

# *Assessing biological exposures in the omics era*

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*The One Health concept is an interdisciplinary approach that recognizes the interconnectedness of human health, animal health, and environmental health*



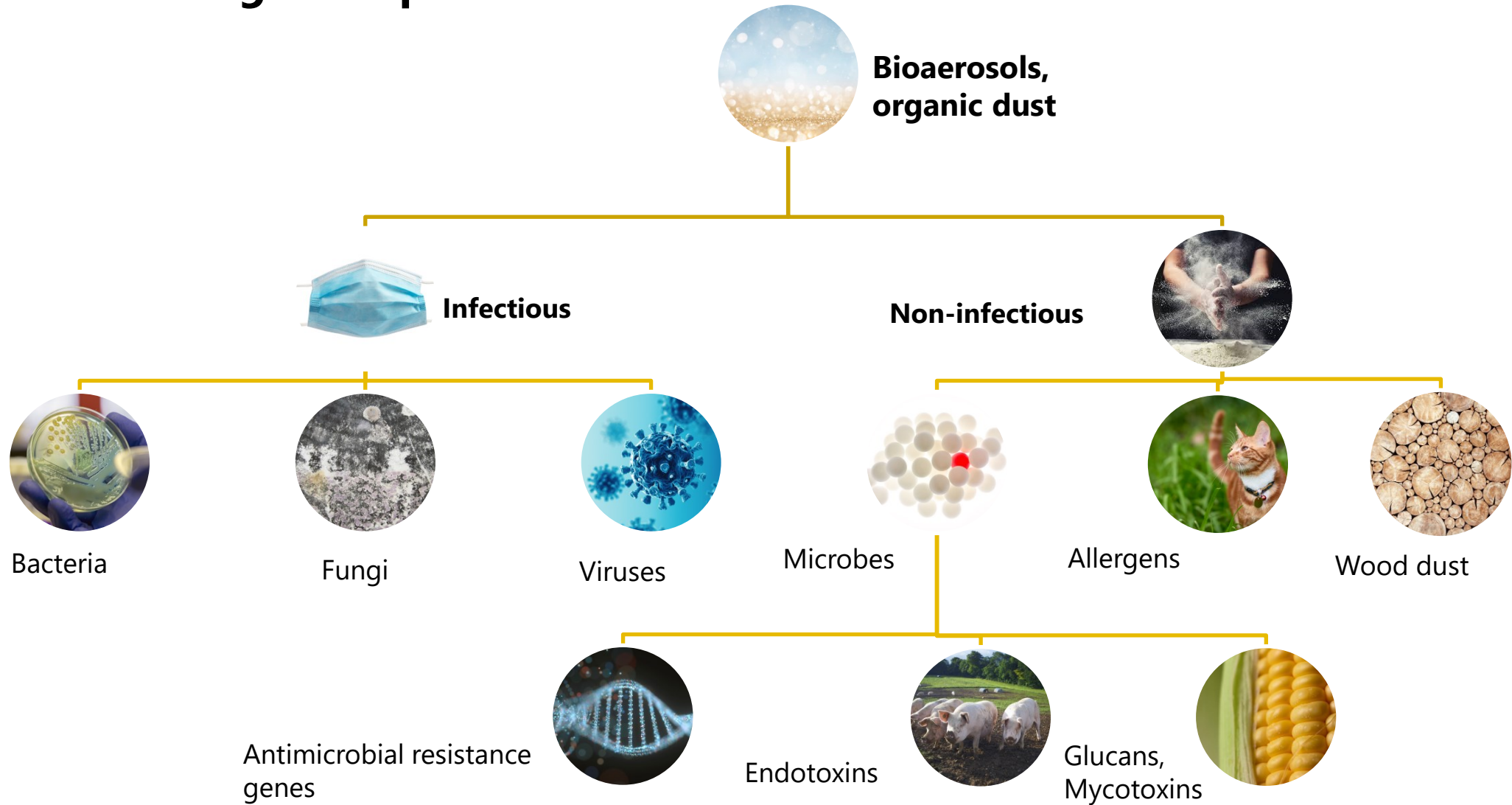




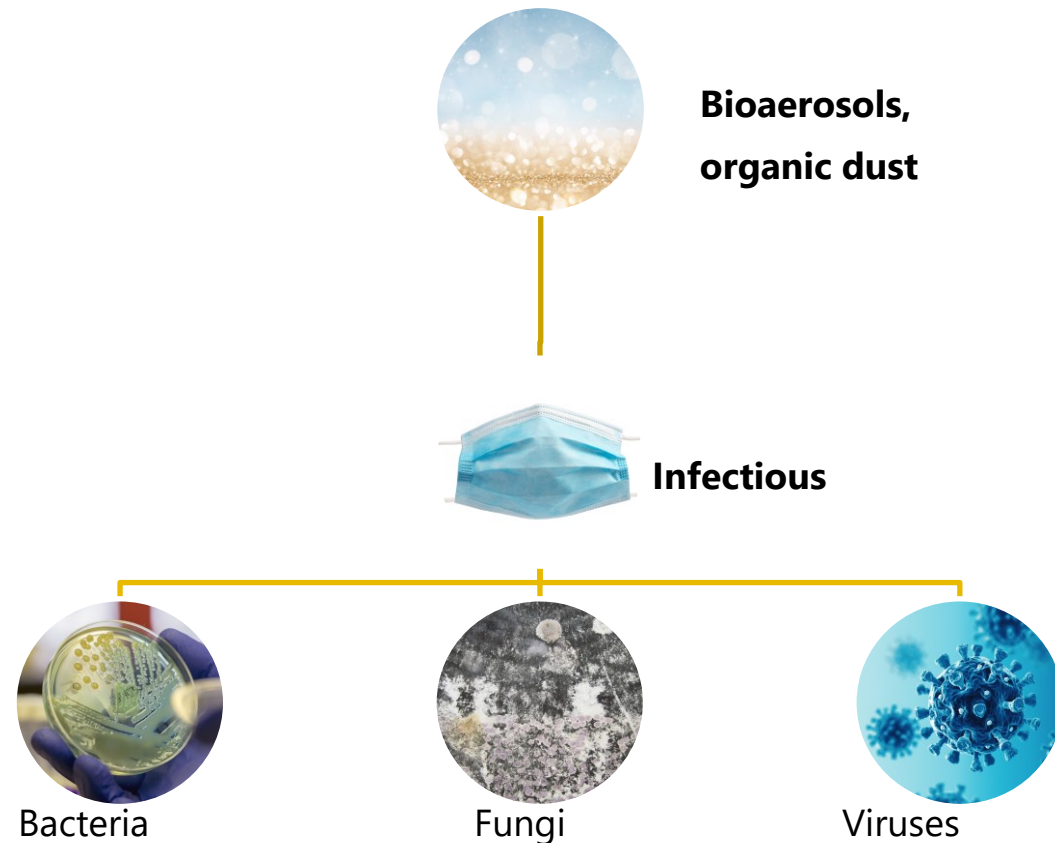




# The Biological Exposome



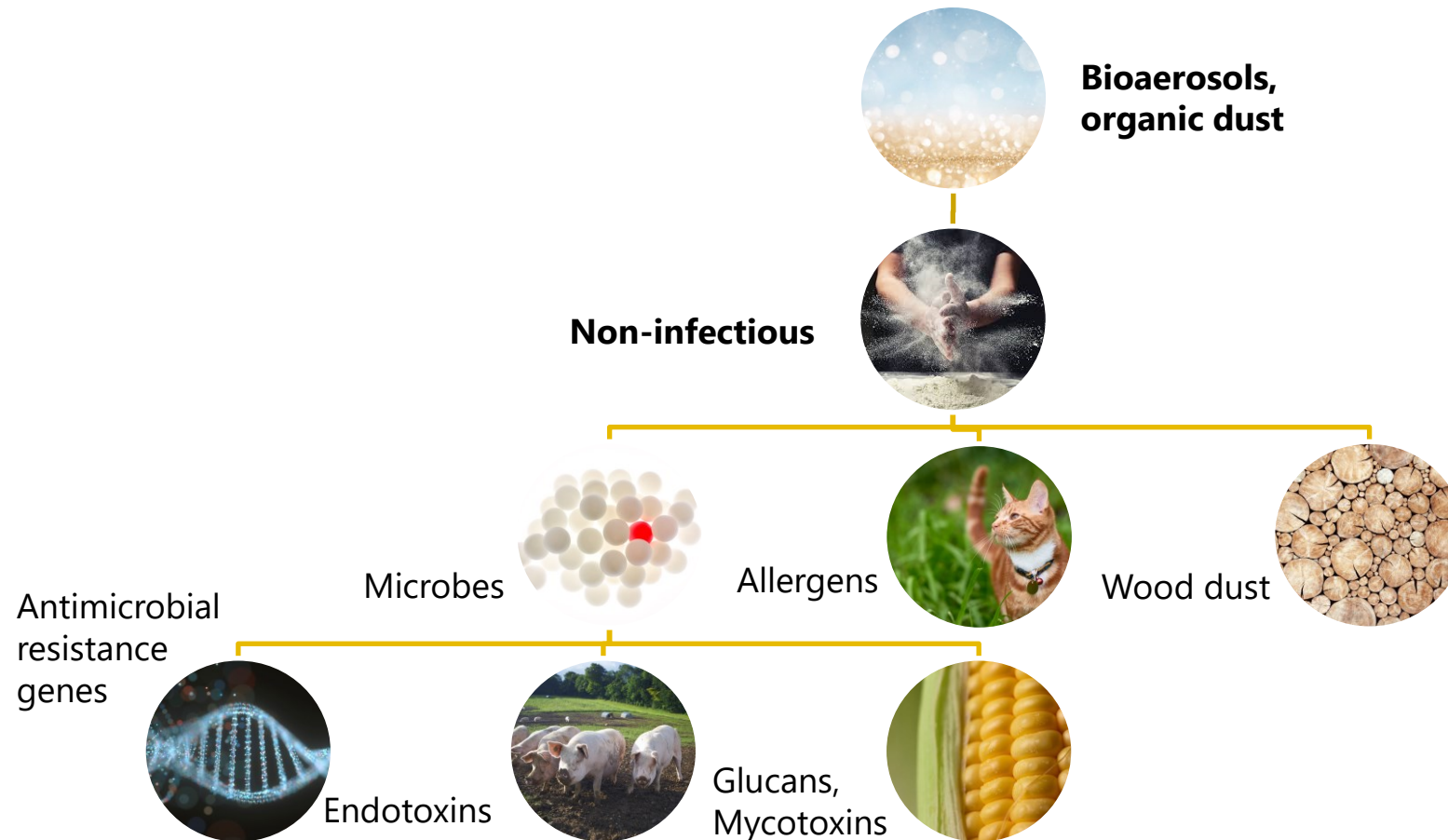
# The Biological Exposome: Health Effects



