Humans China, shrews in Guinea, Belgium, China

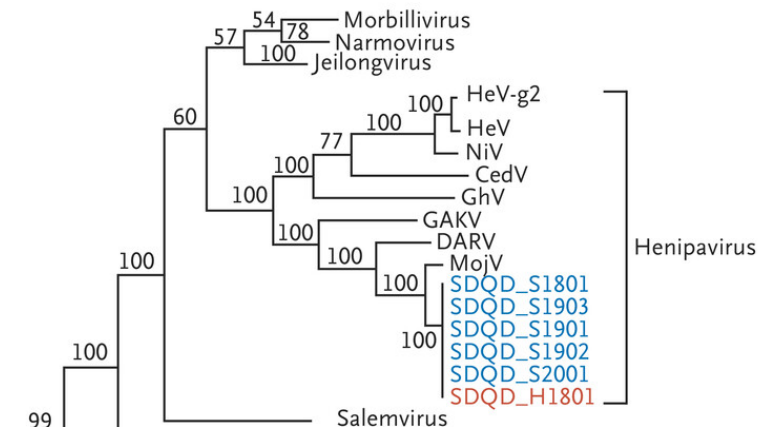


Virus Evol, Volume 8, Issue 2, 2022, veac061



Microb Genom. 2024 May;10(5).
Taiwanese gray shrew

B Phylogenetic Analysis of LayV



N Engl J Med 2022;387:470-472

Nipah Virus R&D @ PSI



A multi-disciplinary research institute hosted by the Nuffield Department of Medicine

Mission: To **discover**, **create**, and **enable** practical solutions to infectious disease threats worldwide – with a focus on equitable access to benefits for all.

- 23 Principal Investigators spanning the 4 university divisions
- ~250 staff



➤ Nipah Virus Diagnostics

- RT-PCR is the predominant diagnostic method
- ELISA – testing for Nipah antibodies
- Need for rapid point-of-care testing:
 - High priority identified by WHO (2019)
 - CEPI and FIND joint call for improved rapid tests for Nipah virus
 - PSI collaboration with Global Access Diagnostics (Gadx) and LSTM via MRC Impact Accelerator Award to develop LFD

BIOPREMIER

Search store



PRODUCTS

ABOUT US SERVICES BLOG

Share:



Home > Veterinary > Virus > Real Time PCR Detection Kit Nipah virus

Real Time PCR Detection Kit Nipah virus

Brand: GPCRs

Nipah virus detection test kit by using qPCR. Nipah virus is a newly emerging zoonosis that causes severe disease in both animals and humans. The natural host of the virus is fruit bats of the Pteropodidae Family. Nipah virus infection in humans has a range of clinical presentations, from asymptomatic infection to acute respiratory syndrome and fatal encephalitis. The virus is also capable of causing disease in pigs and other domestic animals such as dogs, cats, goats, horses, and sheep.

