ZOONOTIC DISEASES AND ONE HEALTH

SOUTH & SOUTHEAST ASIA

PATHOGEN GENOMICS PRIORITIZATION & IMPLEMENTATION WORKSHOP

September 9-13, 2024
Bangkok, Thailand

WORKSHOP PARTNERS

CDC
U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

DukeNUS Medical School
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)

Opening thoughts…

Lower historic investment in animal disease systems means pathogens are often less well characterized

- Foundational surveillance systems may not be robust

Value of genomics use case can be less clear

- When is it worth the investment to develop effective, genomics-informed interventions?
- What needs to be built/improved *before* genomics is added?

Balancing food security, agricultural economic impact, and human health priorities is a big challenge

One Health is hard!

One Health and Zoonotic Diseases

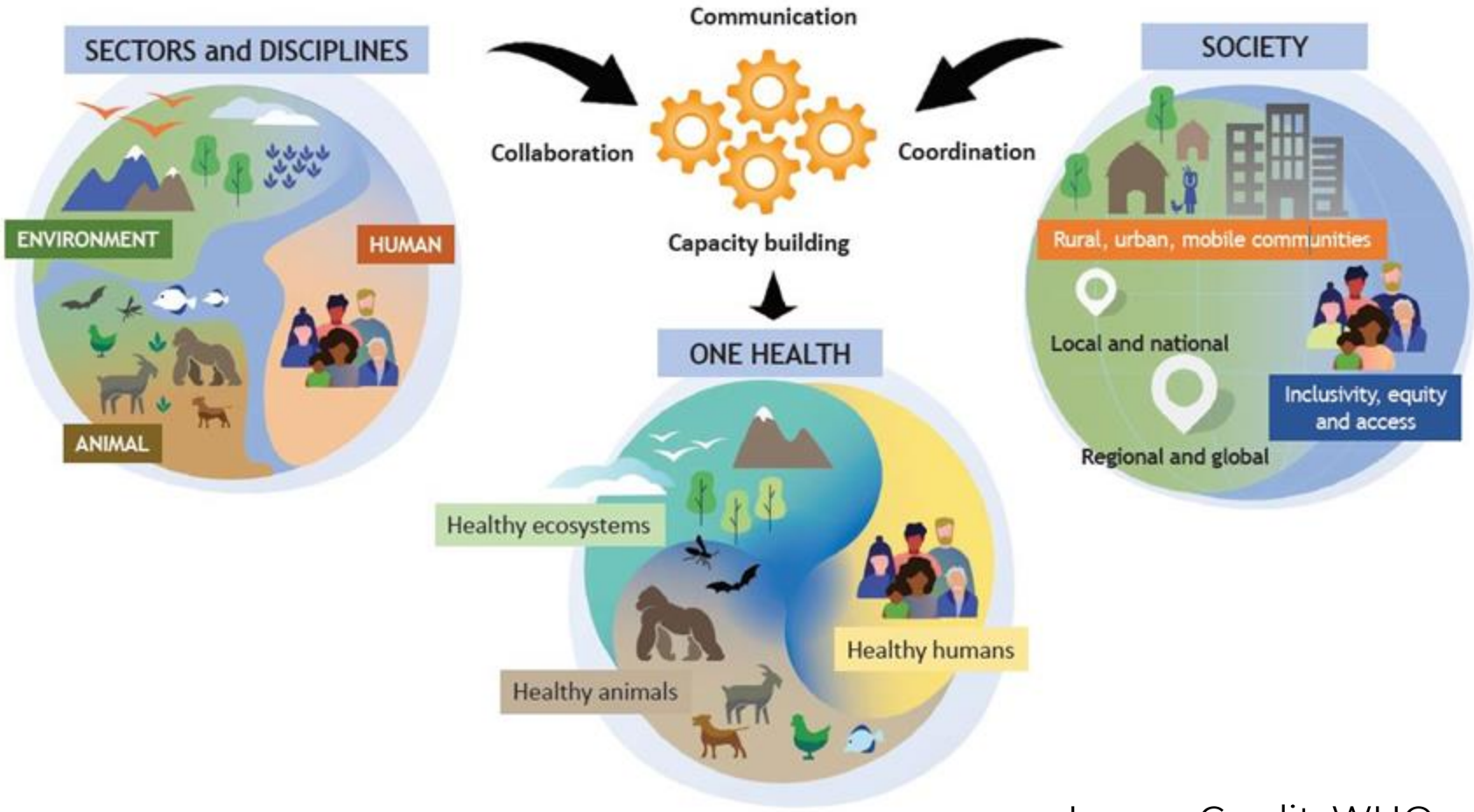


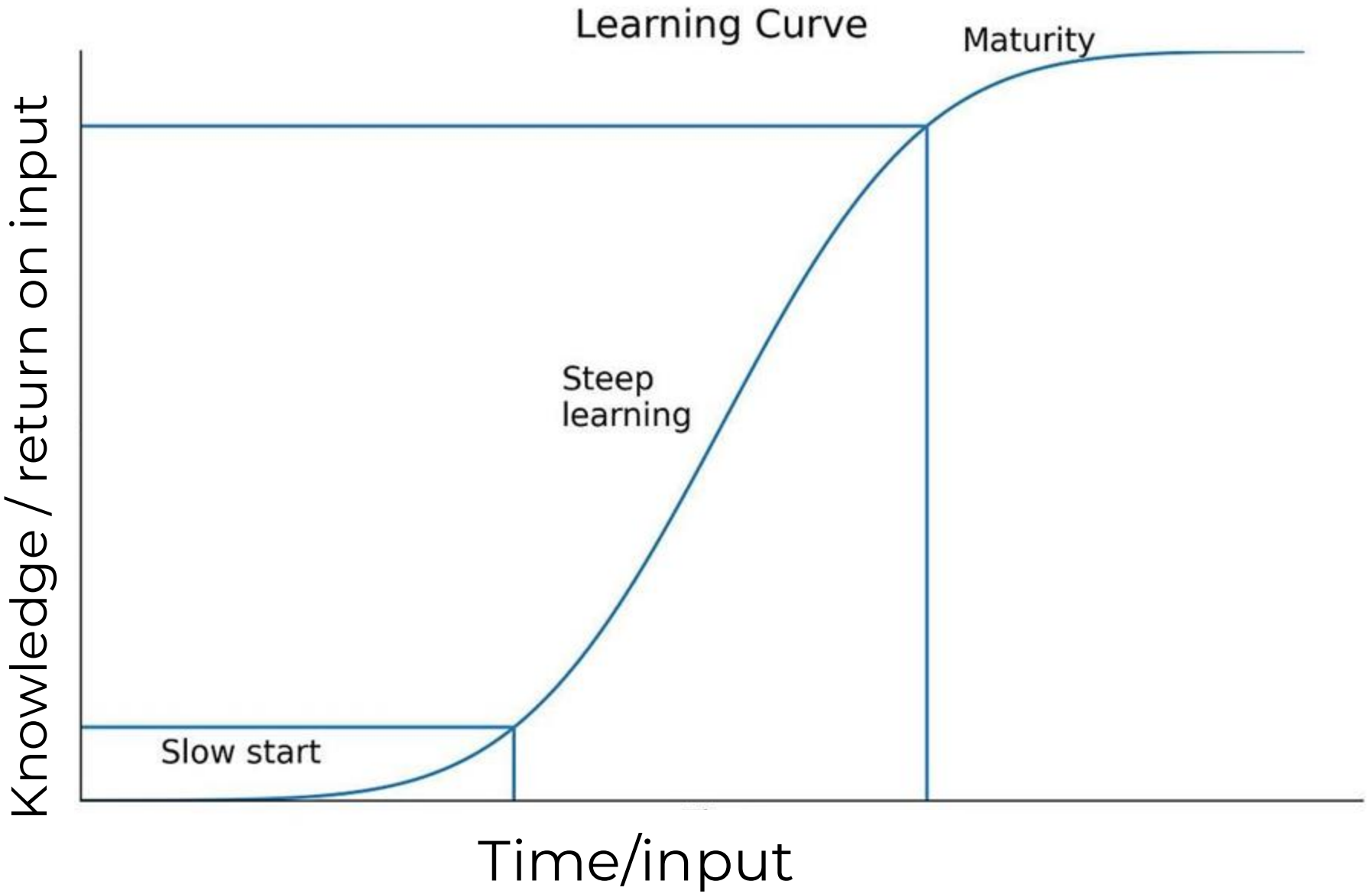
Image Credit: WHO

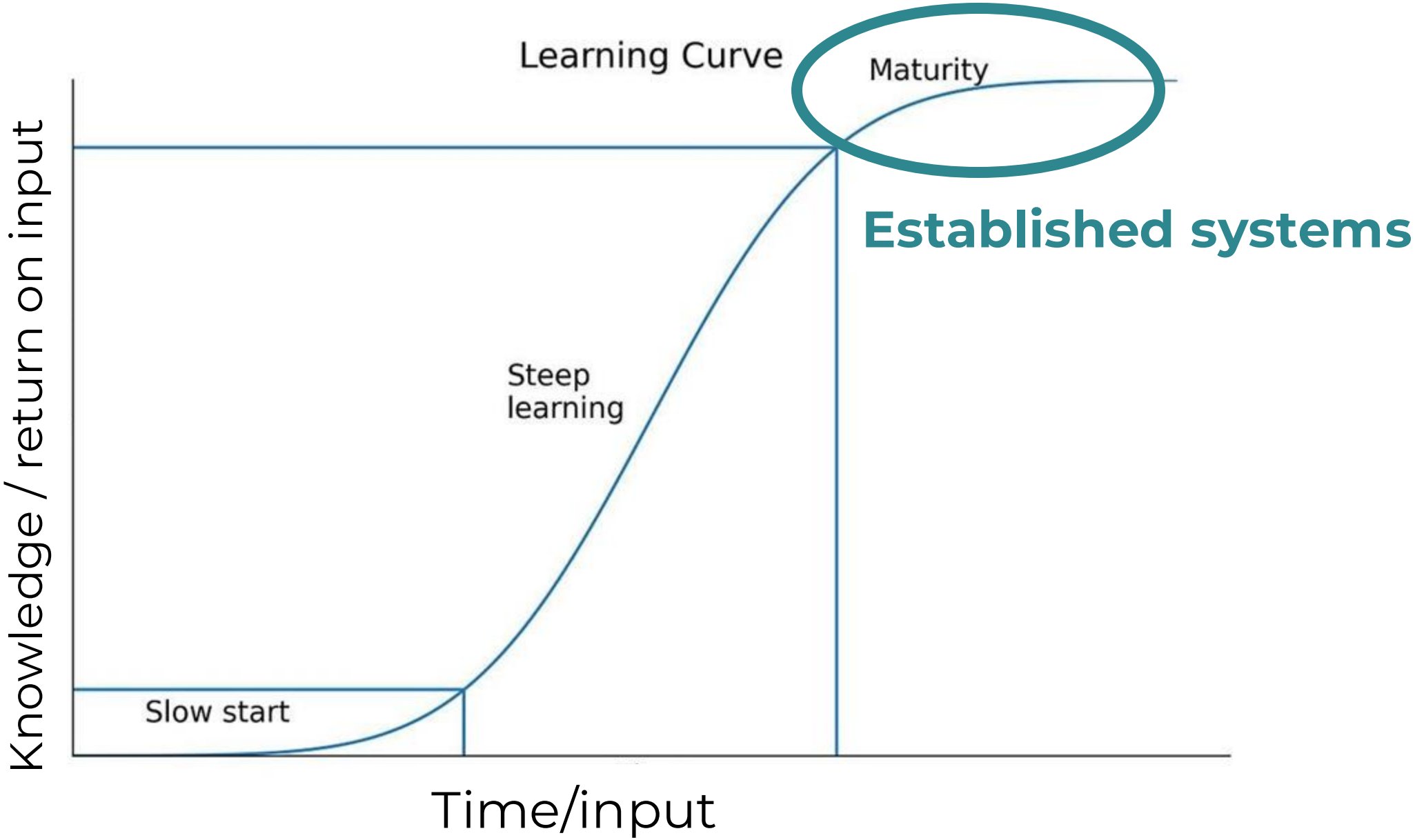
One Health and Zoonotic Diseases

Challenges
Many unknowns
Less funding for animal health
Lack of collaboration
‘Less relevant’
Zoonotic and novel pathogens

One Health and Zoonotic Diseases

Challenges	Opportunities
Many unknowns	Steep learning curve*
Less funding for animal health	Collaboration/shared resources
Lack of collaboration	Coordination/shared knowledge
‘Less relevant’	Animal health = Human health
Zoonotic and novel pathogens	Animals as sentinels


Learning Curve
Maturity
Steep
learning
Slow start
Knowledge / return on input
Time/input


Learning Curve
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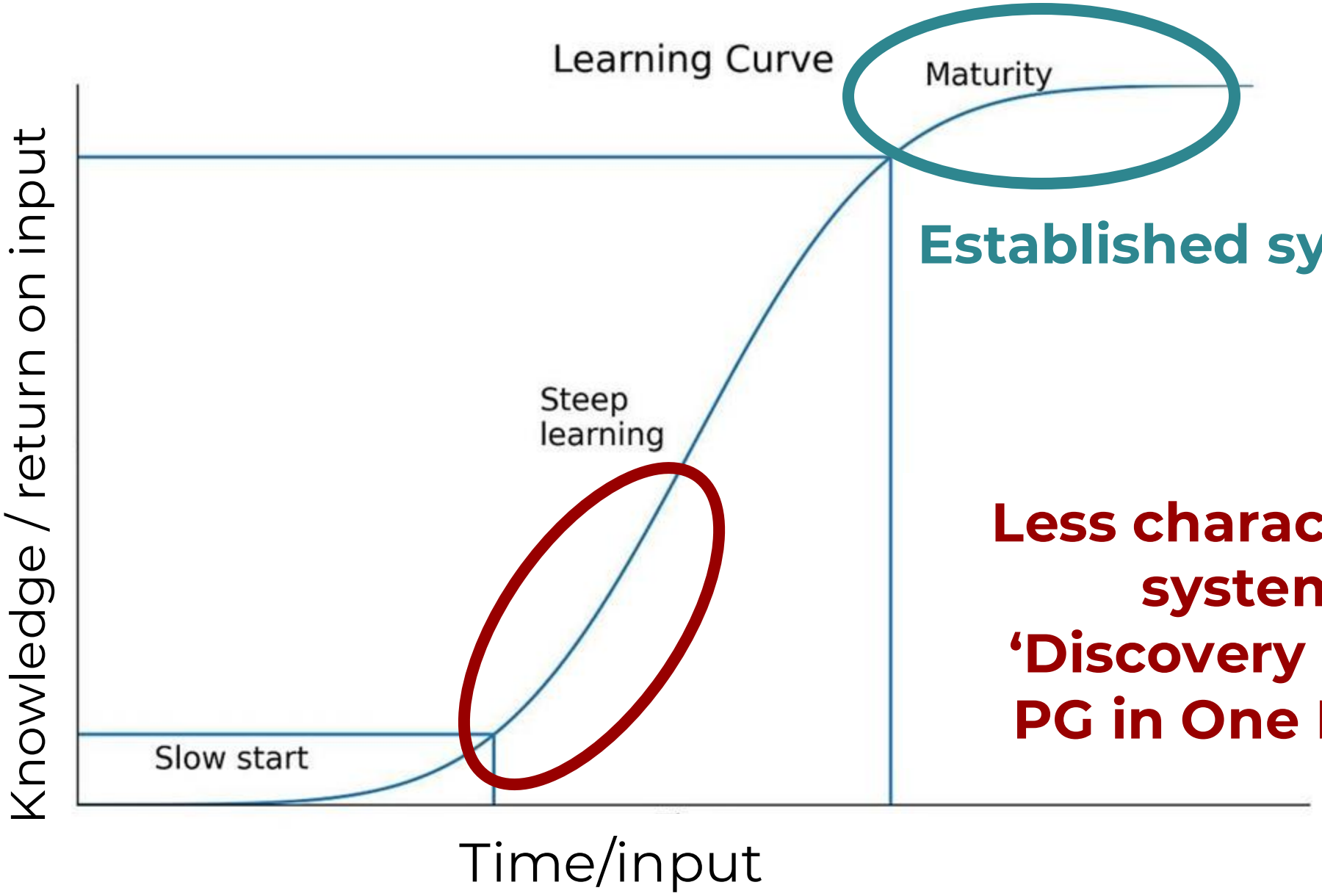


