



CASE STUDY: RESPIRATORY VIRUS & NOVEL PATHOGEN

SOUTH & SOUTHEAST ASIA **PATHOGEN GENOMICS PRIORITIZATION & IMPLEMENTATION WORKSHOP**

*September 9-13, 2024
Bangkok, Thailand*

WORKSHOP PARTNERS



Asia Pathogen
Genomics Initiative



**CENTRE FOR
PATHOGEN
GENOMICS**

Sydney Infectious Diseases Institute
Centre for Infectious Diseases & Microbiology
WHO Southeast Asia Regional Office (SEARO)
WHO Western Pacific Regional Office (WPRO)
WHO International Pathogen Surveillance Network (IPSN)



Case Study 2

Respiratory & Novel Pathogen Case Study

Background



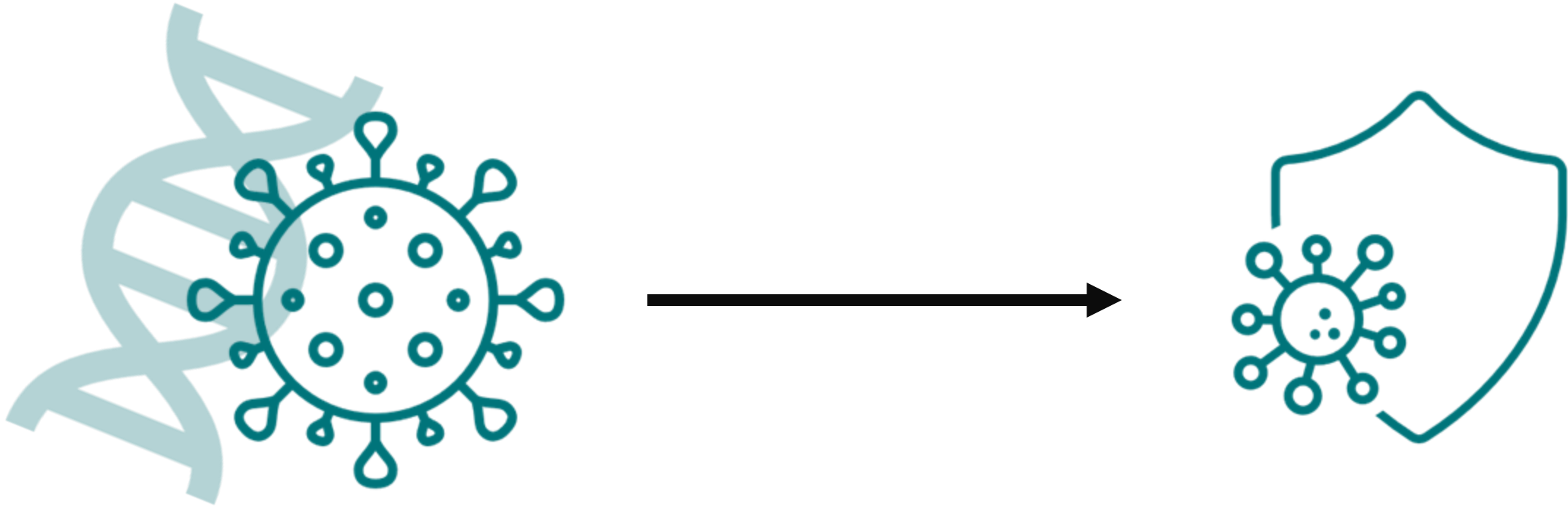
Respiratory & Novel Pathogen Case Study

Outline

1. Learning Objectives
2. Background
3. Scenarios & Discussion
4. Prioritization Activity



Learning Objectives



How do respiratory pathogen genomics support public health preparedness, response, and action?

What are the key considerations when implementing respiratory and novel pathogen genomics?



Learning Objectives



Learning Objectives



Discuss at your table: Are you a laboratorian, bioinformatician, epidemiologist, surveillance expert, or other type of public health practitioner?

Respiratory & Novel Pathogen Genomics



Known respiratory viruses and bacteria



Respiratory & Novel Pathogen Genomics



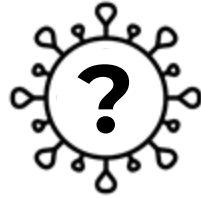
e.g., bordetella pertussis,
burkholderia
pseudomallei,
haemophilus influenzae,
mycoplasma pneumoniae,
and streptococcus
pneumoniae

Known respiratory **viruses and **bacteria****

e.g., coronavirus, influenza, respiratory
syncytial virus, adenovirus, rhinovirus,
parainfluenza virus, enterovirus,
metapneumovirus



Respiratory & **Novel** Pathogen Genomics

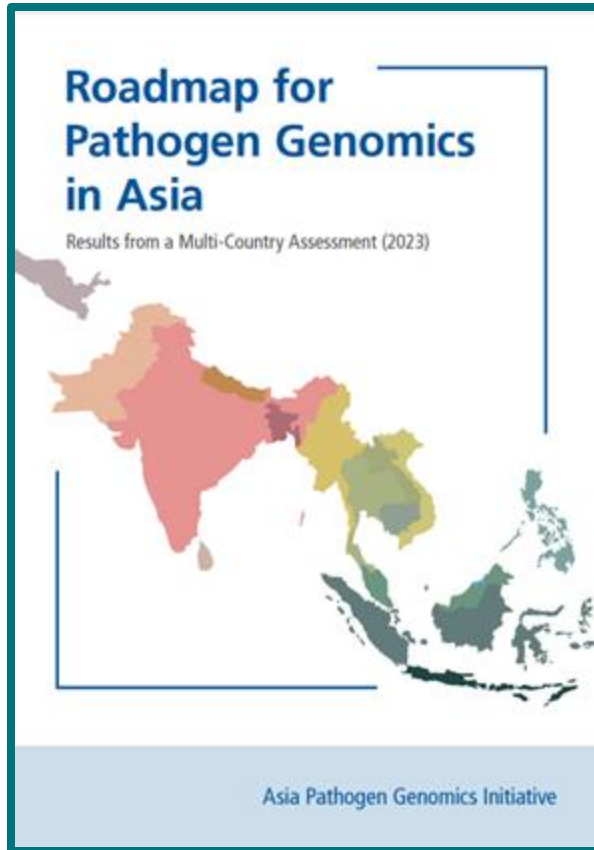


**Unknown respiratory pathogen of
pandemic potential**

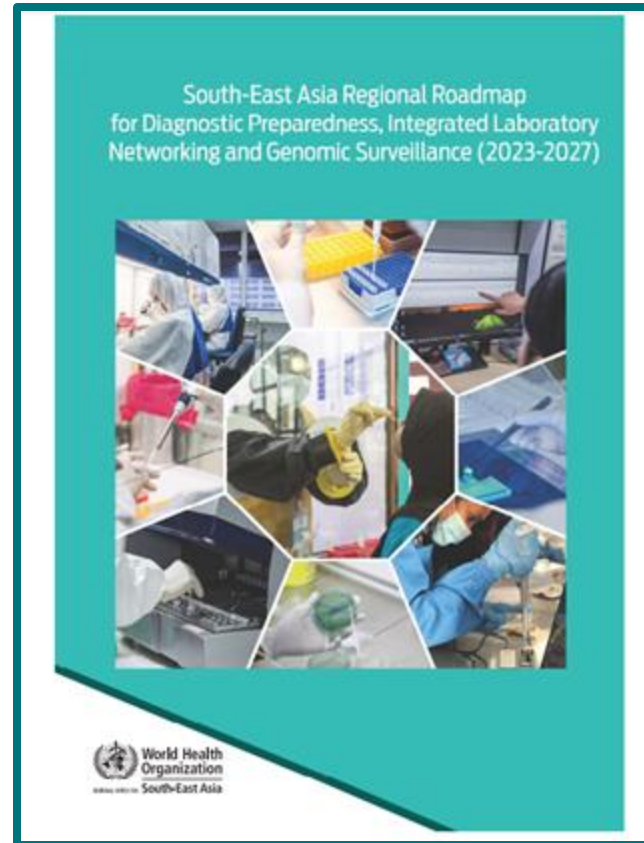


Respiratory & Novel Pathogen Genomics

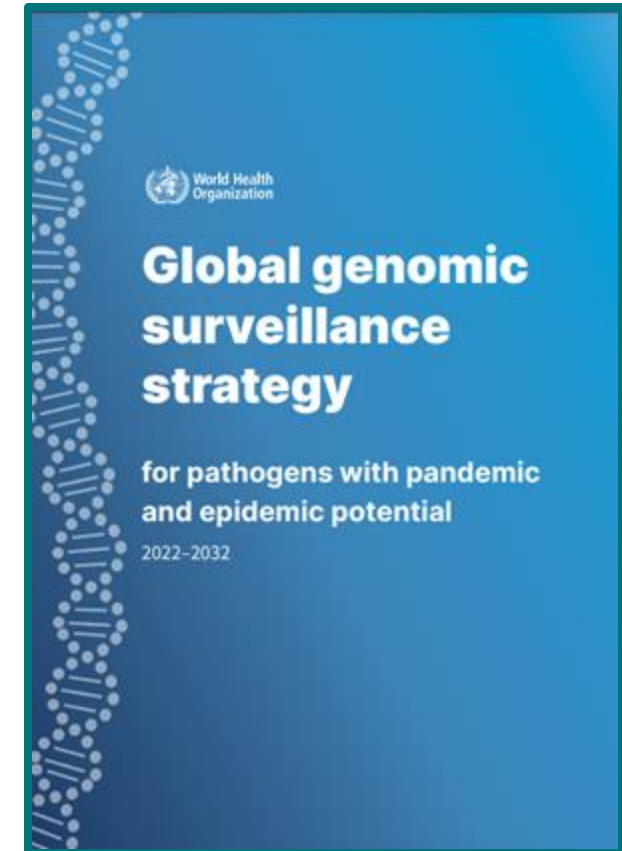
Global, Regional, & National Prioritization



