
"Smart Surveillance*"
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EcoHealth Alliance
* Keusch et al. (2022) Proc. Natl. Acad. Sci.

Pandemic

- Social distancing
- Travel restrictions
- Non-Pharm. Interventions

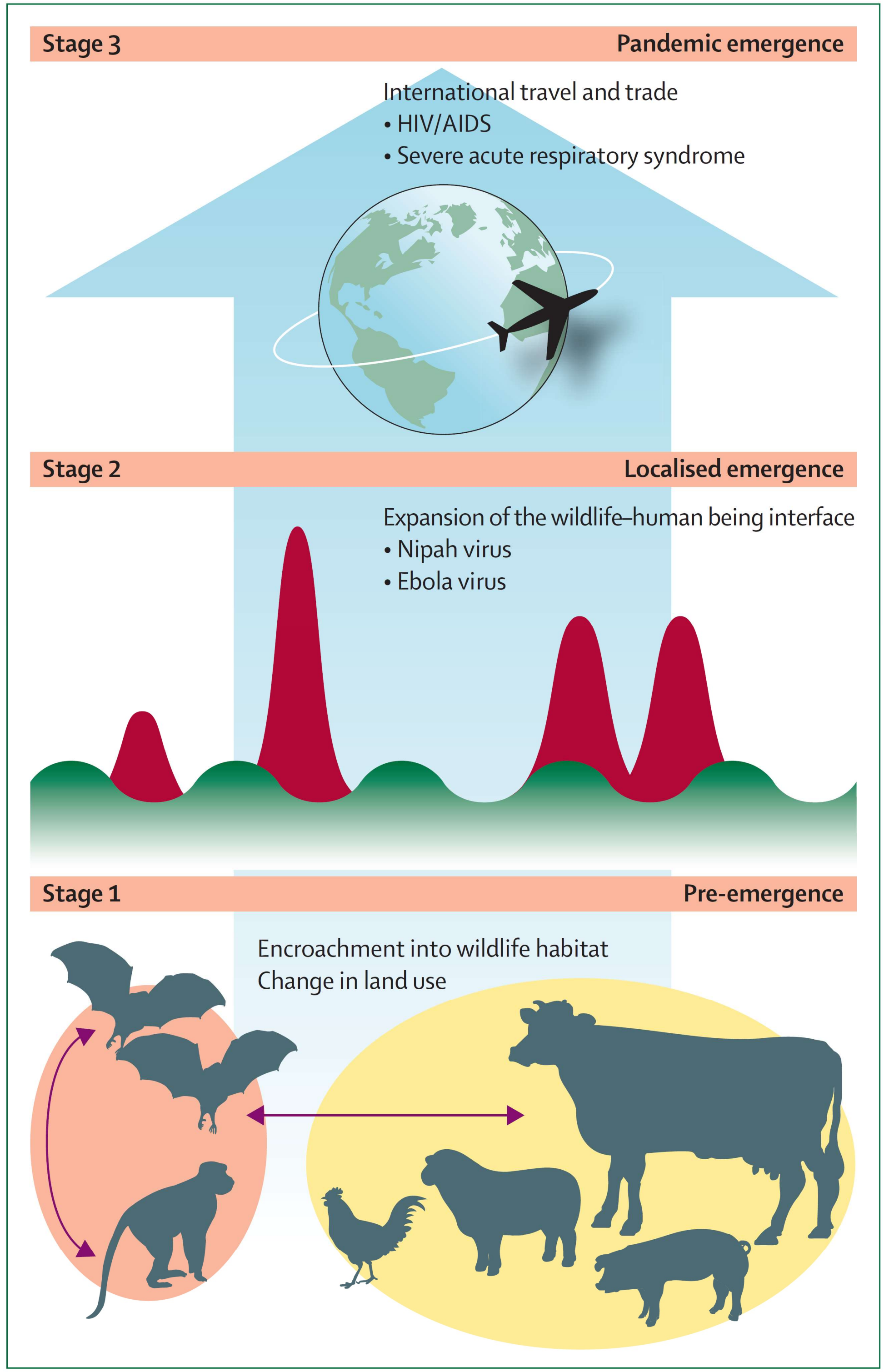
Local → regional outbreak

- Early detection
- National response capacity
- Global Preparedness

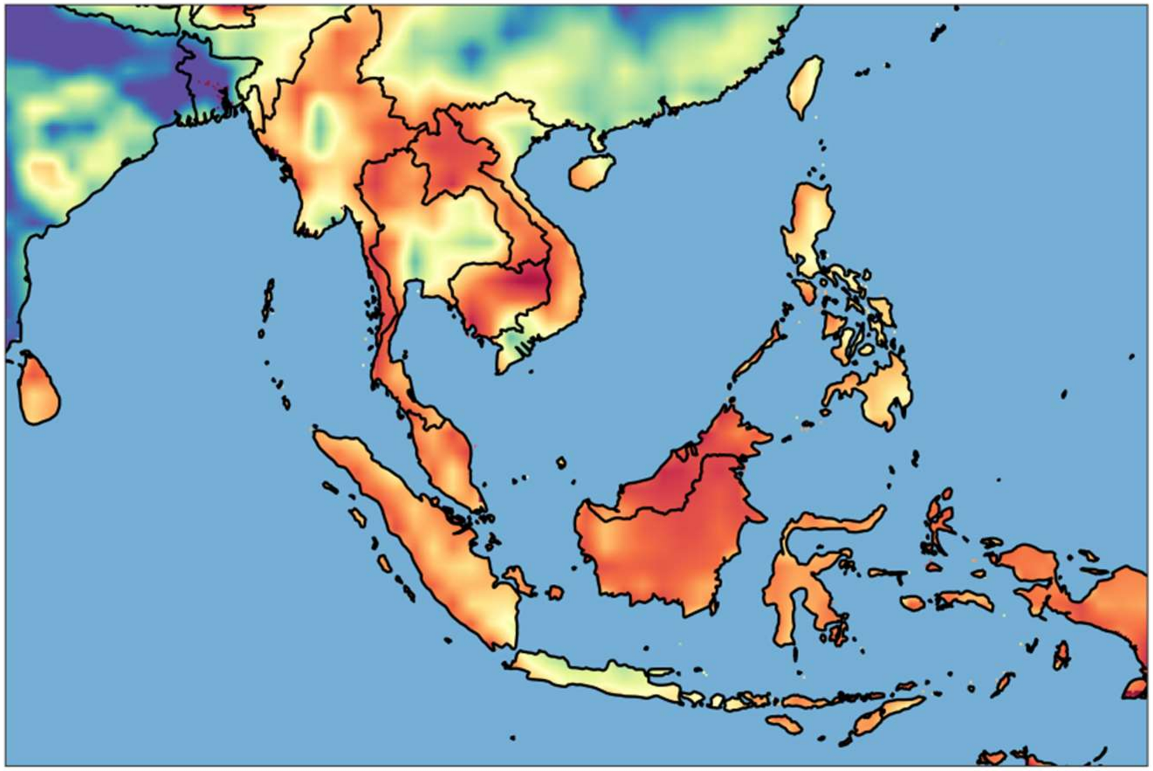
Spillover of Disease X

- Farm biosecurity
- One Health
- Environmental protection

Morse *et al.* (2012) Lancet

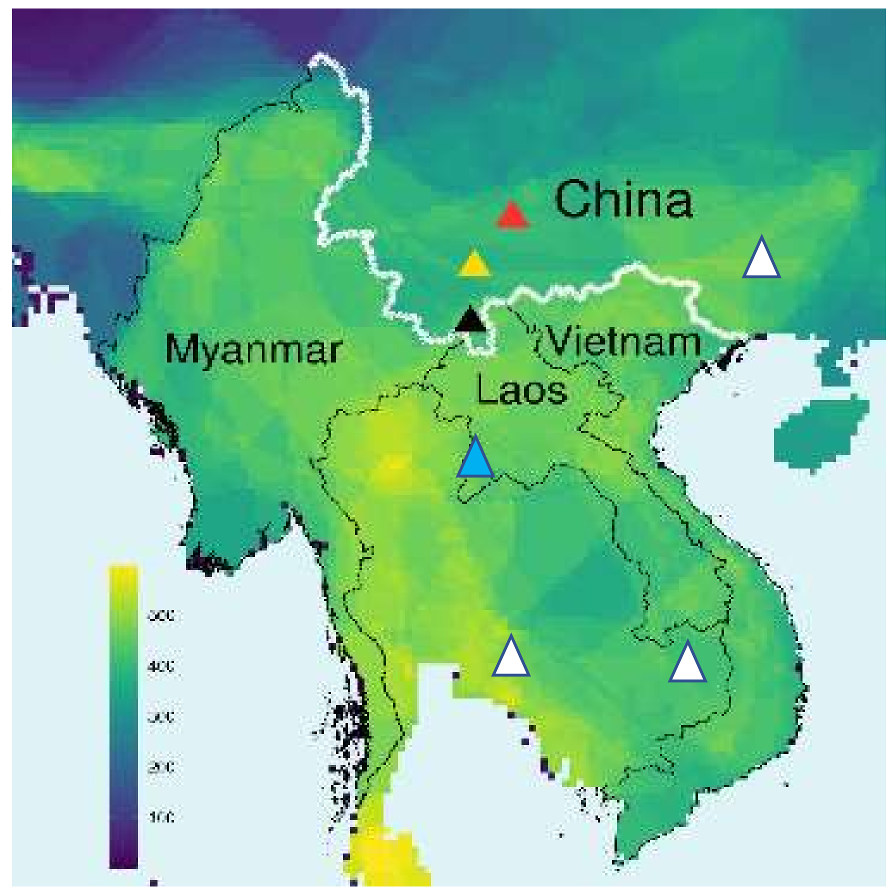


Hotspot maps for viral emergence in Southeast Asia



Emerging disease ‘hotspot’ risk

Allen *et al.* 2017 *Nat. Comm*

