NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

Quid pro Quo:

How Whole Genome Sequencing will enable international connection of food-, water- and human microbiology

– One Health through new methodology

Joergen Schlundt
Professor Food Science
JIFSAN Conference
November, 2019

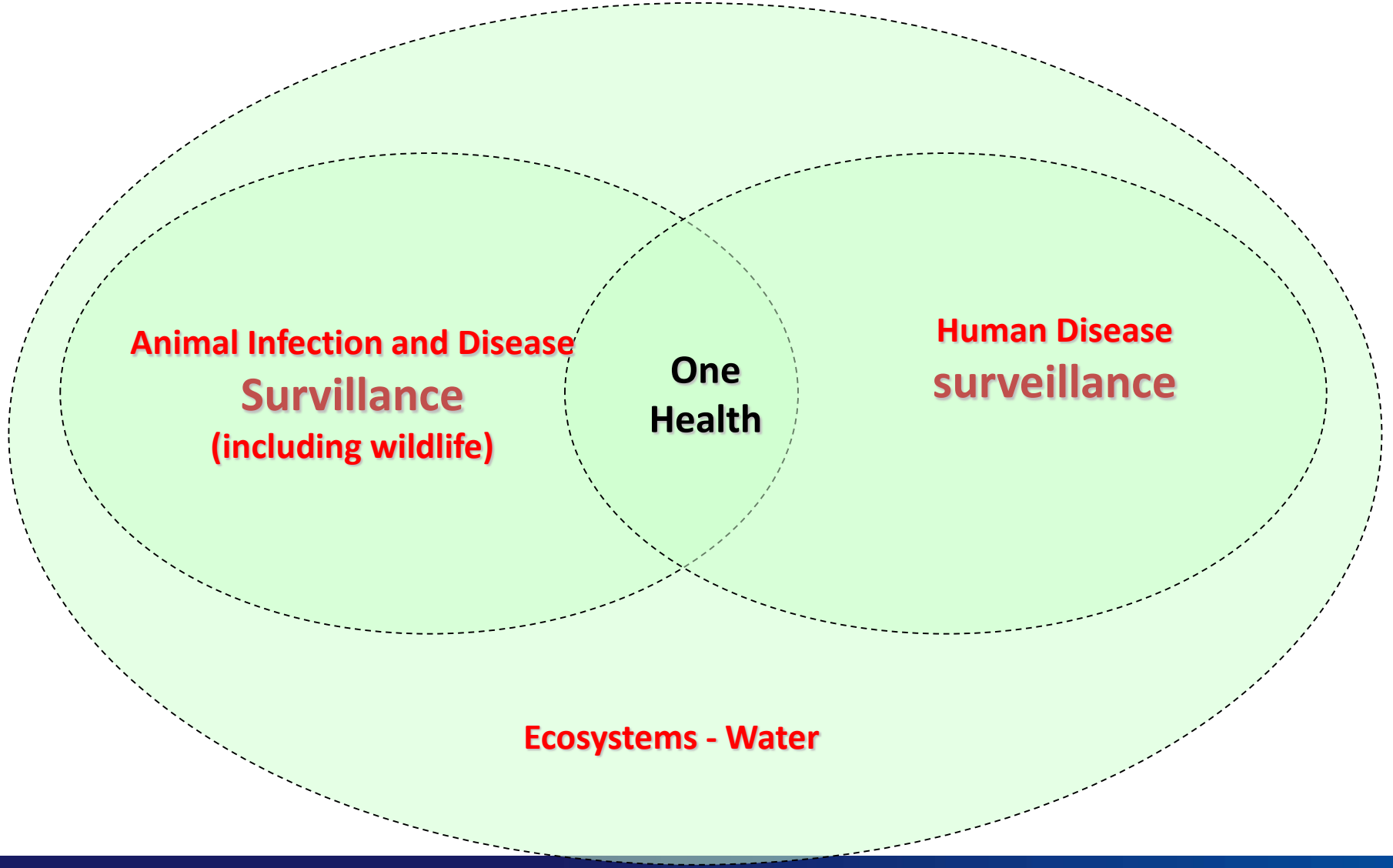
Food safety initiative
World Health Organization

One Health Action?