Asia PGI Roadmap



SEARO Roadmap



WHO Strategy



Global Prioritization

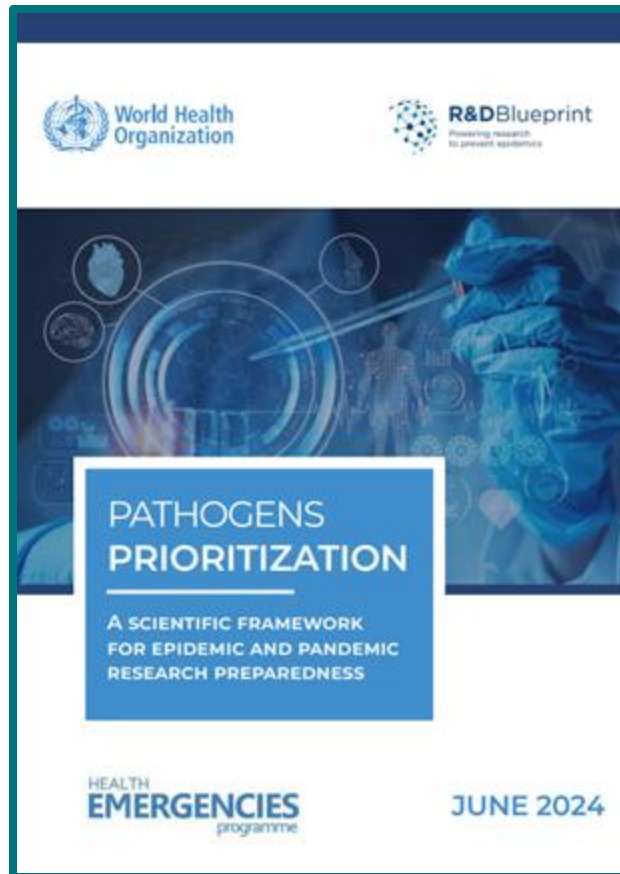
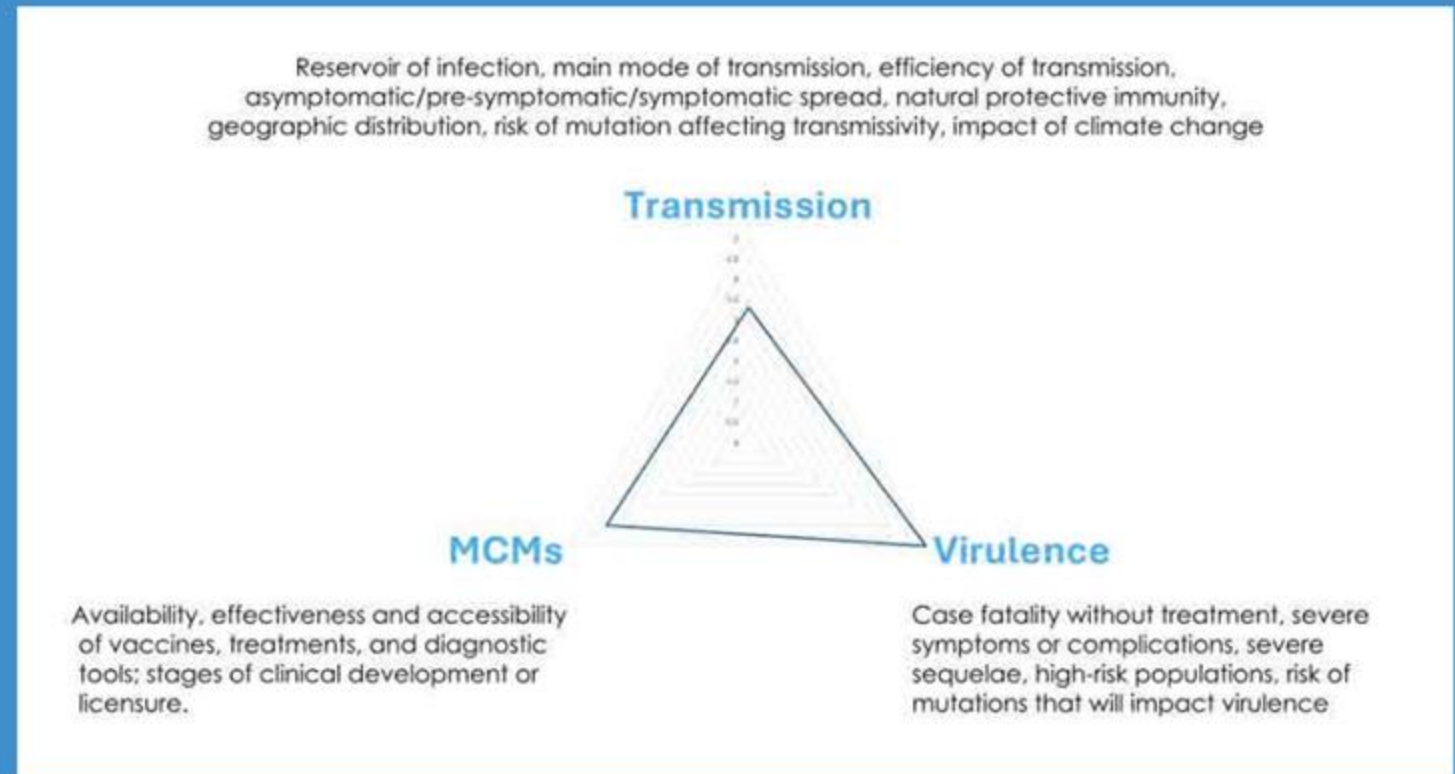


Figure 2. Evidence elements considered to assess a pathogen's potential to cause a PHEIC or pandemic

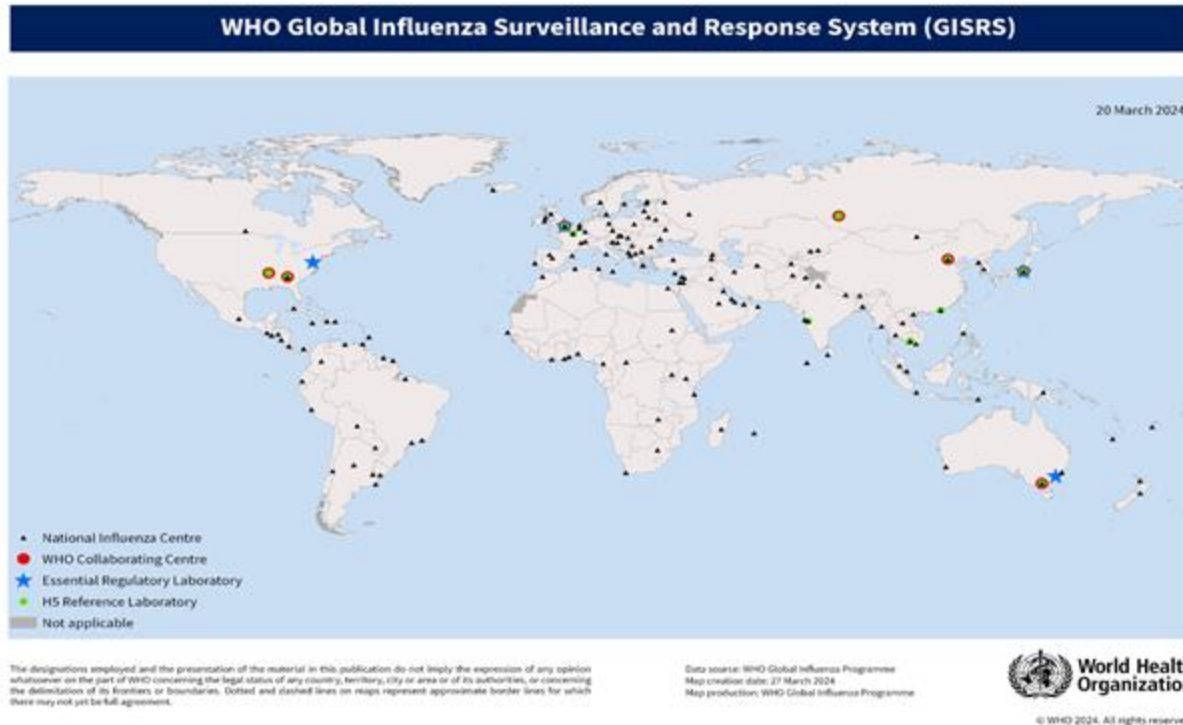


Pathogens prioritization: a scientific framework for epidemic and pandemic research preparedness



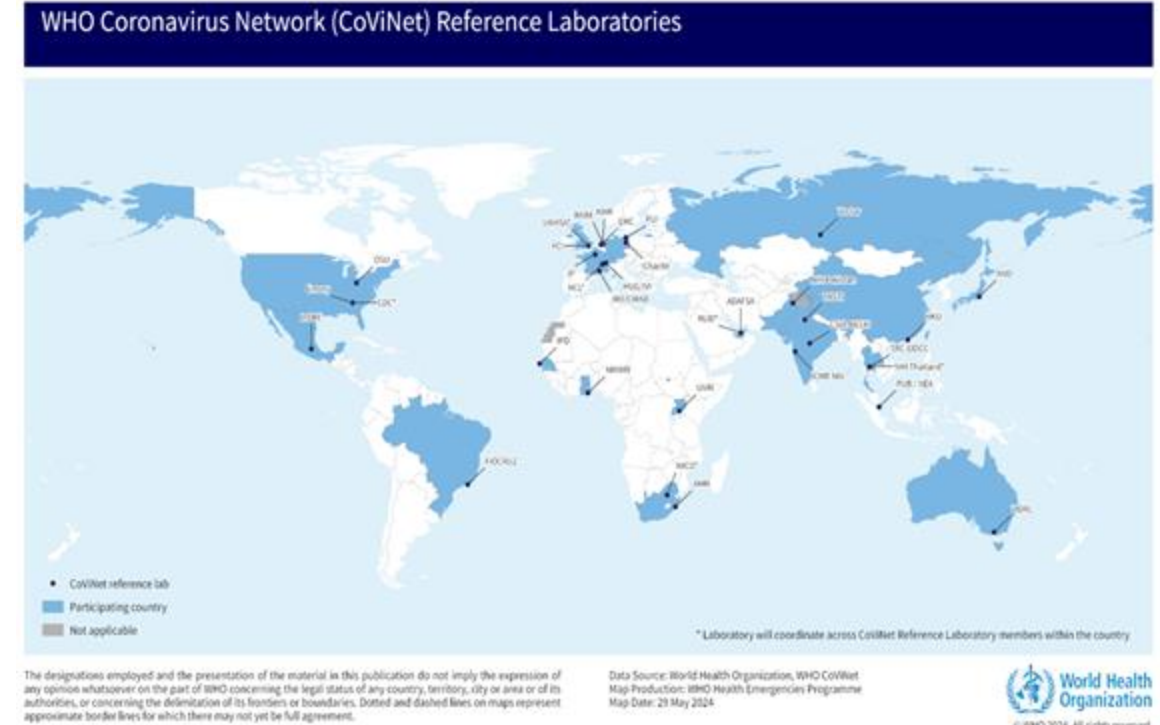
Respiratory & Novel Pathogen Genomics

Global Respiratory Virus Networks



Global Influenza Surveillance and Response System (GISRS)

<https://www.who.int/initiatives/global-influenza-surveillance-and-response-system>