SKU: GPCRsNIV

FIND

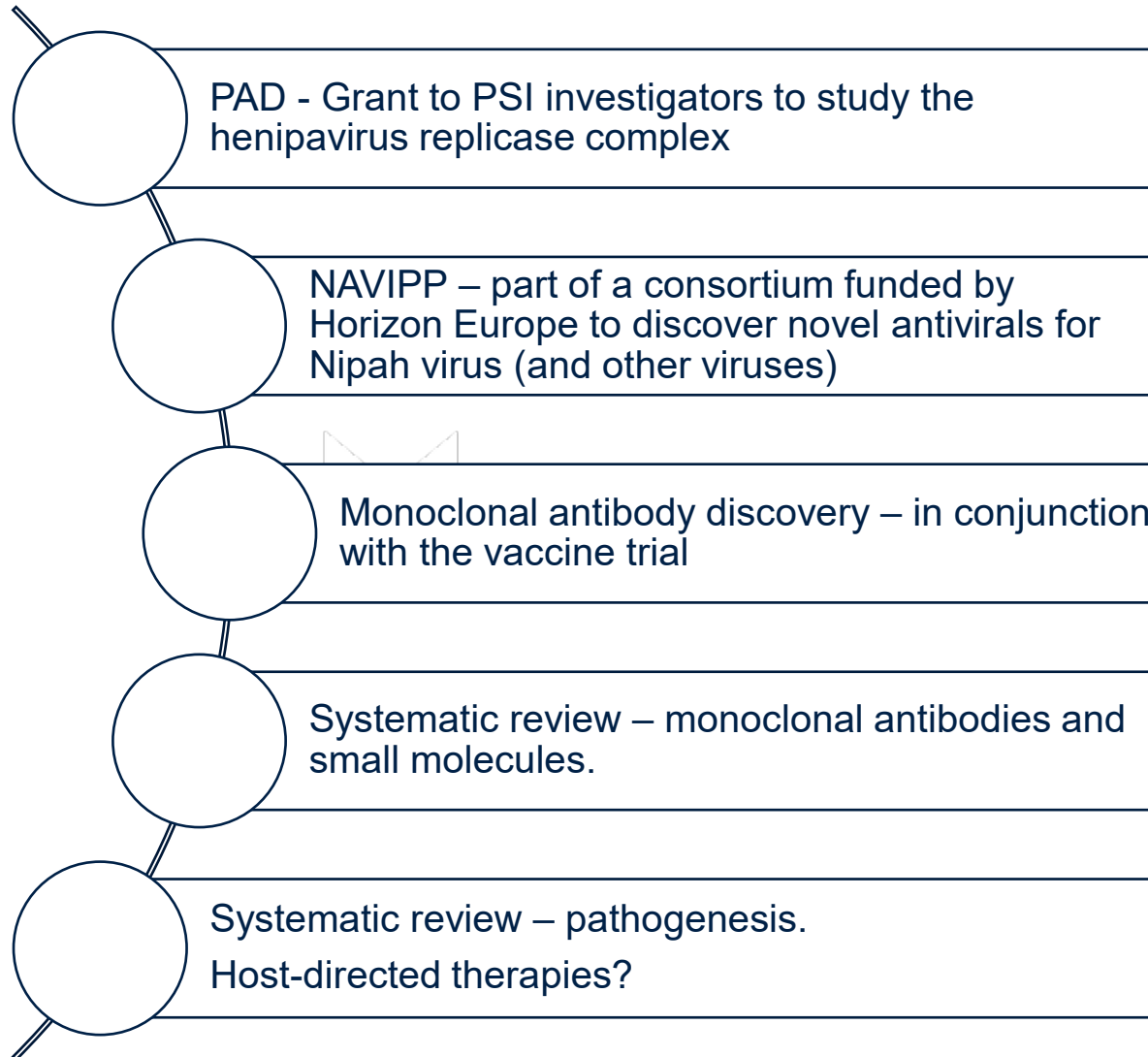
About us What we do Data and impact Publications and statements

Home > Publications and statements > Testing the tests: Scientists seek out best on-the-spot diagnostics for deadly

Testing the tests: Scientists seek out best on-the-spot diagnostics for deadly Nipah and Lassa