## Infectious diseases

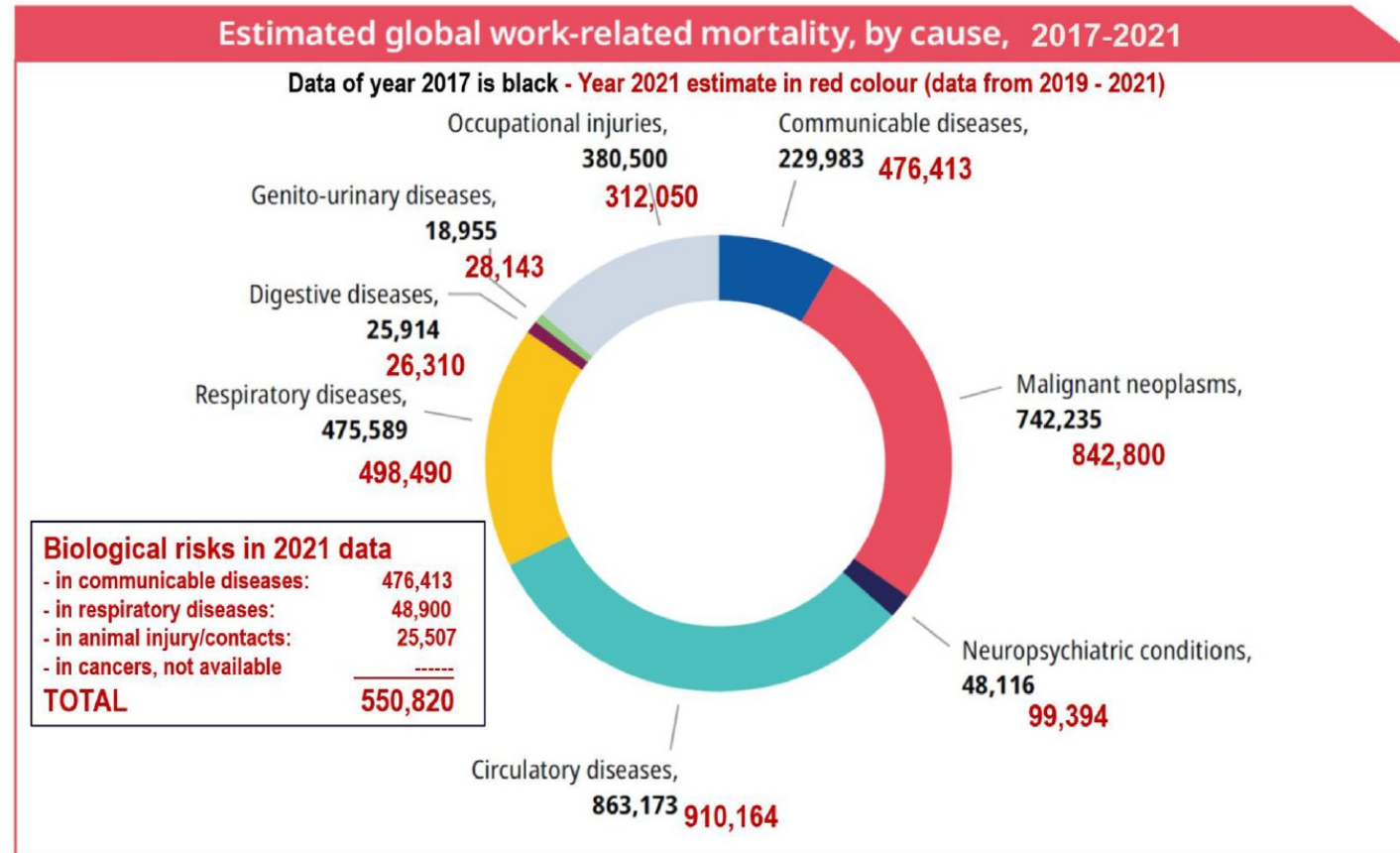
e.g. COVID-19, influenza, tuberculosis, MRSA, aspergillosis, Q-fever, Legionnaires' disease

# The Biological Exposome: Health Effects



- **Asthma**
- **Allergy**
- **COPD**
- **Hypersensitivity pneumonitis**
- **ODTS**
- **Cancer**

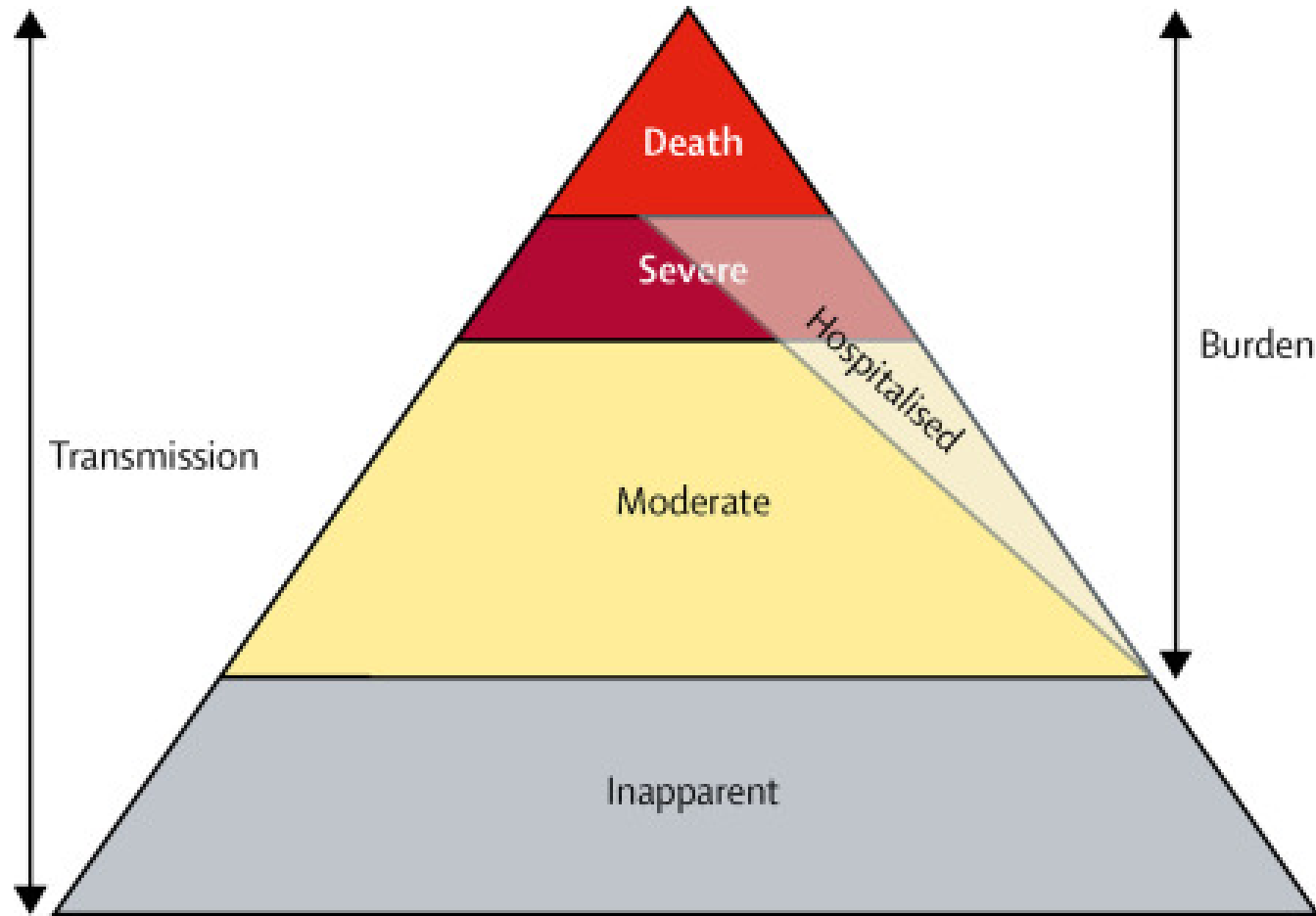
# Mortality due to hazardous biological agents at the workplace



**Biological Risks: Mortality > 500,00 per year**



**Mortality due to infectious diseases within the working population is relatively rare, absence from work is common**



# Biological and chemical exposures interact in occupational and environmental health



Welding fumes and lower airway infection with *Streptococcus pneumoniae*



Respirable crystalline silica exposure and tuberculosis



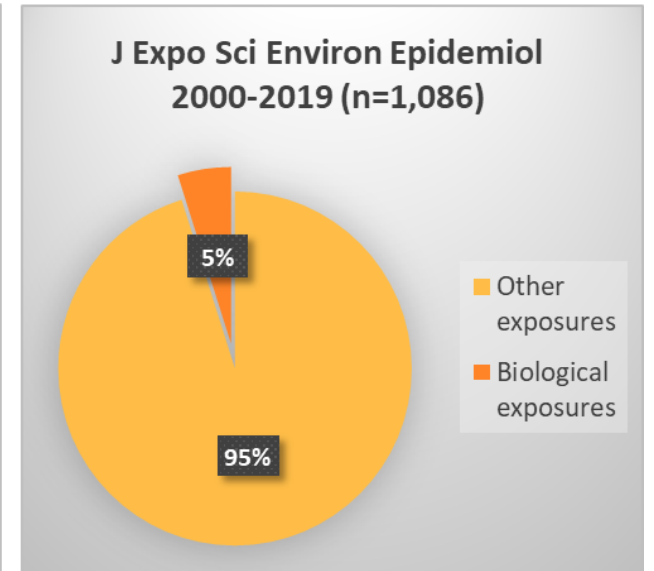
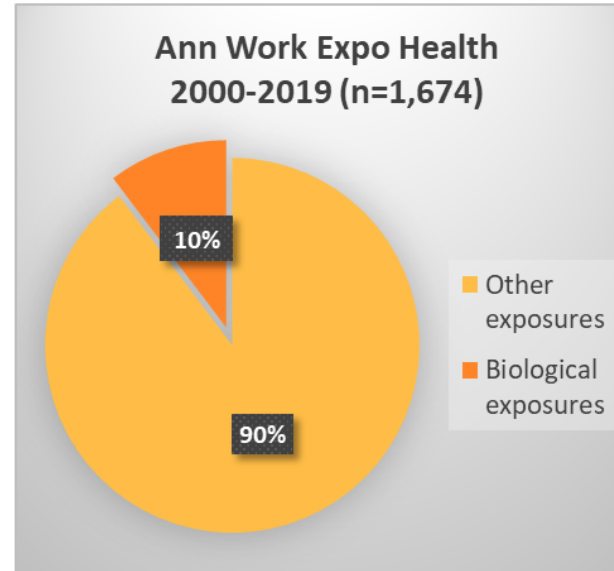
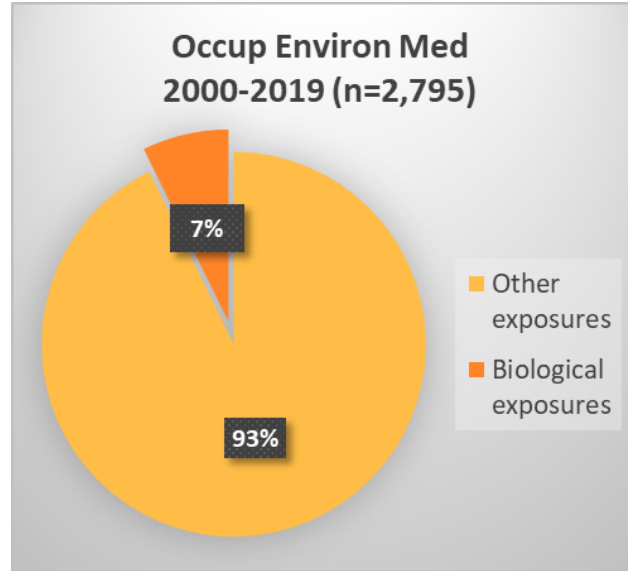
Indoor air pollution and severe lower respiratory tract infections