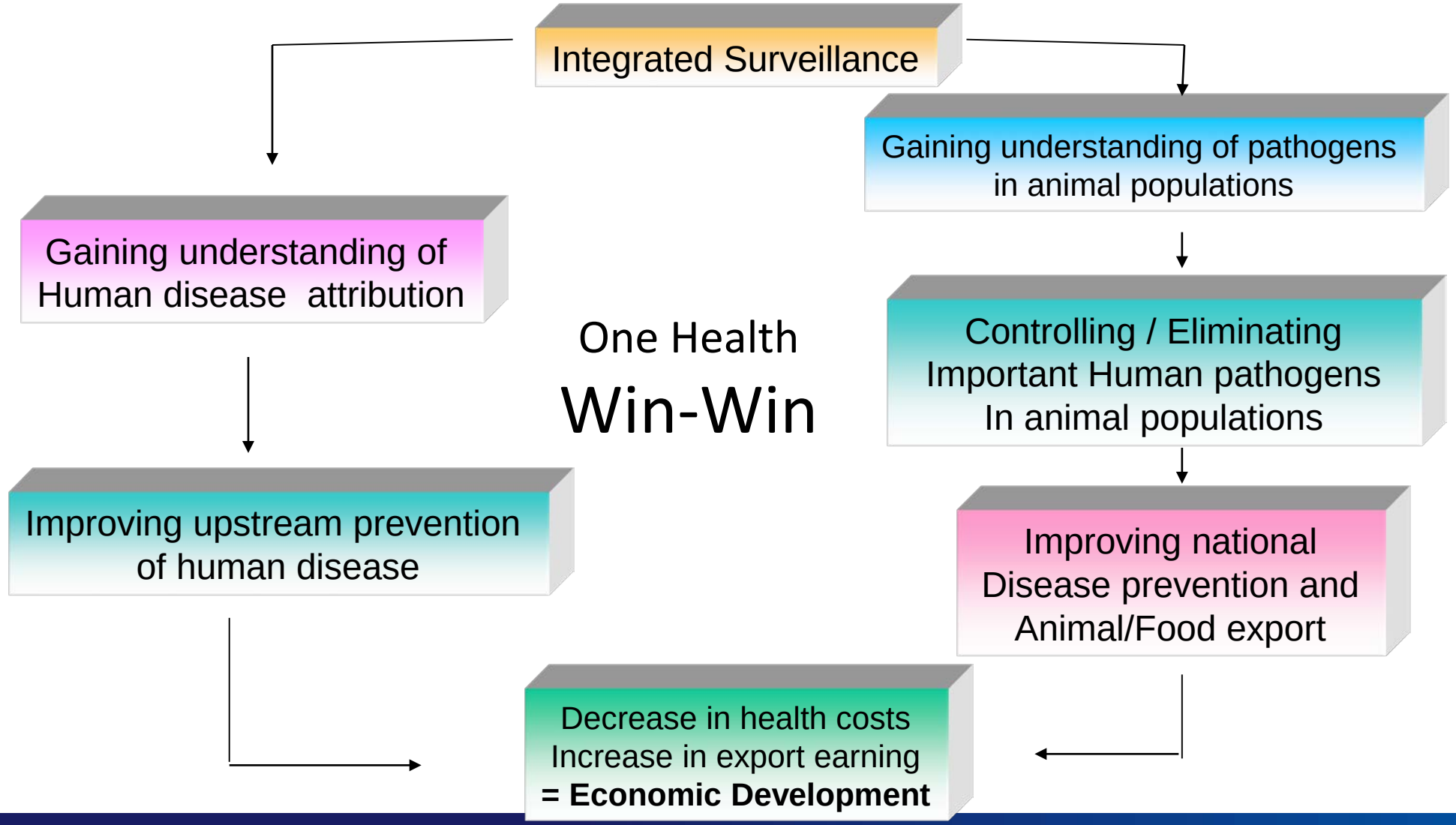
One Health refers to “the collaborative efforts of multiple disciplines working locally, nationally and globally to attain optimal health for people, animals and our environment.”