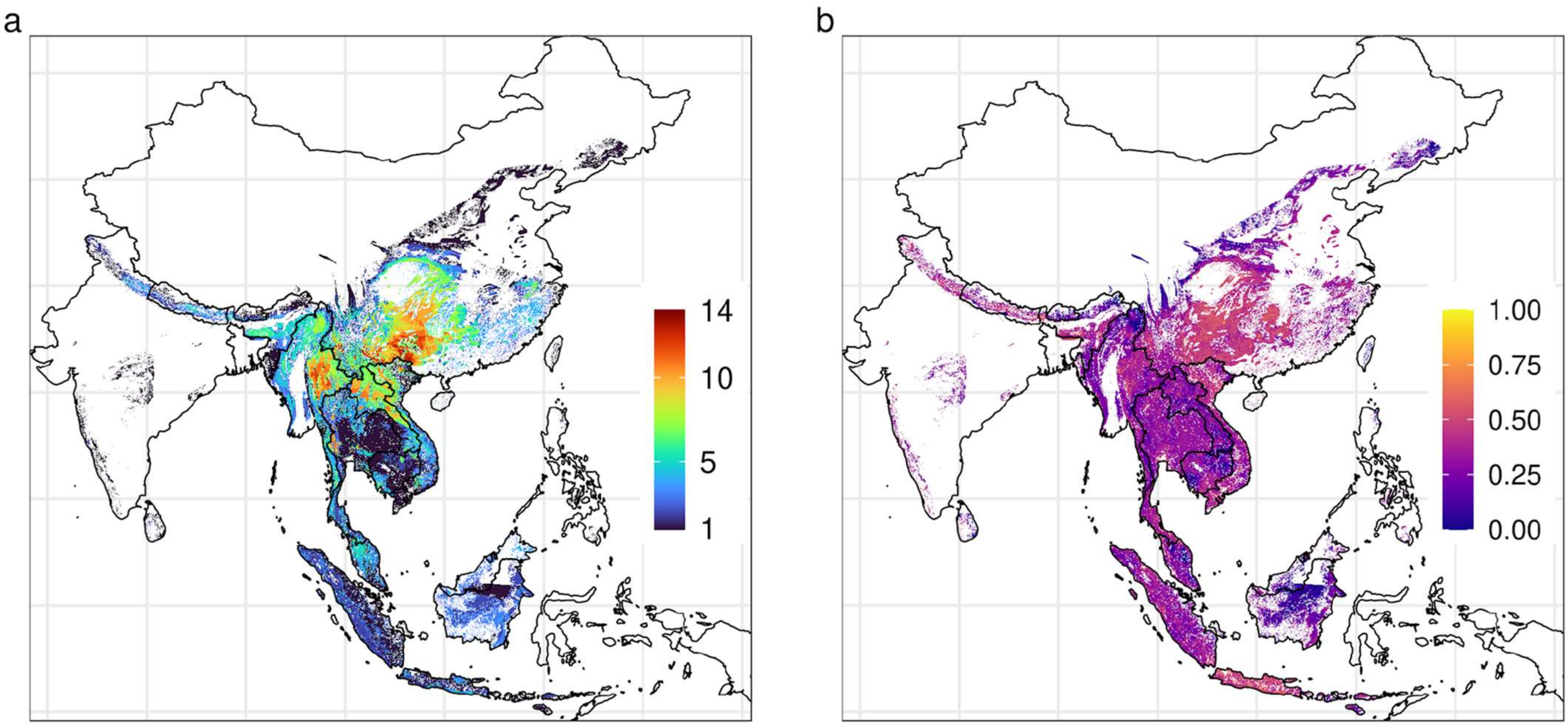


Predicted diversity of undiscovered likely zoonotic viruses (bats)

- ▲ Jinning (serol. Study)
- △ Mojiang (RaTG13)
- ▲ Xishuangbanna (RmYN02)
- ▲ BANAL CoVs (Laos)

Olival et al. 2018 *Nature*

Bat SARSr-CoV spillover risk analysis



Left: SARSr-CoV bat host species richness

Right: Relative outbreak risk (host species richness * human population)

Sánchez *et al*. **medRxiv** (2021)

EID-SEARCH

Emerging Infectious Diseases
South East Asia Research Collaboration Hub

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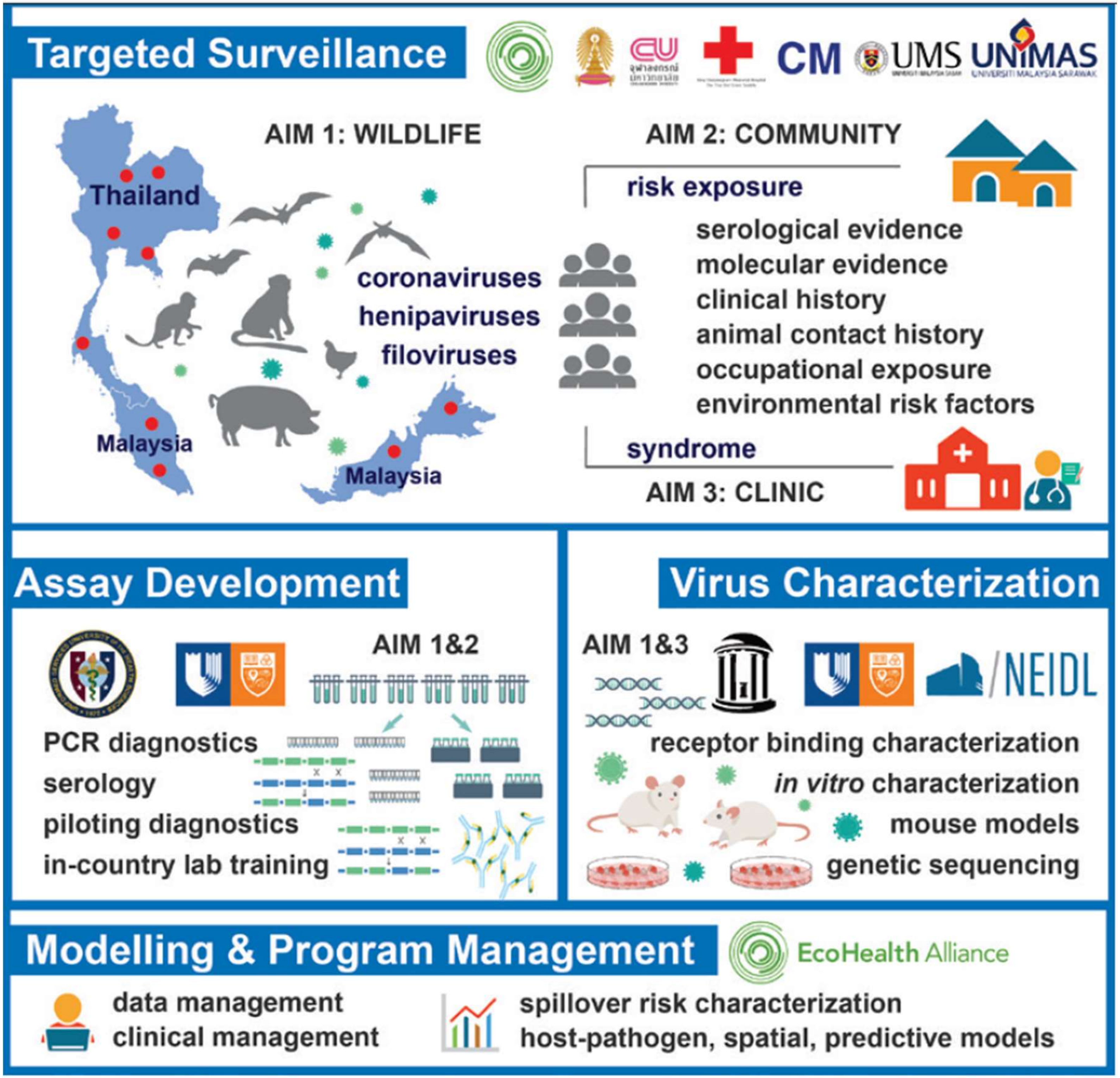
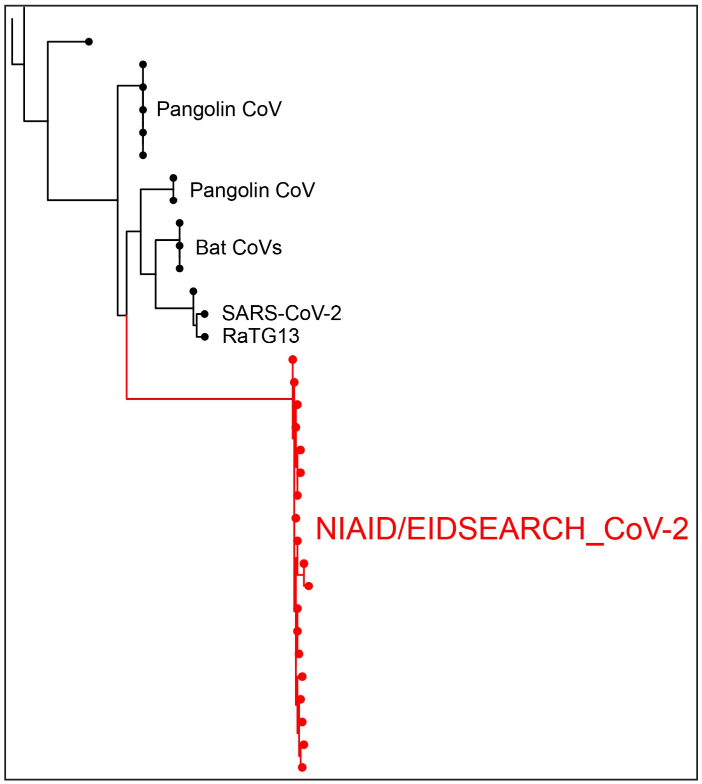
Dr. Keusch
Dr. Corley