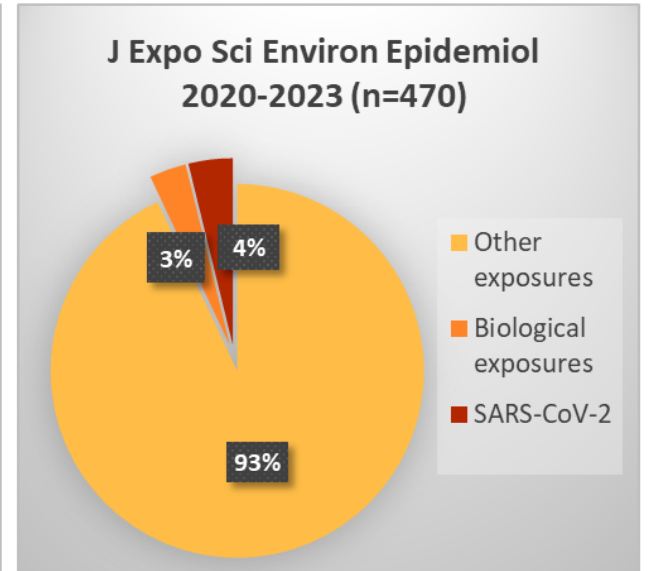
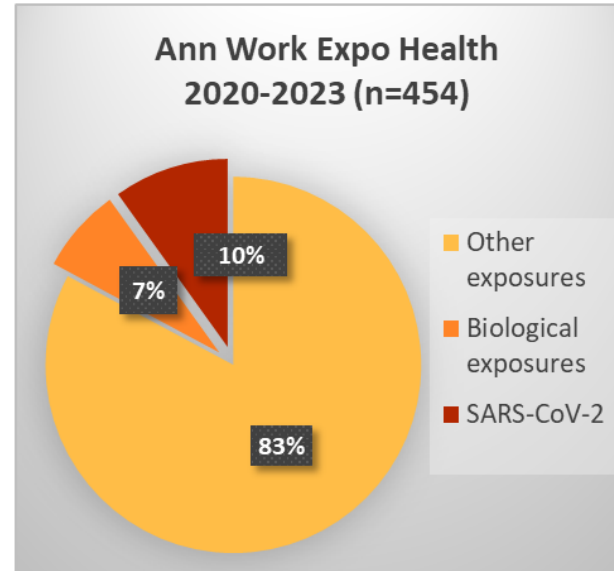
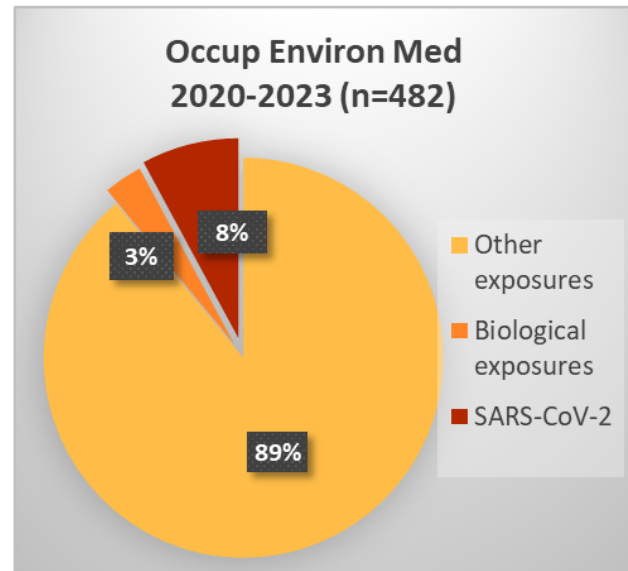
Outdoor air pollution and COVID-19 severity

# Proportion of articles concerning biological exposures\*

2000 – 2019



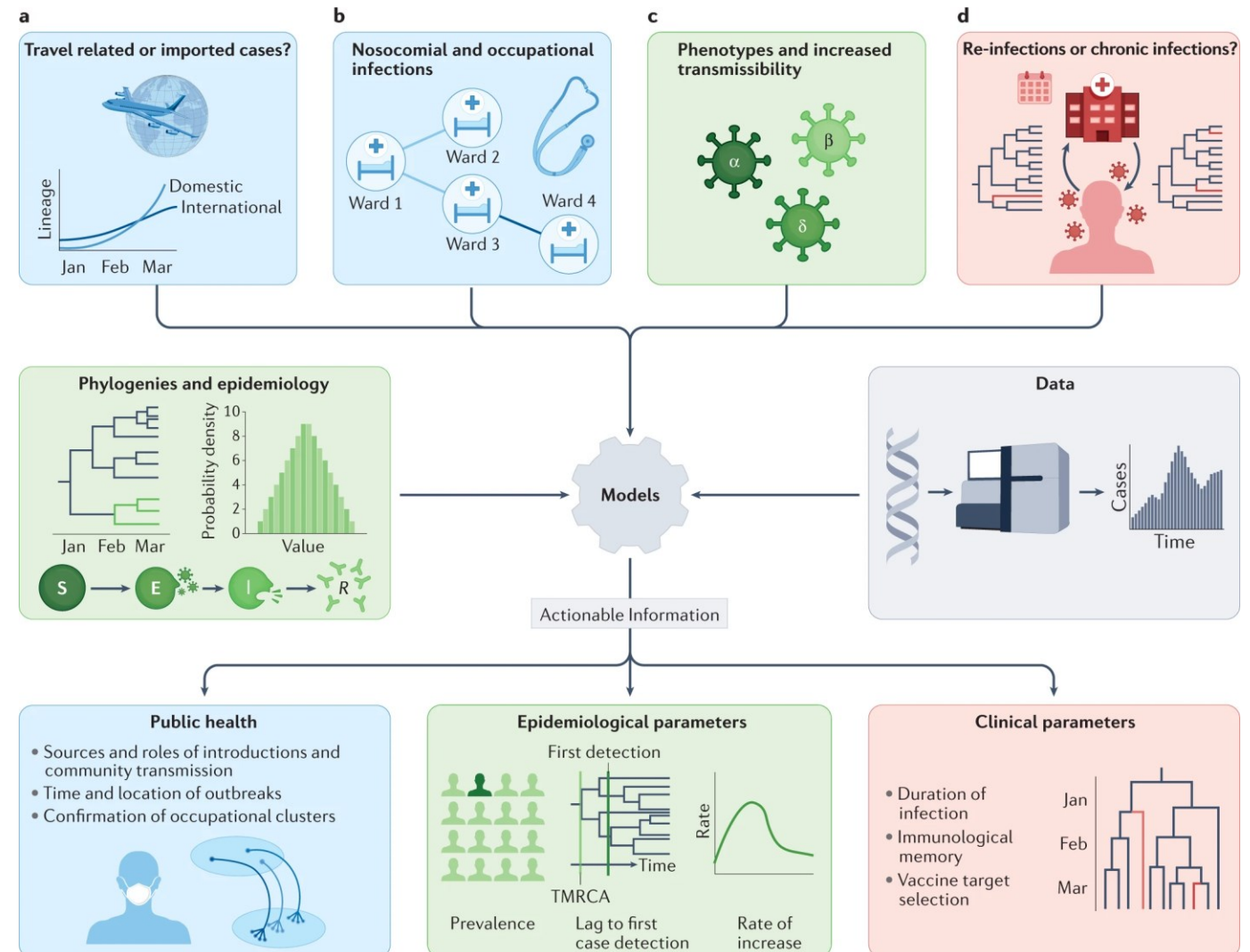
2020 – 2023



\* A broad search term was used to capture exposure to bacteria, fungi, viruses, microbiome, bioaerosols, mycotoxins, endotoxins, and allergens

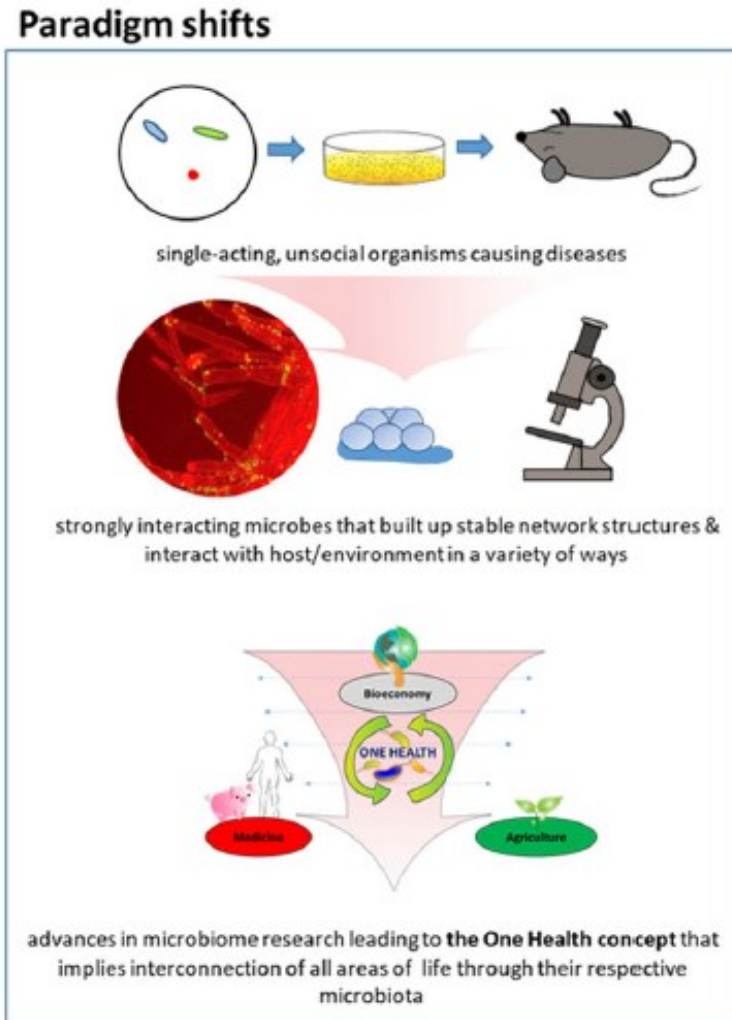
# COVID-19: Increased attention for biological exposure assessment