(from World Bank: PEOPLE, PATHOGENS AND OUR PLANET, Vol. 2: The Economics of One Health, 2012)

One Health: the interface in Infectious Disease Surveillance



One Health – Cost-Benefit – rel. to Food



One Health sharing data and isolates

We need to find mechanisms to share data and actual microorganisms (human/animal)

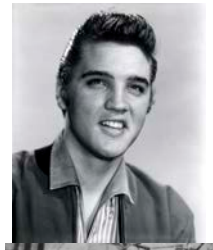
There needs to be clear benefit for all countries involved (industrialized countries -> help developing countries – as per SPS/WTO agreement)

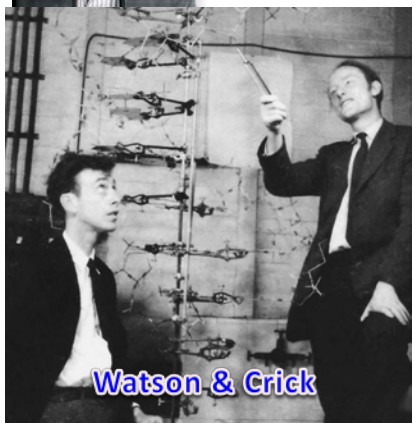
In future, systems will provide dramatically different potential for pathogen characterization and pathogen tracking (global interactive database of total DNA sequencing data)

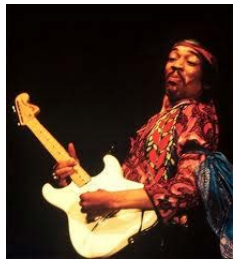
New Opportunities ?

History

454 starts the next generation sequencing era



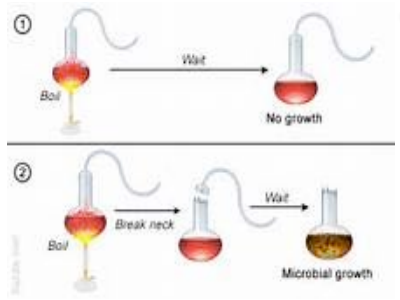




1953 1970 1977 1990 2003 2004

Whole Genome Sequencing (WGS) - The next Milestone

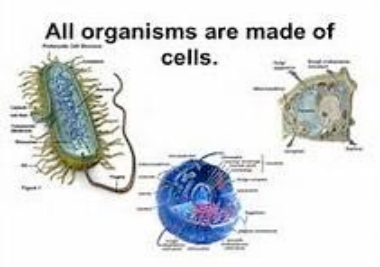
Leeuwenhook – 1676 – Bacteria/Microscopy



Pasteur– 1861– Proves Germ Theory

Invents pure culture technique ***(+ Koch)***

2005 – Next Generation Sequencing (NGS) of microorganisms



Schwann– 1839– Cell Theory

Fleming– 1928– Discovers Antibiotics

NOTEWORTHY MILESTONES IN MICROBIOLOGY

Some see new technologies and ask:
”Why?”

We see dramatic technological improvement, and ask:
”Why not?”

(paraphrased from Robert Kennedy)

Global Microbial Identifier: GMI

A global system will enable two major lines of action:

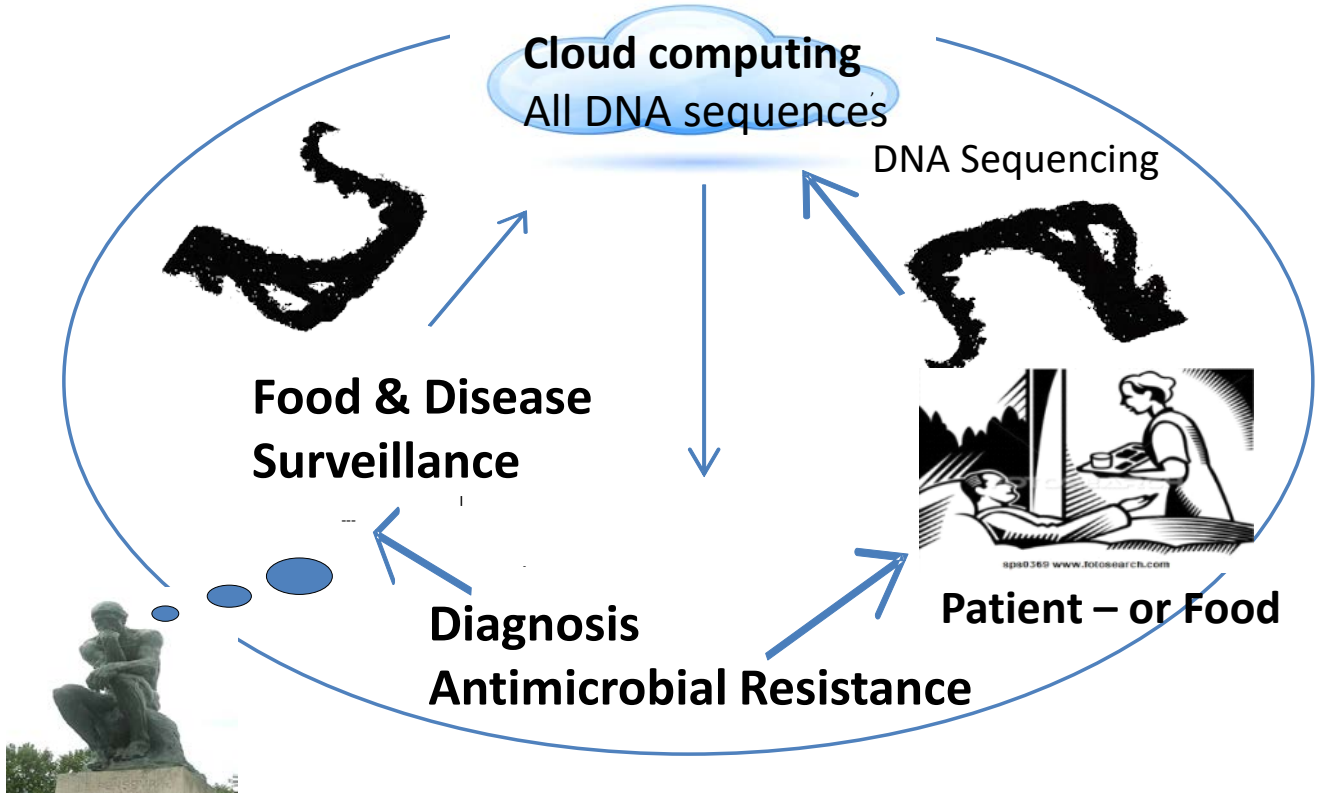
- Simple identification of all microorganisms in clinical (or other) settings, making redundant existing systems, and enabling reduction of total time for characterization down to typical time needed to obtain the original isolate

- A total database of unique sequences of all relevant microbiological strains globally, enabling real-time global surveillance of disease and pathogen developments

FUTURE Global Microbial Identifier: GMI

1st global tool to identify Microorganisms and Antimicrobial Resistance

Independent experts from 57 countries



Still:

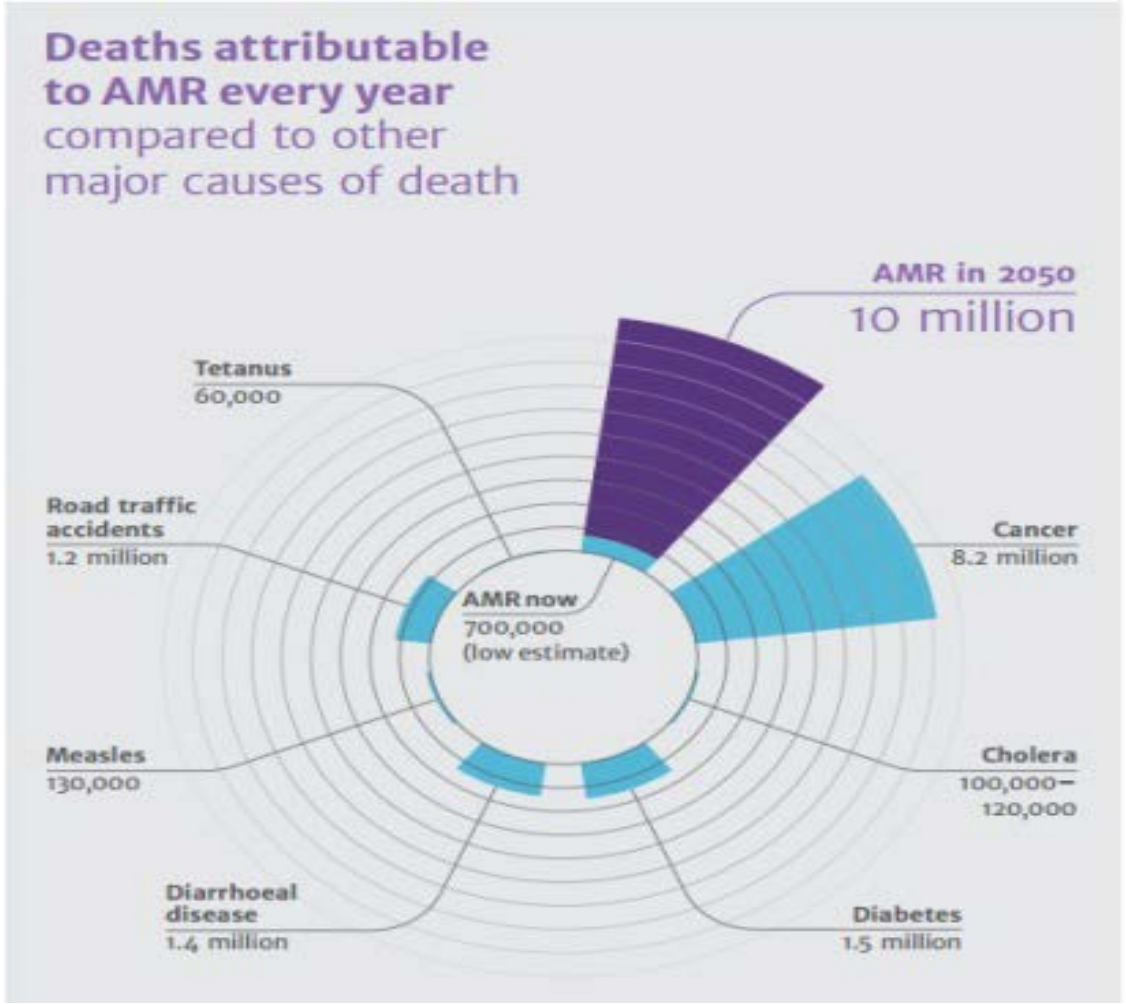
Just an Idea !