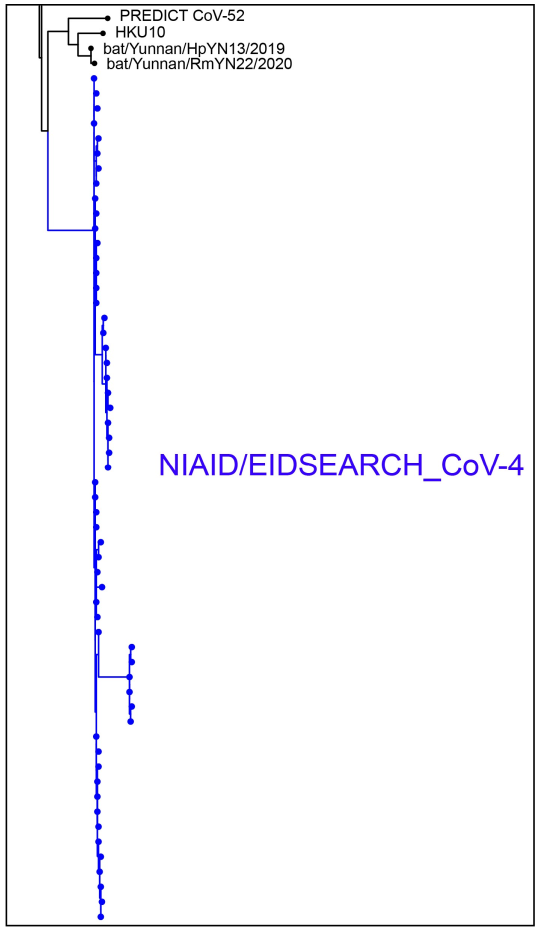
Targeted Surveillance
CM
UMS
UNIMAS
UNIVERSITI MALAYSIA SARAWAK
AIM 1: WILDLIFE
Thailand
Malaysia
Malaysia
coronaviruses
henipaviruses
filoviruses
AIM 2: COMMUNITY
risk exposure
serological evidence
molecular evidence
clinical history
animal contact history
occupational exposure
environmental risk factors
syndrome
AIM 3: CLINIC
Assay Development
AIM 1&2
PCR diagnostics
serology
piloting diagnostics
in-country lab training
Virus Characterization
AIM 1&3
NEIDL
receptor binding characterization
in vitro characterization
mouse models
genetic sequencing
Modelling & Program Management
EcoHealth Alliance
data management
clinical management
spillover risk characterization
host-pathogen, spatial, predictive models

Bat coronavirus discovery

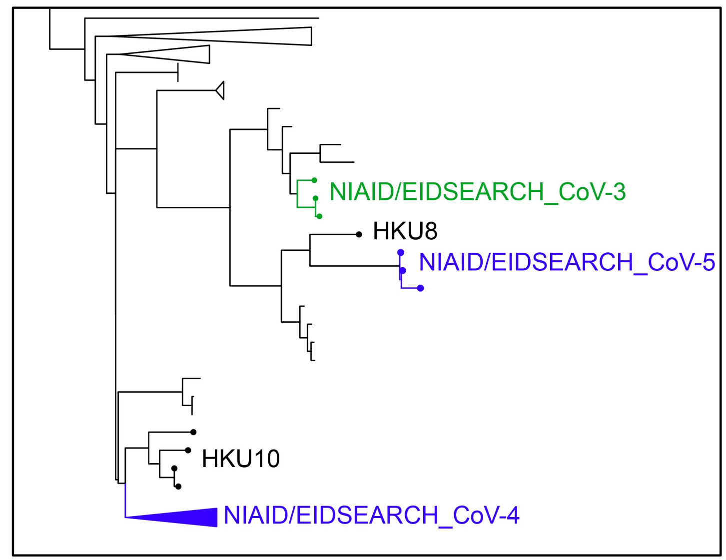
Level 1: Related to viruses with known zoonotic potential