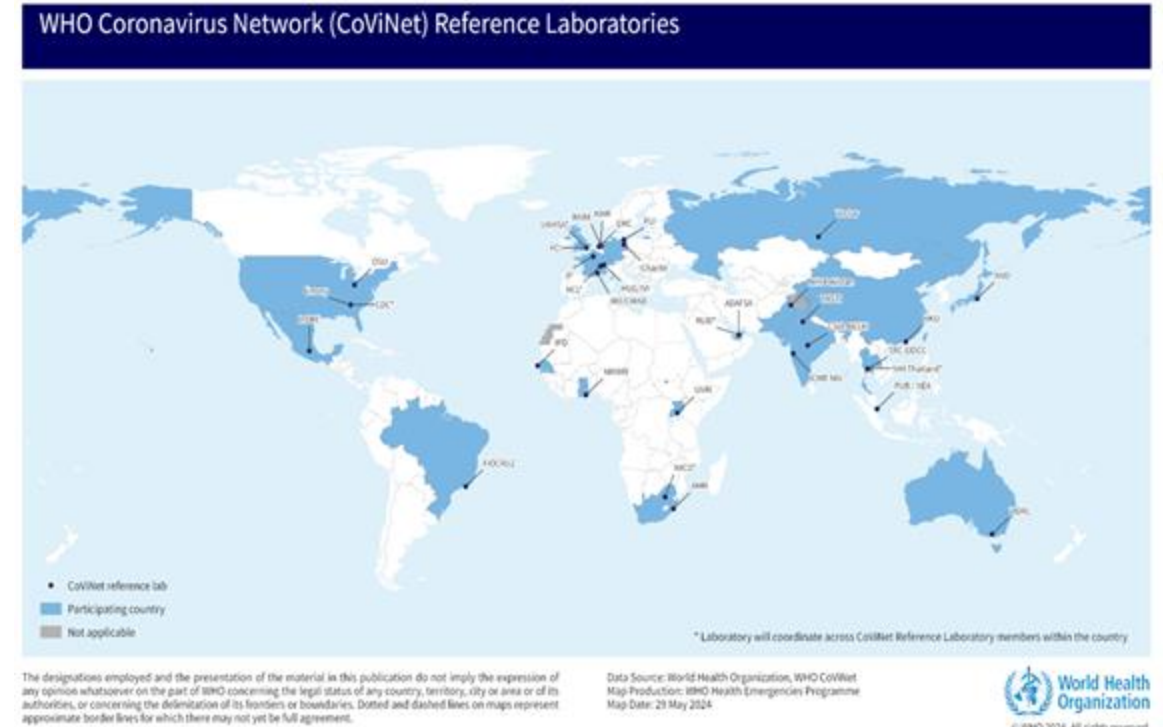
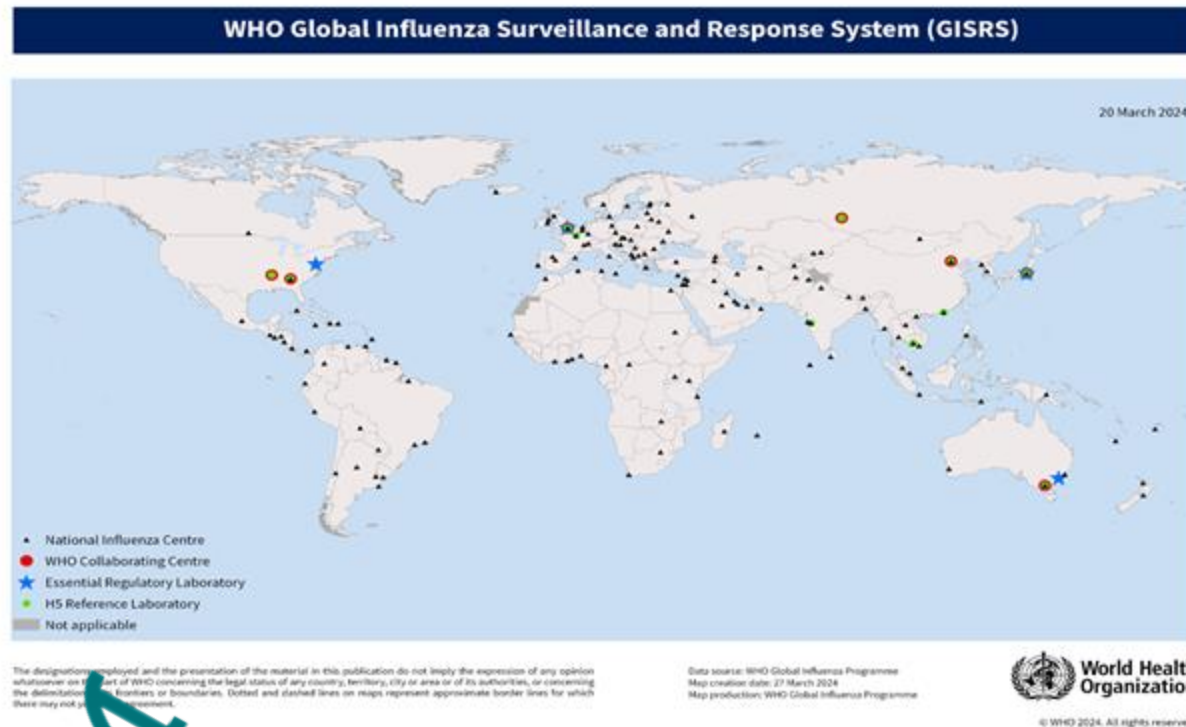
WHO Coronavirus Network (CoViNet)

<https://www.who.int/groups/who-coronavirus-network>



Respiratory & Novel Pathogen Genomics

Global Respiratory Virus Networks



Discuss at your table: Is your country part of one of these global respiratory virus surveillance networks?

Implementation Considerations



Sampling Strategies



Utility and Public Health Action



Multi-Pathogen and Pathogen Flexible Approaches



Existing Surveillance Networks and Capacity



Resources and Sustainability



Preparedness



Implementation Considerations



Respiratory
pathogen
genomics
question
dependent

Sampling Strategies



Multiple existing and in-
development
interventions benefiting
from genomic
surveillance support

Utility and Public Health Action



Similar symptoms,
sentinel populations
and tools for multi-
pathogen and use
approaches; supports
multi-pathogen
sampling strategies

Multi-Pathogen and Pathogen Flexible Approaches



Pre-existing global,
regional, and national
SARS-CoV-2
surveillance networks,
standards, and capacity

Existing Surveillance Networks and Capacity



Seasonal viruses and
countermeasures
may support more
sustainable pathogen
genomics use

Resources and Sustainability

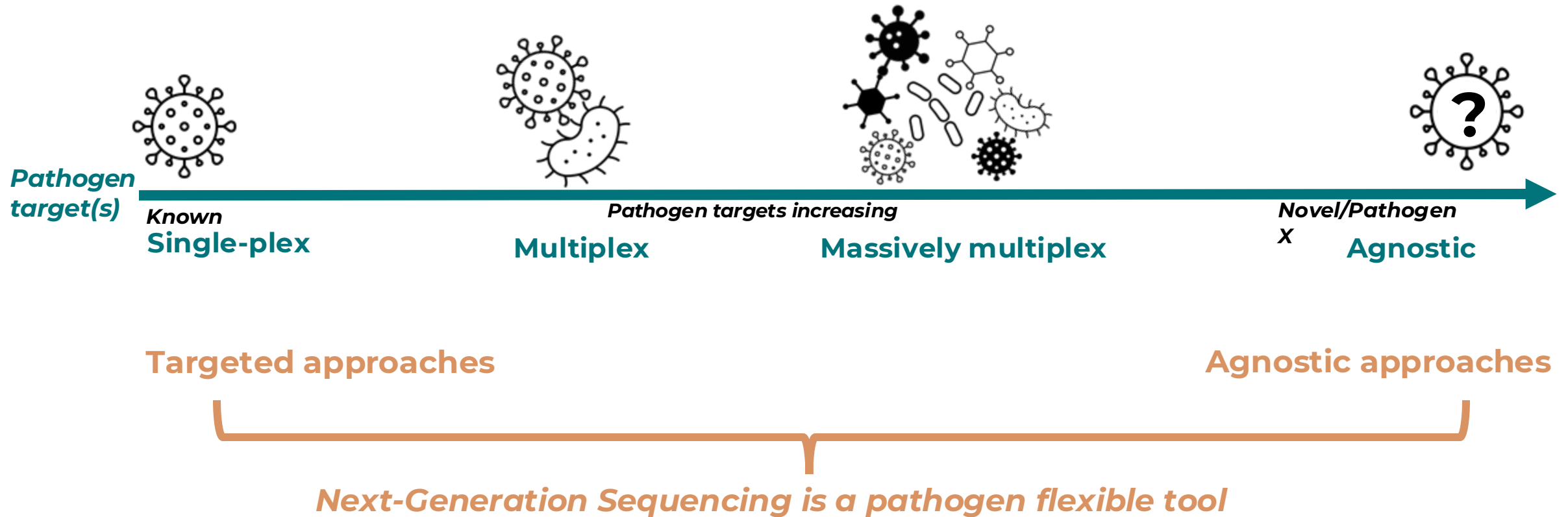


Pathogens of
pandemic
potential are
likely respiratory-
transmission
based, critical
prioritized
pathogens