- Optimal air sampling and analysis methods for airborne viruses?
- **Whole genome sequencing, phylogenetic trees, transmission routes**
- Interventions, prevention, preparedness





# Development of molecular methods: increased attention for microbial exposures



**1670**

Discovery micro-organisms, pathogens

**End 19<sup>th</sup> century**

Microbial ecology, beneficial micro-organisms

**End 20<sup>th</sup> century**

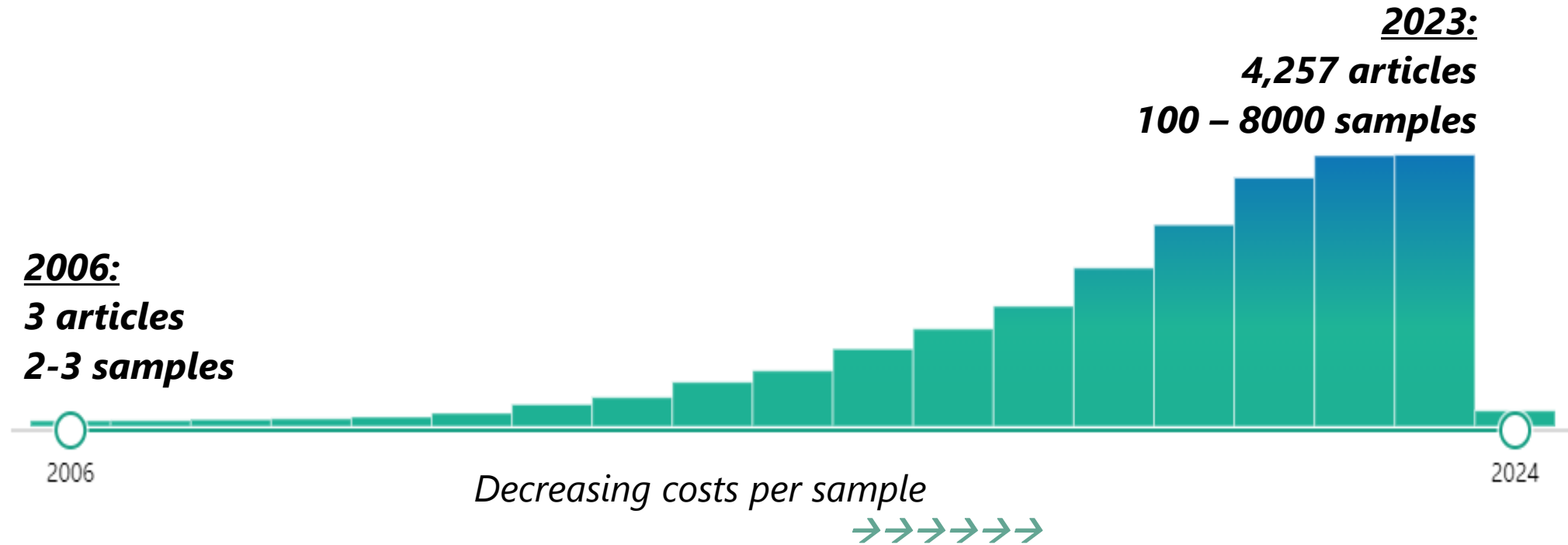
Molecular biology

**21<sup>st</sup> century**

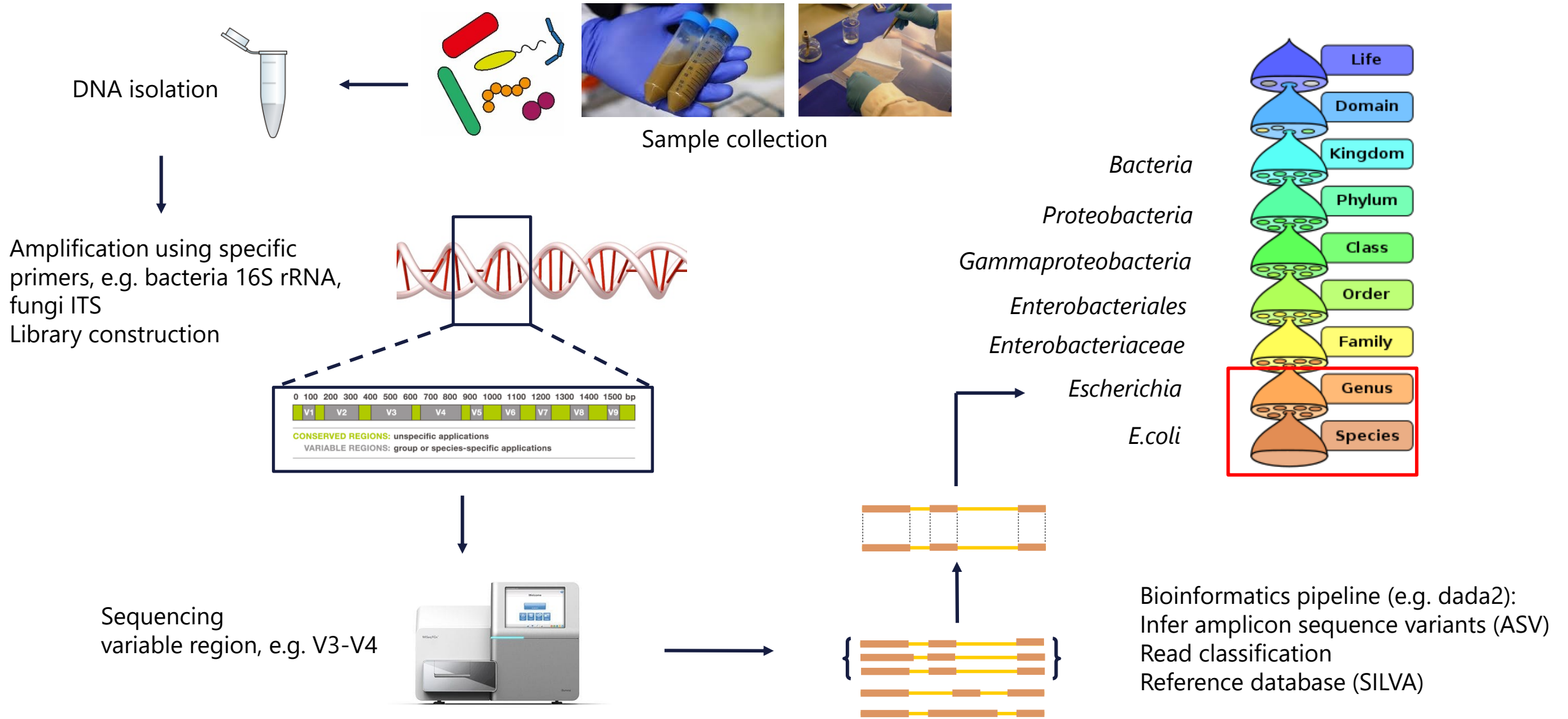
Microbiome, One Health concept

# High throughput sequencing: increased attention for microbial exposures

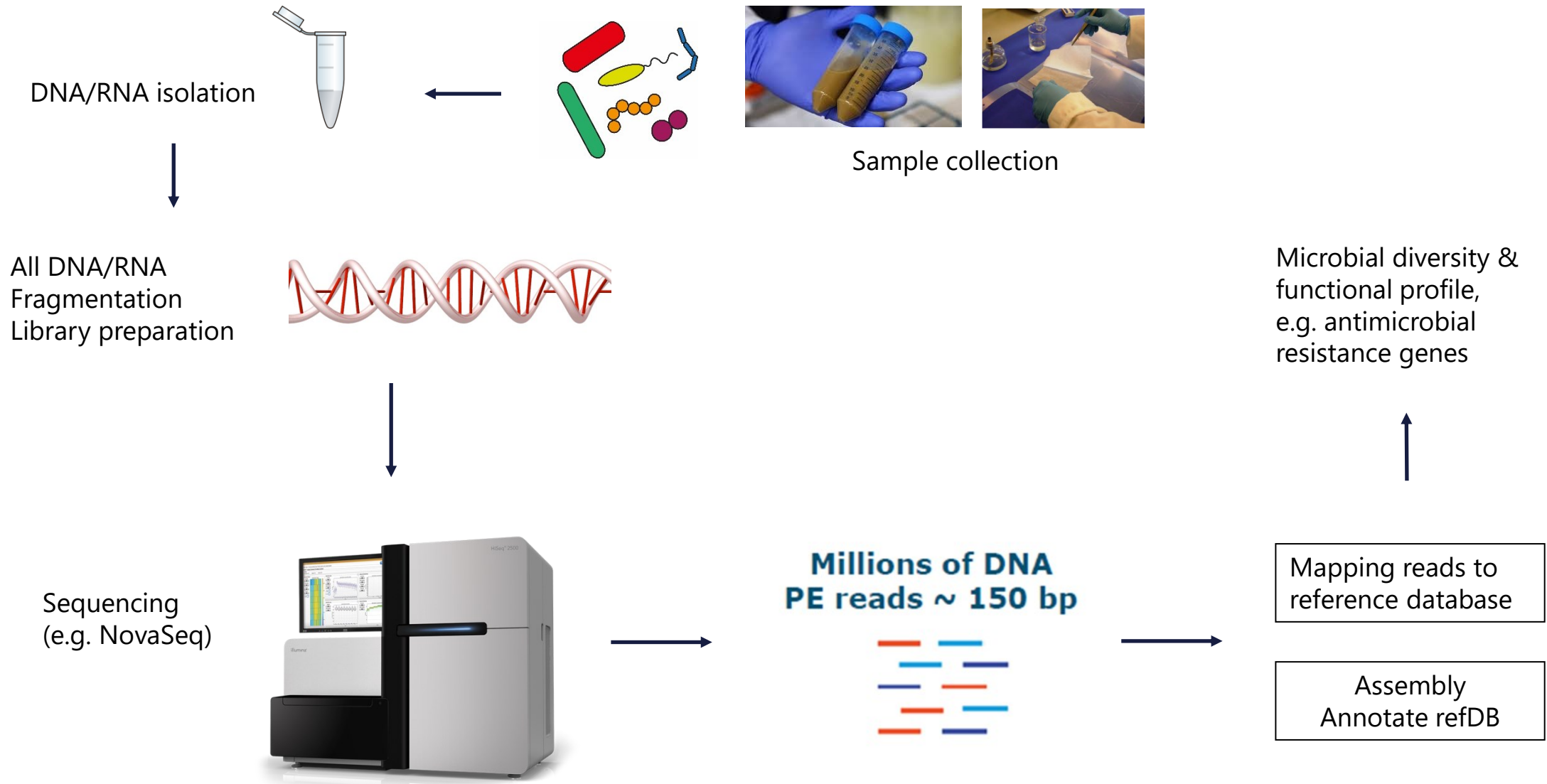
Over 22,500 articles with 'Microbiome' in the title since 2006