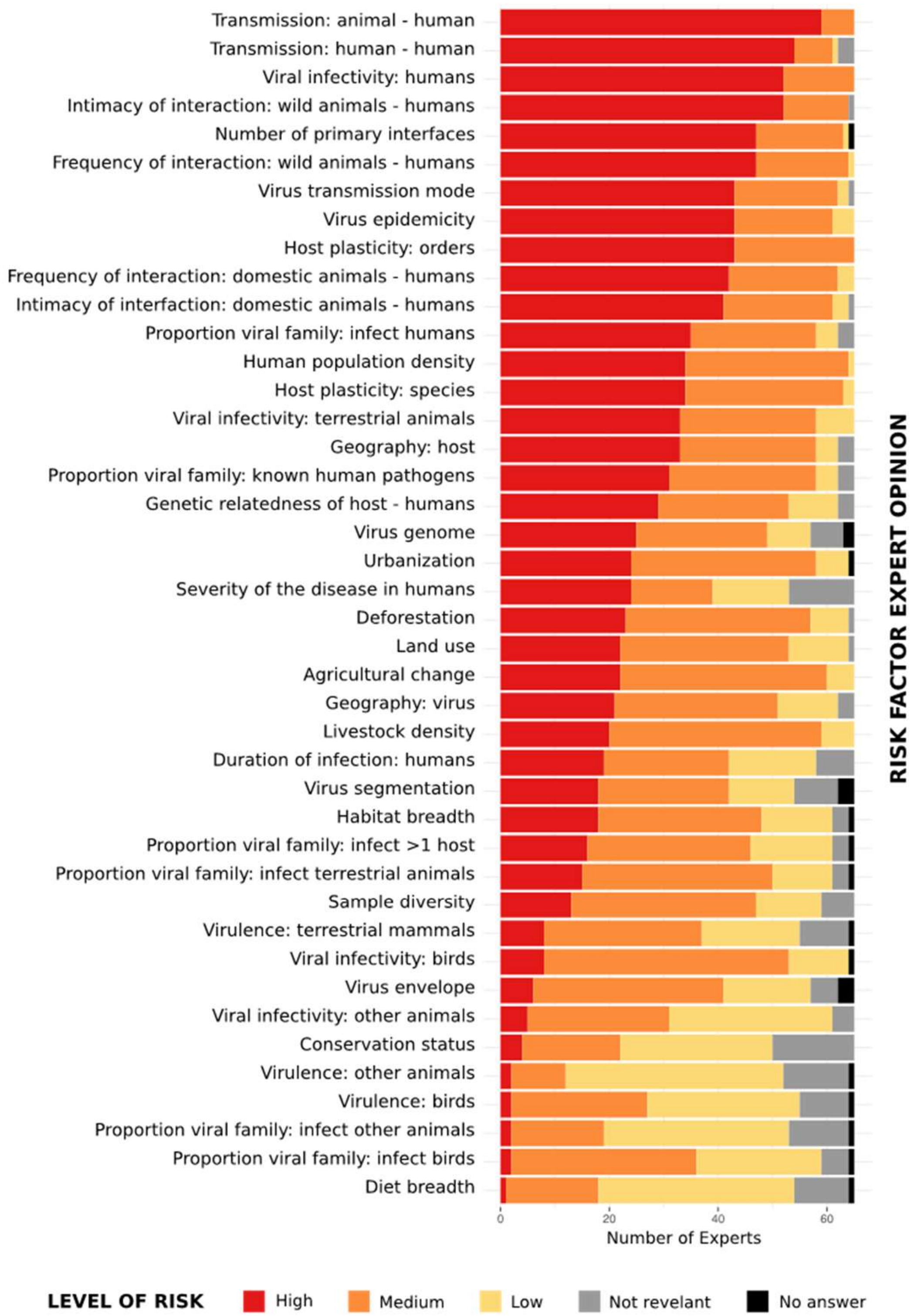


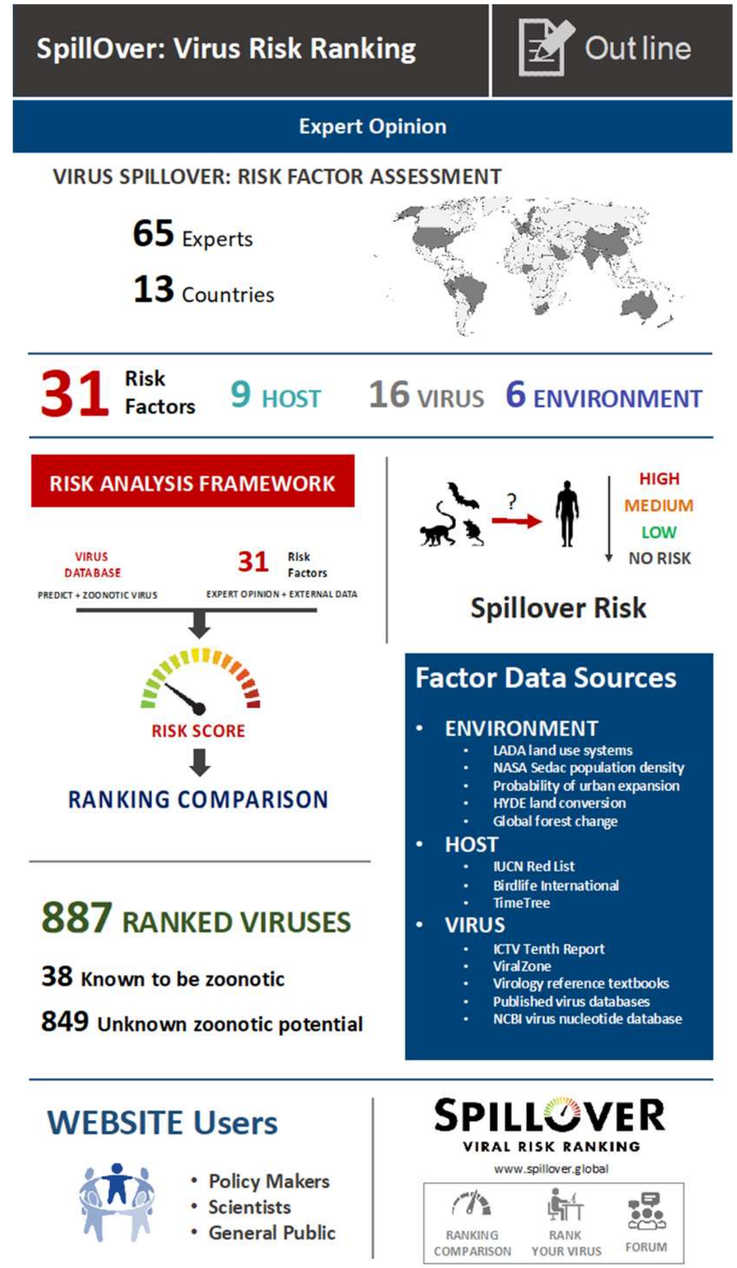
Level 2: Highly prevalent or in multiple taxa



Level 3: Restricted to a single host or at low prevalence



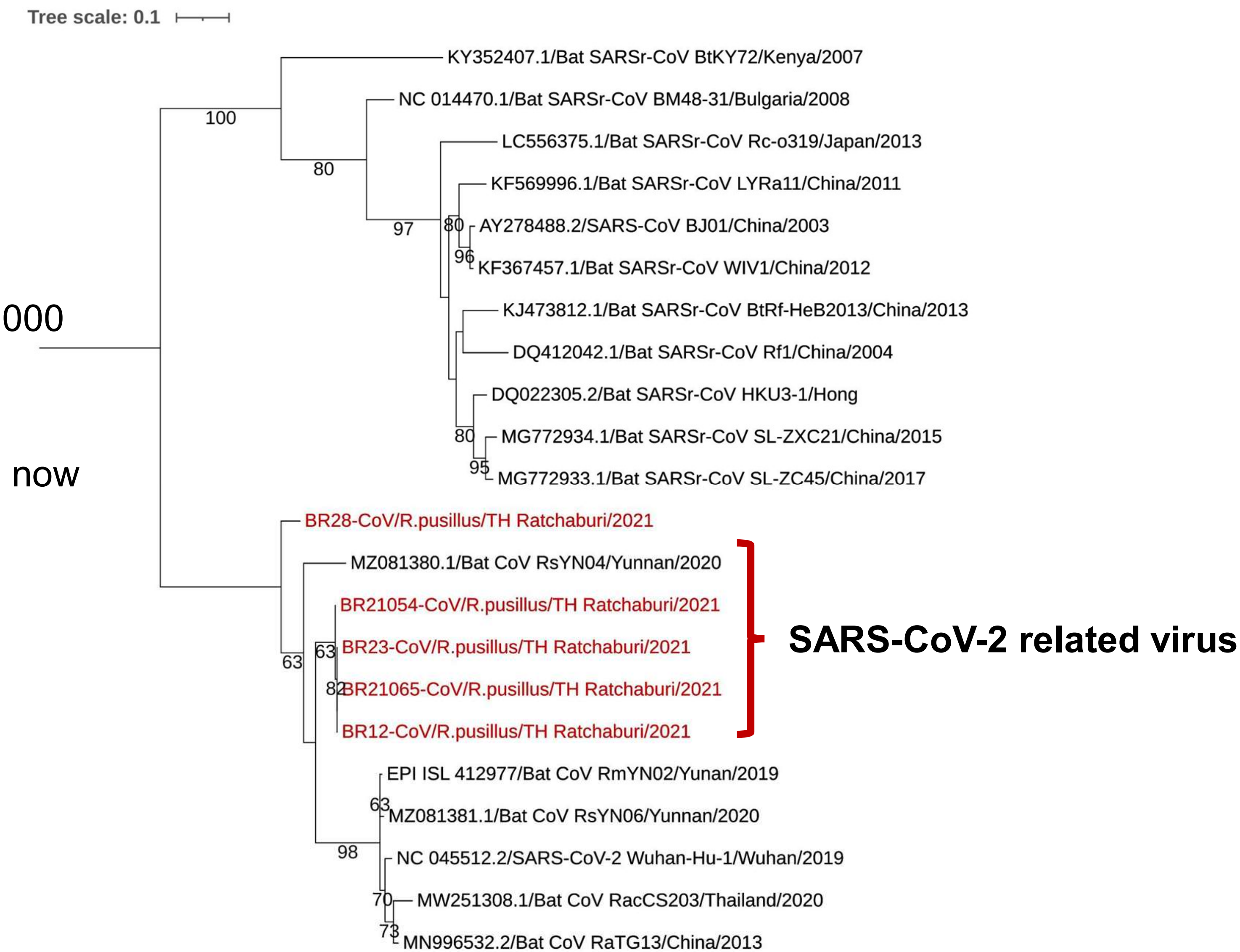




Grange *et al.* PNAS 2021

Wild Animal Surveillance Thailand Year 1

- 1,848 bats and non-human primates sampled with >13,000 specimens collected
- Characterization of newly-discovered CoVs beginning now
- Further testing underway



CREID Centers for Research in Emerging Infectious Disease
EcoHealth Alliance

SARS-CoV-2 related coronaviruses in *Rhinolophus pusillus*, Ratchaburi province, Thailand

4/99 rectal swabs PCR positive for SARS-CoV-2 related (collected in March 2021)

WGS results	Mapping Reads	Genome Completeness %	Length
B21023	13844	87	29829
B21054	218827	85.6	29970
B21065	2202757	100	29845