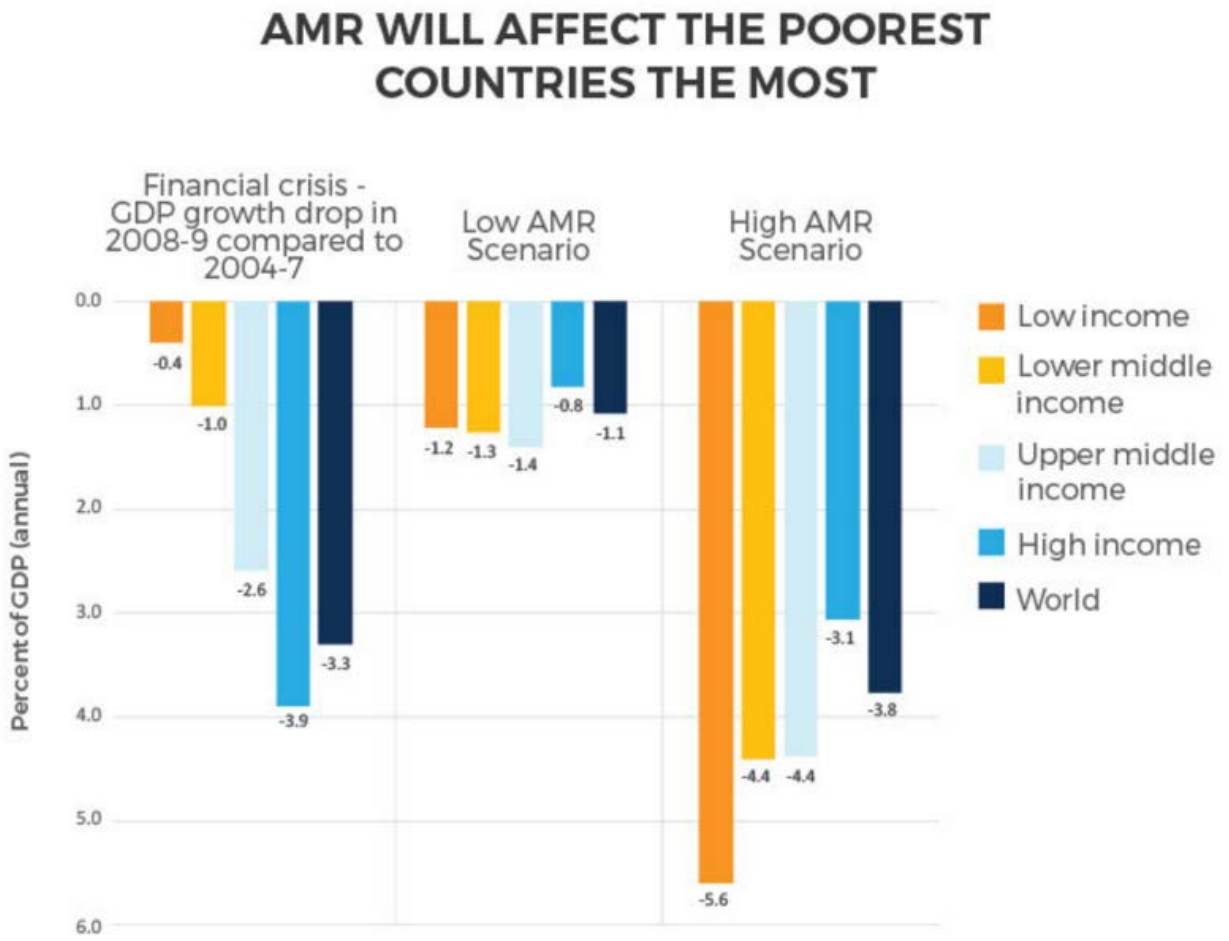
Virus – Bacteria – Parasites
Same - Same