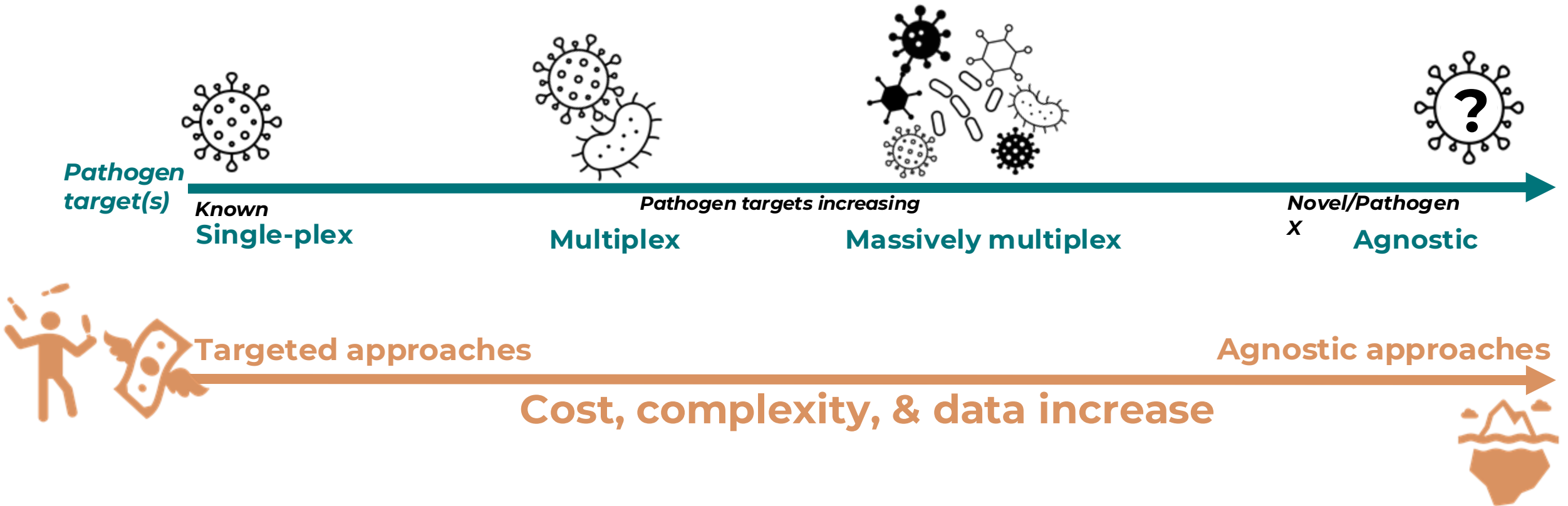
Preparedness



Respiratory & Novel Pathogen Genomics

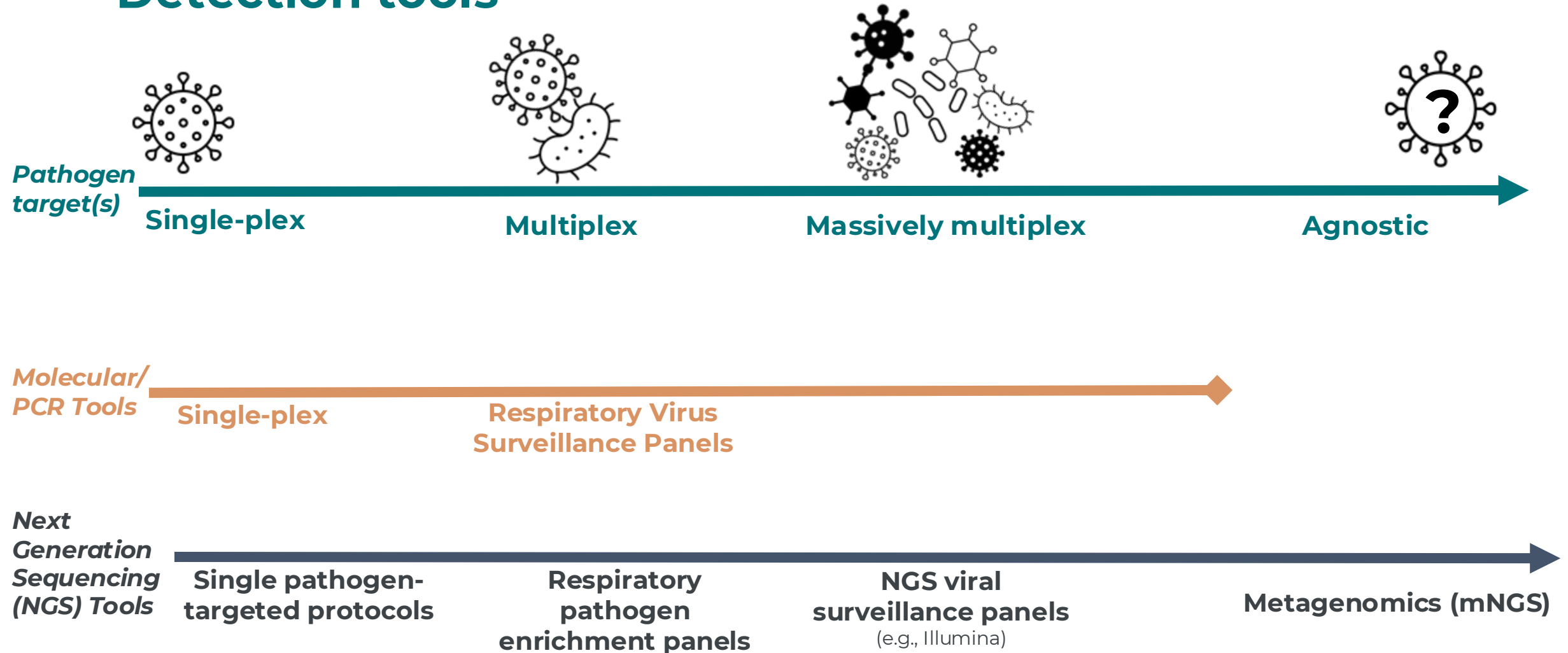


Respiratory & Novel Pathogen Genomics



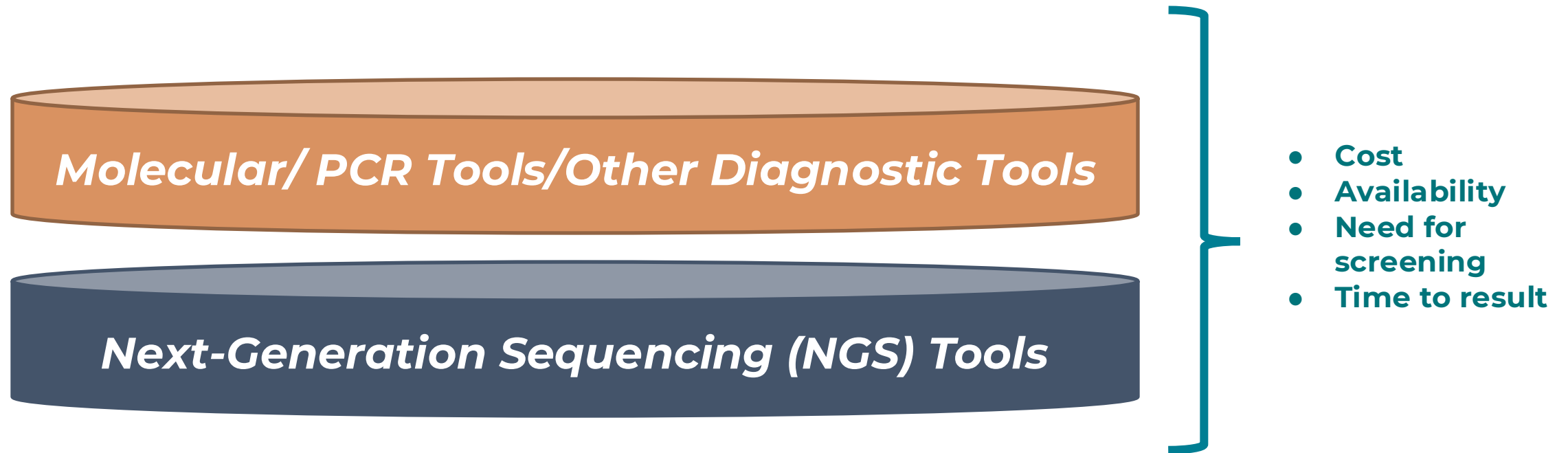
Respiratory & Novel Pathogen Genomics

Detection tools



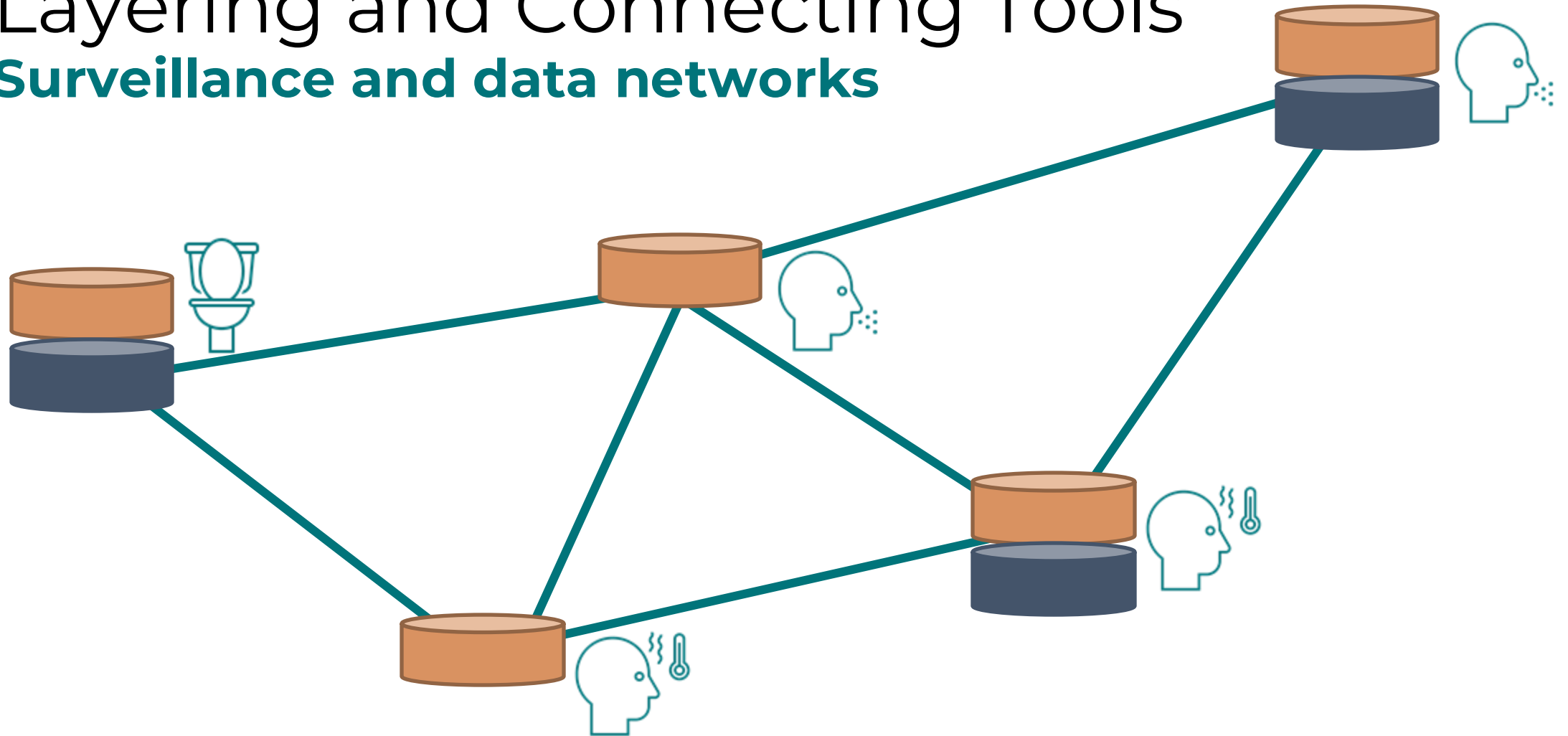
Important to Layer Tools for Public Health

Detection tools



Layering and Connecting Tools

Surveillance and data networks



Respiratory & Novel Pathogen Genomics

Pathogen Genomics Utility & Use Cases



Variant tracking and early warning



Intervention design and deployment



Clinical and characterization
(e.g., severity, unique symptoms)



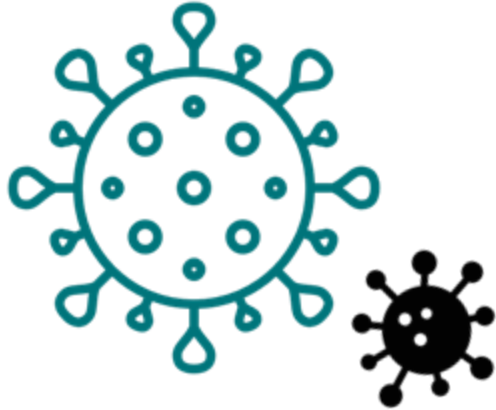
Transmission and outbreak response
(e.g., healthcare setting, outbreak investigation)



One Health interface surveillance



Metagenomics (mNGS) for respiratory virus action



Optimizing respiratory diagnostics and detection



SARI/ILI cases are negative on respiratory PCR panel



Using mNGS for optimizing panels and diagnostic design



Integration for early warning and pandemic prevention



Integrate into ILI/SARI in key populations/settings for early warning



Respiratory & Novel Pathogen Genomics

Utility use cases

Intervention development & evaluation

Clinical characteristics
and public health action



scientific reports

OPEN **Phylogenomic analysis uncovers a 9-year variation of Uganda influenza type-A strains from the WHO-recommended vaccines and other Africa strains**

Grace Nabakooza^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000}

Genetic characterisation of circulating influenza viruses directs annual vaccine strain selection and mitigation of infection spread. We used next-generation sequencing to locally generate whole genomes from 116 A(H3N2)pdm09 and 118 A(H3N2) positive patient swabs collected across Uganda between 2010 and 2018. We recovered sequences from 92% (215/234) of the swabs, 90% (193/215) of which were whole genomes. The newly-generated sequences were genetically and phylogenetically compared to the WHO-recommended vaccines and other Africa strains sampled since 1999. Uganda strain haemagglutinin (n = 206), neuraminidase (n = 207), and matrix protein (M2, n = 213) sequences had 95.23–99.65%, 95.31–99.79%, and 95.46–100% amino acid similarity to the 2010–2020 season vaccines, respectively, with several mutated haemagglutinin antigenic, receptor binding, and N-linked glycosylation sites. Uganda influenza type-A virus strains sequenced before 2016 clustered uniquely while later strains mixed with other Africa and global strains. We are the first to report novel A(H3N2)pdm09 subclades 6B.3A.3, 6B.3A.5a.1b, and 6B.3A.6 (n = 1288) that circulated in Eastern, Western, and Southern Africa in 2017–2018. Africa forms part of the global influenza ecology with high viral genetic diversity, progressive antigenic drift, and local transmissions. For a continent with inadequate health resources and where social distancing is unsustainable, vaccination is the best option. Hence, African stakeholders should prioritise routine genome sequencing and analysis to direct vaccine selection and virus control.