Established systems

Less characterized systems
‘Discovery phase’
PG in One Health

Zoonotic disease/one health resources

Tools to improve capacities and coordination across human and animal sectors

Multisectoral, One Health Coordination

Mapping Country Context

Planning and Preparedness

Surveillance and Information Sharing

Investigation and Response

Joint Risk Assessment

Risk Communication

Workforce Development

Food and Agriculture Organization of the United Nations

World Health Organization

World Organisation for Animal Health
Founded as OIE

Zoonotic disease/one health workshops

International Health Regulation - Performance of Veterinary Services: collaboration for improved prevention, detection, response

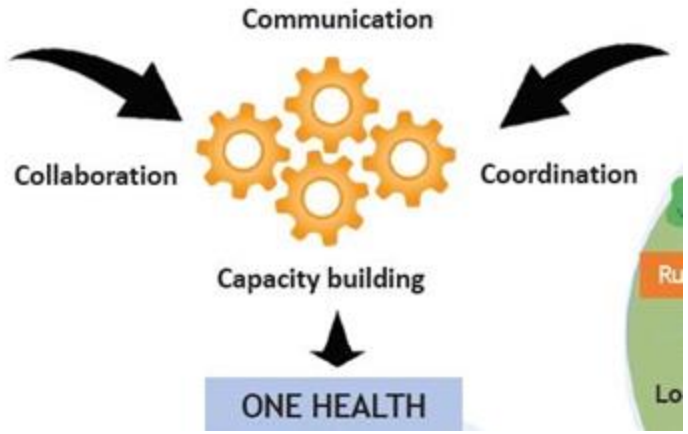
Response Preparedness Program:

Multi-sectoral outbreak response framework

https://www.who.int/activities/bridging-human-and-animal-health-sectors
https://www.who.int/initiatives/tripartite-zoonosis-guide/response-preparedness

Zoonotic disease/one health resources

Tools to improve capacities and coordination across human and animal sectors



Multisectoral, One Health Coordination

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Food and Agriculture Organization of the United Nations

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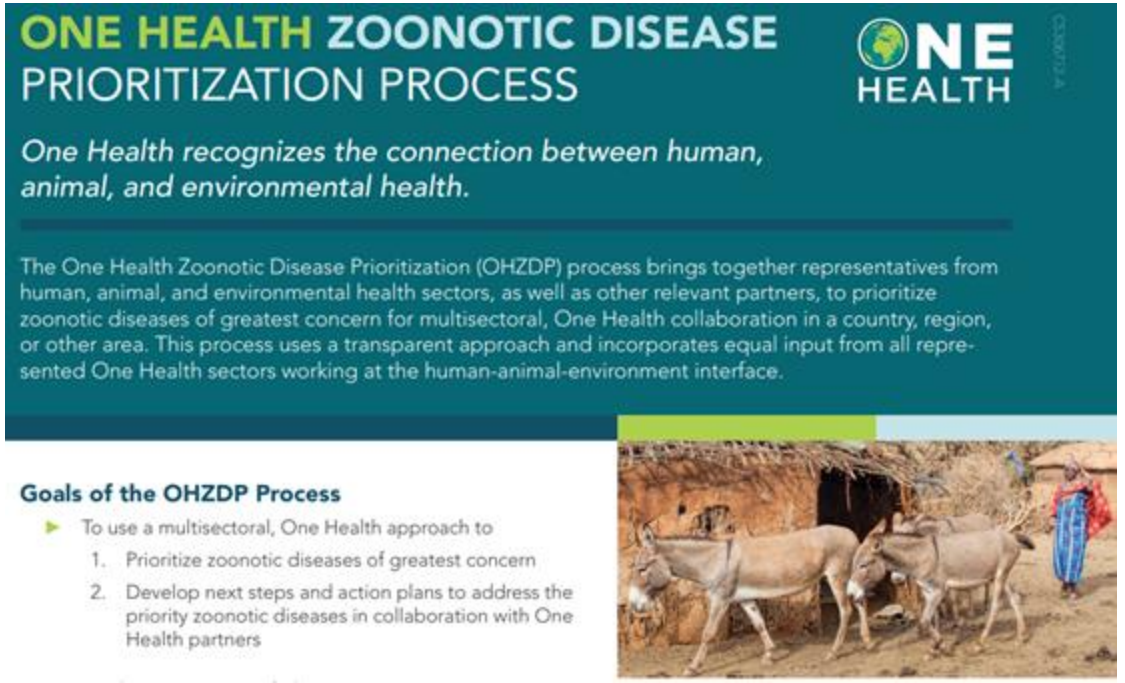
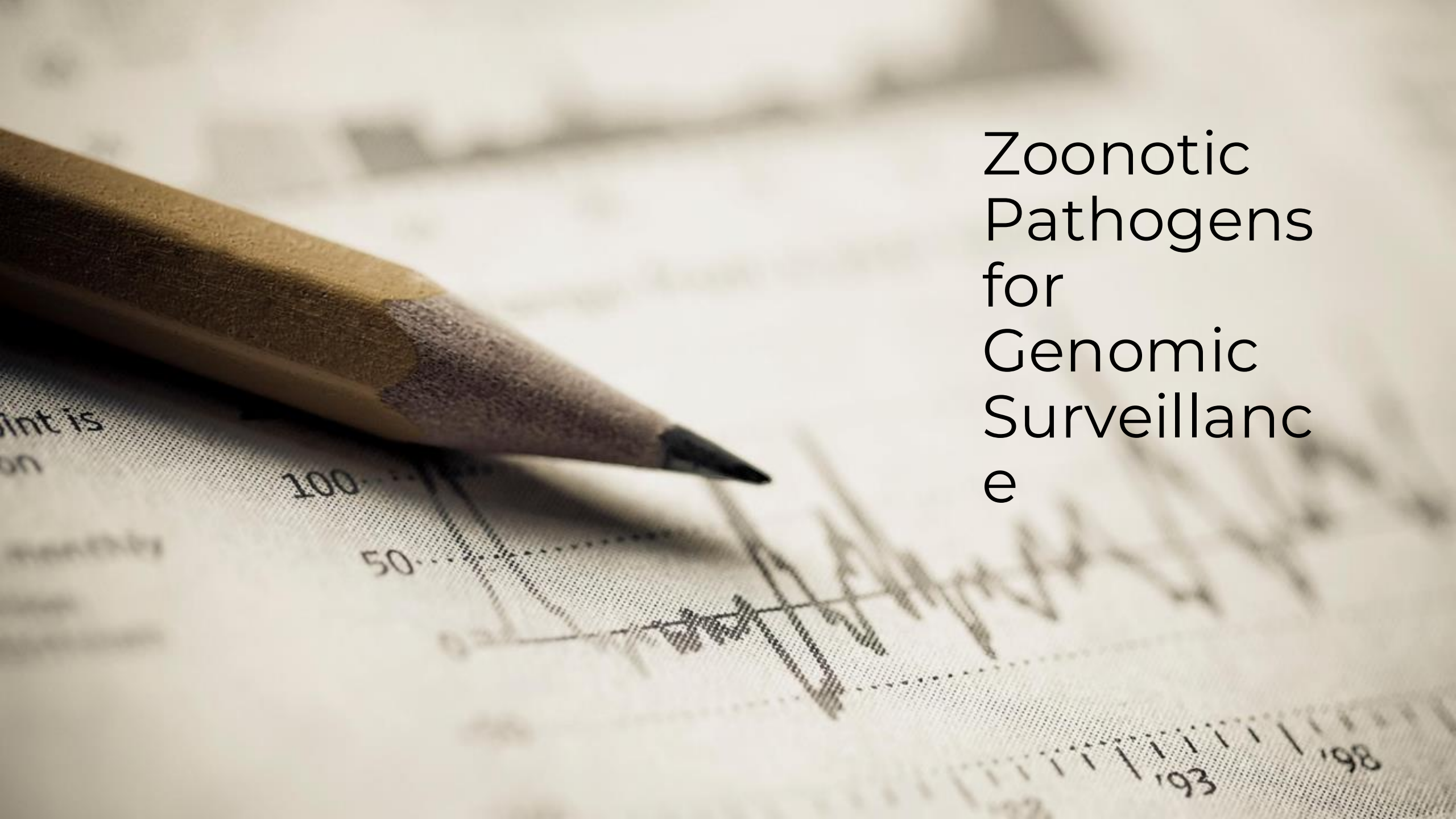
Founded as OIE

Perspective from Pakistan…

Dr. Ayesha Farooq
Senior Scientific Officer/In Charge
Microbiology Laboratory
National Institutes of Health
Pakistan





Zoonotic Pathogens for Genomic Surveillance

Zoonotic Priority Pathogens

- Zoonotic Influenza virus
- Rabies
- CCHF
- Anthrax
- Brucellosis
- Salmonellosis

Priority Zoonotic Pathogens

- Zoonotic Avian Influenza
- Emerging Corona Viruses (COVID -19, SARS, MERS)
- Nipah virus encephalitis
- Rabies
- Ebola

Priority Zoonotic Pathogens

Zoonotic Influenza

Rabies

Nipah virus encephalitis

Anthrax

Brucellosis

Zoonotic Tuberculosis (M. bovis)

Indonesia (Zoonotic priority Pathogens)

- Zoonotic Avian Influenza
- COVID – 19
- Zoonotic Swine Influenza
- Anthrax

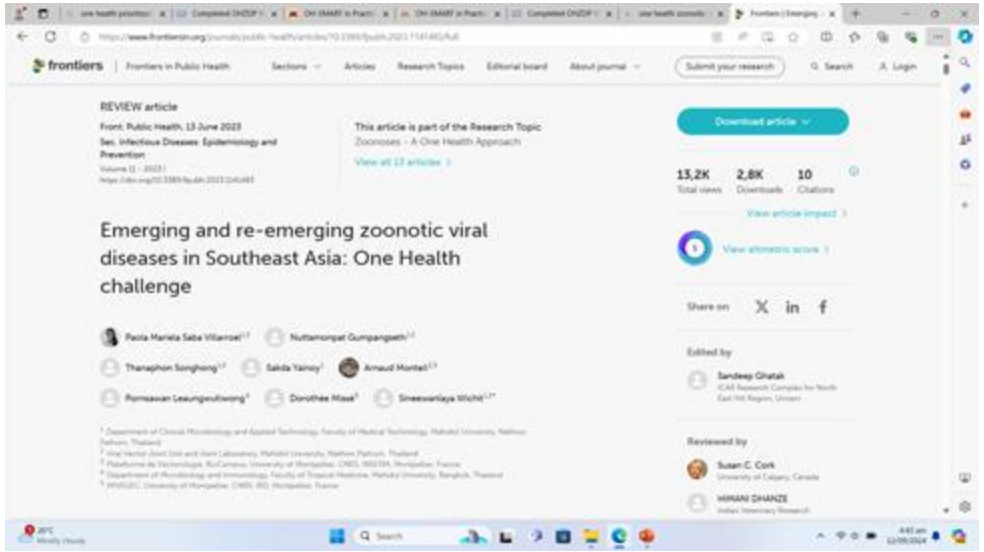
Country Specific Priority Zoonotic Diseases (0HZDP workhop)

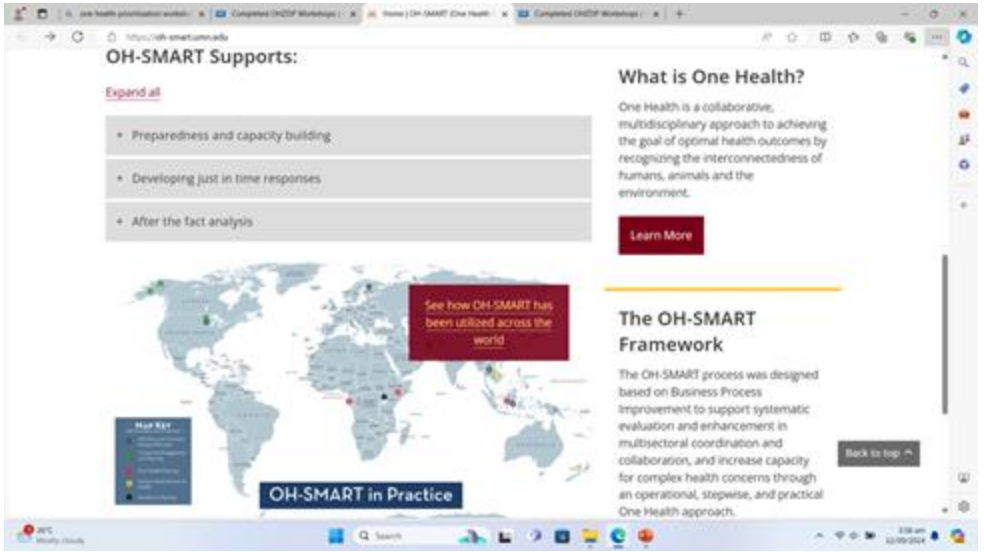
BANGLADESH	THAILAND	INDONESIA	PAKISTAN
Zoonotic Influenza Rabies Nipah virus encephalitis	Zoonotic Avian Influenza Emerging Corona Viruses (COVID-19, SARS, MERS) Nipah virus infection Rabies Ebola	Zoonotic Avian Influenza Covid-19 Anthrax Zoonotic Swine Influenza	Zoonotic Influenza virus Rabies CCHF
Anthrax Brucellosis Zoonotic Tuberculosis			Anthrax Brucellosis Salmonellosis

One Health Prioritization workshop

- One Health Zoonotic Disease Prioritization (OHZDP) workshop, jointly organized by CDC, USDA, US DOI in Dec, 2017. https://www.cdc.gov/one-health/php/prioritization/index.html
- Country specific priority zoonotic diseases were identified using a mixed methods prioritization process, the One Health Zoonotic Disease Prioritization (OHZDP) tool, developed by CDC. https://www.cdc.gov/one-health/php/prioritization/index.html
- One Health Systems Mapping & Analysis Resource Toolkit OH - SMART™ , co- developed by USDA 7 university of Minnesota, used to review & visualize the One Health system in place to address the priority zoonotic diseases.