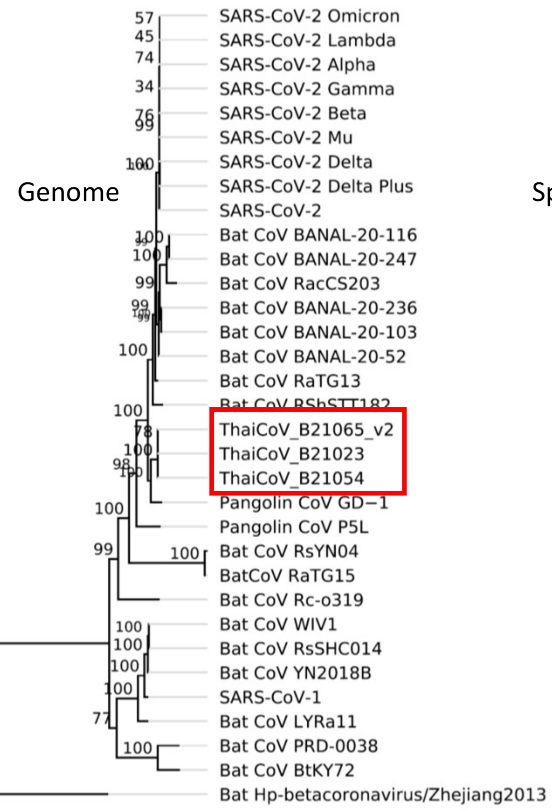
Closely related to bat and pangolin clade 2 sarbecovirus (RaTG13, GD-1, P5L), at some positions closest to SARS-CoV-2

4 amino acid differences in from RaTG13 in RBD region

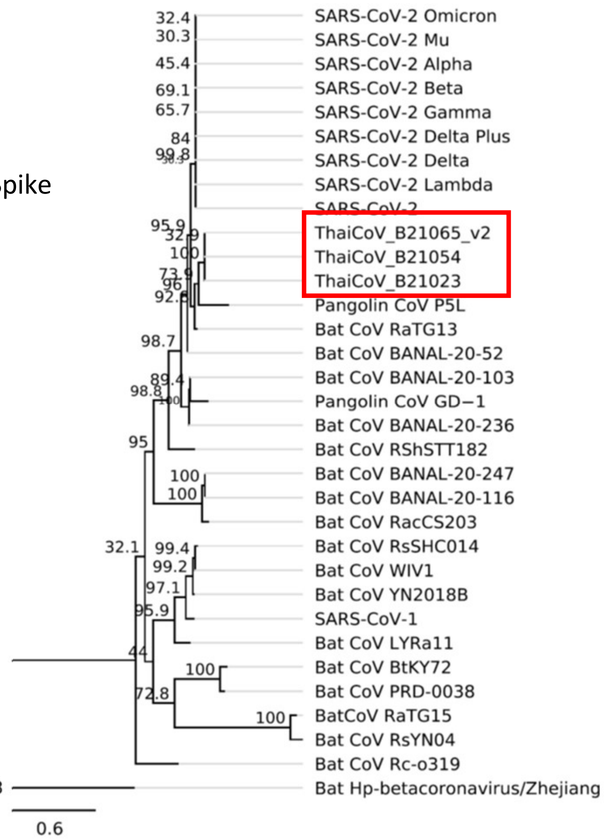
Full genome identity of B21065

Length	Pangolin GD-1	RaTG13	SARS-CoV-2
29845	91.99%	91.91%	91.72%

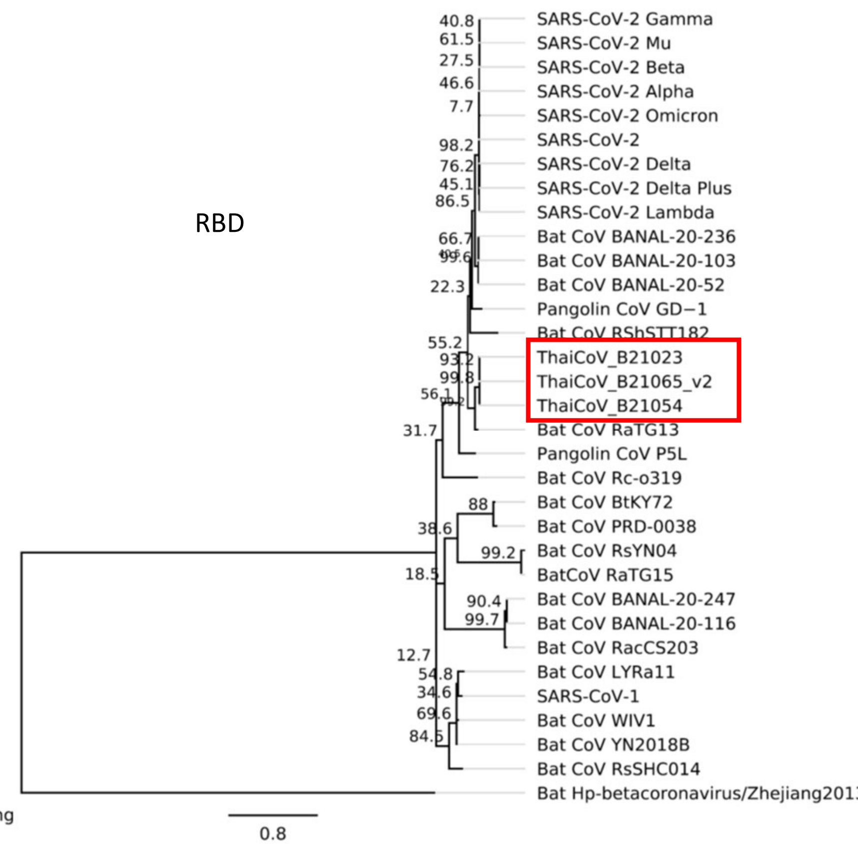
Genome



Spike



RBD



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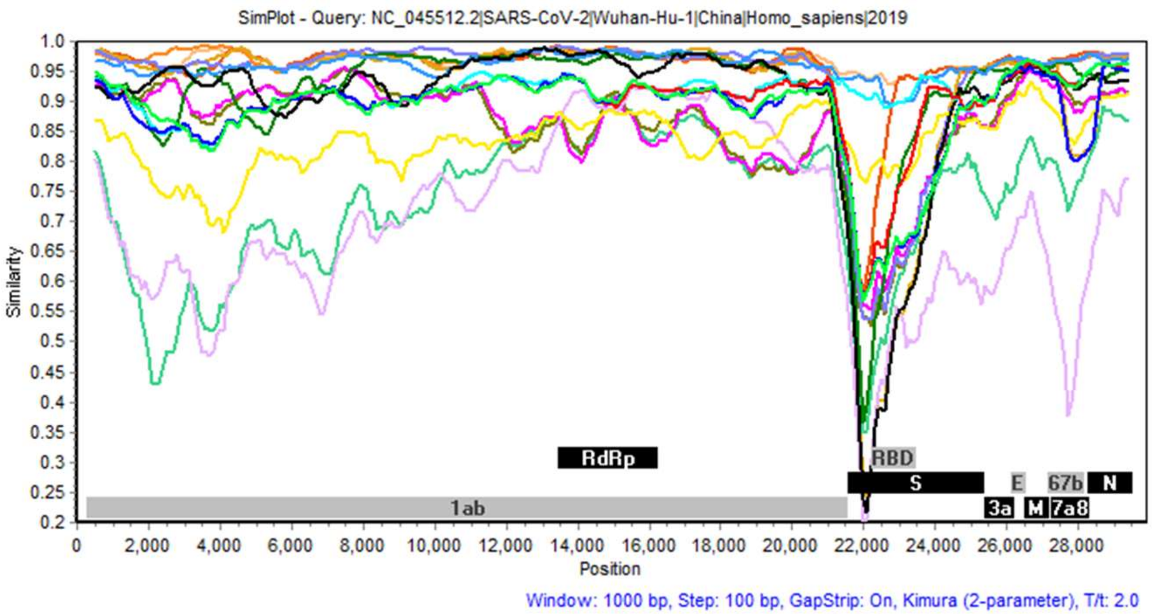
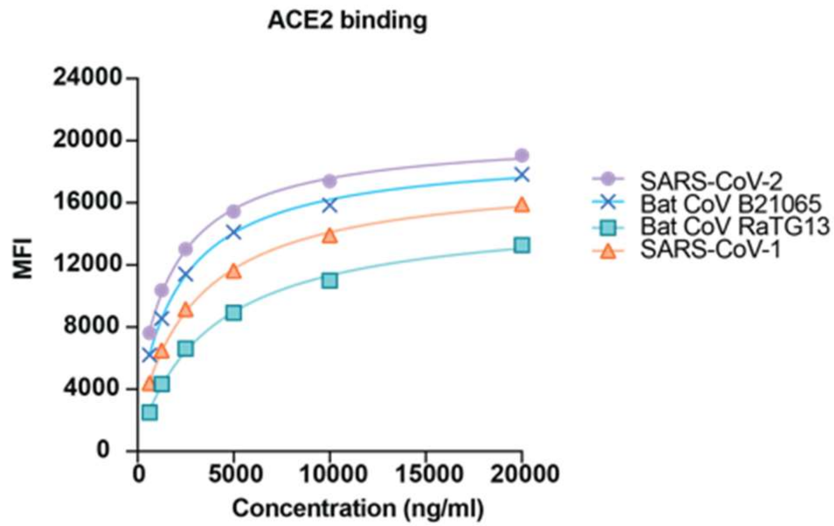
Emerging Infectious Diseases South East Asia Research Collaboration Hub