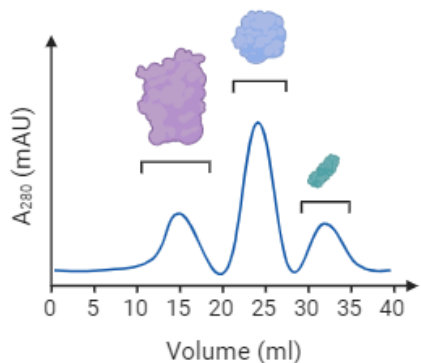
➤ Therapeutics



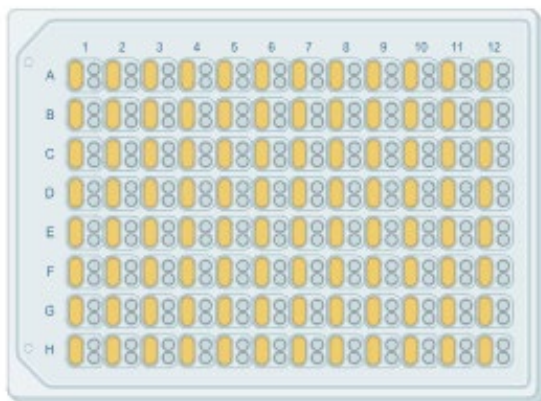
New AntiVirals for Infections with Pandemic Potential

Crystallographic Fragment Screening

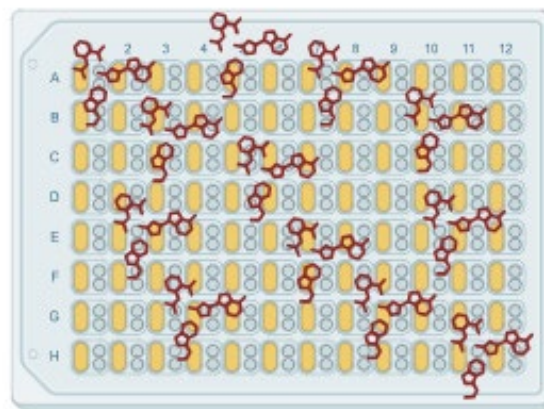
XChem platform in Diamond Light Source



Protein purification

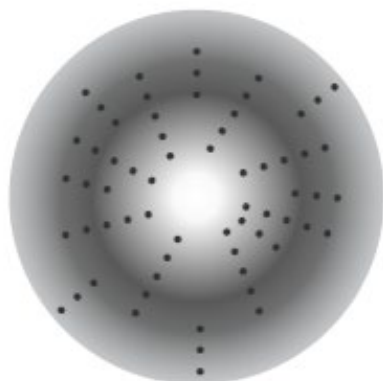


Protein crystallization
**Thousands of crystals grown*

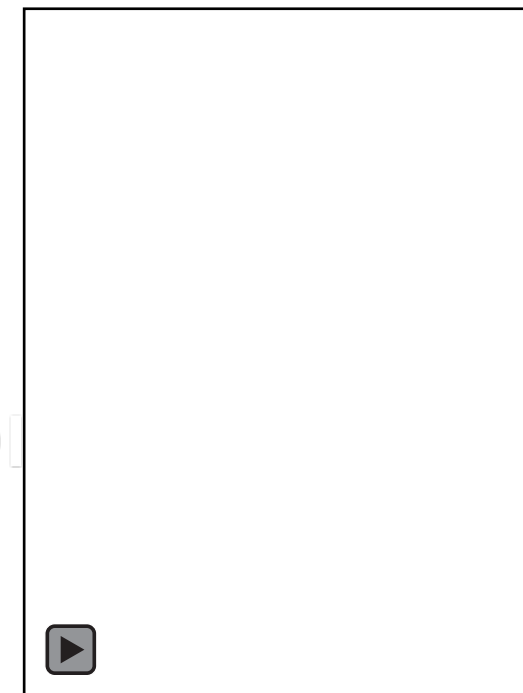


Soaking protein crystals with
fragment libraries

X-ray data collection
and analysis



- ✓ Druggable pockets
- ✓ Fragments as starting points to build into leads



An example of XChem on
SARS-CoV-2, M^{pro}

Douangamath, A. et al. 2020

Antiviral screening platform using rCedV-Luc system

Project Aims:

- Further development of rCedV antiviral screening platform (Broder Lab)
- Establishment of rCedV-Luc **high-throughput 384-well system**
- Assessment of positive controls **Favipiravir & Remdesivir** & screening of **FDA-approved drug library (2,703 compounds)**
- Additional antiviral screening of 'hits' from **X Chem** fragment analysis
- Further validation of antiviral 'hits' via **drug resistance & cytotoxicity** studies & drug combination studies
- Assessment of potential **virus-enhancement** properties of licensed drugs