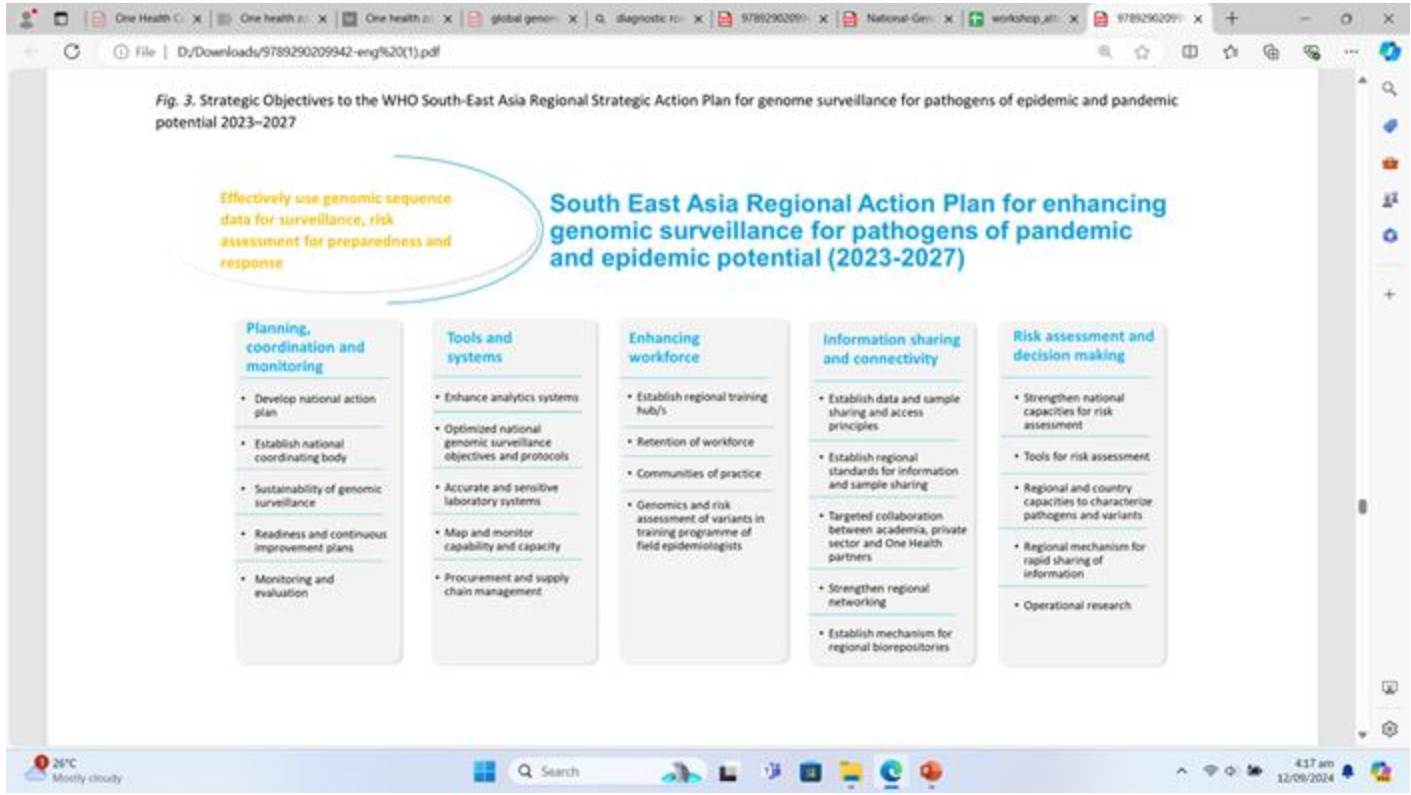
OH-SMART Framework





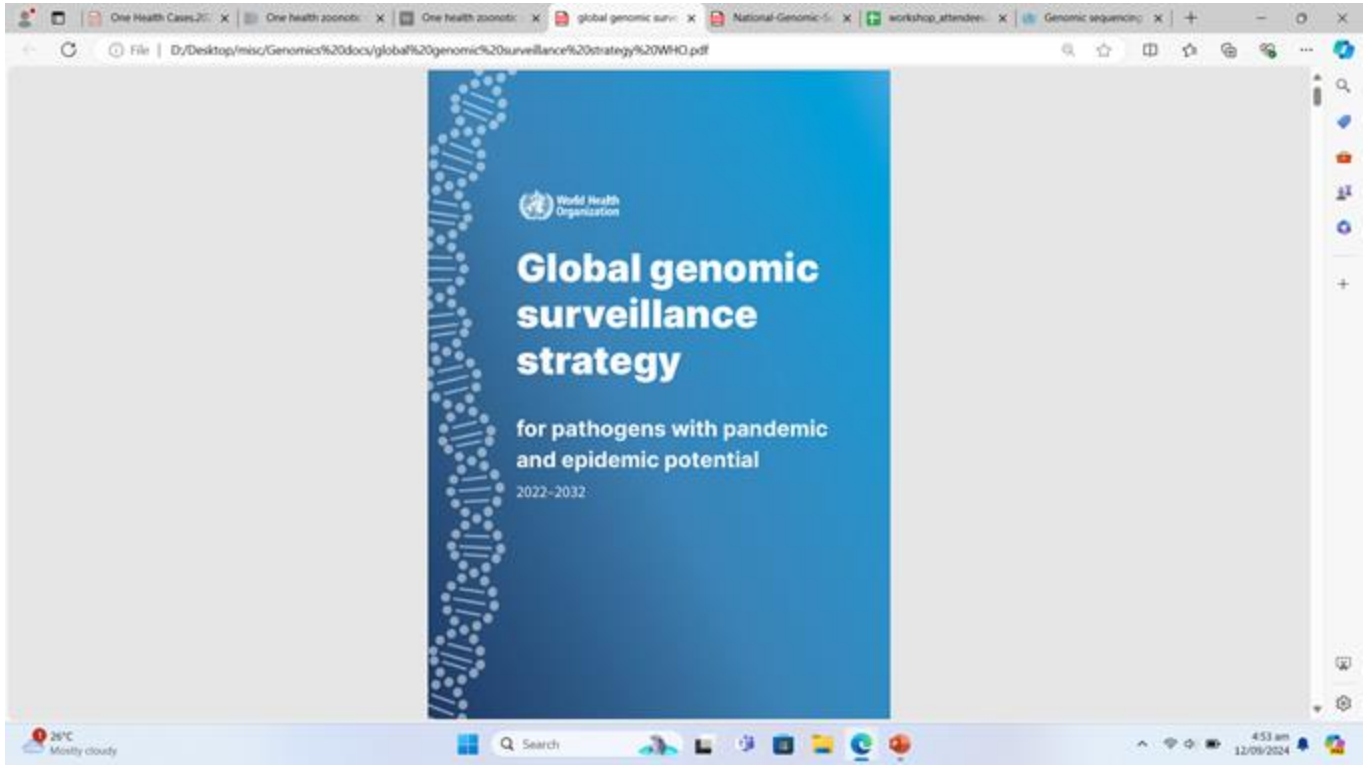
Integrated lab networking & Genomic surveillance

South East Asia regional roadmap for Genomic Surveillance (2023-2027)



Pathogen Selection

Zoonotic pathogens selected by OH- SMART tool can be assessed for potential candidate of Genomic Surveillance for maximum public health impact in specific country context.



Genomic Surveillance for Country specific Zoonotic pathogens

Genomic Surveillance: Objectives & Strategic Actions


File | D:/Desktop/misc/Genomics%20docs/global%20genomic%20surveillance%20strategy%20WHO.pdf
ANNEX 2: KEY WHO ASSETS FOR THE STRATEGY
International Health Regulations (IHR, 2005)
WHO's global footprint
WHO Hub for Pandemic and Epidemic Intelligence
Public health laboratory strengthening
Disease specific networks with genomic surveillance use cases
International Pathogen Surveillance Network + Global Pandemic Radar (IPSN)
Global Outbreak Alert and Response Network (GOARN)
BioHub
Research and Development (R&D) Blueprint
26°C
Mostly cloudy
Search
5:00 am
12/09/2024

- Priority zoonotic diseases are already mapped by most countries according to public health impact.
- Suitable candidate from this list could be selected.
- Consortia could be made with different research and surveillance groups working in different countries

Candidates for Genomic Surveillance

- Case histories can be build around:
- Brucella
- Leptospira
- AMR Bacteria (CRE KP)

Novel Pathogen Genomic Surveillance

- Clinical cases of Malaria
- Negative for all available ICT testing methods
- Could it be

Menti Responses

What One Health efforts are happening in your countries?

In planning, in progress, completed

CASE STUDY#6: ZOONOTIC DISEASE
HYPOTHETICAL BACTERIAL PATHOGEN INFECTING LIVESTOCK AND HUMANS

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Core process of MSCS strengthening

Decision Scenarios → Surveillance Objectives → Surveillance Approaches → Operationalization (Priority Actions to advance MSCS)

Public health investigation
Reactive investigation in response to event
- Support/refute source of infection(s) & outbreaks
- Tracing of transmission chains and networks

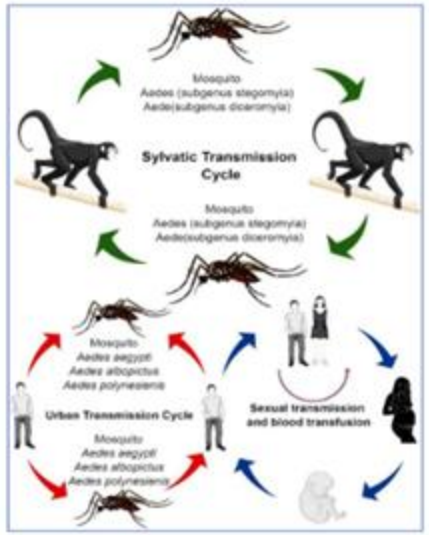
Surveillance
Systematic, ongoing collection of data on pathogen or syndrome

Control-focused
- Detect cases & outbreaks of priority AMR pathogens
- Identify high-risk clones & at-risk groups

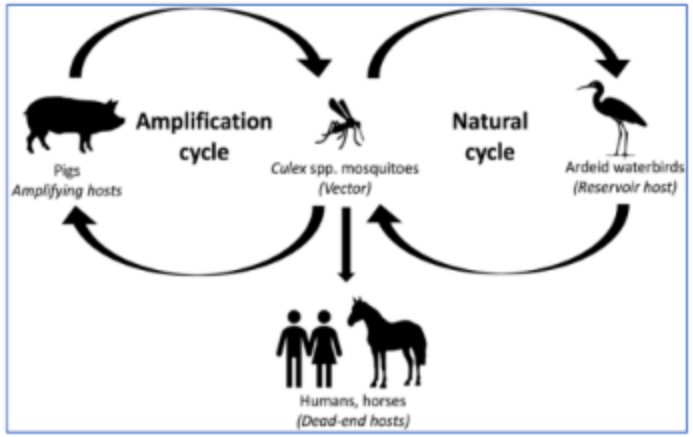
Strategy-focused
- Monitor circulating resistance mechanisms & strains
- Investigate pathogen factors associated with severity, outcome & transmissibility

Research
Targeted data to drive knowledge
- Identify pathways & drivers of AMR evolution
- Characterise new mechanisms of resistance
- Develop point of care tests

ZIKA transmission cycle



JEV transmission cycle

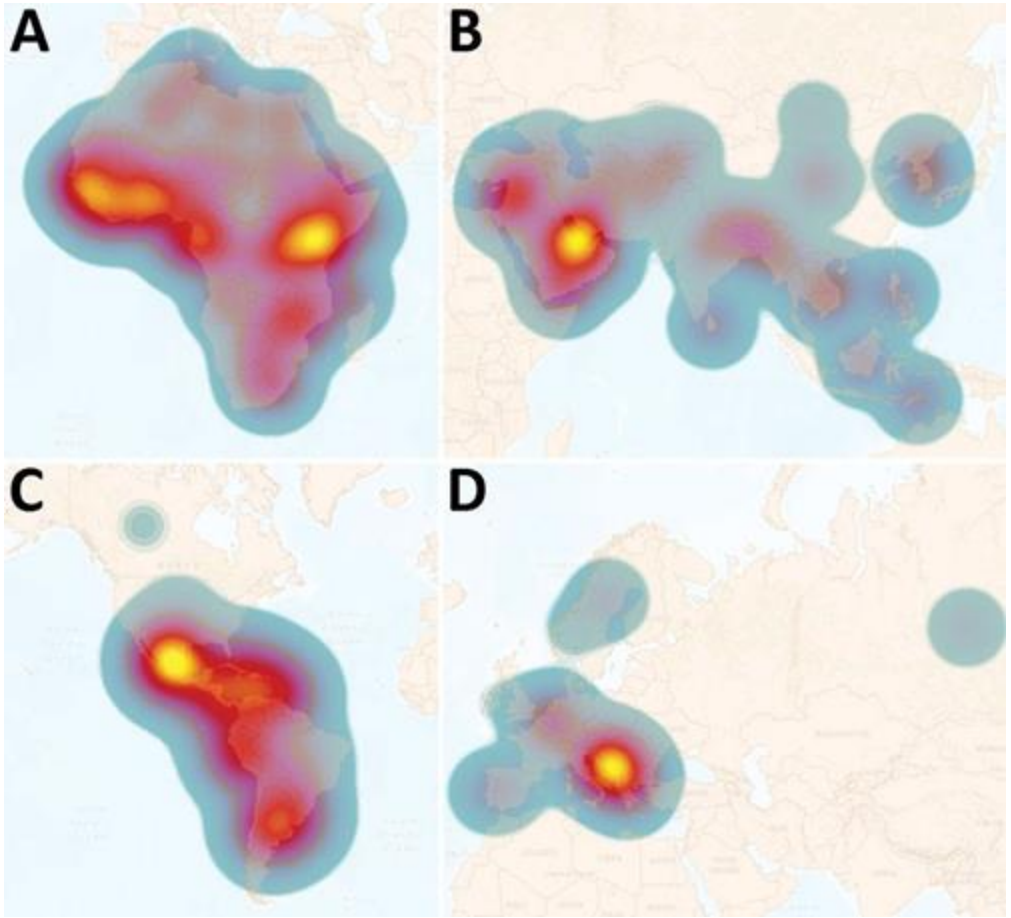


Background – ‘Bruntellosis’

- Livestock are important for human health and economics
- Many of Asia's ecosystems & agriculture conducive to zoonotic diseases

- **Bruntellosis**: A significant threat affecting livestock and human health
- *Critical food safety/security issue*

Background – ‘Bruntellosis’



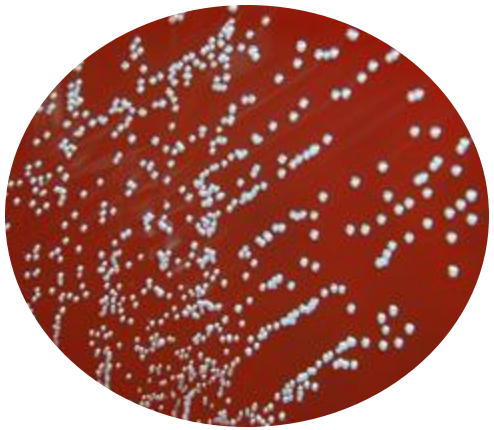
Heatmaps of annual incidence of human bruntellosis estimated per 1 million population at risk.

In Asia the average risk is ~500 cases per million population with a high of ≥4000.

Incidence has been increasing rapidly across the region

https://wwwnc.cdc.gov/eid/article/29/9/23-0052_article

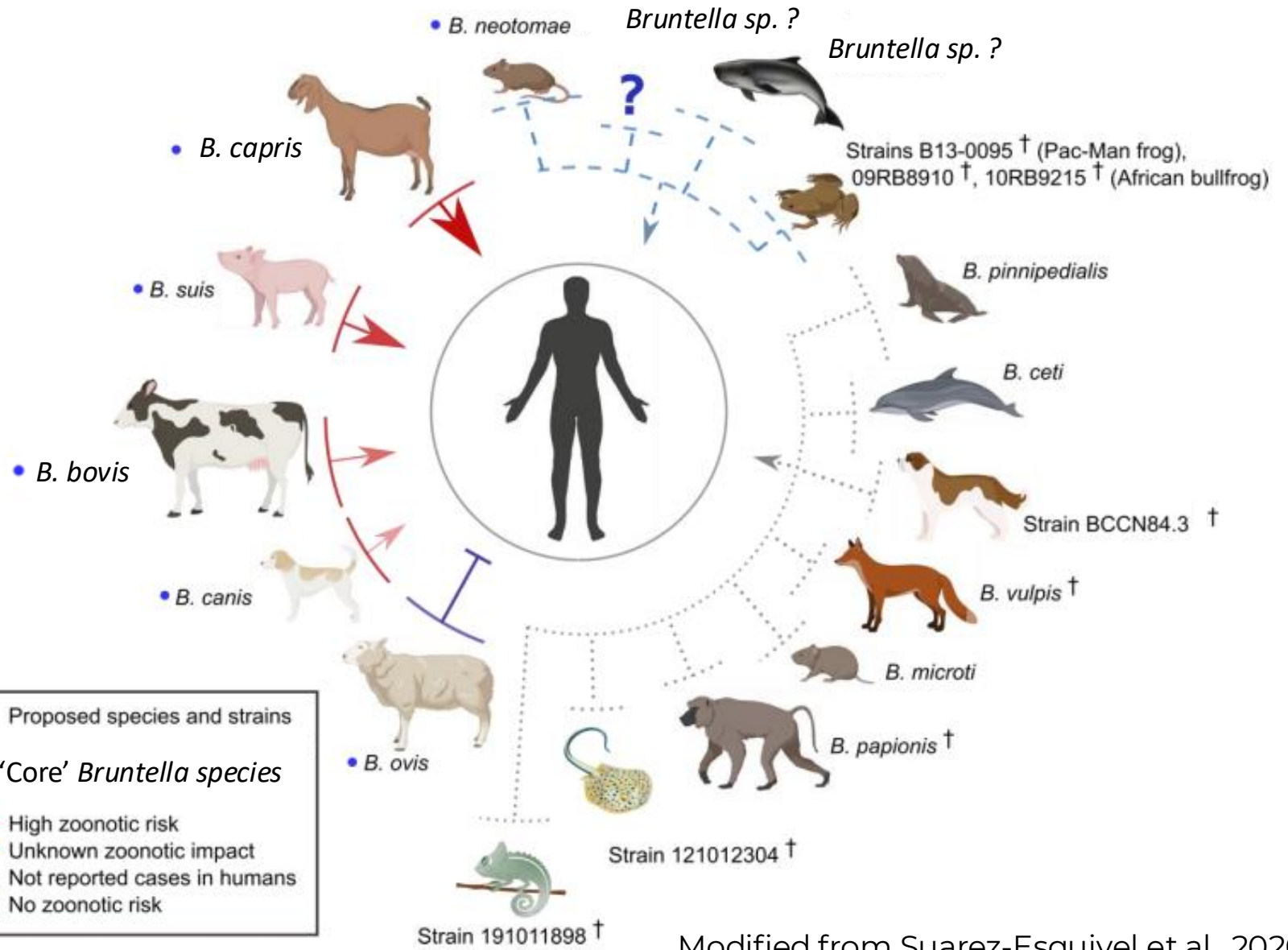
Bruntella pathogen



- Many species/strains in *Bruntella* genus
- Gram negative coccobacilli bacteria
  - Small, non-motile, facultative intracellular
- Mutates slowly
- Stable in environment for prolonged periods
- Virulence factors known to vary across species/strains
- Antimicrobial resistance is common…