Novel influenza type-A viruses (IAV) cause human respiratory infections that lead to social lockdowns, economic losses, and millions of deaths¹. Genomic sequencing and characterisation of circulating IAVs are important to differentiate them from other viruses causing similar clinical symptoms for effective viral control and

<https://www.nature.com/articles/s41598-023-30667-z>

scientific reports

OPEN **A pan-influenza monoclonal antibody neutralizes H5 strains and prophylactically protects through intranasal administration**

Anna L. Beukenshorst^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,668,669,670,671,672,673,674,675,676,677,678,679,680,681,682,683,684,685,686,687,688,689,690,691,692,693,694,695,696,697,698,699,700,701,702,703,704,705,706,707,708,709,710,711,712,713,714,715,716,717,718,719,720,721,722,723,724,725,726,727,728,729,730,731,732,733,734,735,736,737,738,739,740,741,742,743,744,745,746,747,748,749,750,751,752,753,754,755,756,757,758,759,760,761,762,763,764,765,766,767,768,769,770,771,772,773,774,775,776,777,778,779,780,781,782,783,784,785,786,787,788,789,790,791,792,793,794,795,796,797,798,799,800,801,802,803,804,805,806,807,808,809,810,811,812,813,814,815,816,817,818,819,820,821,822,823,824,825,826,827,828,829,830,831,832,833,834,835,836,837,838,839,840,841,842,843,844,845,846,847,848,849,850,851,852,853,854,855,856,857,858,859,860,861,862,863,864,865,866,867,868,869,870,871,872,873,874,875,876,877,878,879,880,881,882,883,884,885,886,887,888,889,890,891,892,893,894,895,896,897,898,899,900,901,902,903,904,905,906,907,908,909,910,911,912,913,914,915,916,917,918,919,920,921,922,923,924,925,926,927,928,929,930,931,932,933,934,935,936,937,938,939,940,941,942,943,944,945,946,947,948,949,950,951,952,953,954,955,956,957,958,959,960,961,962,963,964,965,966,967,968,969,970,971,972,973,974,975,976,977,978,979,980,981,982,983,984,985,986,987,988,989,990,991,992,993,994,995,996,997,998,999,1000}

Avian A(H5N1) influenza virus poses an elevated zoonotic threat to humans, and no pharmacological products are currently registered for fast-acting pre-exposure protection in case of spillover leading to a pandemic. Here, we show that an epitope on the stem domain of H5 haemagglutinin is highly conserved and that the human monoclonal antibody CR1114, targeting that epitope, potently neutralizes all pseudotyped H5 viruses tested, even in the rare case of substitutions in its epitope. Further, intranasal administration of CR1114 fully protects mice against A(H5N1) infection at low dosages, irrespective of pre-existing immunity conferred by the quadrivalent seasonal influenza vaccine. These data provide a proof-of-concept for broad, pre-exposure protection against a potential future pandemic using the intranasal administration route. Studies in humans should assess if autonomous administration of a broadly-neutralizing monoclonal antibody is safe and effective and can thus contribute to pandemic preparedness.

Highly pathogenic avian influenza virus poses an elevated zoonotic threat¹ to humans, especially A(H5N1), given its recent unprecedented spread among wild birds, poultry, and mammals in 67 countries on five continents^{2,3}. Since 2020, A(H5N1) has become a year-round rather than a seasonal infection, resulting in a dramatic increase in poultry losses due to death, measurable declines in wildlife bird populations in many regions of the world, and culling (c. 190 M in 2021–2022 alone, compared to c. 195 M in 2010–2019)⁴. The World Health Organisation has reported 878 cases of human infection with A(H5N1) since 2005, of which 456 were fatal (case fatality rate of 52%)⁵. However, to date the basic reproductive number R_0 in these outbreaks has been below unity in value and hence they have not triggered epidemics in humans. The threat to humans has been growing, however: spillover into mammals has led to mammalian adaptation and resulted in mutations previously shown to enable airborne transmission between ferrets in gain-of-function experiments (e.g. PB2 627K)^{6,7}. No fast-acting prophylactics are available to prevent infection with a future A(H5N1) strain that could be transmitted between humans. Some existing antiviral drugs for seasonal influenza cross-protect against A(H5N1), but these are mostly suitable as post-exposure treatments and concomitant risk of resistance from viral escape mutants^{8,9}. Post-exposure transfer of convalescent serum is effective, but supply constraints and cost make this an unsuitable treatment on a larger scale¹⁰. Some governments have a stockpile of H5 vaccines (US—vaccine doses for 20 million people^{11,12}) or advance purchase agreements (UK—100 million vaccine doses¹³). However, these vaccines may not work if another H5 subtype (e.g. H5N2, H5N8) spills over to humans. Furthermore, the recent SARS-CoV-2 pandemic showed that vaccination, although important to avert severe disease, does not necessarily prevent infection and associated spread¹⁴, especially when vaccine roll-out is still ongoing and before the vaccine has elicited antibody responses in a sufficient proportion of the population. Therapeutic monoclonal antibodies have saved lives of infected patients during the SARS-CoV-2 pandemic, but no prophylactic

<https://www.nature.com/articles/s41598-024-53049-5>

nature communications

Article **Targeted metagenomics reveals association between severity and pathogen co-detection in infants with respiratory syncytial virus**

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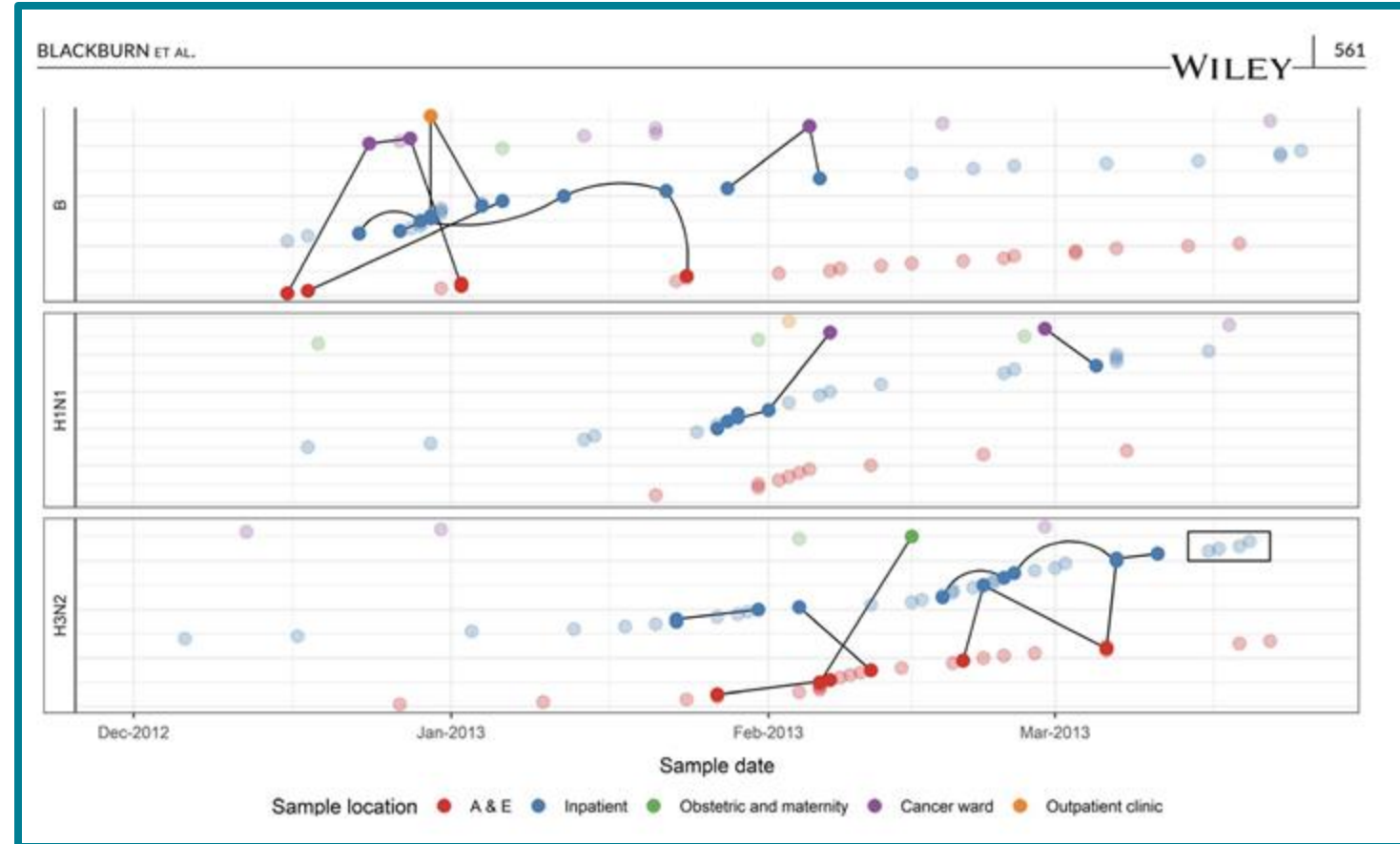
Gu-Lung Lin^{1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100,101,102,103,104,105,106,107,108,109,110,111,112,113,114,115,116,117,118,119,120,121,122,123,124,125,126,127,128,129,130,131,132,133,134,135,136,137,138,139,140,141,142,143,144,145,146,147,148,149,150,151,152,153,154,155,156,157,158,159,160,161,162,163,164,165,166,167,168,169,170,171,172,173,174,175,176,177,178,179,180,181,182,183,184,185,186,187,188,189,190,191,192,193,194,195,196,197,198,199,200,201,202,203,204,205,206,207,208,209,210,211,212,213,214,215,216,217,218,219,220,221,222,223,224,225,226,227,228,229,230,231,232,233,234,235,236,237,238,239,240,241,242,243,244,245,246,247,248,249,250,251,252,253,254,255,256,257,258,259,260,261,262,263,264,265,266,267,268,269,270,271,272,273,274,275,276,277,278,279,280,281,282,283,284,285,286,287,288,289,290,291,292,293,294,295,296,297,298,299,300,301,302,303,304,305,306,307,308,309,310,311,312,313,314,315,316,317,318,319,320,321,322,323,324,325,326,327,328,329,330,331,332,333,334,335,336,337,338,339,340,341,342,343,344,345,346,347,348,349,350,351,352,353,354,355,356,357,358,359,360,361,362,363,364,365,366,367,368,369,370,371,372,373,374,375,376,377,378,379,380,381,382,383,384,385,386,387,388,389,390,391,392,393,394,395,396,397,398,399,400,401,402,403,404,405,406,407,408,409,410,411,412,413,414,415,416,417,418,419,420,421,422,423,424,425,426,427,428,429,430,431,432,433,434,435,436,437,438,439,440,441,442,443,444,445,446,447,448,449,450,451,452,453,454,455,456,457,458,459,460,461,462,463,464,465,466,467,468,469,470,471,472,473,474,475,476,477,478,479,480,481,482,483,484,485,486,487,488,489,490,491,492,493,494,495,496,497,498,499,500,501,502,503,504,505,506,507,508,509,510,511,512,513,514,515,516,517,518,519,520,521,522,523,524,525,526,527,528,529,530,531,532,533,534,535,536,537,538,539,540,541,542,543,544,545,546,547,548,549,550,551,552,553,554,555,556,557,558,559,560,561,562,563,564,565,566,567,568,569,570,571,572,573,574,575,576,577,578,579,580,581,582,583,584,585,586,587,588,589,590,591,592,593,594,595,596,597,598,599,600,601,602,603,604,605,606,607,608,609,610,611,612,613,614,615,616,617,618,619,620,621,622,623,624,625,626,627,628,629,630,631,632,633,634,635,636,637,638,639,640,641,642,643,644,645,646,647,648,649,650,651,652,653,654,655,656,657,658,659,660,661,662,663,664,665,666,667,66}