➤ Nipah virus therapeutics development plan

1) Research agenda

- a) Review of therapeutic options (what is in the pipeline?)
- b) Review of pathogenesis data (target tissues, therapeutic window etc.)
- c) Observational study to complete missing clinical data

2) Define Use cases

3) Define Target Product Profile

4) Protocol development

5) Partnership development and governance structures

6) Trial site identification and capacity development



Clinical trials platform: syndromic approach

Problems

- Insufficient data on clinical epidemiology and usual care of Nipah virus disease to design a clinical trial
- Too few Nipah cases for a clinical trial

Solutions

- Concentrate on Acute Encephalitis Syndrome (AES), the primary and predominant clinical presentation of NiVD (97% of patients in India, 90% in Bangladesh, 88% in Singapore, 64% in Philippines and 55% in Malaysia)
- Conduct an observational study of AES, including NiVD, to inform clinical trial design
- Consider feasibility of trial of therapeutic approaches for all-cause AES in NiVD endemic regions (host-directed)
- Consider feasibility of pharmacometric trial of antivirals in NiVD

Bangladesh Acute Encephalitis Syndrome cohort study

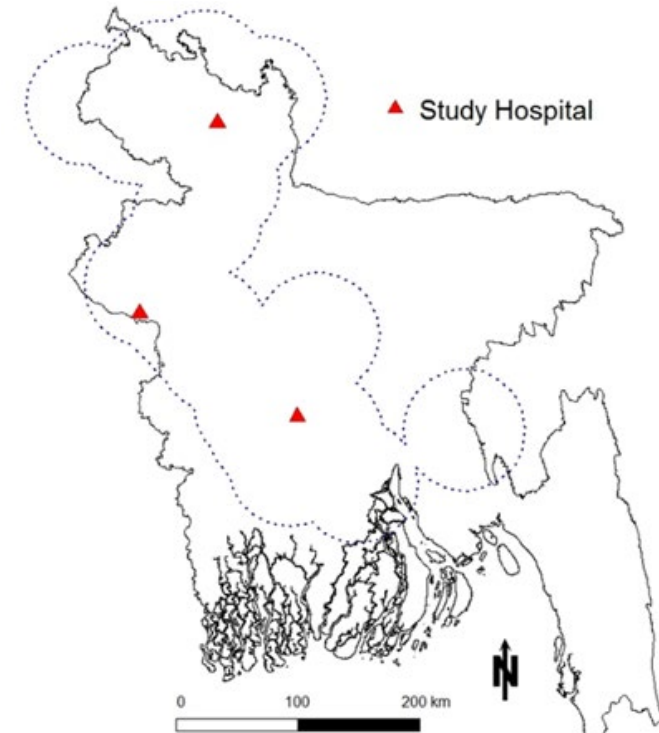
Objective: To describe the patient population, clinical presentation, natural history, common infectious aetiologies, treatment practices, and clinical outcomes of patients presenting with acute encephalitis syndrome (including NiVD) to inform the design of clinical treatment trials.

Design Prospective cohort

Sample size 2000 participants

Inclusion Criteria

Patients of any age and sex admitted with suspected acute encephalitis:



Hospital	Recruitment
Rajshahi Medical College Hospital	79
Rangpur Medical College Hospital	55
Faridpur Medical College Hospital	43
Total	177