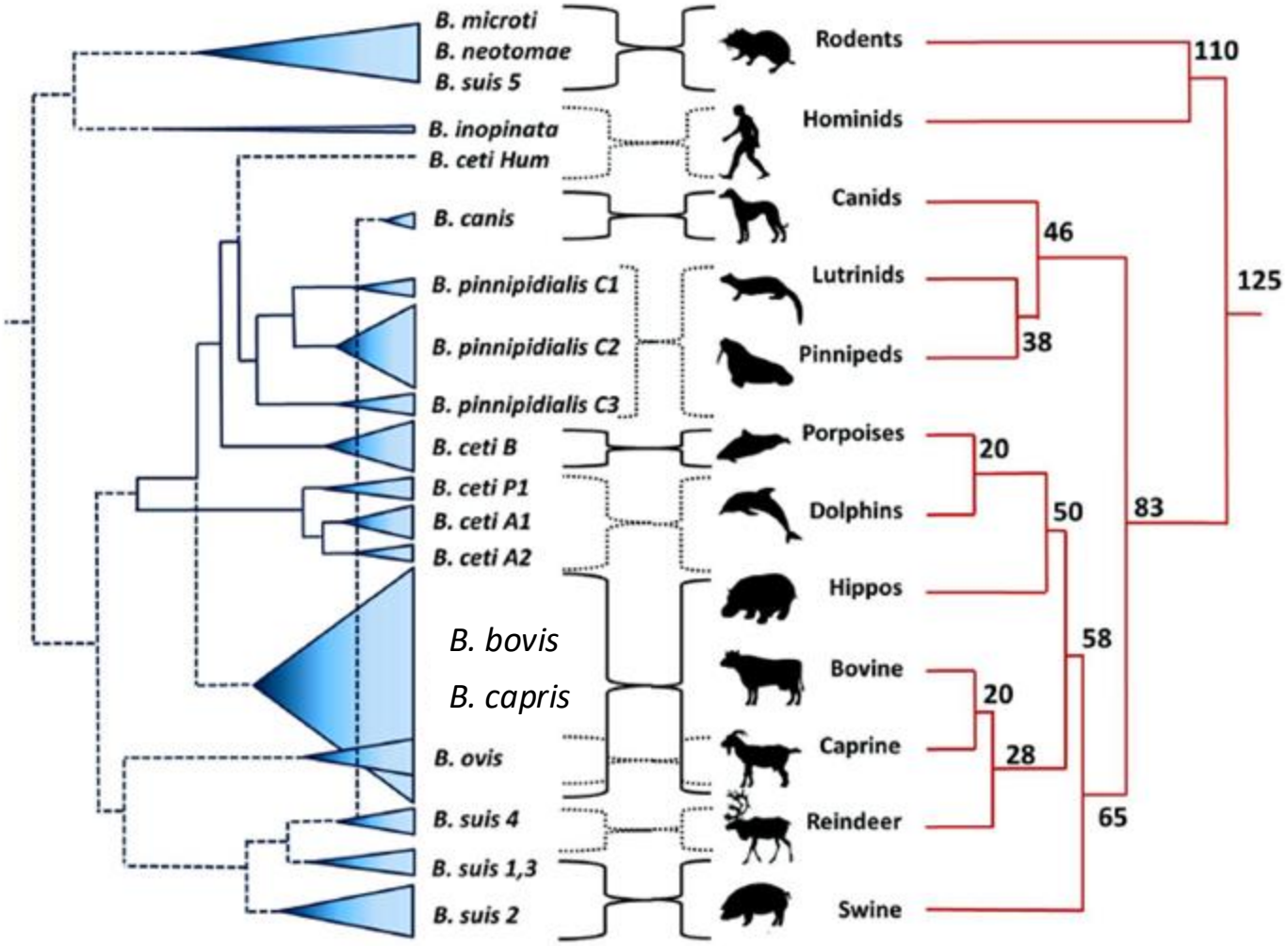
  …genetic markers for AMR poorly characterized

Diversity and Zoonotic Risk



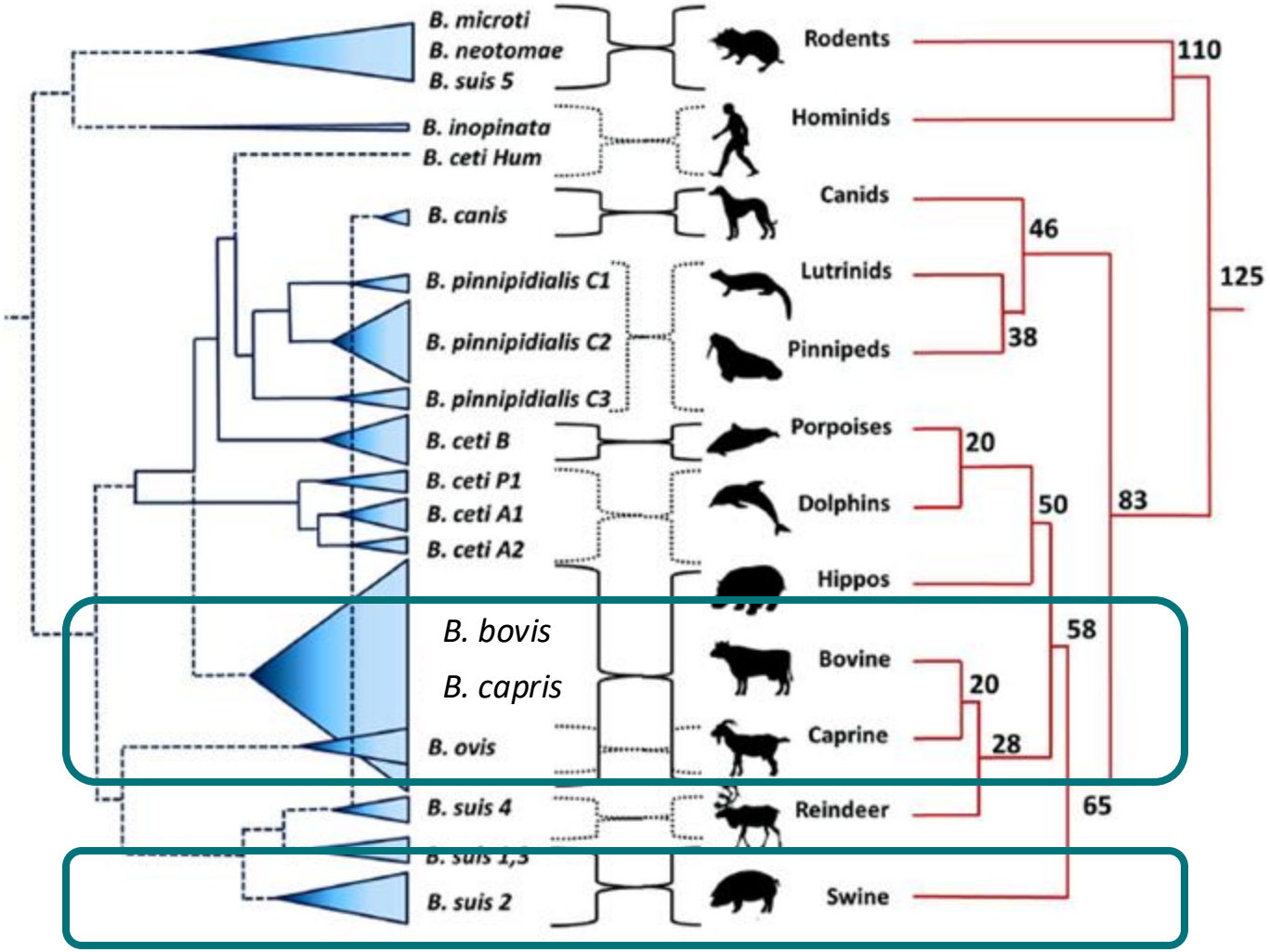
Modified from Suarez-Esquivel et al., 2020