# 16s rRNA, ITS Amplicon sequencing

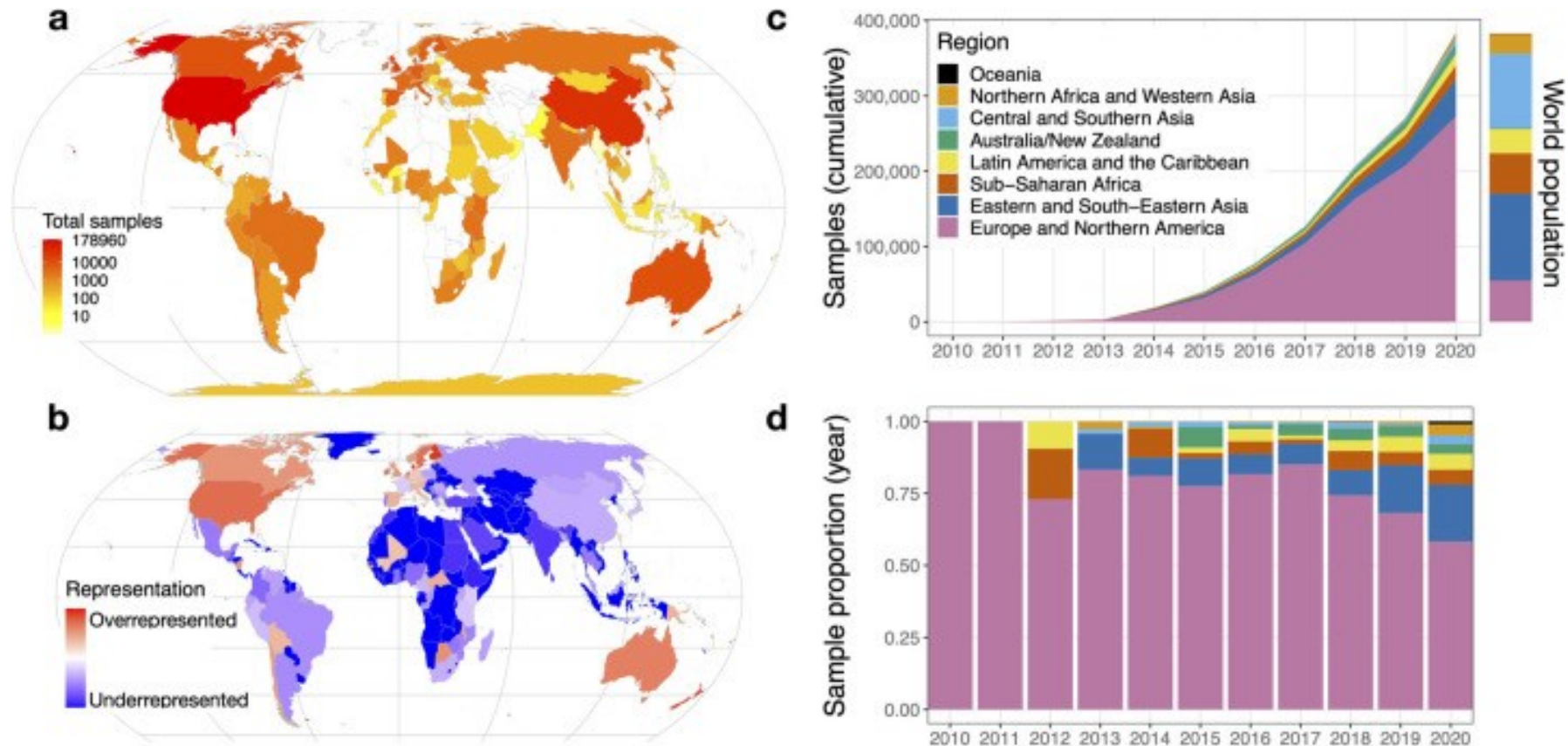


# Shotgun metagenomic sequencing





# Public human microbiome data are dominated by highly developed countries



## Assessing biological exposures using sequencing: different study aims

- Describe composition, function, and determinants of the biological exposome
- Explore biological agents as risk factors for disease
- Investigate outbreaks
- Surveillance, detection of novel variants



# Antimicrobial resistance in the food chain

Shotgun metagenomics: microbiome & resistome

- Farmers, slaughterhouse workers



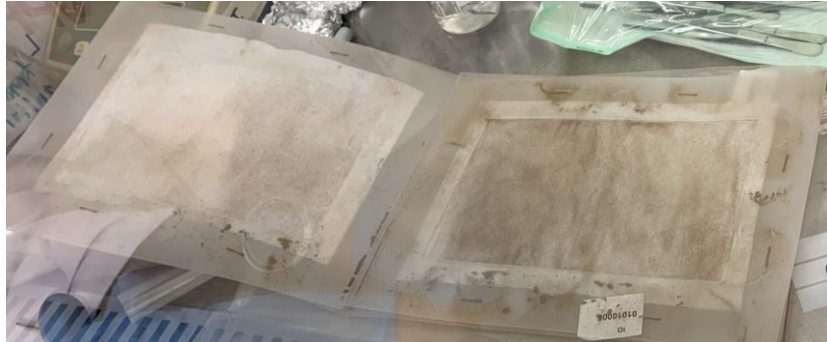
- Pigs, poultry, veal calves...