Respiratory & Novel Pathogen Genomics

Utility use cases



Transmission and outbreak response



<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6800305/pdf/IRV-13-556.pdf>



Opportunities & Obstacles

Opportunities	Obstacles
<ul style="list-style-type: none">• Pre-existing infrastructure and surveillance networks (influenza and SARS-CoV-2)• High utility of pathogen genomics to answer key public health and clinical questions• Strong actionability for intervention development; investment case• Existing detection tools• Seasonality• Diversity of pathogens and characteristics• Similar symptoms and target populations; multi-pathogen sampling strategies• Importance for maintain pathogen genomics sustainability for pandemic prevention and preparedness• National, regional, and global data, protocols, and standards sharing• One Health applications: clinical, environmental, and zoonotic opportunities• Serve as a pandemic prevention and preparedness warm-base	<ul style="list-style-type: none">• Diversity of pathogens• Integrating pathogens into a multi-pathogen approach• Varying complexity of workflows• Workforce and resource cost and sustainability• Diverse host ranges and critical interfaces• Screening approaches and sampling strategies• Balancing prioritization of endemic pathogens vs. emerging threats and future pandemics• Integration into pre-existing surveillance systems and structures• Specimen transport and genetic material stability• Maintaining political will and prioritization• Supply chain, procurement, and platforms• Complex and big data and bioinformatics• Building horizontal surveillance and lab workflows• Training a horizontal workforce





Case Study 2

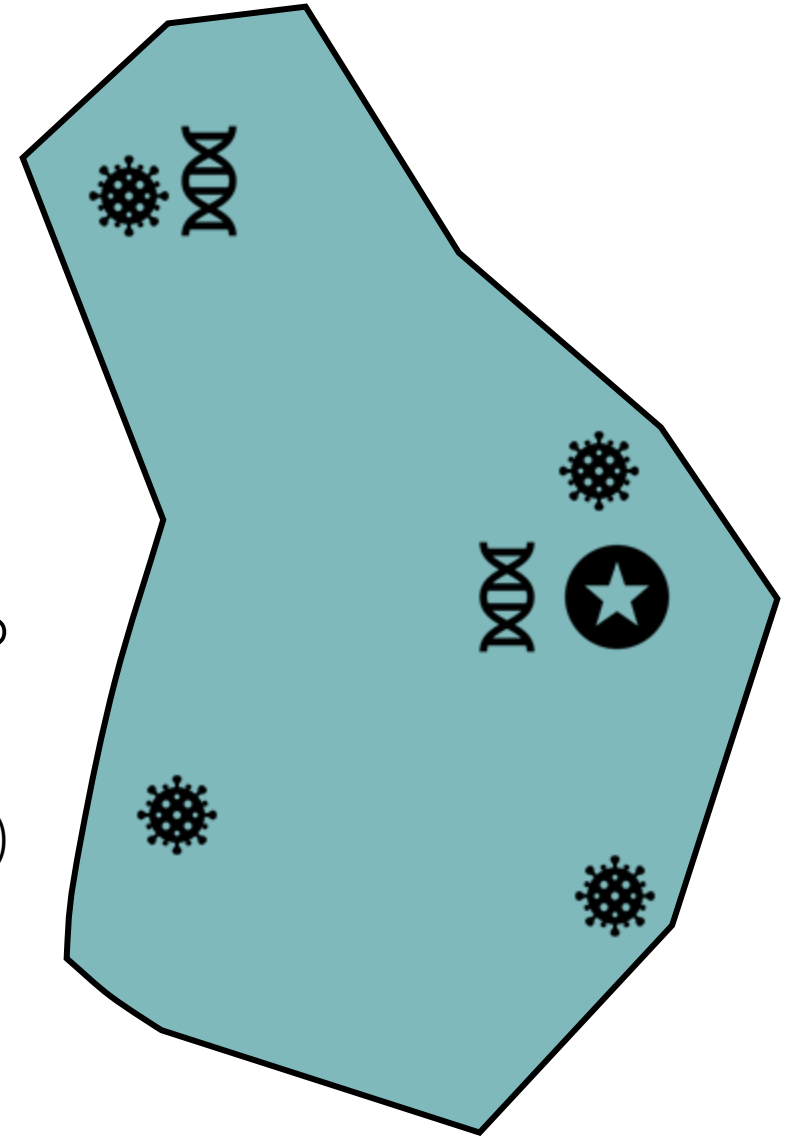
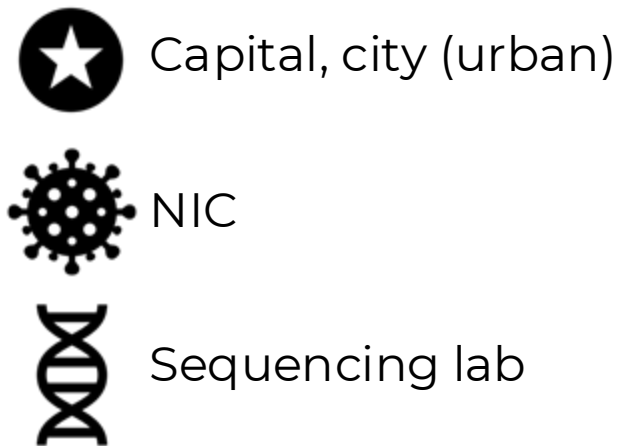
Respiratory & Novel Pathogen Case Study

Scenarios & Discussion



Setting the Stage

- Has a National Influenza Center (NIC) and SARI/ILI sentinel surveillance sites
- NICs incorporated SARS-CoV-2 diagnostic testing
- Developing National Pathogen Genomics Strategy
- 12 health districts
- Sequencing capability exists at central government lab and one academic urban hospital



Scenario - Part 1



A local school has a respiratory outbreak. The local NIC tested for influenza and SARS-CoV-2 via RT-PCR, and these tests are negative.

What are some potential next steps?



Scenario - Part 1



A local school has a respiratory outbreak. The local NIC tested for influenza and SARS-CoV-2 via RT-PCR, and these tests are negative.



Cases are increasing, and a few local infants have been hospitalized. Further diagnostic respiratory panel investigation indicates this outbreak may be caused by respiratory syncytial virus (RSV).



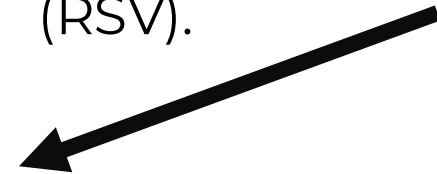
Scenario - Part 1



A local school has a respiratory outbreak. The local NIC tested for influenza and SARS-CoV-2 via RT-PCR and these tests are negative.



Cases are increasing, and a few local infants have been hospitalized. Further diagnostic respiratory panel investigation indicates this outbreak may be caused by respiratory syncytial virus (RSV).



A few NICs also see upticks in sentinel respiratory samples that are negative for influenza and SARS-CoV-2. Some of these specimens are confirmed RSV and are from other districts, including a village outbreak.

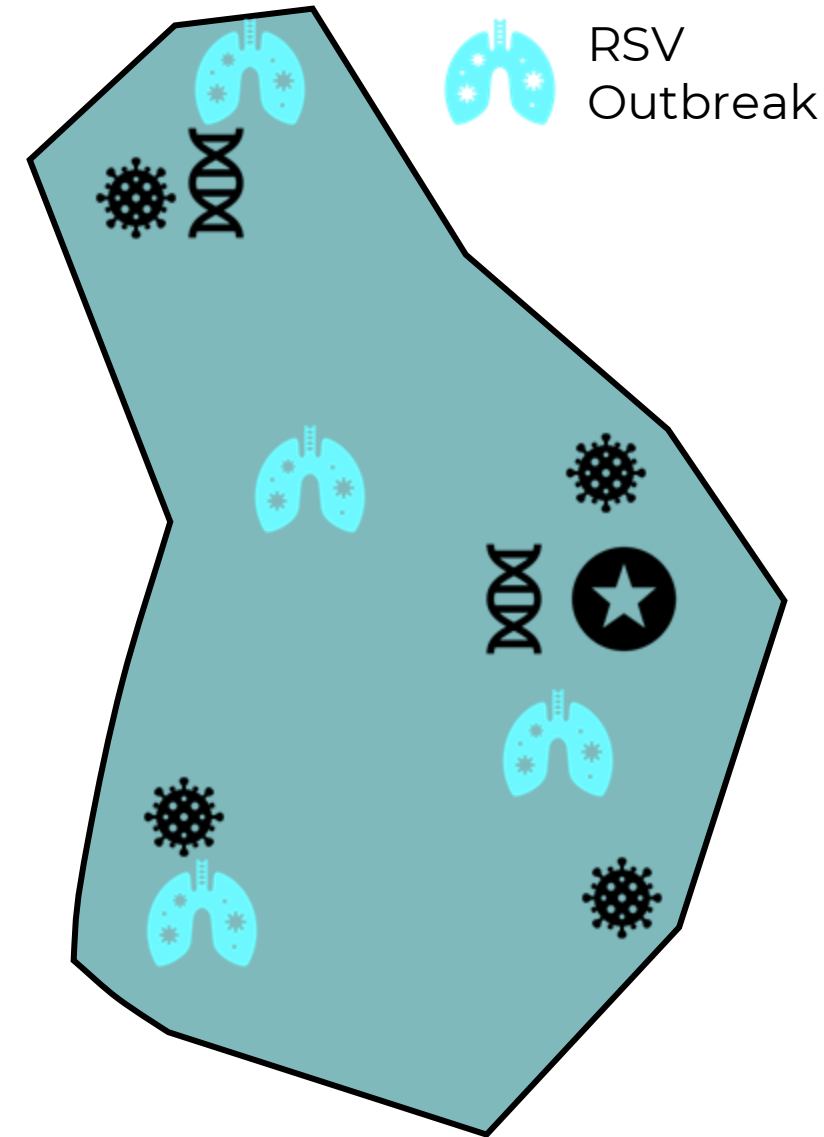
- **What questions arise?**
- **How can pathogen genomics potentially answer some of these questions?**



Scenario - Part 1



- How can pathogen genomics support outbreak response and public health action?
- How does the location of labs and sequencing capacity impact outbreak response and pathogen genomics integration?