Bacteria/Host Relationships



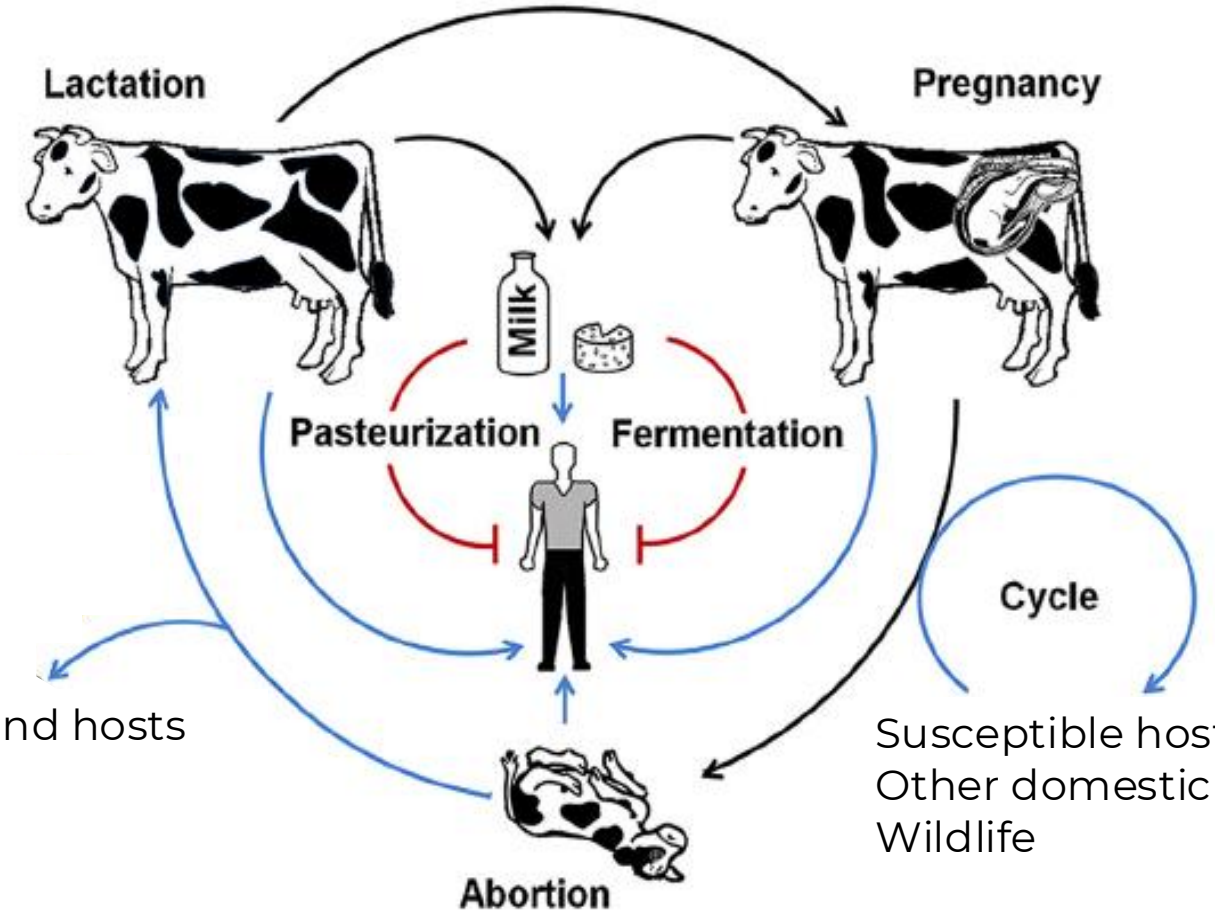
Modified from Moreno, 2014

Bacteria/Host Relationships



Modified from Moreno, 2014

Transmission of *B. bovis*

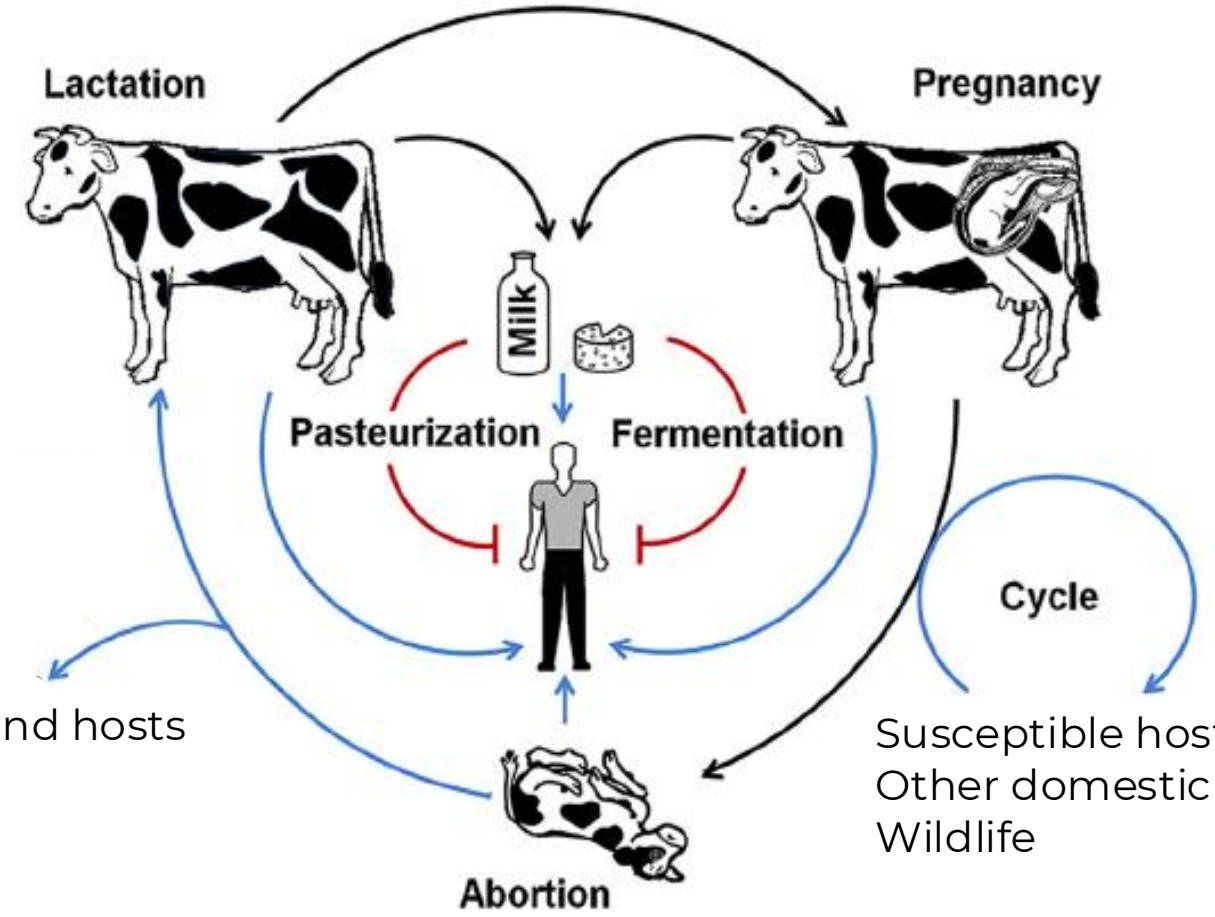


Dead end hosts

Susceptible hosts:
Other domestic animals
Wildlife

Modified from Moreno, 2014

Transmission of *B. bovis*



High risk populations

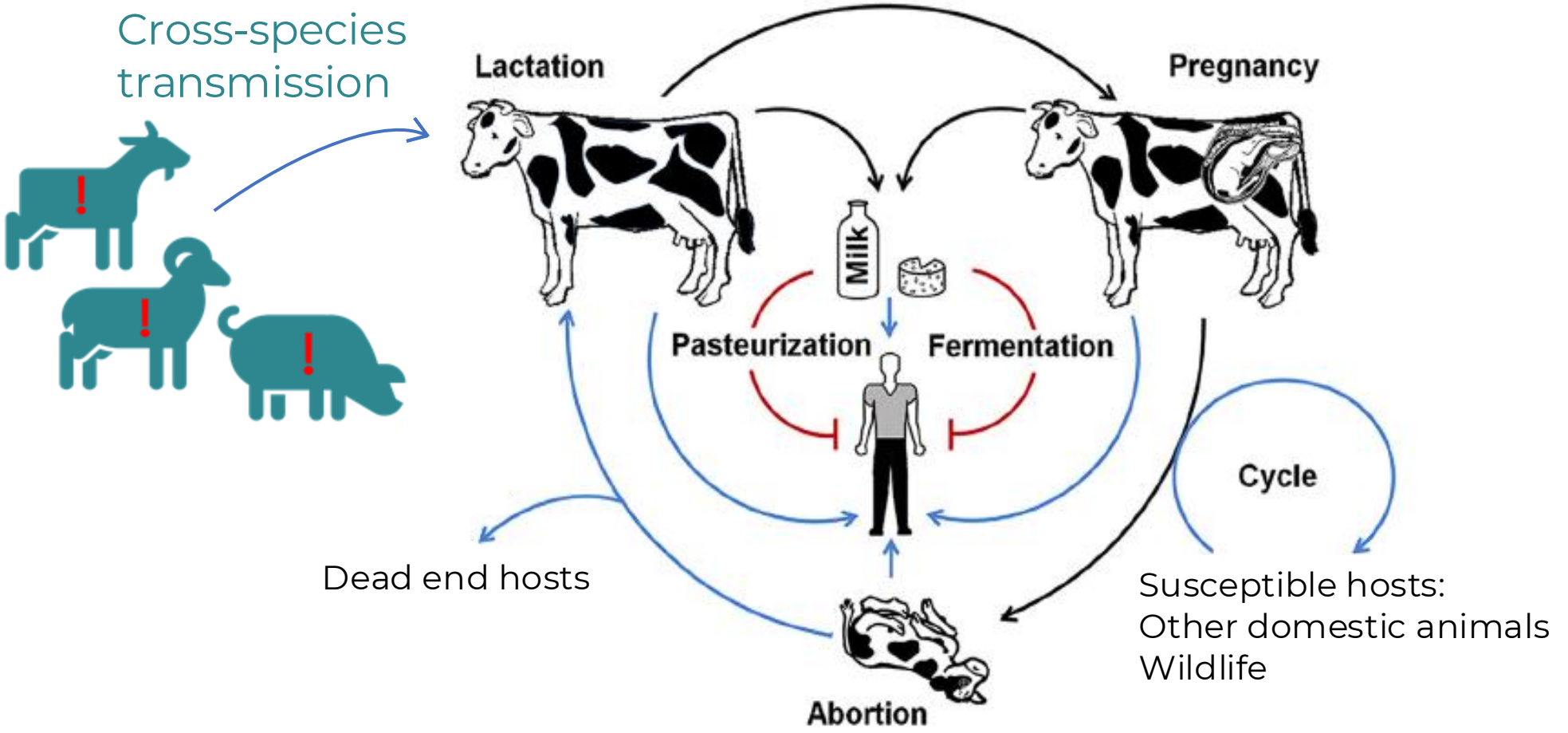
20% of people have regular contact with livestock

30% of people routinely consume unpasteurized foods

Modified from Moreno, 2014

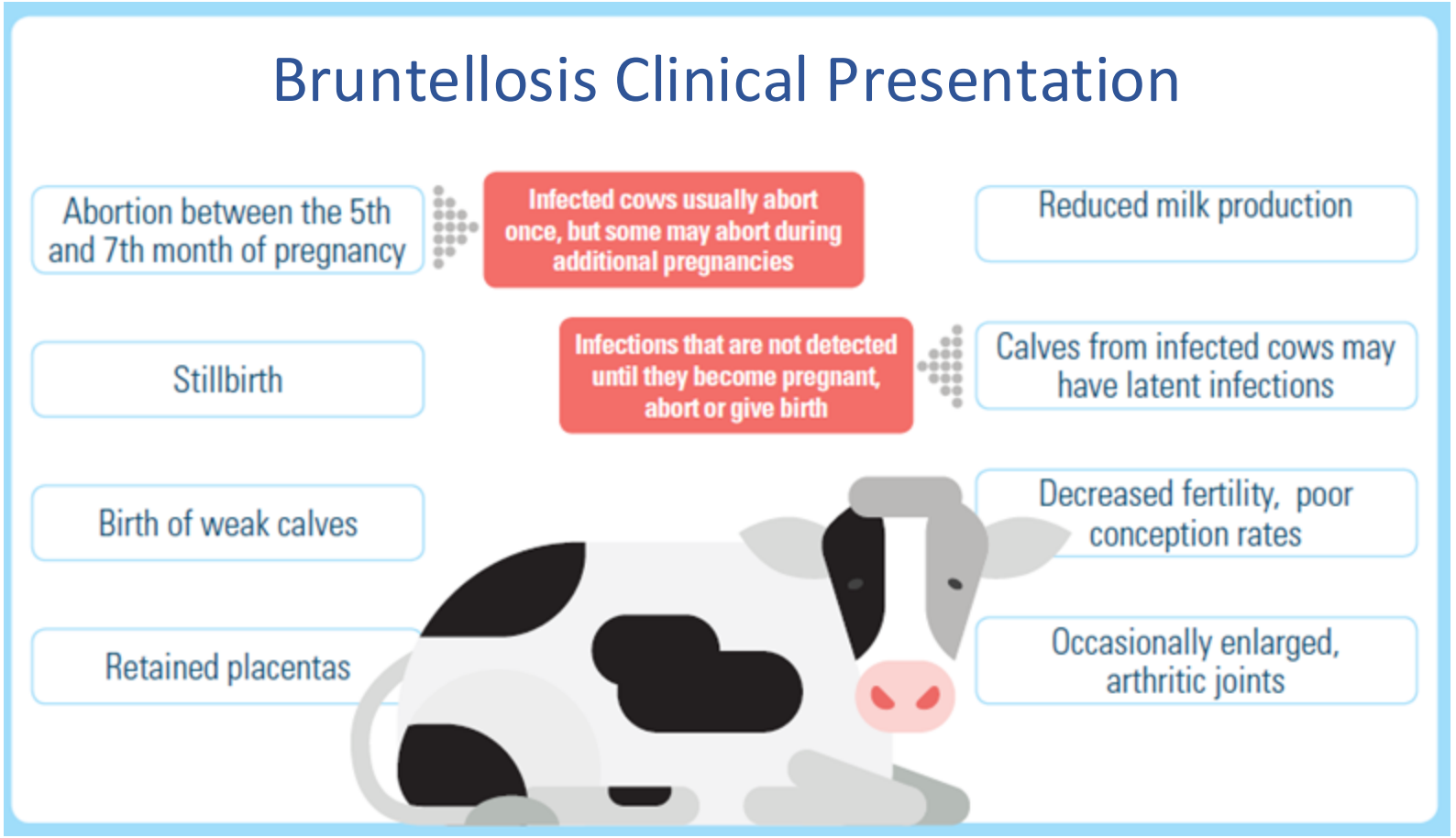
Transmission *B. bovis*

Cross-species transmission

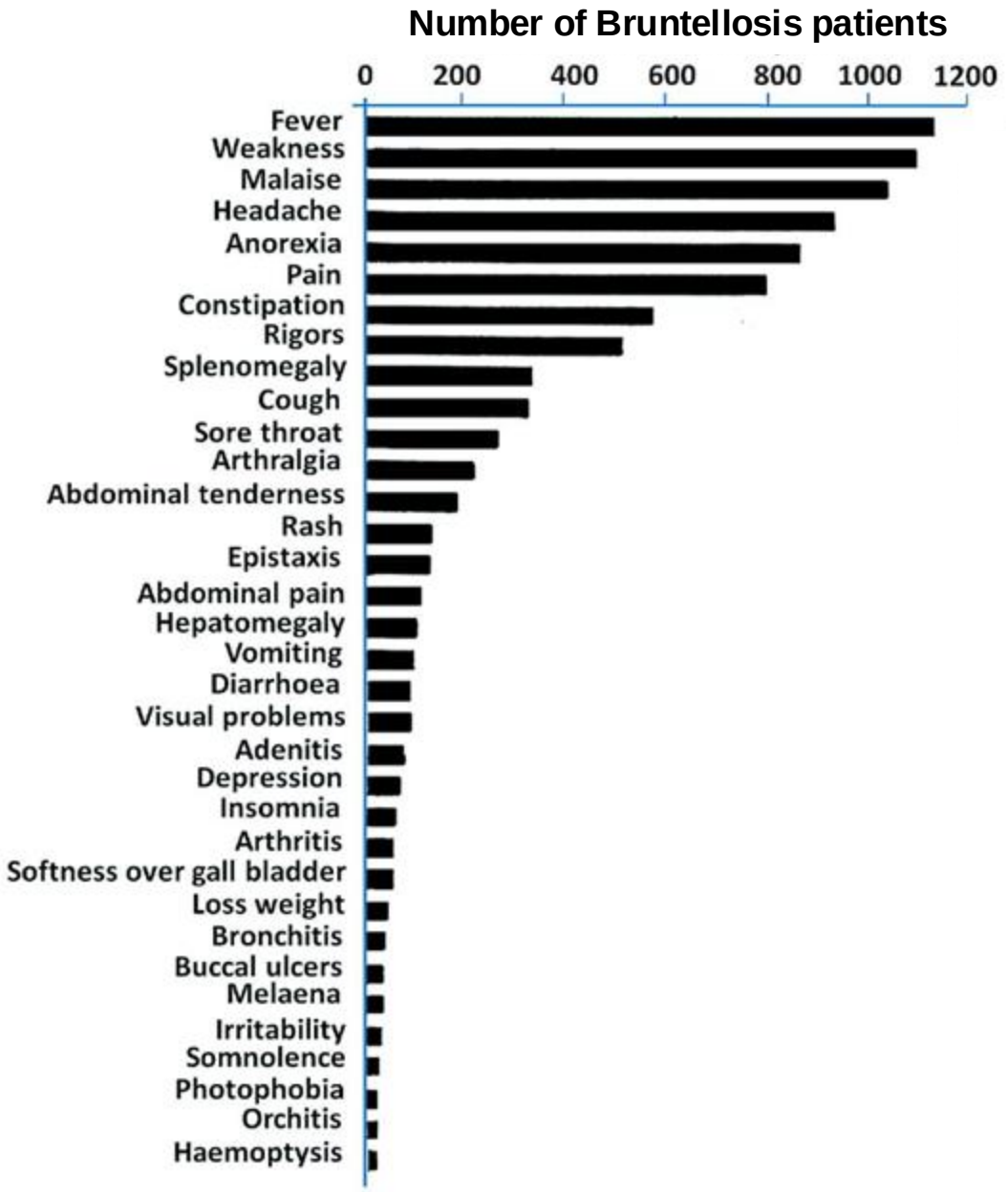


Modified from Moreno, 2014

Disease in animals



Merck Veterinary Manual



Human Disease

Non-specific clinical presentation

Mild to severe*
2% case fatality rate

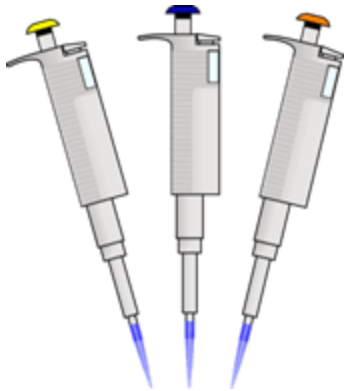
Not prioritized for testing

Underdiagnosed

Moreno, 2014

Bruntella Detection

- Laboratory tests available for detecting bacteria (PCR) & antibodies (ELISA)
    - Do not differentiate species (genus only)
    - Clinicians rarely order tests



- Species identification requires extensive microbiological characterization or specialized molecular assays (*rarely performed*)

- Whole genome sequencing is only way to characterize strains
- No point-of-care/rapid tests available

Genetic diversity

No information about the genetic diversity of Bruntella is known in your country…

…Neighboring countries that have done genomic surveillance typically characterize 3 - 6 genetically distinct strains per species

Bruntella Control

	Human	Animal

Vaccine	• Does not exist	• 2 vaccines available for animals targeting *B. bovis* or *B. capris*
		  • BUT not currently in use in your country
		  • Vaccine effectiveness 40% - 70% (reported)*

Bruntella Control

	Human	Animal

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		  • Vaccine effectiveness 40% - 70% (reported)*

Treatment	• 45-day course of antibiotics
	  • Reported: 80% cure/20% relapse (but unknown in your country)
	  • Resistance markers unknown
		• Cull/removal from heard

Scenario

- The nation-wide prevalence of Bruntellosis has been increasing in animals and people
- Most human cases can be epidemiologically linked to cattle (*B. bovis* suspected but *B. suis* and *B. capris* also circulate)
- Only large-scale agricultural operations (> 500 animals) are included in current test/cull surveillance (~60% of total livestock)
- Primary transmission routes among animals/herds unknown
- Test and cull of positive animals is only current control strategy

Your task

You are assigned to be part of a team tasked with recommending a public health response that will lead to a decrease in the incidence of bruntellosis among people (and animals).

Given your background, they ask you to investigate if genomic sequencing can help inform the planning, monitoring, and evaluation of new control efforts.

Assume your country has medium capacity for human health and low capacity for animal health. Please draw on and compare experiences from your home country throughout the discussion.

Menti response

Intervention

List as many possible pharmaceutical and non-pharmaceutical interventions as you can that could be considered to reduce human cases of bruntellosis.

Questions for discussion

1. What are some questions for which genomic data could add actionable information about this disease system?

   For each question you generate, describe a public health intervention that could be designed, refined, or improved using the genomic surveillance data

1. Why might it be important to understand if/how cross-species transmission among different livestock (cattle, sheep, goats, pigs) is occurring?
2. What are some sampling strategies and metadata would you need to inform the use of pathogen genomics for the following? Be specific :)

   Table 2 - Differences in animal vaccine effectiveness across bacterial species/strains

   Table 3 - Potential impact of genotype on disease outcomes and AMR

   Table 4 - Identifying key transmission pathways among animals within the country

   Table 5 - Determining if import of new cases from neighboring countries is a major factor in the epidemiology

4. What stakeholders should be involved in your genomic surveillance and control program and what roles would they play in the surveillance/control efforts you are planning?

5. What components of this system are unique because the focal pathogen is zoonotic?

Menti responses

Characterization

Currently your country is only identifying Bruntella bacteria at the genus level…

Why is accurate identification of bacterial **species and strains** important in when planning/monitoring control efforts?

Parting thoughts…

Balancing food security, economic impact, and human health is a big challenge

Lower historic investment means animal disease systems are often less well characterized

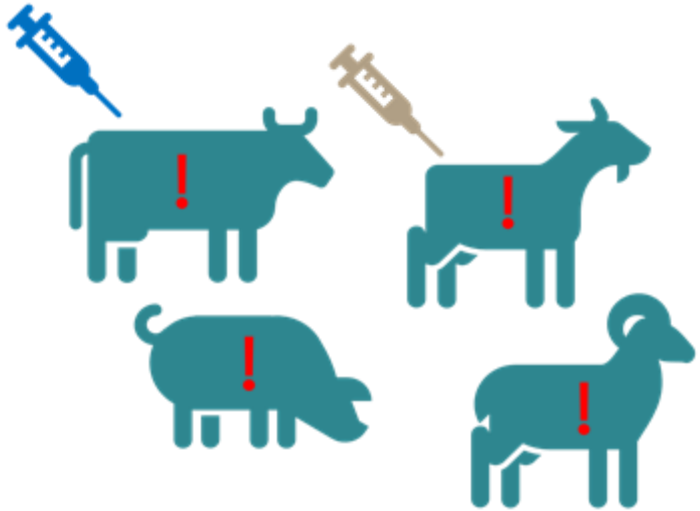
- Foundational surveillance systems may not be robust
- Value of genomics use case can be less clear/immediate

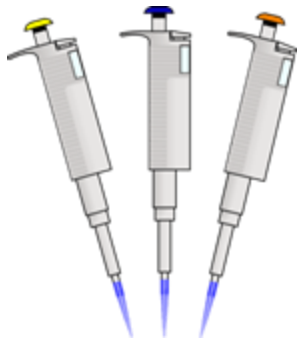
Would the country be better off with more effective Bruntella control? YES!