➤ Nipah virus vaccine

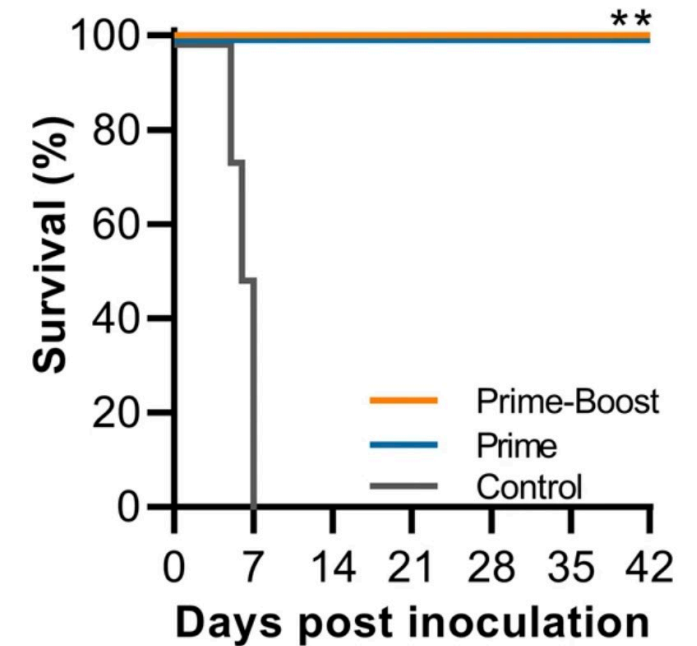
- Several vaccines show protection in animal models
- Four vaccines had advanced to Phase I clinical trial: HeV-sG-V, PHV02, mRNA-1215, ChAdOx1