TRC EIDCC

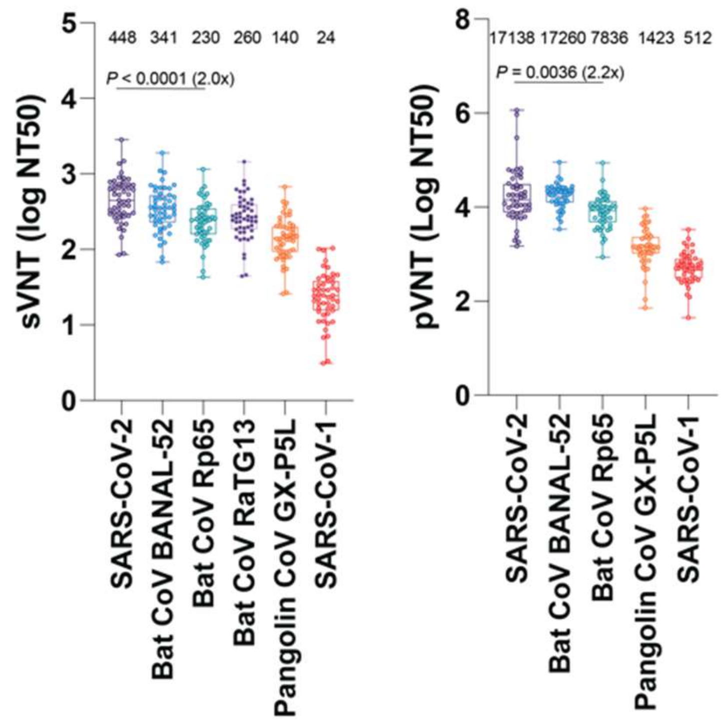
DukeNUS Medical School

Spillover risk assessment of a novel bat SARS-CoV-2-related CoV





	Genome	RdRp	Spike	RBD
THAB21065	**91.76**	**92.31 (99.25)**	**90.57 (97.56)**	**86.40 (91.48)**
THAB21105	90.34	92.42 (99.25)	80.65 (86.25)	72.94 (75.78)
THAB21140	88.96	92.63 (99.25)	75.31 (80.05)	66.22 (66.37)
THAB21146	89.60	92.56 (99.36)	75.28 (79.89)	66.37 (66.37)



High risk community – bat guano collectors

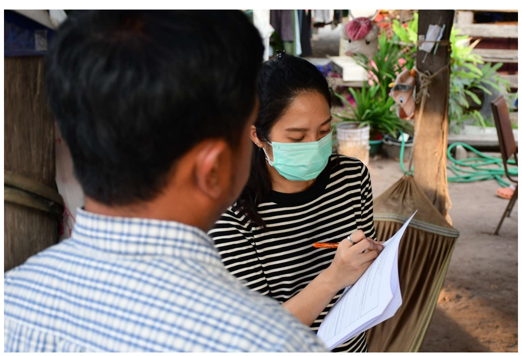
- 7/56 tested positive for PMV
- 4/56 tested positive for FV
- 34/56 tested positive for CoV

Cryptic spillover among local communities #1

Presence of antibodies reactive to henipavirus or filovirus envelope glycoproteins using MMIA (n = 237)

	# positive	Seroprevalence
Henipavirus seropositive	**64**	**27.00**
Single reactive	50	21.10
Ced	2	0.84
HeV	1	0.42
NiV	1	0.42
MojV	45	18.99
GhV	1	0.42
Cross reactive	14	5.91
Filovirus seropositive	**45**	**18.99**
Single reactive	30	12.66
EBOV	20	8.44
BDBV	6	2.53
RESTV	1	0.42
MLAV	1	0.42
RAVV	2	0.84
Cross reactive	15	6.33

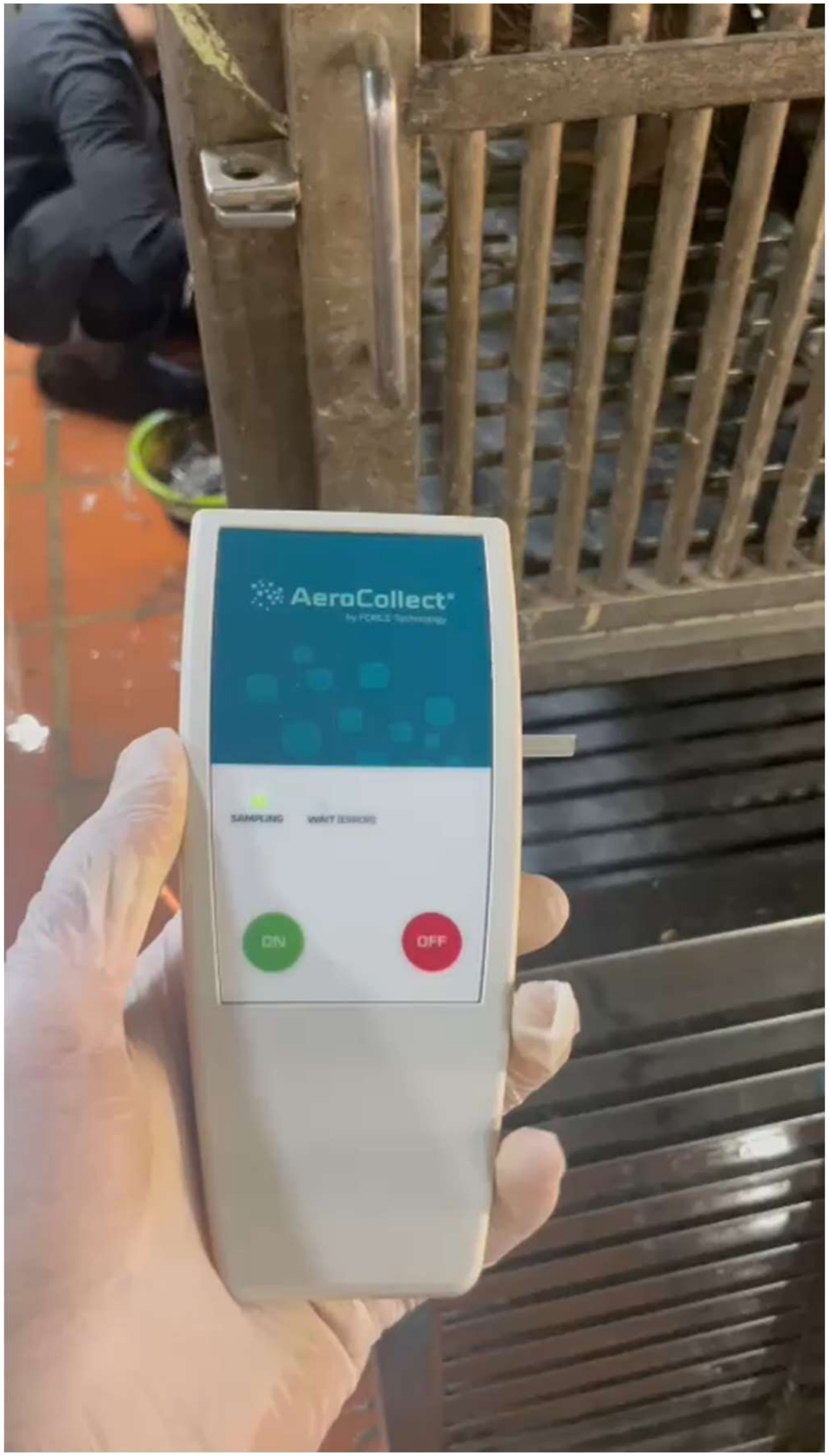
Cryptic spillover among local communities #2



Factors associated with Mojiang-related virus and Filovirus seropositivity among surveyed population (n = 237)