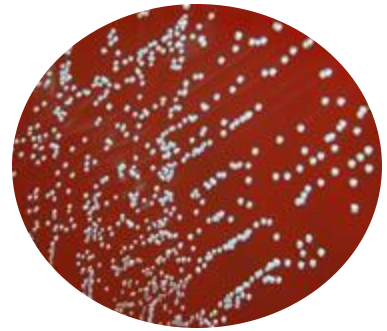
Is it worth the investment to develop effective, genomics-informed interventions to get there???

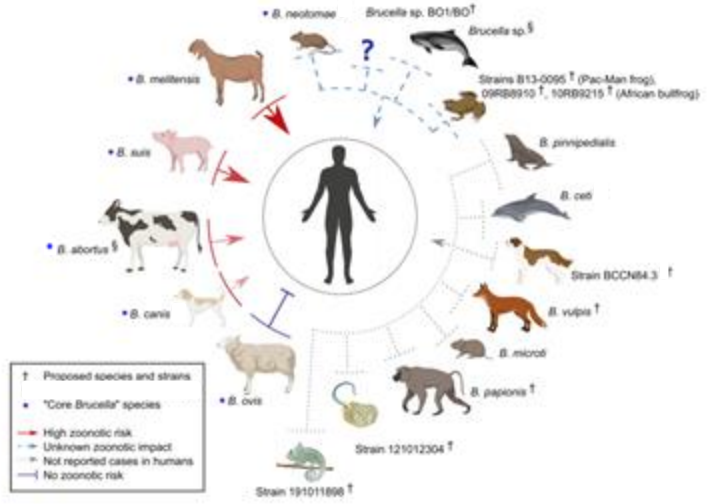
One Health is hard!

The end ☺








B. neotomae
Brucella sp. BO1/BO†
Brucella sp.§
B. melitensis
?
Strains B13-0095 † (Pac-Man frog),
09RB8910 †, 10RB9215 † (African bullfrog)
B. suis
B. pinnipedialis
B. ceti
B. abortus §
Strain BCCN84.3 †
B. canis
B. vulpis †
B. microti
B. ovis
B. papionis †
Strain 121012304 †
Strain 191011898 †
† Proposed species and strains
• "Core Brucella" species
High zoonotic risk
Unknown zoonotic impact
Not reported cases in humans
No zoonotic risk

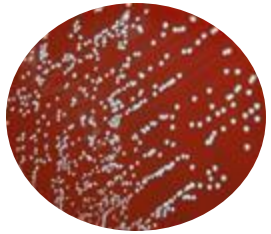
Pathogen prioritisation tool

Implement and monitor control program

Of the many control efforts you plan to use, we will focus on…

1. Start a vaccination campaign among cattle

2. Monitor:
   - incidence in humans & cattle
   - genetic diversity of *Bruntella* over time



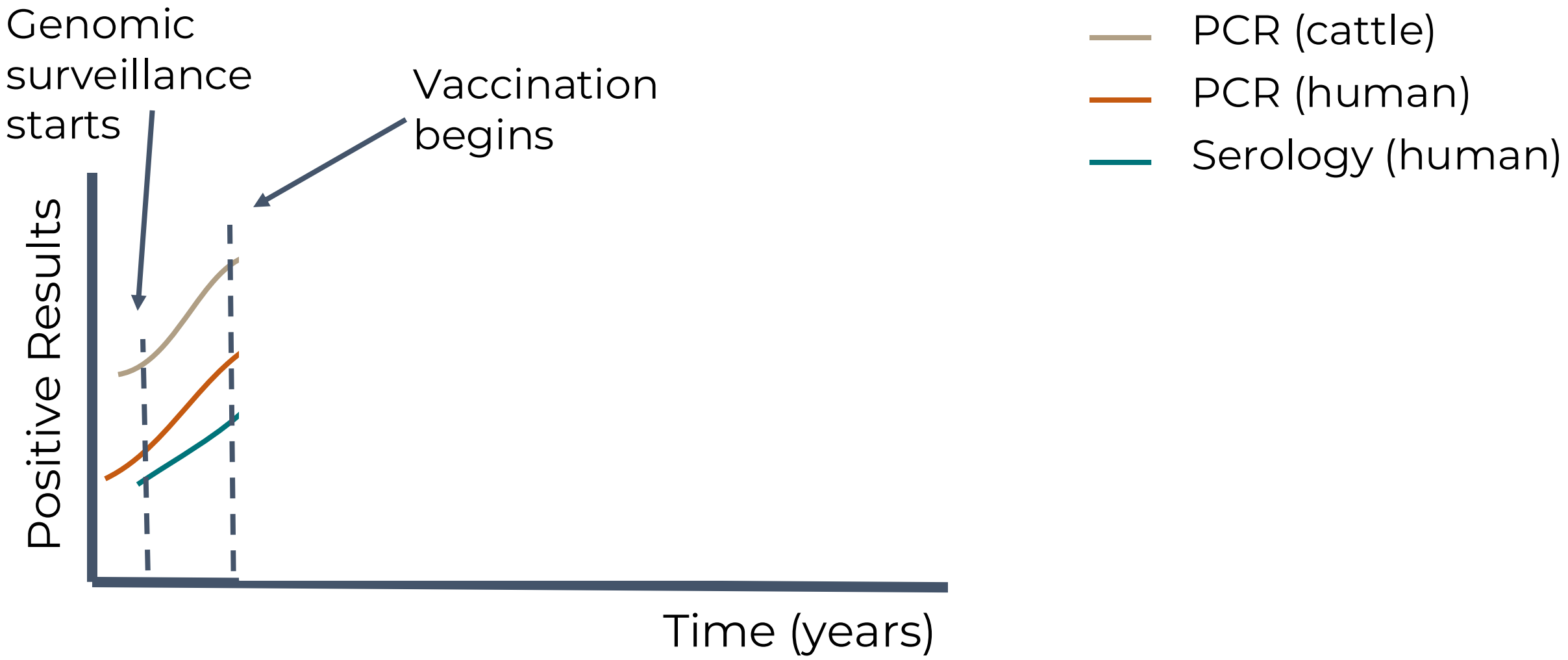
You convene the stakeholders…

Cross-sector collaboration is difficult!

It takes 18 months to develop a surveillance strategy and start to implement the testing and sequencing plans.

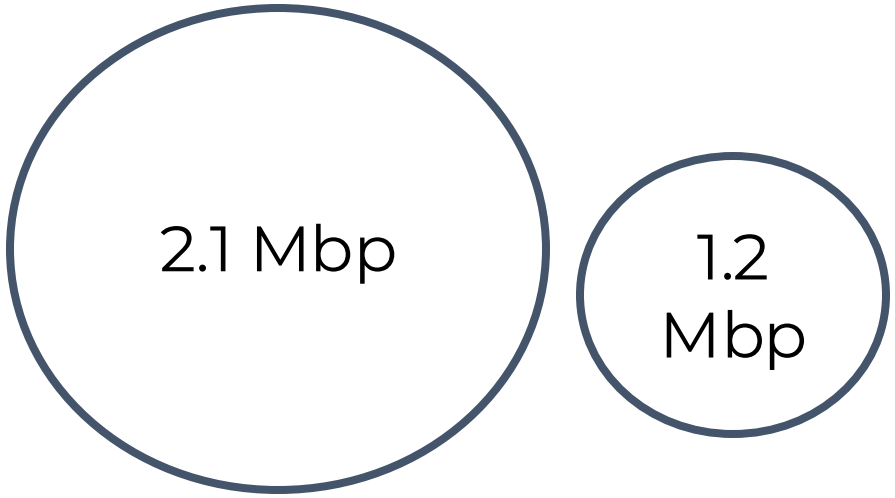
In the meantime…cases continue to rise

Monitoring interventions

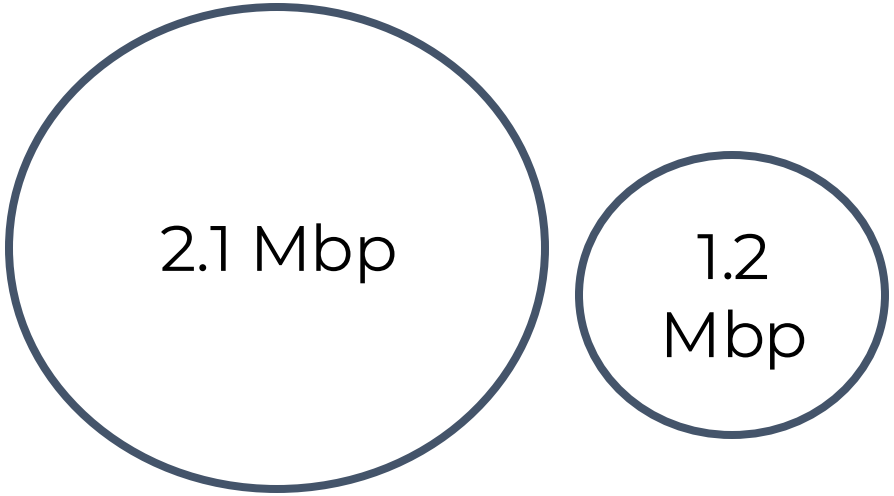


Preliminary results…

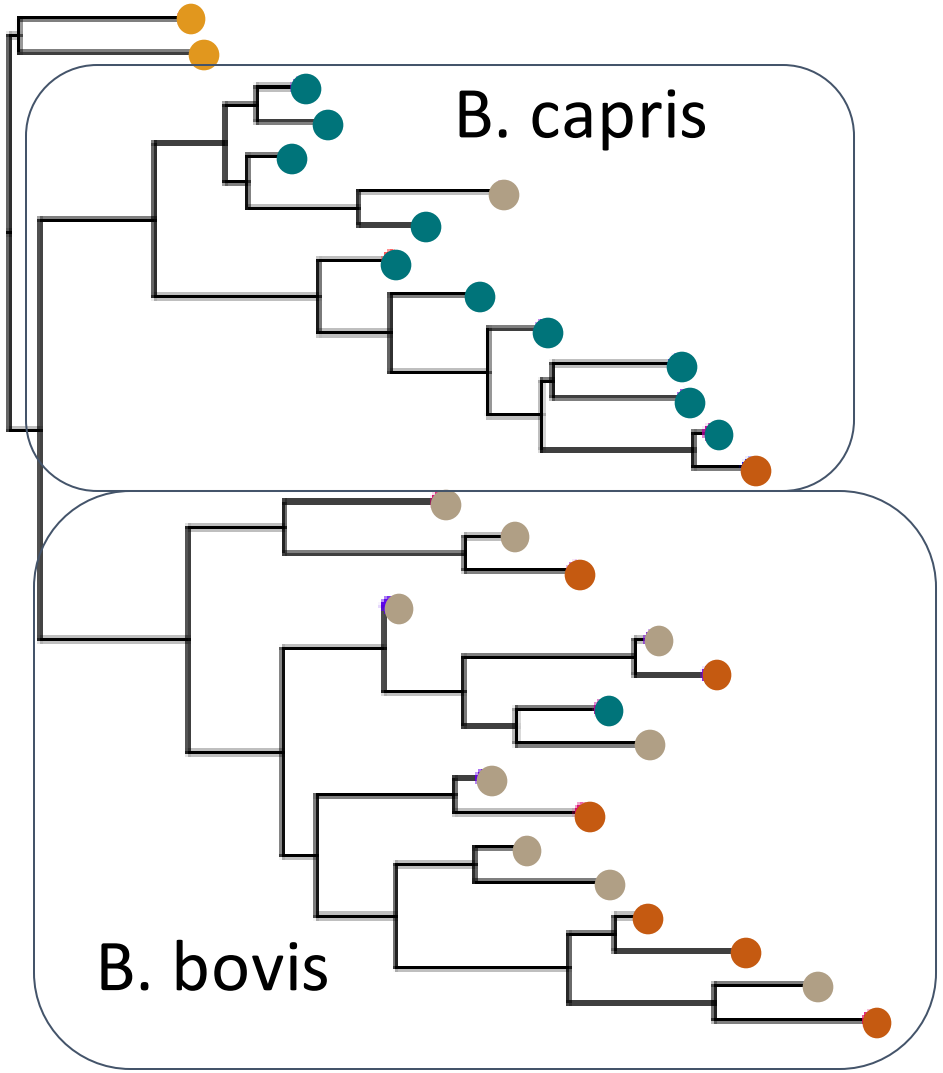
B. bovis Reference genome



Assemble genomes



Bruntella WGS Phylogeny

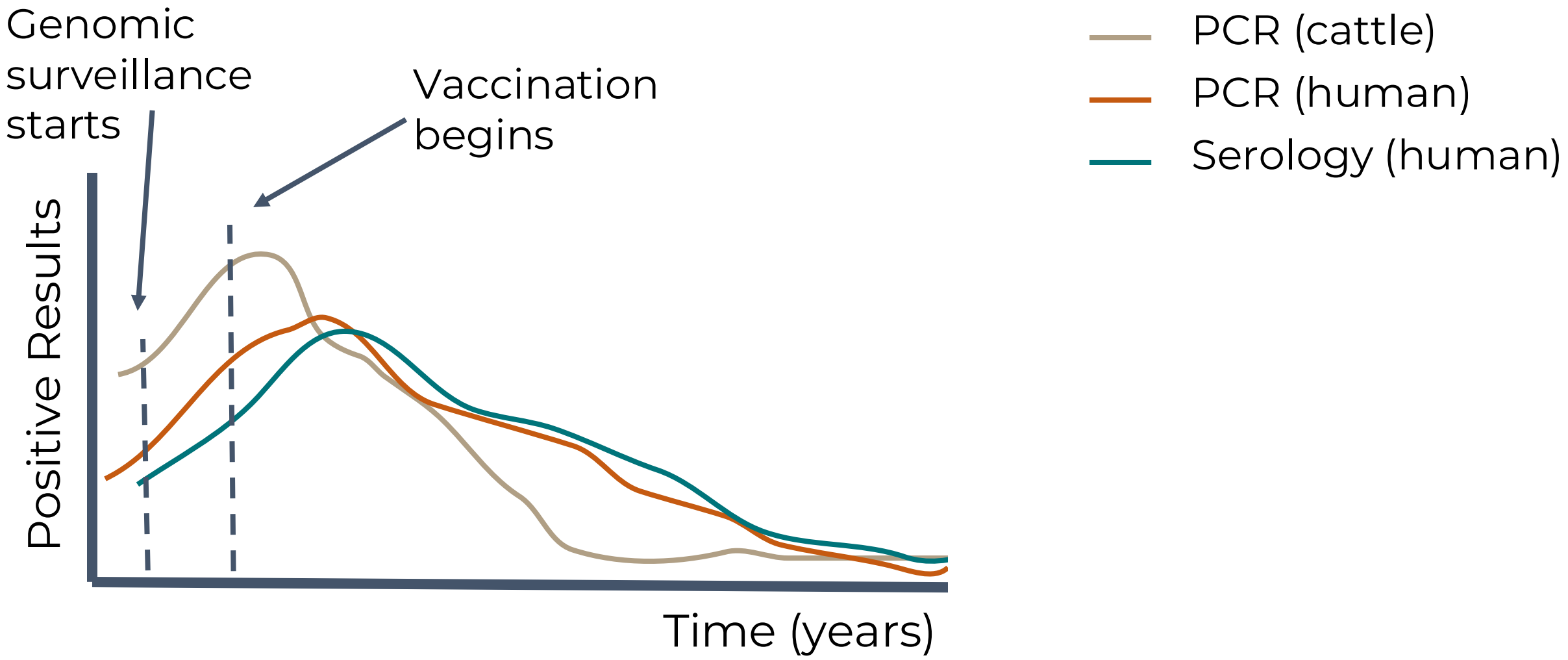


Specimen Source

What preliminary conclusions can be drawn from these results?

Is this what we expected?

Monitoring interventions



Success! Layered interventions work!