- Air, dust, surfaces

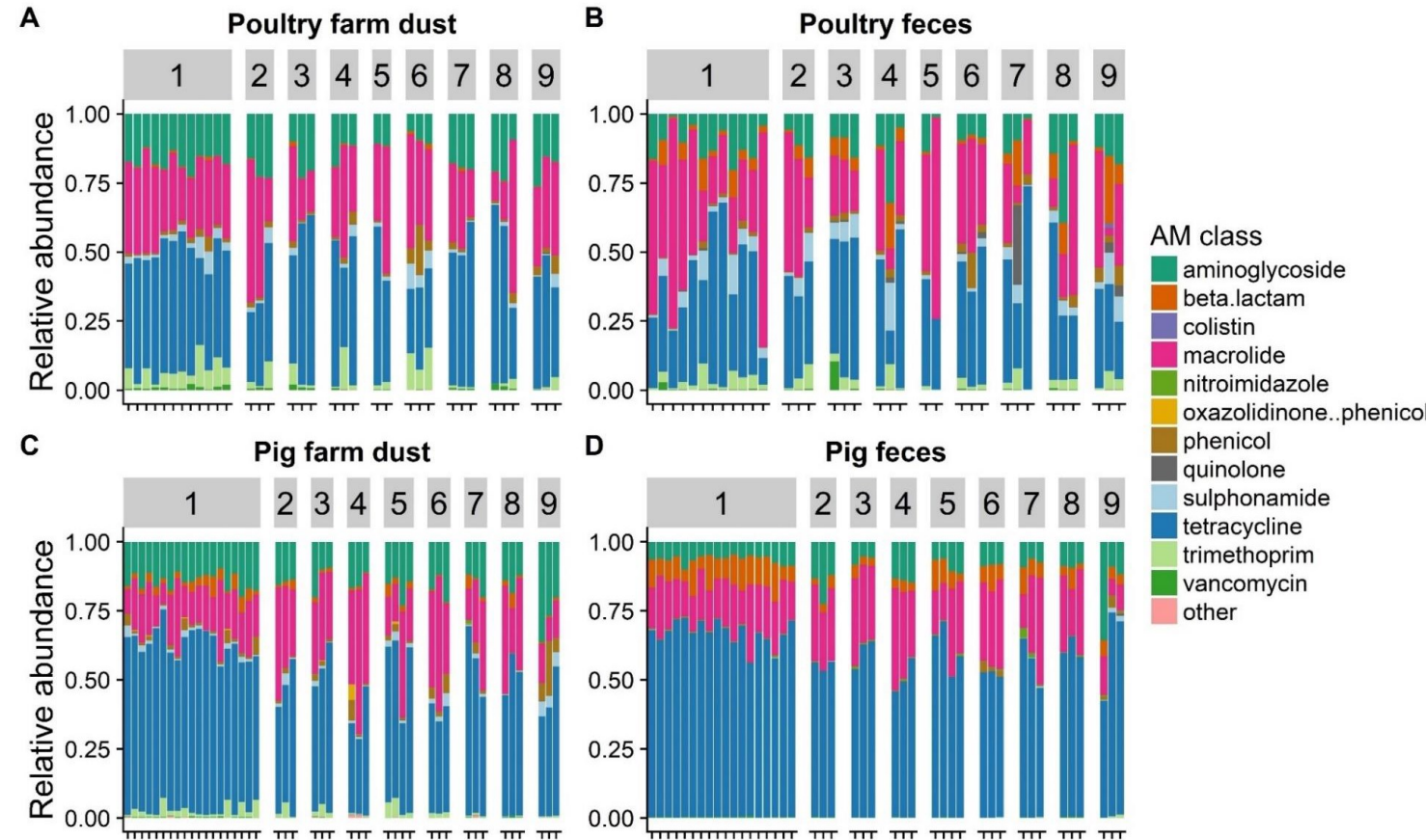


# AMR abundance and composition in pig and poultry farm dust



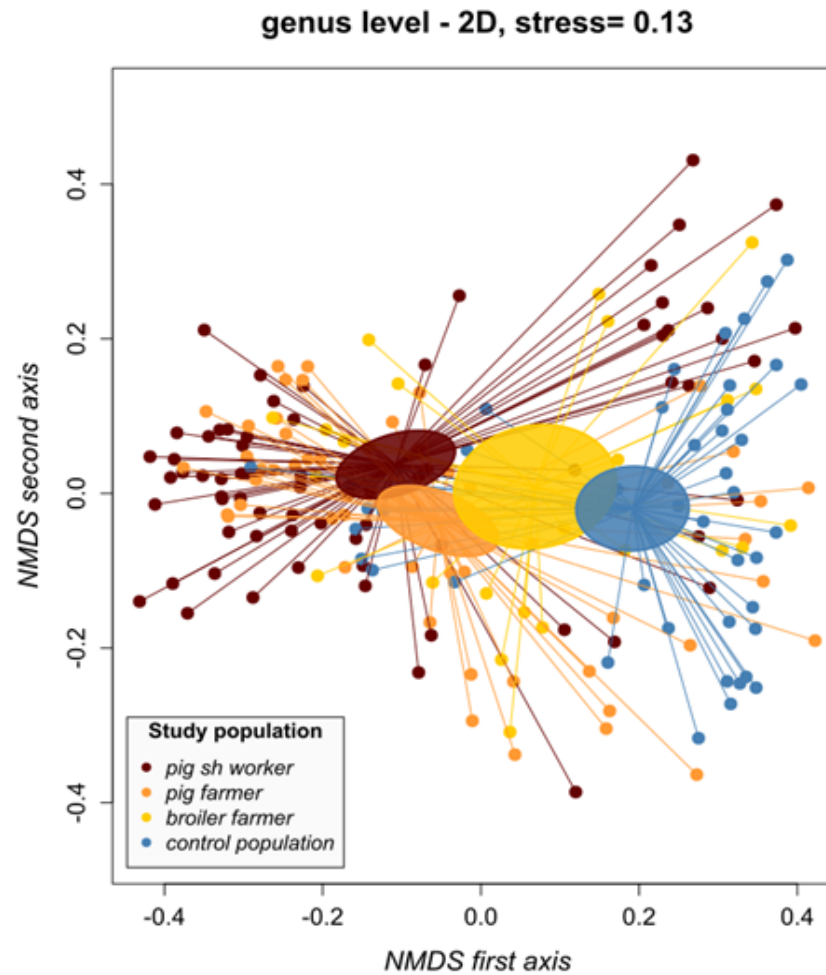
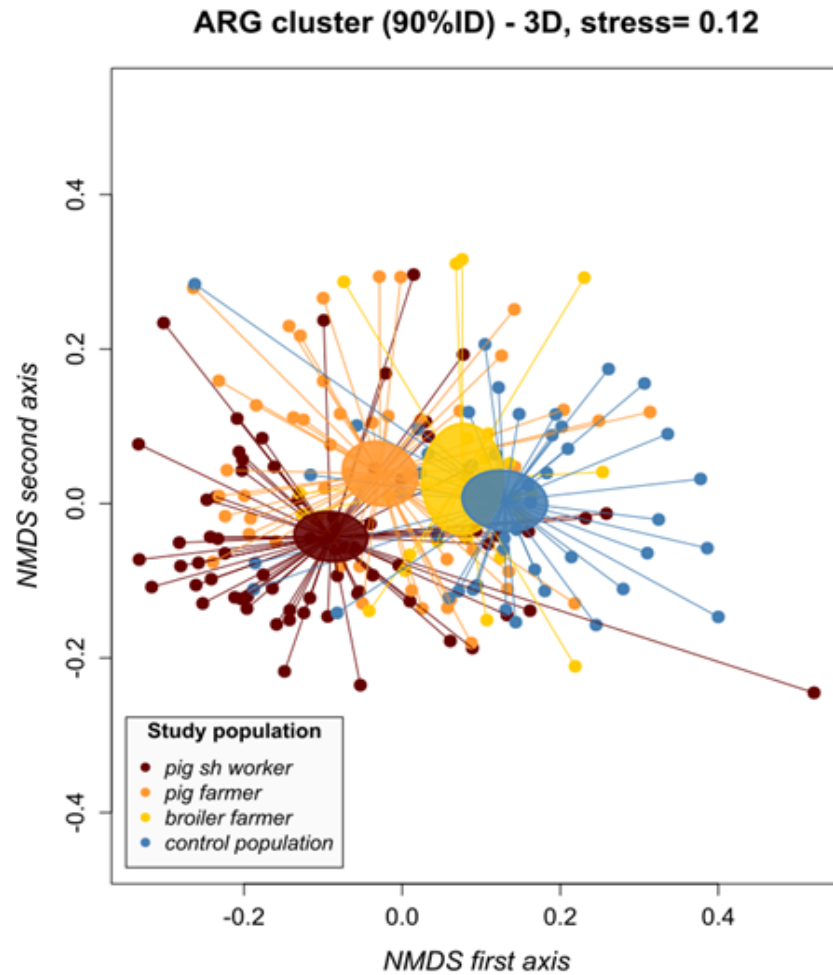
## The farm dust resistome is:

- equally or more abundant and rich than the resistome of poultry and pig feces.
- clearly, but not only, determined by the animal fecal resistome from the animals in the same stable and by the underlying farm dust bacterial microbiome.
- more abundant if antimicrobial usage on the farms is higher.



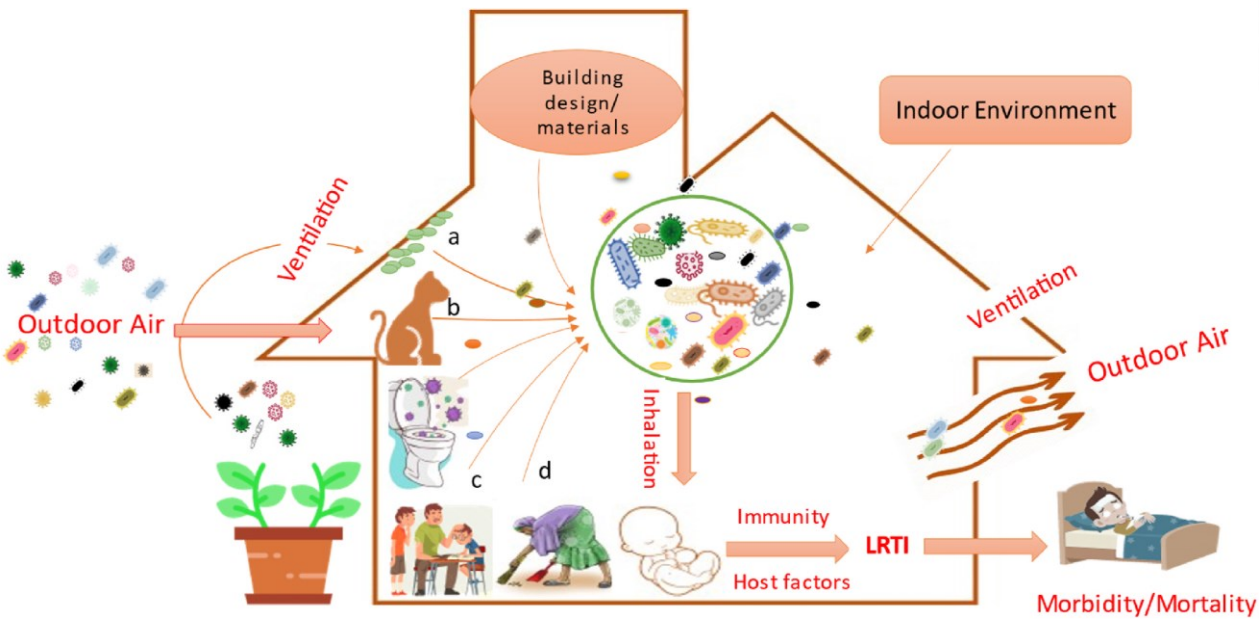


# Human faecal resistome and bacteriome

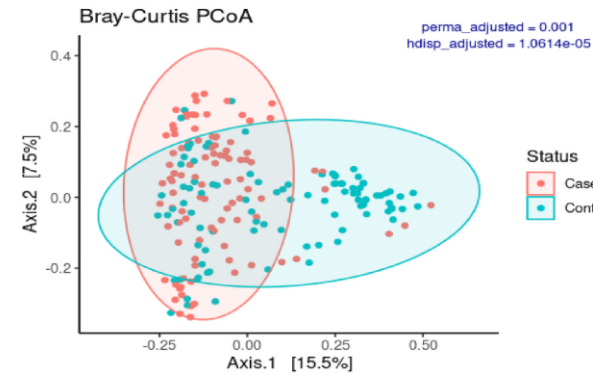


- Ellipses represent the 95% standard error of the centroid per group
- Independent of individual antibiotic use

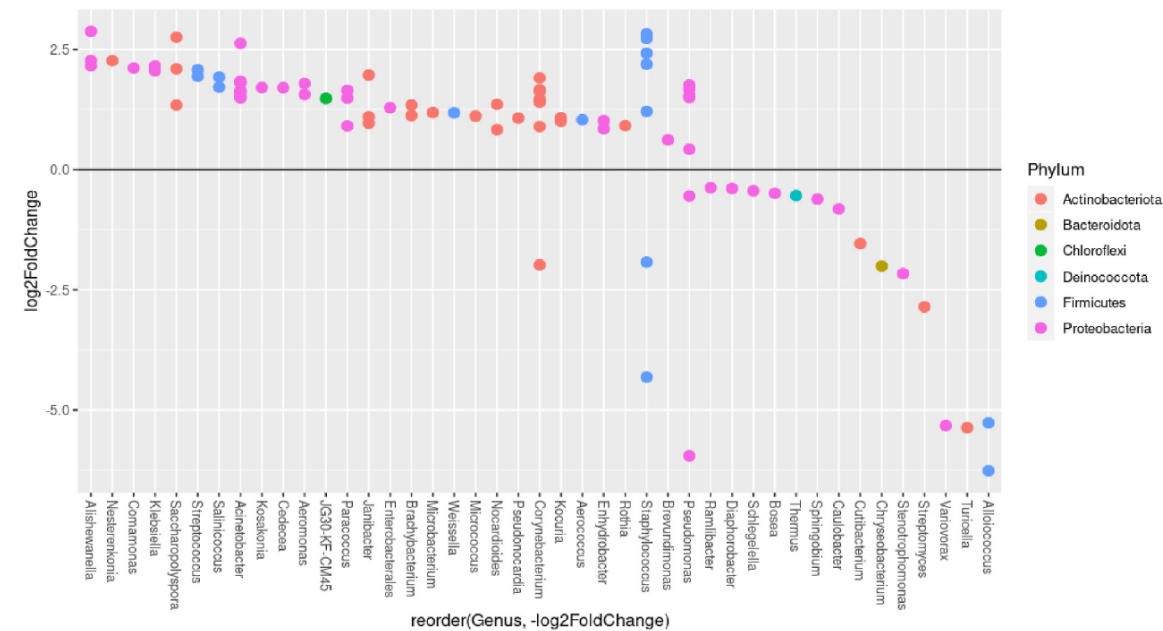
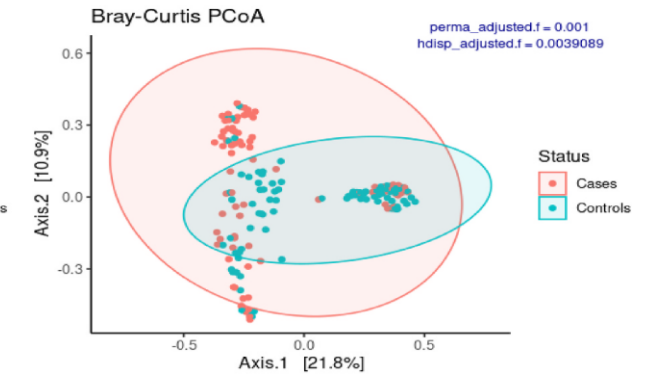
# Residential airborne Bacteriome and Mycobiome in Nigerian children, linked to severe lower respiratory tract infections