www.globalmicrobialidentifier.org

Global Microbial Identifier

The most important One Health issue: AMR - A global emerging threat





World Bank Group, March 2017, Drug-resistant Infections – A threat to our economic future/ Review on AMR, Dec. 2014

What is needed!

- Real-time sharing of data on occurrences of all infectious agents including AMR data
- Bioinformatic tools for automatically detections of related clusters in time and space
- Possibilities to observe trends in clones and species as well as resistance, virulence, and other epidemiological markers
- Ability to rapidly compare between all types of data; genomic, epi, explanatory variables

Now – we all know USA is the greatest !
(GenomeTrakr and Pulsenet just a few examples)

But sometimes other countries can contribute also

Especially - if you can get them to share their …

SEWAGE

And although the idea is not from Norway – its close

You guessed it – its from **Denmark**

Monitoring large healthy populations using a metagenomic approach

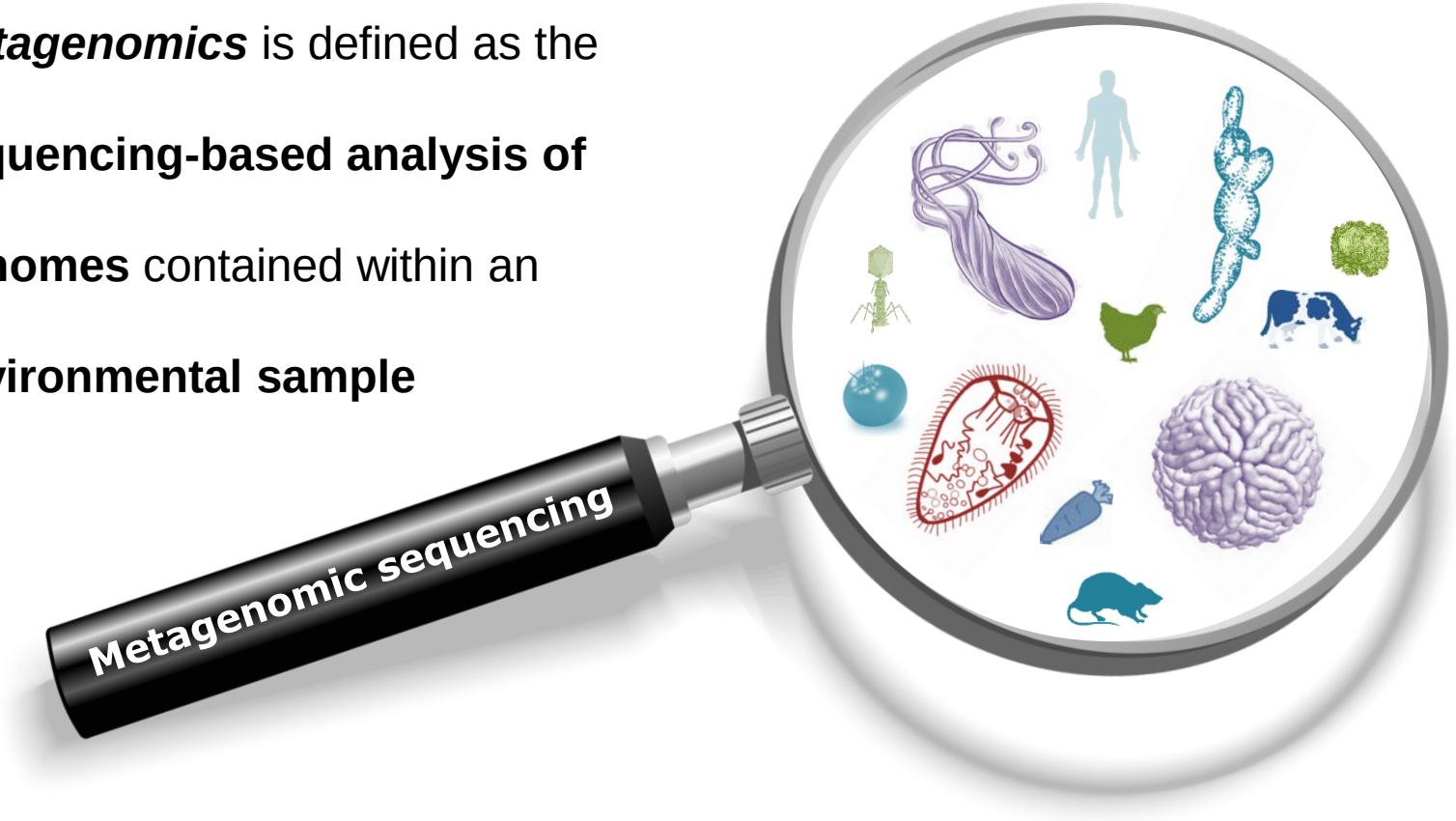
Metagenomics – One technology that takes all