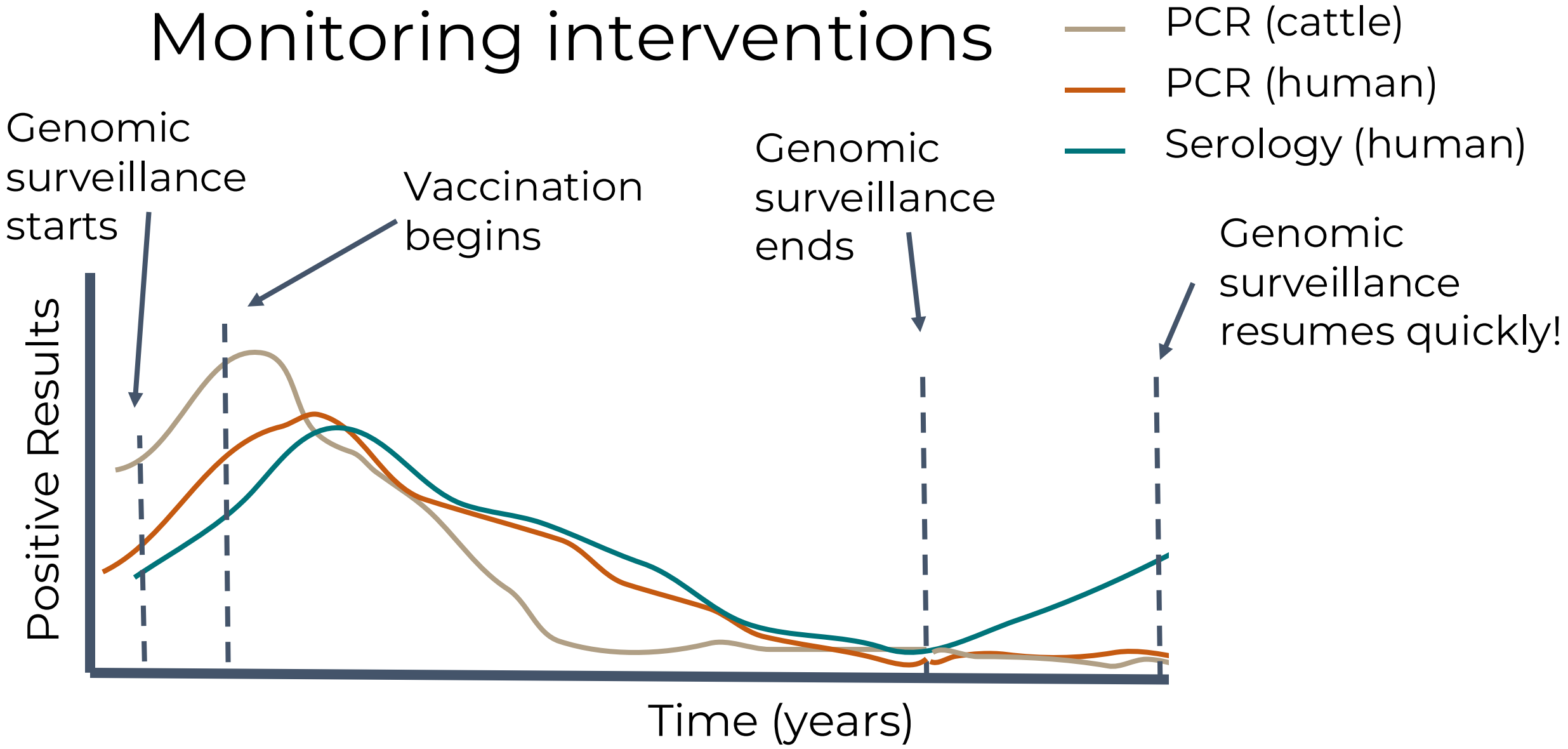
Prevalence in both cattle and humans decreases!!!

You've saved lives and the agricultural industry of your country…

Genomic surveillance is ended to move resources to higher priority diseases.

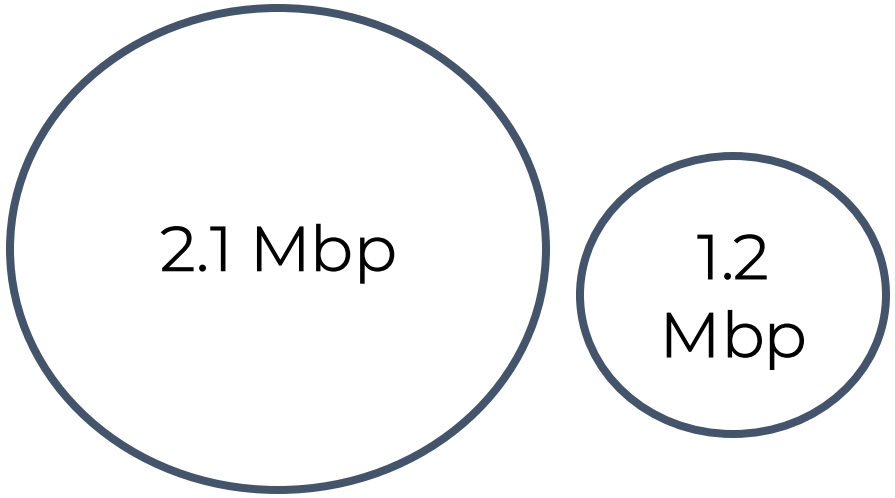
Surveillance returns to PCR and serologic assays only :(

Monitoring interventions

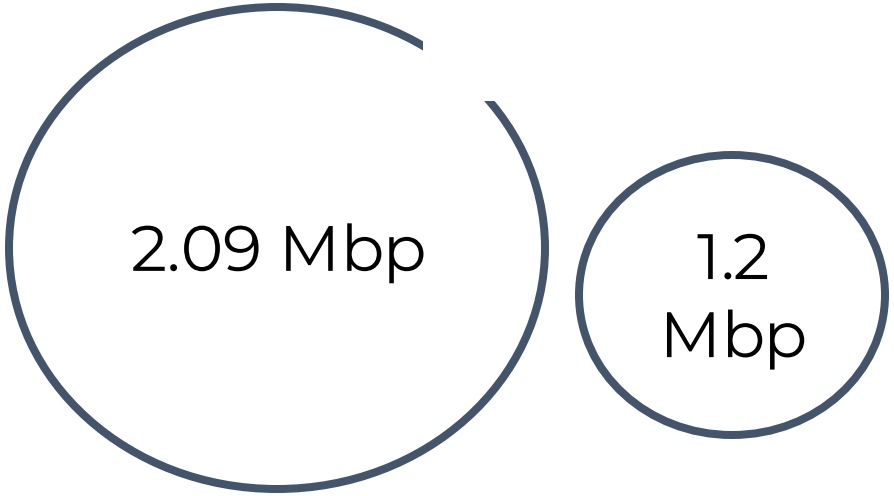


Preliminary results...

Reference genome

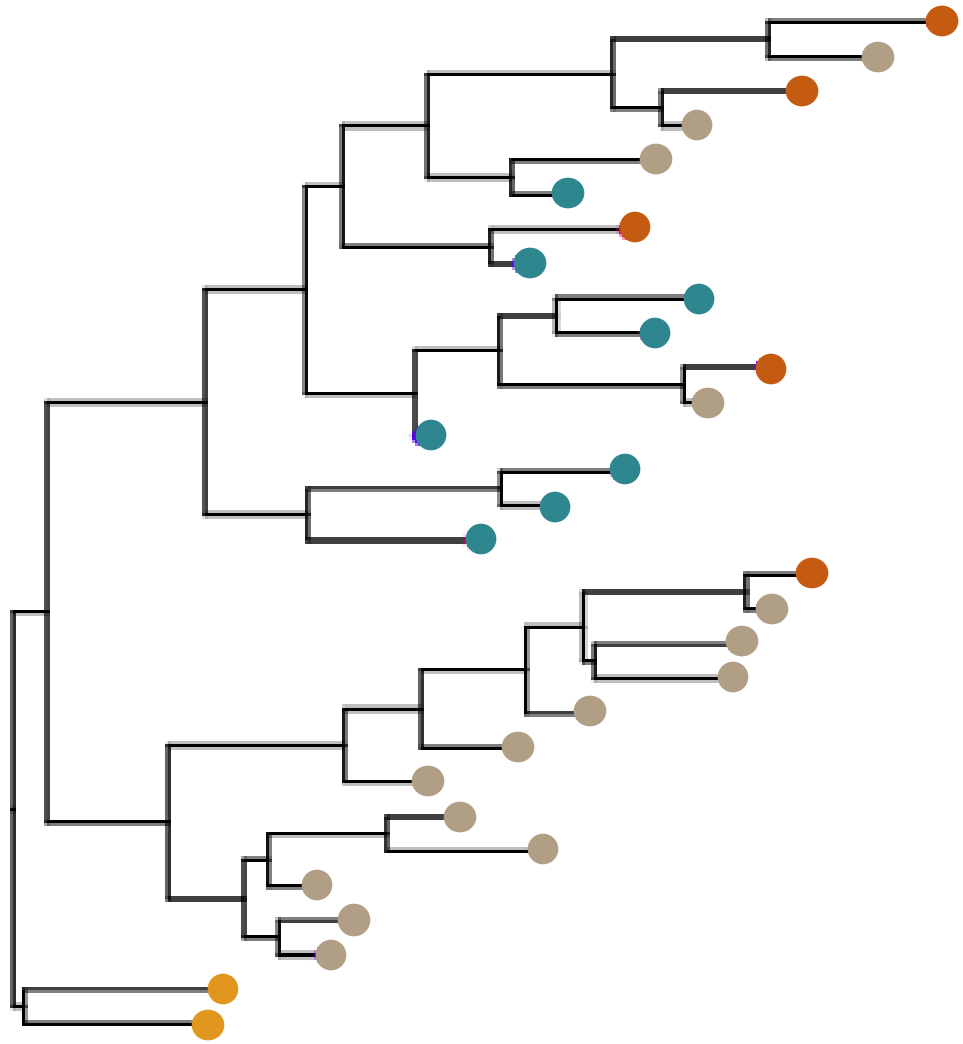


Assemble genomes



Notable deletion in one bacterial chromosome

Bruntella WGS Phylogeny

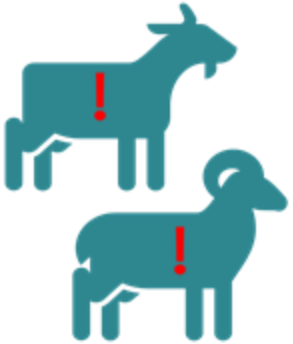


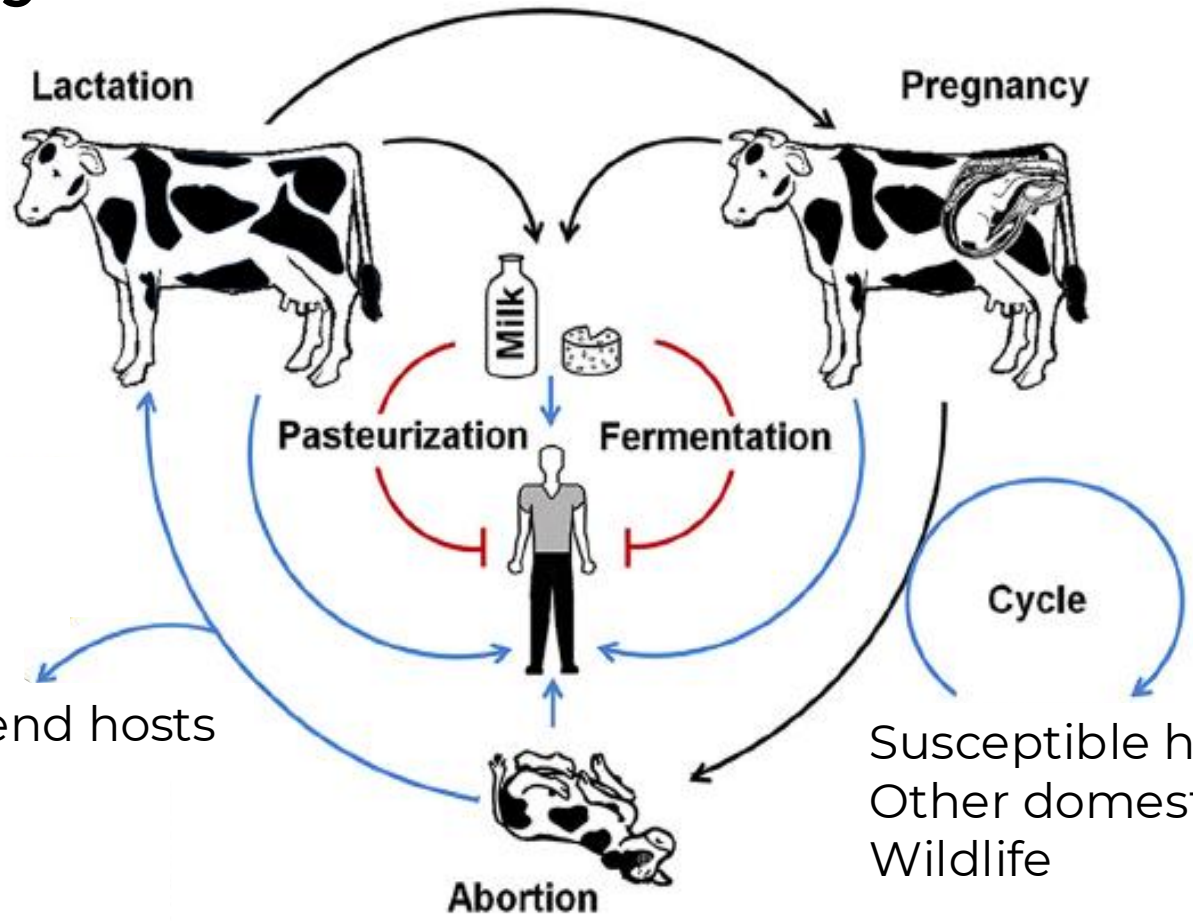
Specimen Source

What preliminary conclusions can be drawn from these results?

How might this change your surveillance & intervention efforts?

What role could cross-species transmission play?