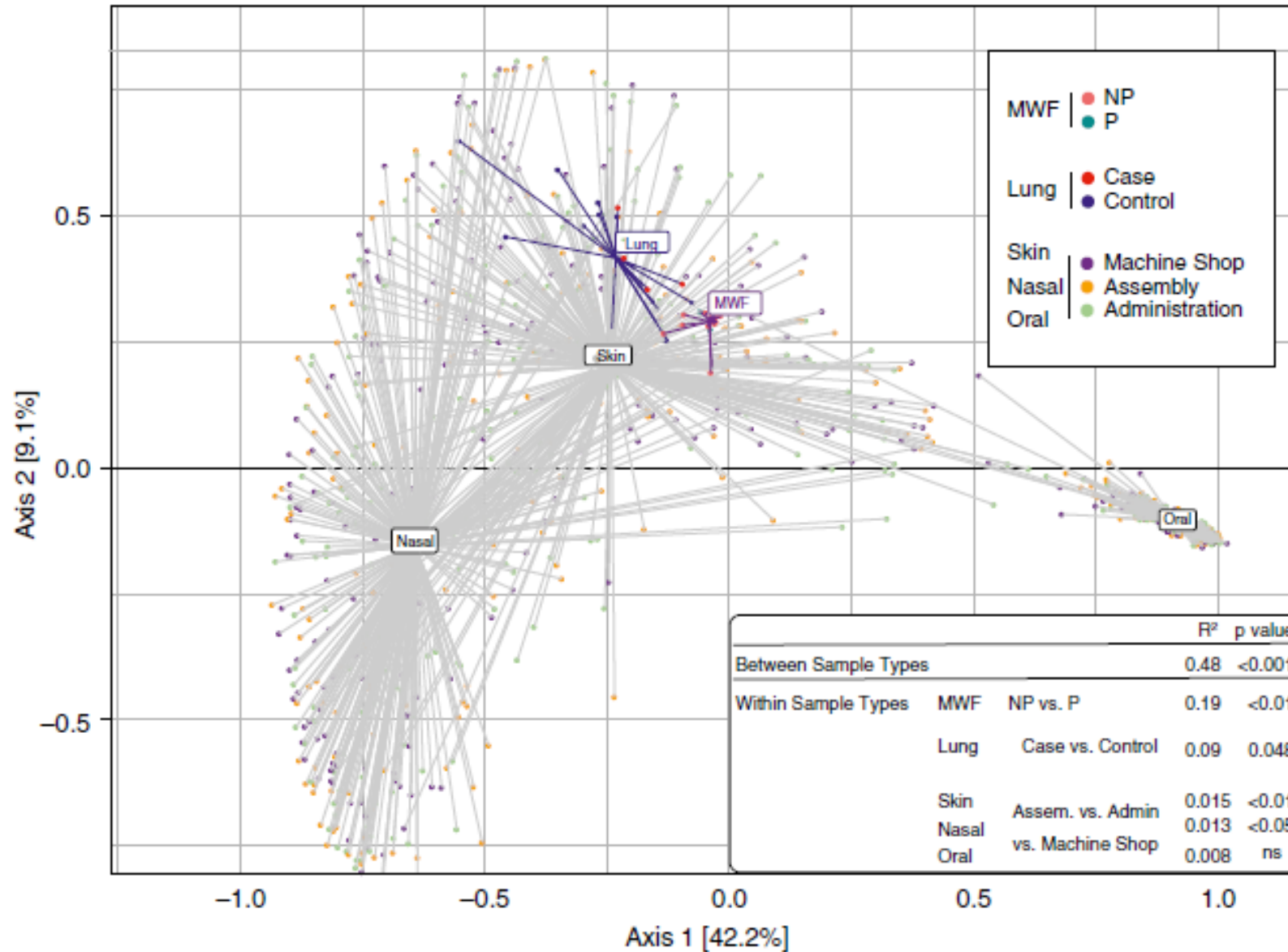
(A) Bacteria



(B) Fungi



# Metal working fluids, cluster of unexplained respiratory conditions

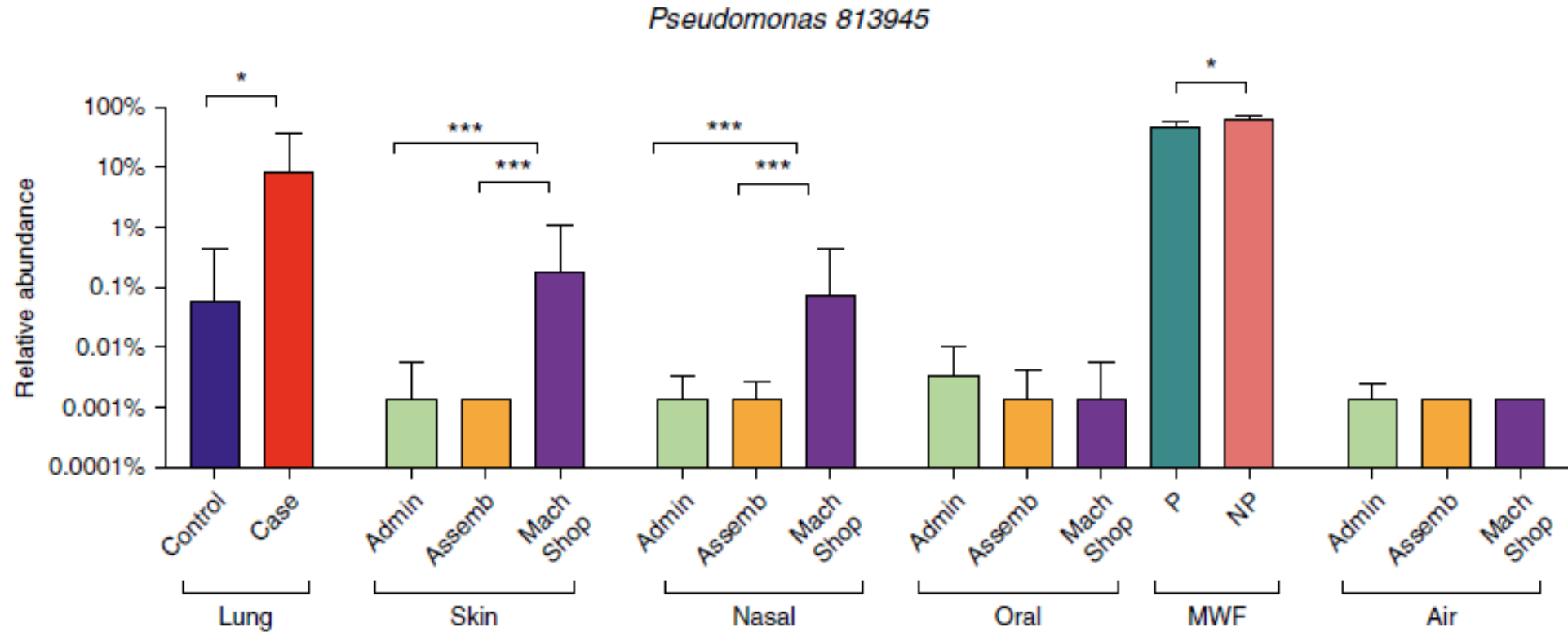


Beta-diversity  
Bacteriome lung tissue, MWF,  
etc

MWF and patients more similar  
than MWF and controls (lung)

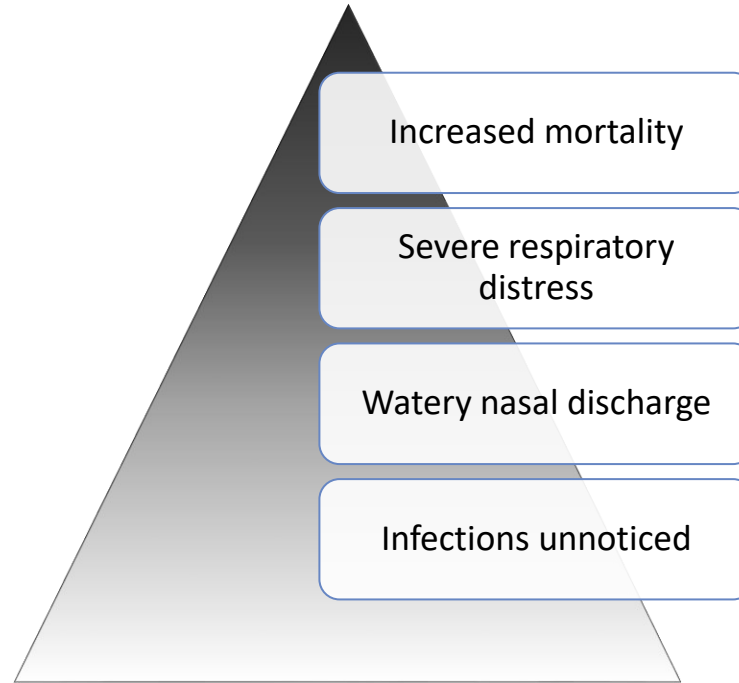
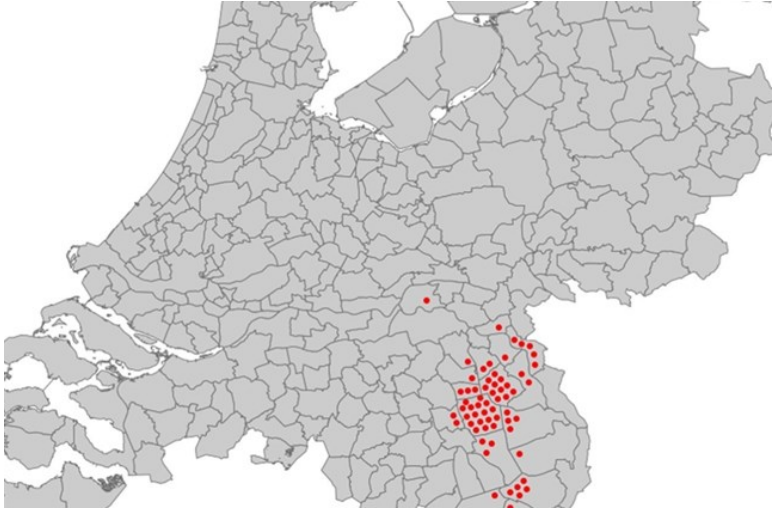
# A *Pseudomonas* operational taxonomic unit (OTU) found to be differentially enriched in human and environmental samples

Metagenomic sequencing: *P. pseudoalcaligenes*





# SARS-CoV-2 infection in mink farms



- Initiated by human-to-mink transmission
- Until end 2020: 68 out of 126 farms in NL infected - despite preventive measures
- January 2021: mink farming in NL banned
- Worldwide, 12 countries reported infected mink farms