	Henipavirus serological results					Filoviruses serological results				
	+/total (% of positive)	Bivariant		Multivariable		+/total (% of positive)	Bivariant		Multivariable	
		OR	P value	OR	P value		OR	P value	OR	P value
Non-animal business										
No **Yes**	42/165 (35%) 21/72 (29%)	1.20	0.664	0.99	0.986	26/165 (16%) 17/72 (24%)	1.65	0.208	5.82	0.029
Bat guano collection										
No **Yes**	45/165 (27%) 18/72 (25%)	0.89	0.838	1.97	0.210	28/165 (17%) 15/72 (21%)	1.29	0.599	8.84	0.007
Forestry station worker										
No **Yes**	57/217 (26%) 6/20 (30%)	1.20	0.923	1.82	0.454	40/217 (18%) 3/20 (15%)	0.78	1*	10.55	0.029
Raised animals										
No **Yes**	26/75 (35%) 37/162 (23%)	0.56	0.079	0.34	0.036*	13/75 (17%) 30/162(19%)	0.97	1.084	0.43	0.137
Raised dogs										
No **Yes**	28/113 (25%) 35/124 (28%)	1.19	0.651	2.16	0.072	16/113 (14%) 27/124 (22%)	1.68	0.177	2.59	0.037
Slaughtered animal										
No **Yes**	62/219 (28%) 1/18 (6%)	0.15	0.048	0.19	0.127	40/219 (18%) 3/18 (17%)	0.90	1*	1.50	0.612
Rodent contact										
No **Yes**	53/206 (26%) 10/31 (32%)	1.37	0.582	1.46	0.420	37/206 (18%) 6/31 (19%)	1.10	1	1.55	0.421
Bat contact										
No **Yes**	54/176 (31%) 9/61 (15%)	0.39	0.024	0.32	0.035	37/176 (21%) 6/61 (10%)	0.41	0.078	0.27	0.052

Live Bird Market (Phnom Penh, Cambodia)
Wash water
Feathers
Cages
Surfaces
Air


AeroCollect®
SAMPLING
WAIT (ERROR)
ON
OFF

Environmental samples: pro and cons

Advantages:

- Cost effective, Rapid
- Convenient, Flexible
- Wider net at high-risk interfaces
- Biosafety, biosecurity
- Animal welfare

Disadvantages:

- Sensitivity
- Sample types
- No individual level (meta/epi)data
- Bioinformatics
- PCR inhibition, sample degradation
- SOP

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VIROLOGY UNIT

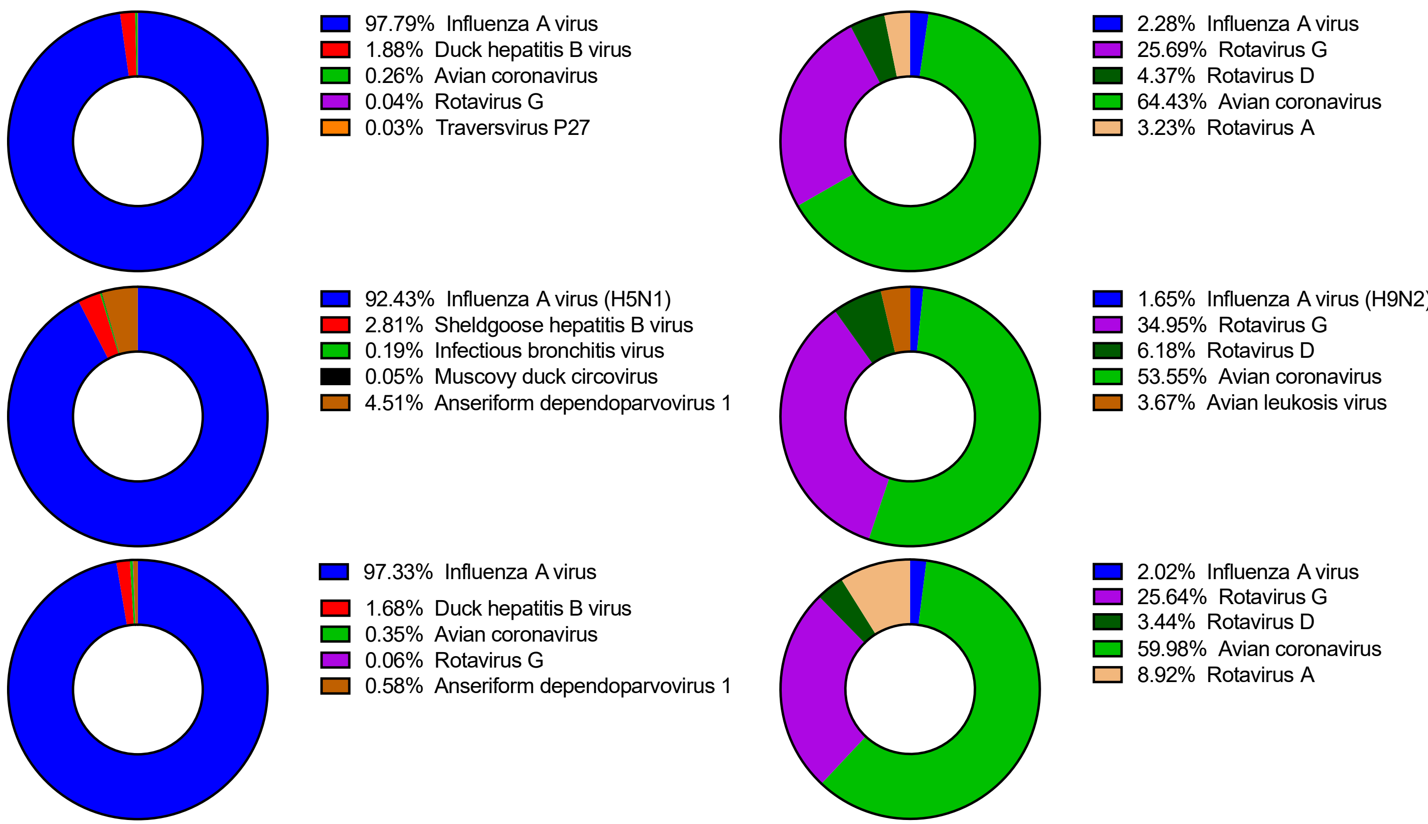
Live bird swabbing vs. air sampling; qPCR vs. metagenomics

Swabbing live birds

Air sampling bird market

Duck (throat) qPCR: A/H5N1

Air (slaughter area) qPCR: A/H9N2, A/H5N1



Influenza A Virus

Conclusion and future plans

Environmental sampling

- Similar/better resolution in detection
- Easy, less risks for humans and animals

Metagenomics

- Bigger = better: reference database
- Less sensitive to primer mismatch
- Metagenomic bycatch
- Whole genomes (phylogenetics)

Improve/expand metagenomic data analysis

- Benchmark analysis pipelines with "Golden standard"
- Develop custom/standardized thresholds
- Visualize complex metagenomics data, α/β diversity
- Feedback to OneCodex,GenomeDetective,CZID, EHA

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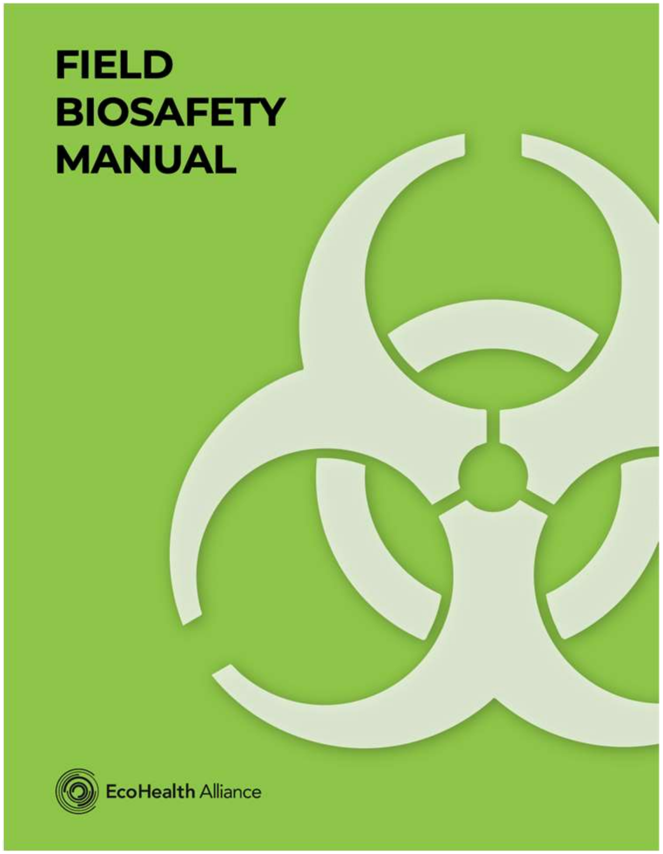
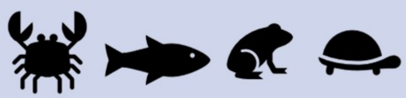
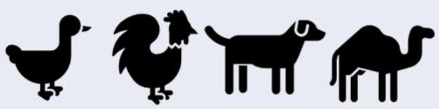
Coming soon: Field biosafety manual