Vaccine comprising the ChAdOx1 vector with the NipahB G protein

Shows protection in lethal AGM NiV challenge model

Phase I (safety and immunogenicity) trial launched in Oxford

Next phase administration to health care workers in Bangladesh

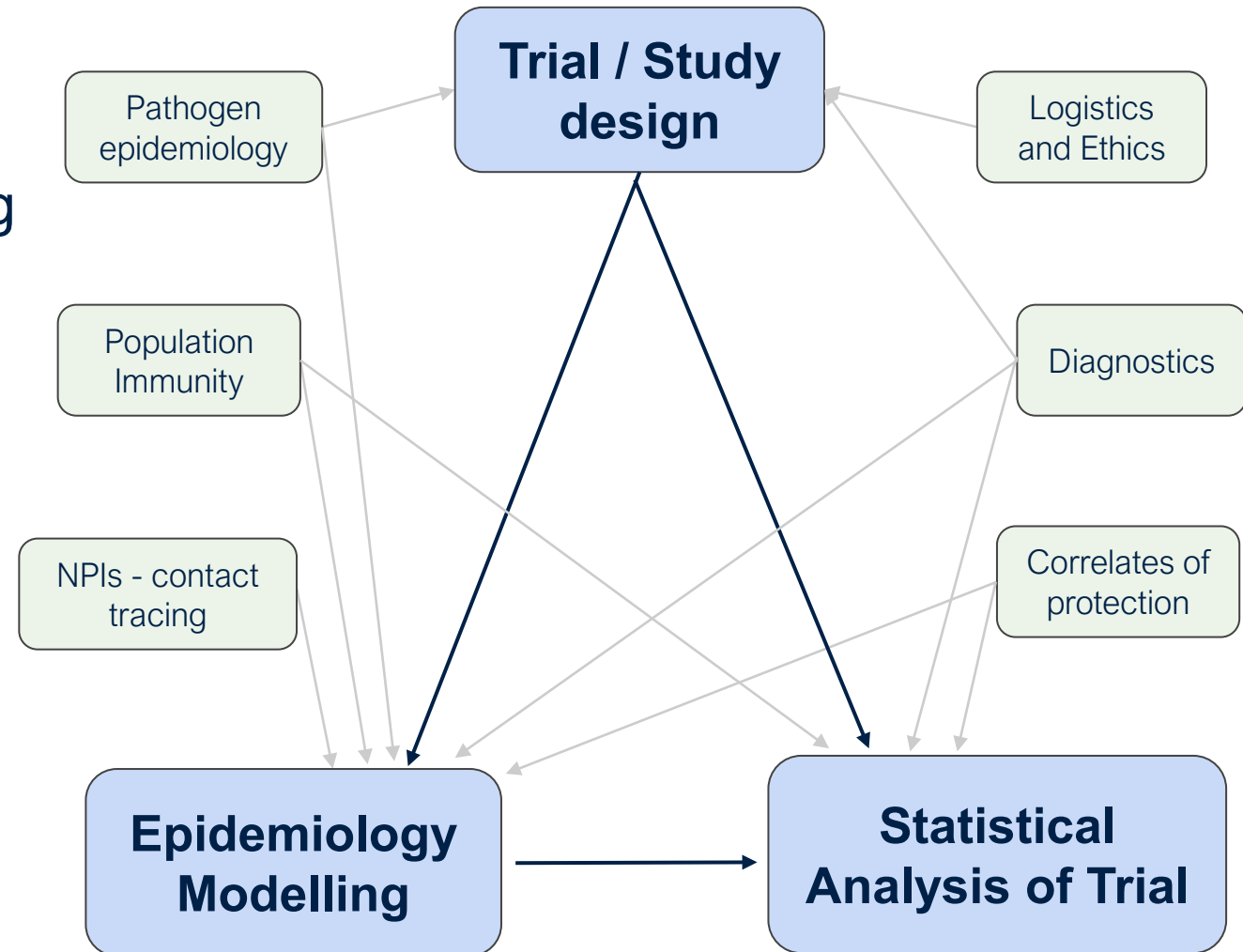


NPJ Vaccines . 2022 Dec 21;7(1):171.



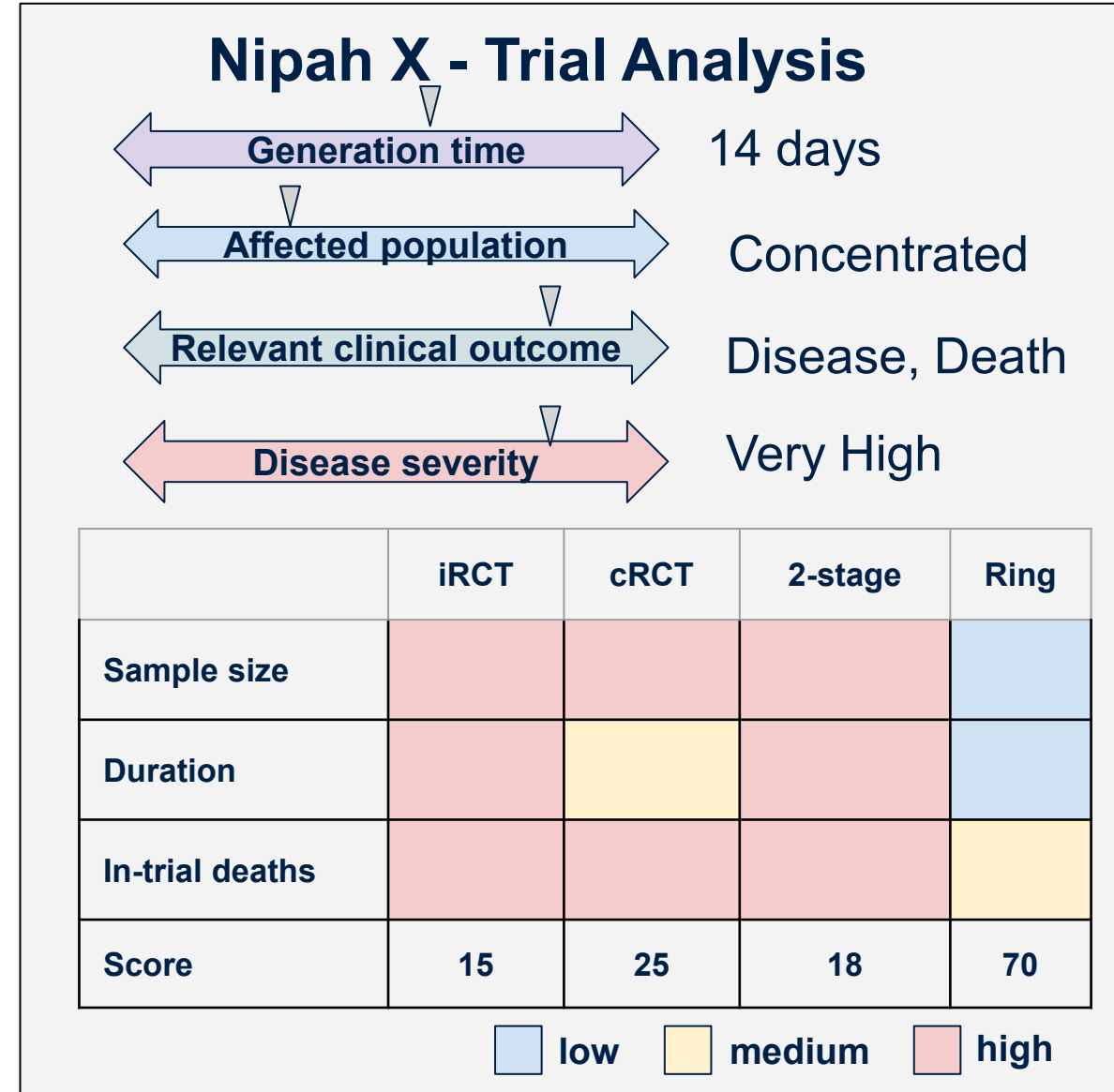
➤ Vaccine trial design modelling [PRESTO PREpare by Simulations and Trial Optimisation]