# Environmental sampling SARS-CoV-2 RNA

Mink housing

Outdoor air,  
premises



Indoor air

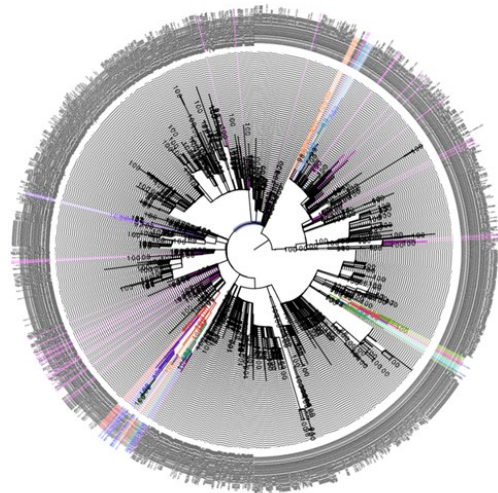
Outdoor air >25m  
from farm



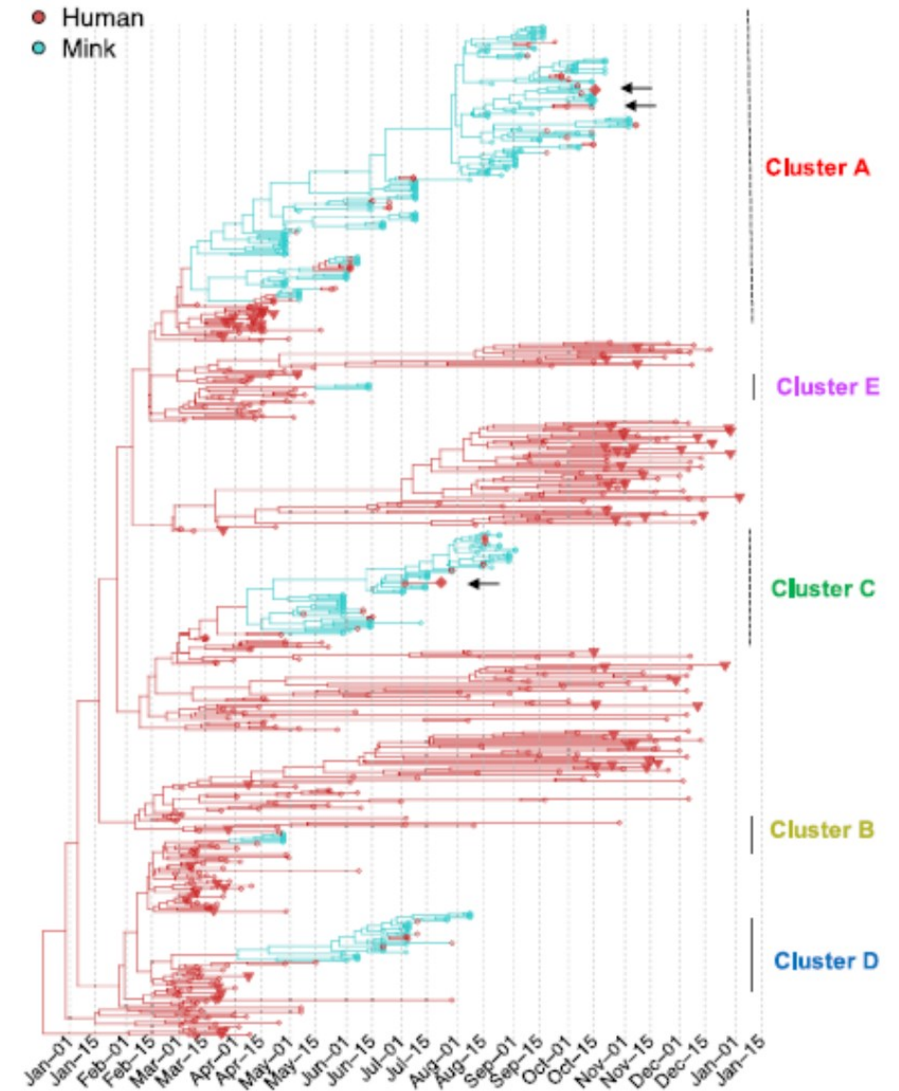


# Mink-to-human infections

- Confirmed human cases at 41/68 farms
- Five independent mink virus clusters: sequences belonging to all were found in human samples
- All 52 human sequences were closely related to the sequences of the minks on the same farm



- Limited spillover and onward transmission to local human population



# Farm environment: sampling for viral surveillance

## Genome Sequence of a *Minacovirus* Strain from a Farmed Mink in The Netherlands

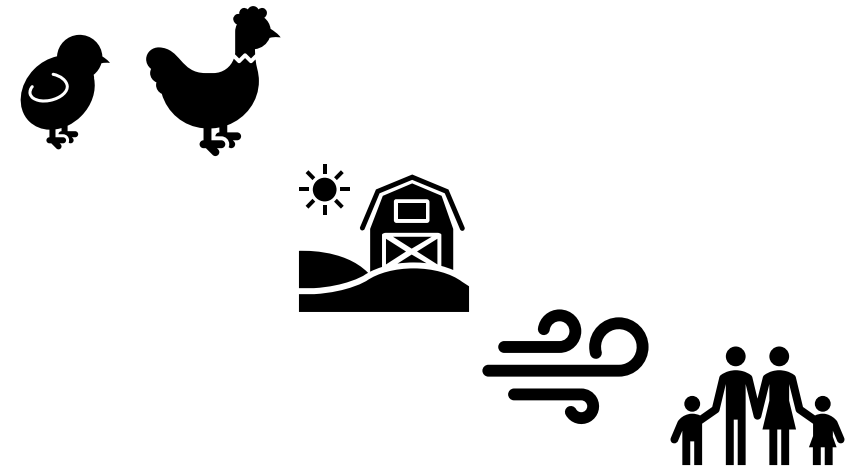


Agnostic deep sequencing

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 My V. T. Phan<sup>a</sup>

Sample types		Chicken feces (N=51)	Farm dust (N=13)
Virus family	<i>Astroviridae</i>	42 (82%)	11 (85%)
	<i>Caliciviridae</i>	40 (78%)	9 (69%)
	<i>Coronaviridae</i>	19 (37%)	3 (23%)
	<i>Parvoviridae</i>	51 (100%)	13 (100%)
	<i>Picobirnaviridae</i>	8 (16%)	2 (15%)
	<i>Picornaviridae</i>	51 (100%)	11 (85%)
	<i>Reoviridae</i>	7 (14%)	3 (23%)

Chicken feces ~ Poultry farm dust



# Differences and similarities chemical and biological exposure assessment

## **Biological agents (derived from) living organisms:**

- Multiplication, survival characteristics
- Growth can be host and/or environment dependent
- Dynamics over time/space
- Beneficial microbes

## **Standardization is key:**

In microbiome analysis, sample collection, transport and storage, DNA extraction, sequencing and data analysis methods can have a large influence on the study results

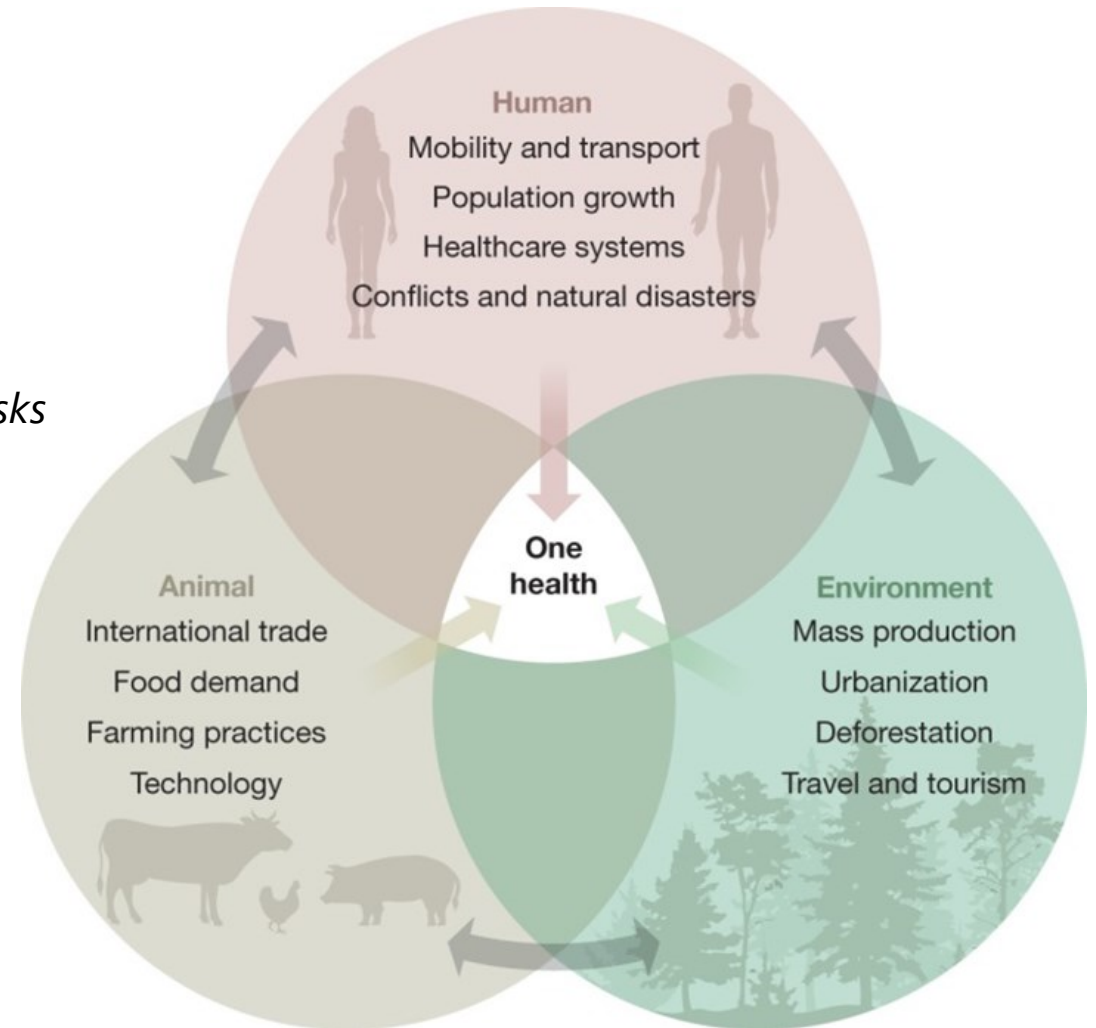
## **Innovation:**

- Spatial modelling is possible, but generally less % variance explained (*see e.g. Cornu-Hewitt Environ Pollut 2024*)
- Sensoring, real-time exposure assessment
- Biomonitoring
- Understand exposure-response relationships, and establish tools and regulations

## Global changes and emerging biological (and chemical) risks

- Climate change
- Urbanisation and deforestation
- Circular economy
- Energy transition
- Agricultural transition

>> a *One Health* approach is needed to study emerging biological risks







**Utrecht  
University**

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*shaping tomorrow*