1. Introduction
2. Hazard Identification
3. Risk Assessment
4. Field Biosafety Levels
5. Risk Mitigation Protocols
6. Emergency Response & Exposure
7. Appendices



RISK GROUP	ANIMAL SPECIES	ENVIRONMENT	FBSL
1		Not known to be ideal for agents greater than WHO/NIH RG 1 	1
2		Not known to be ideal for agents greater than WHO/NIH RG 2 	2
3		Not known to be ideal for agents greater than WHO/NIH RG 3 	3
4	Any RG species population known/ suspected to harbor a WHO/NIH RG 4 agent	Any risk group areas or a transient conditions known or suspected to be ideal for a WHO/NIH RG 4 agent	4

FIELD BIOSAFETY LEVELS 1-4

FIT-TEST KITS USED MUST MEET [OSHA PERFORMANCE CRITERIA FOR FIT-TESTING RESPIRATORS]

WHEN TO CONDUCT RESPIRATOR (FFR) FIT-TESTING

- All new personnel
- Each new FFR type
- Annually
- Change to facial structure
  - Weight fluctuation
  - Trauma and/ or surgical correction
  - Dental change
  - Facial scars

WHEN TO REPLACE FFRs

- Broken seal
- Soiled
- Wet from fluids/ sweat
- Increasingly difficult to breathe through
- Continuous use for 8 hours

Personal Protective Equipment (PPE) – Disposable FFR Fit Testing

For FFRs to function as intended, the product must be "fit-tested" to each individual to ensure a complete facial seal prevents any air leakage. Incomplete seals allow for potential pathogens to evade filtration. To ensure an FFR is tightly fit, a fit-test must be conducted (if first time) or a pressure seal check (each time it is placed on).

All field participants that need to wear an FFR must be fit-tested for the mask intended for use. While wearing a specialized hood and the selected FFR, an examiner puts the user through a series of exercises that mimic how a user would wear the FFR regularly. A safe flavor chemical is circulated through the hood that can only be detected by the user if there is an incomplete seal.

ENSURING RESPIRATORS (FFRs) ARE TIGHTLY FIT TO USERS FACE

1
KEEP FACE FREE OF FACIAL HAIR FOR A COMPLETE SKIN SURFACE CONTACT

2
WEAR APPROPRIATELY – DO NOT CROSS STRAPS

3
CONDUCT A PRESSURE SEAL CHECK (IF ALREADY FIT-TESTED)

Personal Protective Equipment (PPE) – Elastomeric Facepiece Respirator (EFR) & Power Air-Purifying Respirators (PAPR)

Alternatives to disposable filtering facepiece respirators (FFRs) are the reusable elastomeric facepiece respirators (EFR) and power air-purifying respirators (PAPR). These respirators should be considered if an individual fails the fit-test or has an aversion to any of the supplied NIOSH approved FFRs. Follow model instructions for fit-testing and use.

ELASTOMERIC FACEPIECE & POWER AIR-PURIFYING RESPIRATORS

EFR

Half mask (elastomeric) — Full facepiece (elastomeric)

- Tight fitting respirator
- Fit-testing required, must be NIOSH-approved
- Reusable/ Can be disinfected
- Filtration level dependent upon replaceable filters
- BUT has exhalation valve – consider reverse zoonoses
- COST: Usually ~ $15 to $30, but can be up to $500

PAPR

Loose-fitting powered air-purifying respirator (PAPR) — Hood powered air-purifying respirator (PAPR)

- Loose fitting respirator, battery powered
- Fit-testing NOT required, but must be NIOSH approved
- Reusable/ Can be disinfected
- Typically exceeds N95 level filtration
- Units that filter exhaled air are preferred
- COST: Usually ~ $800 +

OPTIONS FOR WHEN FIT-TESTS FAIL OR WHEN USE OF A NIOSH-APPROVED DISPOSABLE RESPIRATOR (FFR) IS NOT POSSIBLE

- TRY AN ALTERNATE NIOSH - APPROVED FFR SIZE/ MODEL
- CONSIDER AN ELASTOMERIC RESPIRATOR
- CONSIDER A POWER AIR-PURIFYING RESPIRATOR
- CONSDIER AN UNDER-RESPIRATOR BEARD COVER

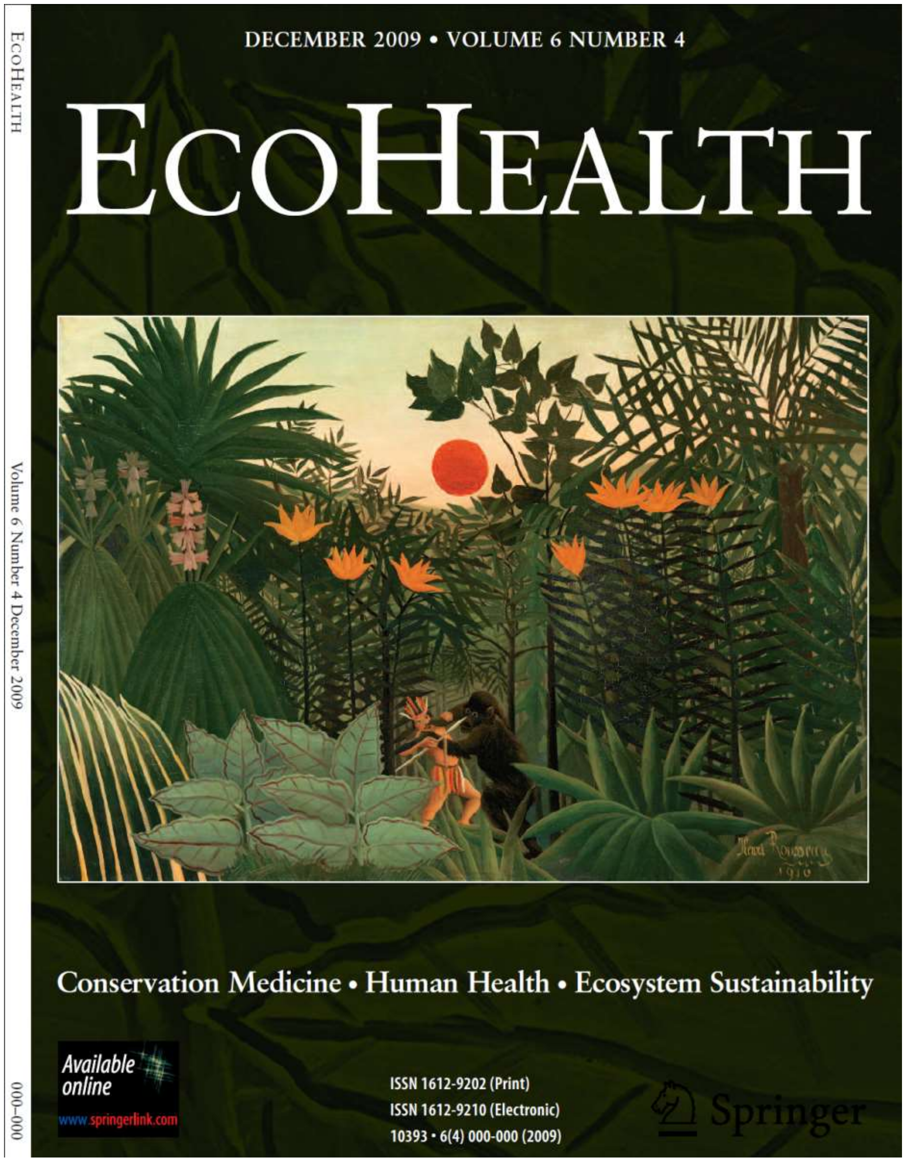
UNDER-RESPIRATOR BEARD COVER

SINGH-THATTHA TECHNIQUE

A final alternative for beard presence when PAPRs are not an option is the application of a beard cover. Use of a synthetic elastic cover to contain the beard and to make complete contact with skin and the respirator (FFR or EFR) may be attempted but still requires fit-testing.

https://www.journalofhospitalinfection.com/article/S0195-6701(20)30459-X/fulltext

Collaborators



- 100+ partners in 30+ countries
- NIAID CREID Center Grant partners: USU, UNC, Duke-NUS, Thai Red Cross EIDCC, Chulalongkorn Univ, Conservation Medicine Malaysia, BU NEIDL
- Dr. Wacharapluesadee, Dr. Opass
- Wuhan Inst. Virology (Zhengli Shi, Peng Zhou)
- Duke-NUS Singapore (Linfa Wang , Chee-Wah Tan)
- Pasteur Inst. Cambodge (Erik Karlsson; Jurre Siegers)

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