- Acceleration of vaccine efficacy trials by optimising designs using modelling
- Comprehensive modelling of key factors which influence trial design and length of trials
- Disease-specific analyses for epidemic versions of existing priority pathogens
- Real-world evaluation of vaccine efficacy when Phase III not possible



PRESTO “Nipah X”

- Epidemiology of the pathogen determines trial design (e.g. concentrated epidemics with long generation times suggest ring trials)
- Evaluate trial designs in a consistent framework estimating key trial metrics for each design
- Trial design optimisation and analysis of correlates of protection



➤ **Ethics and social sciences**

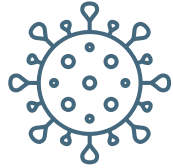
Public health ethics

- Stigmatisation and politicisation of control measures may occur. How can we avoid increasing stigma for disadvantaged populations?
- The most disadvantaged populations may face the most surveillance and containment burden. How should we compensate for these burdens?

Research ethics

- Phase III trials may be implausible due to low frequency of cases. How should we proceed in the face of uncertain recruitment and utility.

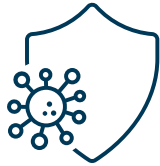
Summary: practical solutions to NiV threat



PSI & Partners Nipah Research and Development Programme



Improving early diagnosis
(development of POC)



Medical countermeasures
(vaccine, therapeutics – antivirals, mAbs)



Designing clinical trials



Involving and engaging affected communities

Acknowledgements

Syed M Satter

Kamal Ibne Amin Chowdhur

Tonmoy Sarkar

Sharful Islam Khan

Wasik Rahman

Dewan Intiaz Rahman

Zakiul Hassan

Mohammad Ziaur Rahman

Piero Olliaro

Xin Hui Chan

Amy Paterson

Amanda Rojek

Nina Gobat

Ashleigh Cheyne

Mike Parker

Tess Johnson

Euzebiusz Jamrozik

Phaik-Yeong Cheah

Ervin Fodor

Jonathan Grimes

Loic Carrique

Jeremy Keown

Juan Sandoval Valencia

Miles Carroll

Esra Balikci-Akil

Emily Clayton

Kuang Yu Chen

Haitian Fan

Franziska Guenl

Lucie Abeler-Dörner

Robert Hinch

Luca Ferretti,

James Hay

Jasmina Panovska-Griffiths

Christophe Fraser