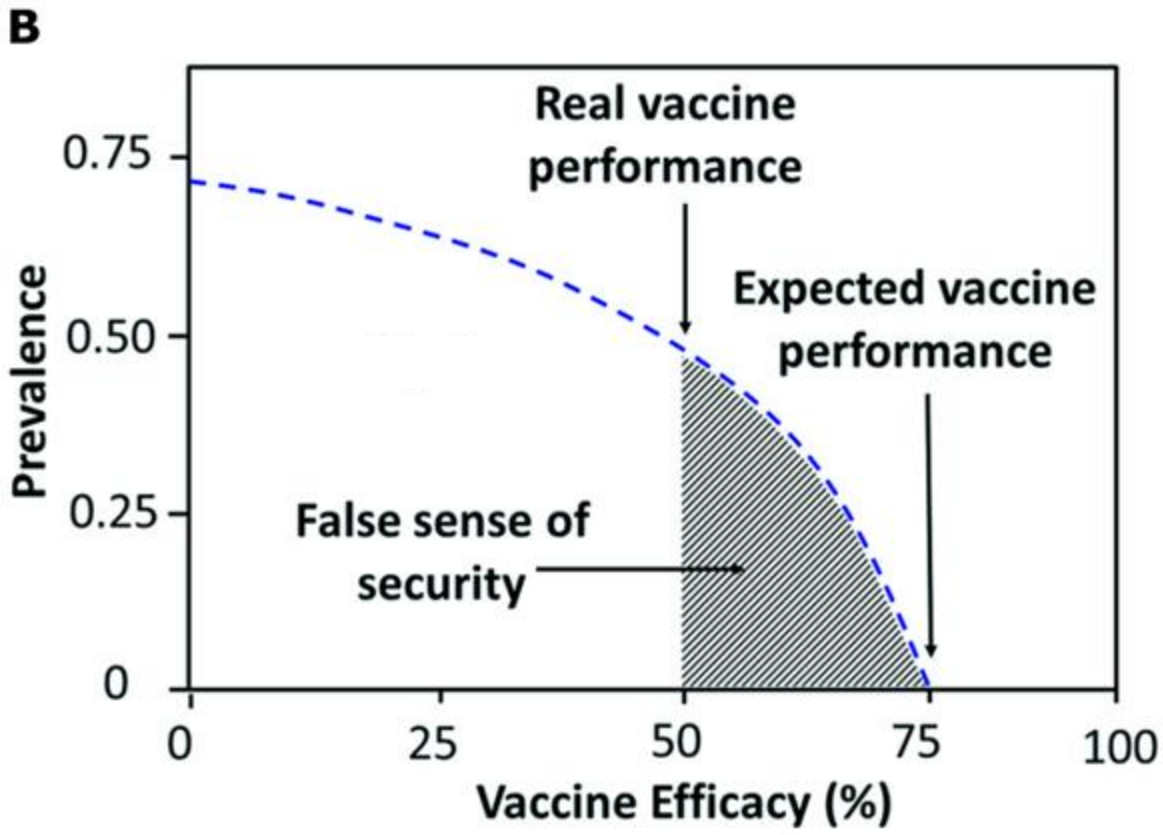
Dead end hosts

Susceptible hosts:
Other domestic animals
Wildlife

Modified from Moreno, 2014

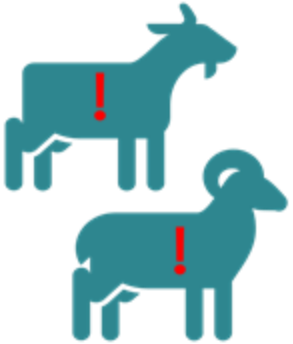
Monitoring Vaccine Effectiveness

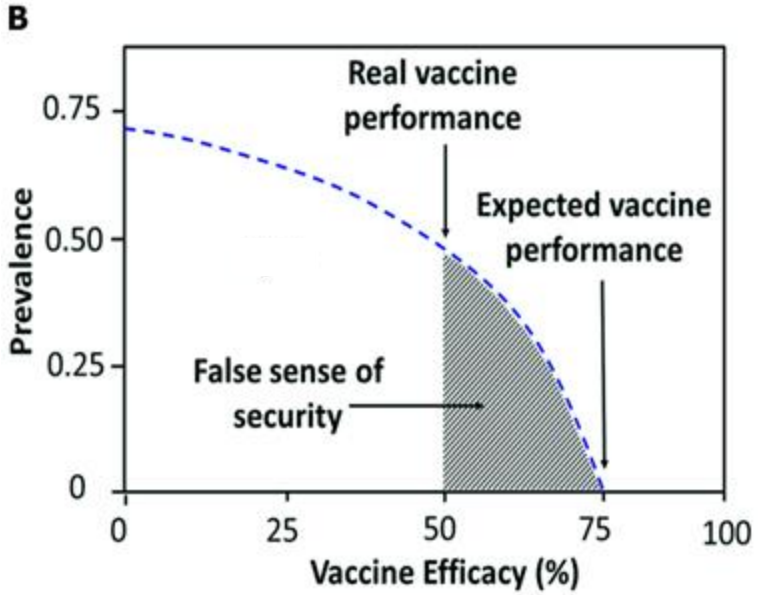
Cattle vaccines are for B. bovis

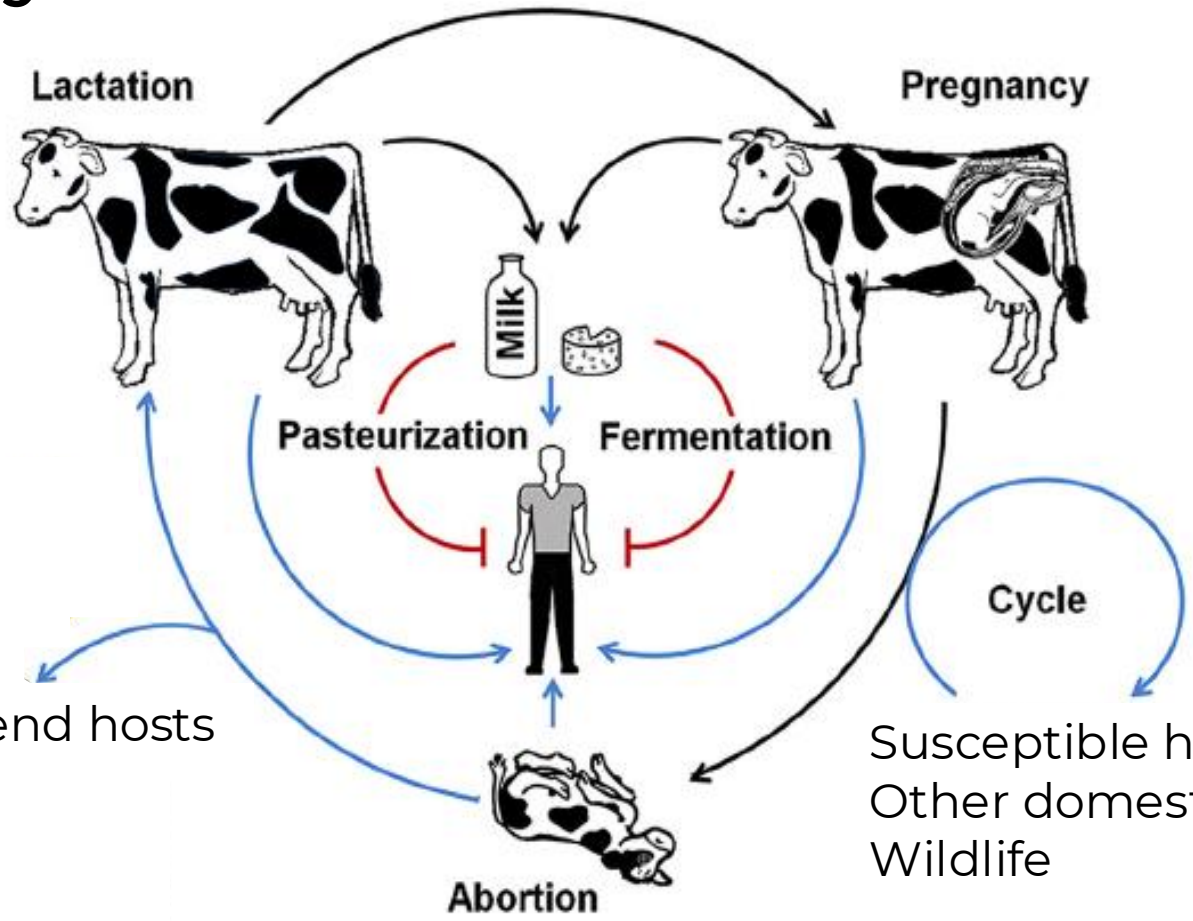


Moreno, 2014

What role could cross-species transmission play?







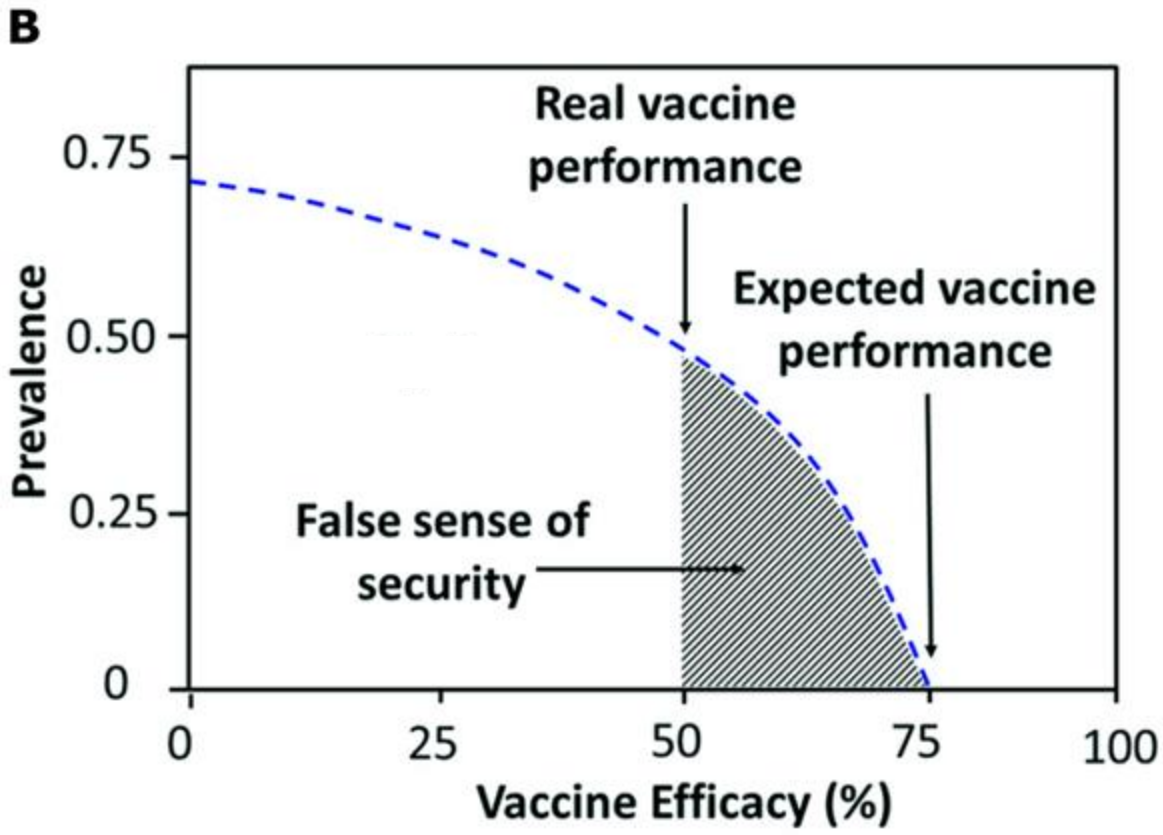
Dead end hosts

Susceptible hosts:
Other domestic animals
Wildlife

Modified from Moreno, 2014

Monitoring Vaccine Effectiveness

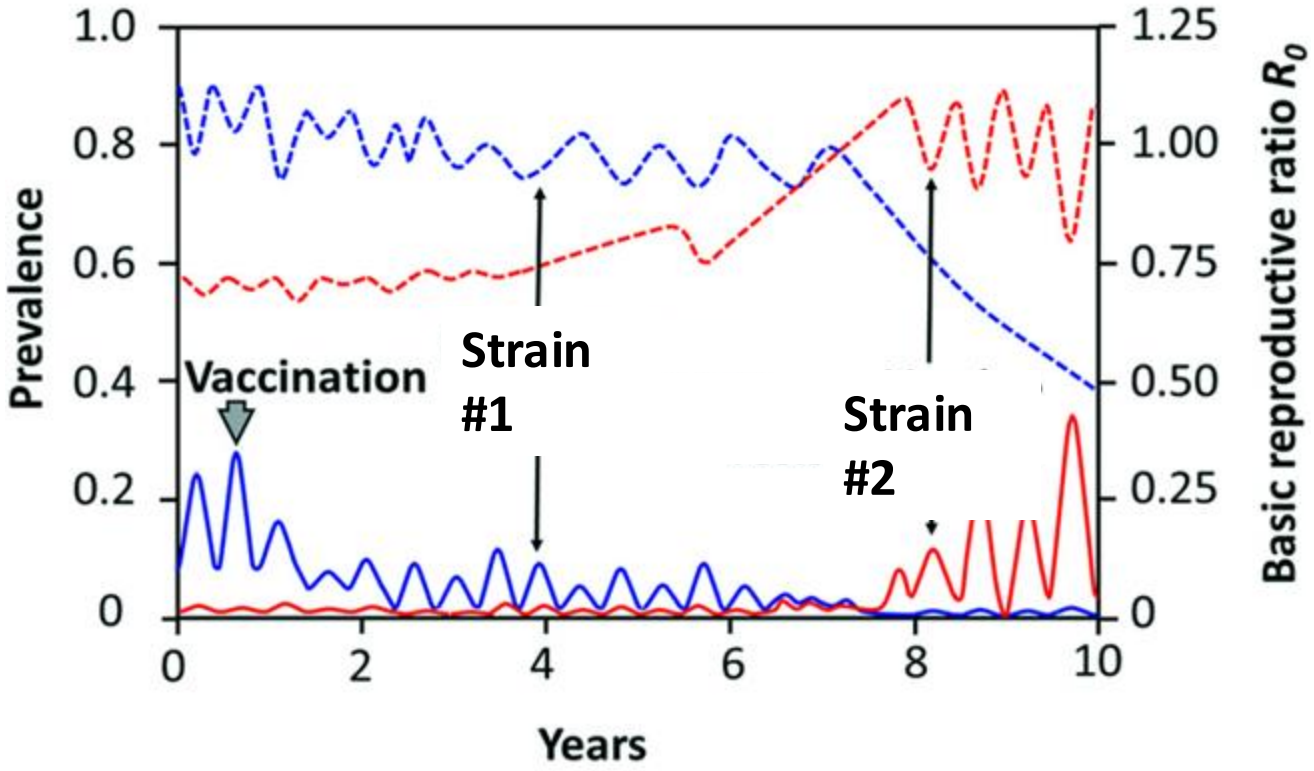
- Is vaccine effectiveness the same in different hosts?
- Does it provide protection against multiple species of *Bruntella*?
- How effective is it against different bacterial strains?
- Which hosts/populations should be vaccinated to have the biggest reduction in to humans transmission?



Moreno, 2014

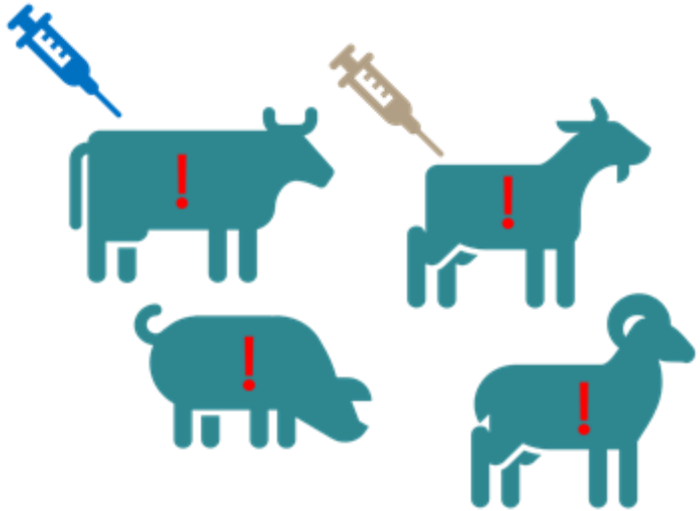
Monitoring Vaccination - Diversity

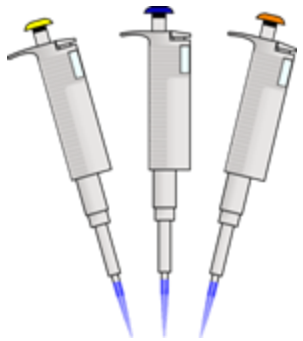
- Vaccine effectiveness
- Changes in strain/species abundance over time

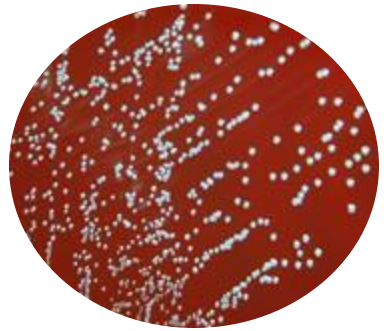


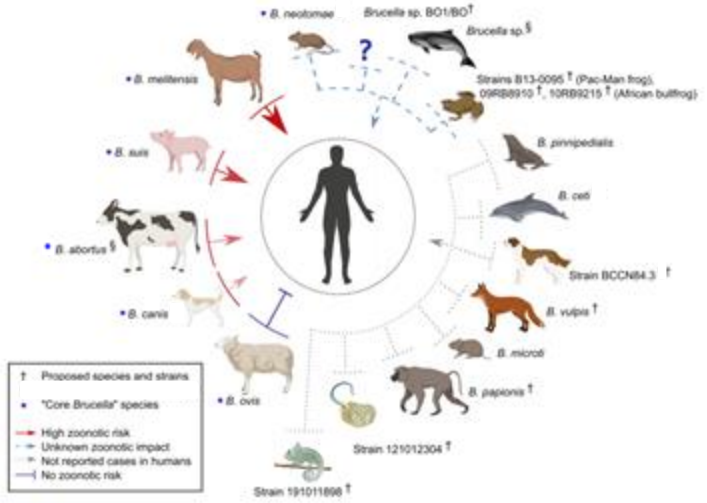
Moreno, 2014

The end ☺








B. neotomae
Brucella sp. BO1/BO†
Brucella sp.§
B. melitensis
Strains B13-0095 † (Pac-Man frog),
09RB8910 †, 10RB9215 † (African bullfrog)
B. suis
B. pinnipedialis
B. ceti
B. abortus §
Strain BCCN84.3 †
B. canis
B. vulpis †
B. microti
B. ovis
B. papionis †
Strain 121012304 †
Strain 191011898 †
† Proposed species and strains
• "Core Brucella" species
High zoonotic risk
Unknown zoonotic impact
Not reported cases in humans
No zoonotic risk

THANK YOU!

WORKSHOP PARTNERS

CDC
U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

DukeNUS Medical School
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)