Respiratory Syncytial Virus (RSV)

“An estimated 33 million RSV-associated lower respiratory tract infections (LRTI) occur in children under five every year, leading to 3.6 million hospital admissions. What’s more, over 95% of these infections occur in low- and middle-income countries.”



Scenario - Part 2



6 months later...

There is a new pediatric vaccine for RSV. After these widespread RSV outbreaks, the Ministry of Health is thinking about working with GAVI and WHO to procure RSV vaccines.



Scenario - Part 2



6 months later...

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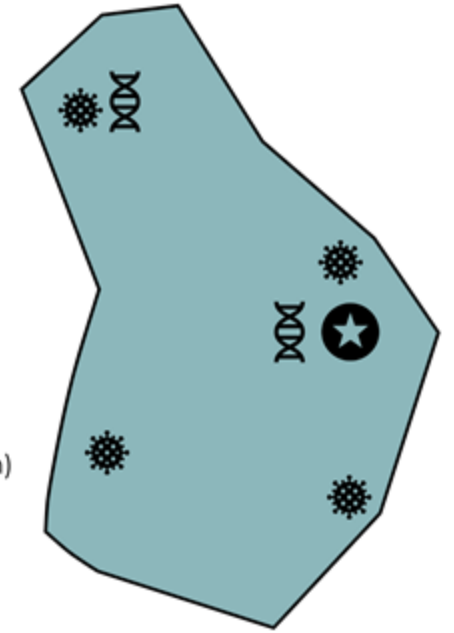
This Minister of Health has asked your team, **how can pathogen genomics support vaccination rollout and evaluation?**



Scenario - Part 2



The Minister of Health decides to include RSV into the routine pediatric vaccination program.



- Is there utility to integrate RSV genomic surveillance into National planning?
- What are the key implementation and actionability considerations?
- Would this decision vary between **high, moderate, and low genomic capacity** countries? How so?
- What types of experts would you consult? How would you try to integrate RSV?
- For countries currently integrating RSV, what has been the most difficult step?



Scenario - Part 3

A month later...



An adolescent is admitted to a local hospital with severe respiratory symptoms. They are negative for influenza and SARS-CoV-2, and this is the only respiratory test able to be run at this hospital.

- **What are some potential next steps?**
- **How could you layer different detection tools?**
- **What do you think is making the patient ill?**



Scenario - Part 3

A month later...



An adolescent is admitted to a local hospital with severe respiratory symptoms. They are negative for influenza and SARS-CoV-2, and this is the only respiratory test able to be run at this hospital.

- **What are some potential next steps?**
- **What do you think is making the patient ill?**



This patient is getting worse and tests negative on a multi-respiratory panel, which is confirmed at the central lab. All tests are coming up negative. Two healthcare workers have now fallen ill.

- **What are some next testing steps?**
- **What capabilities are needed?**



Scenario - Part 3



- 1. How can you confirm this is a novel pathogen? What are the implications if this is a novel pathogen?**



Scenario - Part 3



- 1. How can you confirm this is a novel pathogen? What are the implications if this is a novel pathogen, Disease X?**
- 2. How can pathogen genomics support novel virus response at the local, national, regional, and global levels?**



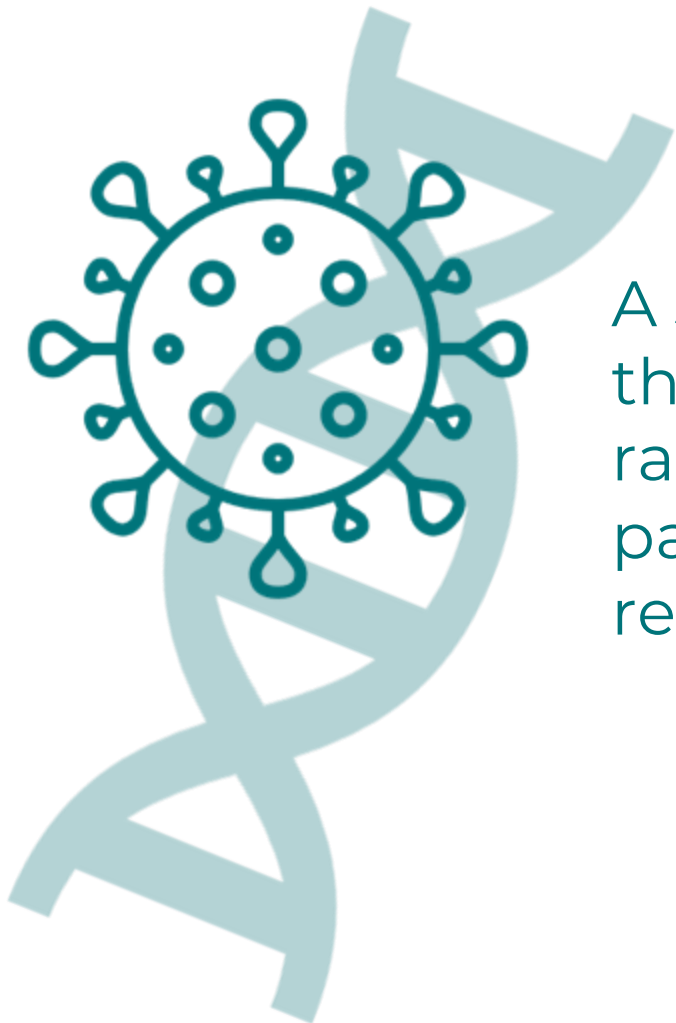
The levels of contribution of genomics per pathogen and surveillance objectives for public health decision-making

Pathogens / surveillance objectives	Public Health Surveillance						Special Studies				Clinical Mangement
	1 Early detection	2 Pathogen characterization	3 Pathogen genetic epidemiology & transmission patterns	4 Contact tracing	5 Outbreak investigation (detection or management)	6 Pathogen elimination surveillance	7 Diagnostics, Vaccines and Therapeutics: Research and Development	8 Diagnostics, Vaccines and Therapeutics: Monitoring and Evaluation	9 Non Pharmacological Countermeasures: Monitoring and Evaluation	10 Clinical Characterization and Severity Assessment	11 Clinical management (at patient level to guide individual patient treatment)
Pathogens or pathogen groups											
Pathogens with pandemic potential (from WHO Blueprint)											
Disease X	3	3	3	3	3		3	3	3	3	2
SARS-CoV-2	3	3	3	2	3		3	3	3	3	2
MERS-CoV and SARS	2	3	3		3		3	3	2	2	1
Crimean-Congo haemorrhagic fever		3	2		2		3			2	1
Ebola and Marburg diseases	2	3	1	1	3		3	3	1	2	1
Lassa fever	1	3	2	1	2		3	1		2	1
Nipah and henipaviral diseases	1	3	1	1	1		3	1	1	2	1
BRI Valley fever	1	3	2	1	1		3	1		2	1
Arbovirus Zika	2	3	2		3		3	2	2	3	1
AMR bacteria (GLASS priority list)	1	3	3	2	3		2	2	2	2	2
AMR fungus (GLASS priority list)	1	3	3	2	3		2	2	2	2	1
Chikungunya Arbovirus	2	3	2		3		3	3	2	2	1
Cholera	1		3	1		2	1			1	1
Dengue Arbovirus	1	3	3	1	3		3	3	2	2	1
Food borne pathogens	1	3	3	1	3		1	1	1	1	2
Hepatitis (C or E)	2	3	2	1	3		3	2	2	2	1
HIV	1	3	2	2	3		3	3	2	3	3
Influenza, avian & zoonotic	3	3	3	2	3		3	3	2	3	2
Influenza, seasonal	1	3	3	1	3		3	3	2	2	1
Malaria	2		1				2	3			1
Measles	1	3	3	2	3	3	1	2	2	1	1
Meningitis	2	3	3	2	2		2	2	2	2	1
Mpox	1	3	3		2	3	3	2	2	1	1
Neisseria gonorrhoeae	2	3	3	2	3		3	3	2	3	2
Polio	2	3	3	2	3	3	2	3	2	2	
Rubella	1	3	3	2	3			2	2	2	1
Tuberculosis (TBx)	2	3	2	2	2		3	2		1	3
Yellow fever Arbovirus	1		1	1	2		2	2	1	1	
Pathogen-agnostic surveillance											
Environmental surveillance	2	3	3	1	2		3	1		1	1
Water surveillance (incl. wastewater)	2	3	3		2		3	1		1	1
Air surveillance	1	3		1	2		3	1		1	1
Meta genomics	3	3	3	1	2	3	1	1	1	2	2

Genomics contribution for PH impact	
1	low contribution
2	medium contribution
3	high contribution

IPSN yesterday

Vertical, horizontal and diagonal read-outs



A sequence can be the backbone to a rapid, targeted novel pathogen, **Disease X** response



Viral characterization



Vaccines



Diagnostics



Therapeutics



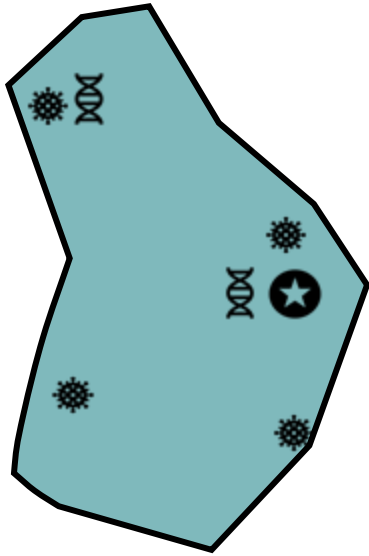
Global situational awareness



Evolution and mutation tracking



Final Exercise



National



Regional



Global

**Thinking the transition to horizontal vs. vertical systems,
and ready/flexible genomic surveillance systems...**



Global genomic respiratory virus surveillance networks

WHO Global Influenza Surveillance and Response System (GISRS)



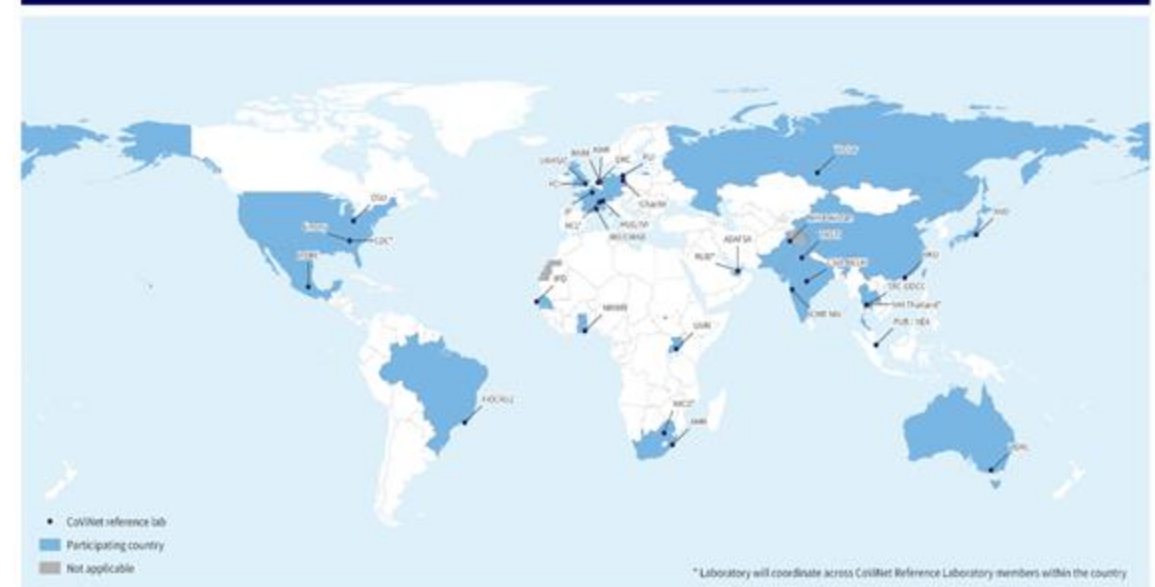
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Data source: WHO Global Influenza Programme
Map creation date: 21 March 2024
Map production: WHO Global Influenza Programme



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WHO Coronavirus Network (CoViNet) Reference Laboratories



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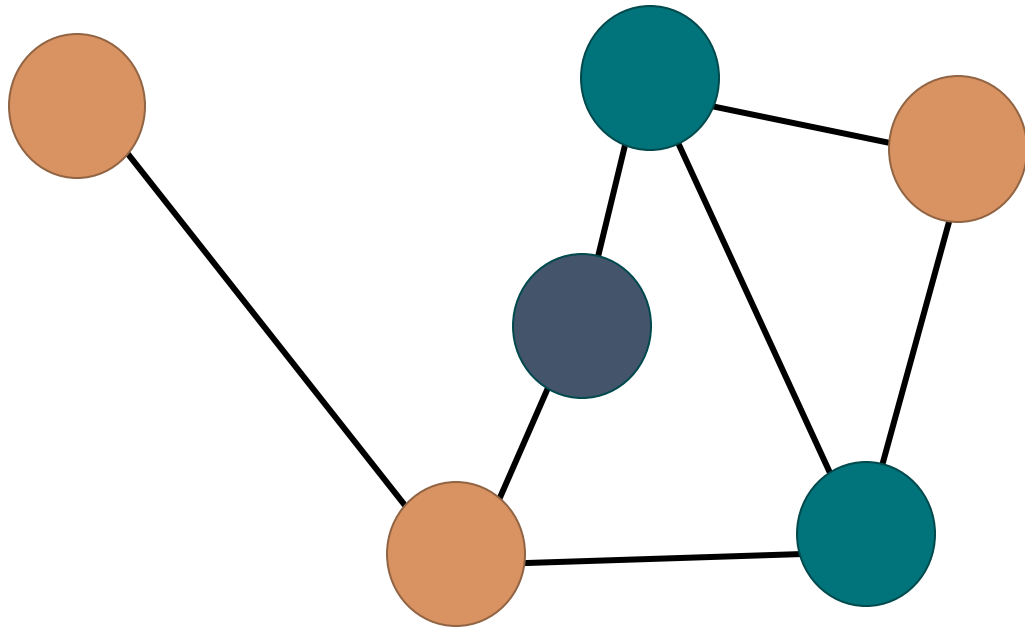
Data Source: World Health Organization, WHO CoViNet
Map Production: WHO Health Emergencies Programme
Map Date: 29 May 2024



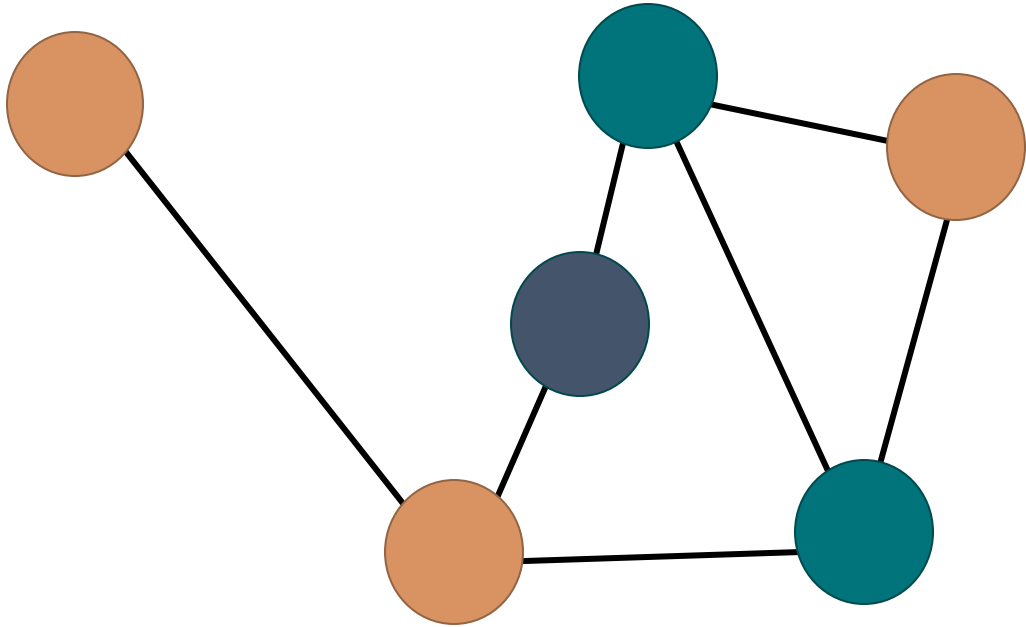
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Using your large notepad: Design a **regional/national early warning genomic surveillance network for novel pathogen**, Pathogen X, detection using pre-existing respiratory virus surveillance systems or network (sentinel systems, SARI/ILI, WHO network, etc.) in your countries.

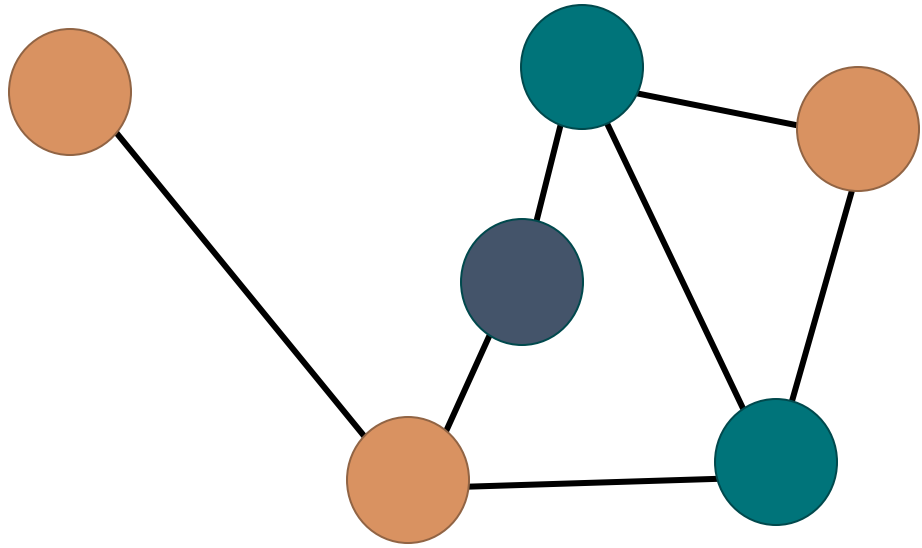


Using your large notepad: Design a **regional/national early warning genomic surveillance network for novel pathogen**, Pathogen X, detection using pre-existing respiratory virus surveillance systems or network (sentinel systems, SARI/ILI, WHO network, etc.) in your countries.



- What kinds of **sites** would you use?
- How would you **layer detection tools**? Molecular and what types of sequencing?
- What kinds of **specimens and sampling**?





Final Discussion

- How do we maintain global genomic surveillance **preparedness for future pandemics** and novel pathogens?
- How can **SARS-CoV-2, influenza, and RSV sequencing** serve as a backbone for transitioning to novel pathogen detection?
- Can and should novel pathogen surveillance tools be integrated into existing respiratory virus surveillance systems? How does **capacity-level** play a role?





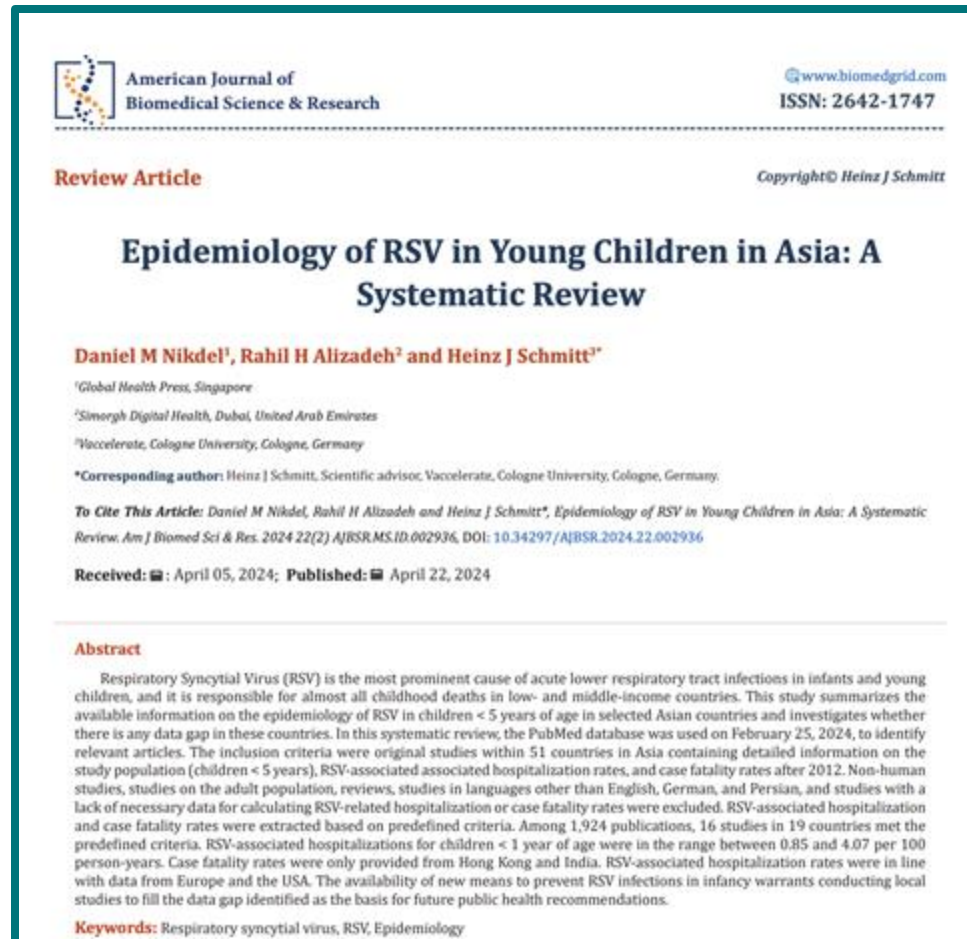
Case Study 2

Respiratory & Novel Pathogen Case Study

Recap & Prioritization Activity



Pathogen prioritisation activity



<https://biomedgrid.com/pdf/AJBSR.MS.ID.002936.pdf>



Pathogen prioritisation tool





Thank you!

The findings and conclusions in this presentation are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

WORKSHOP PARTNERS



Asia Pathogen
Genomics Initiative



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