Metagenomics is defined as the

sequencing-based analysis of

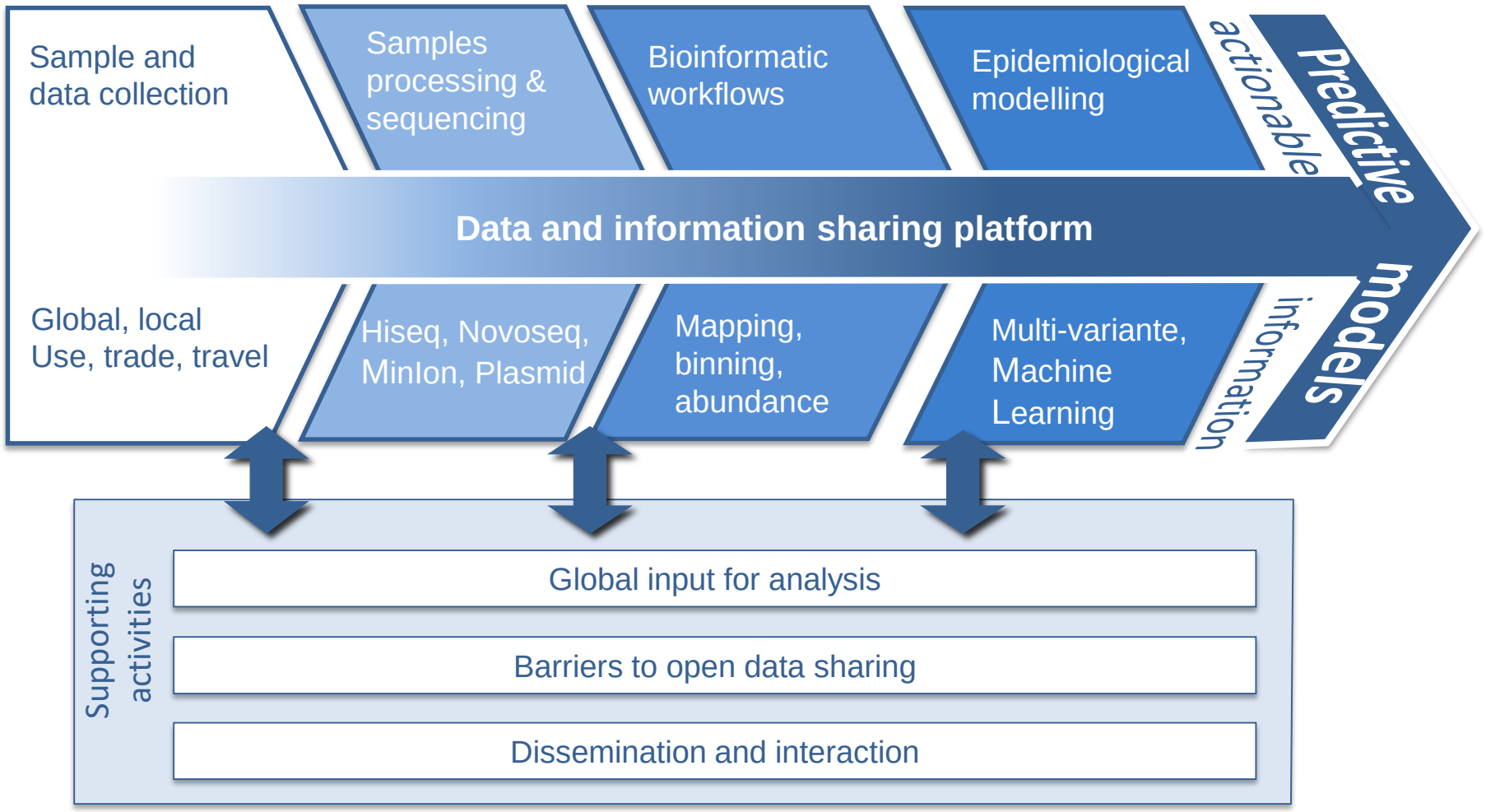
genomes contained within an

environmental sample

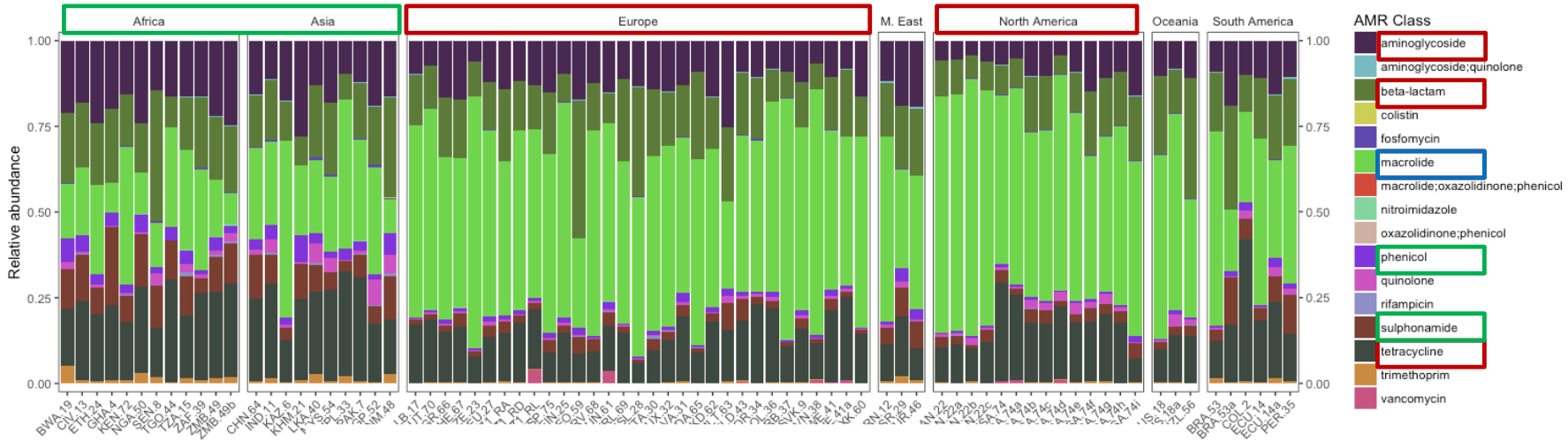


WHO - NNF - EU/COMPARE - Global Sewage Surveillance project 2016

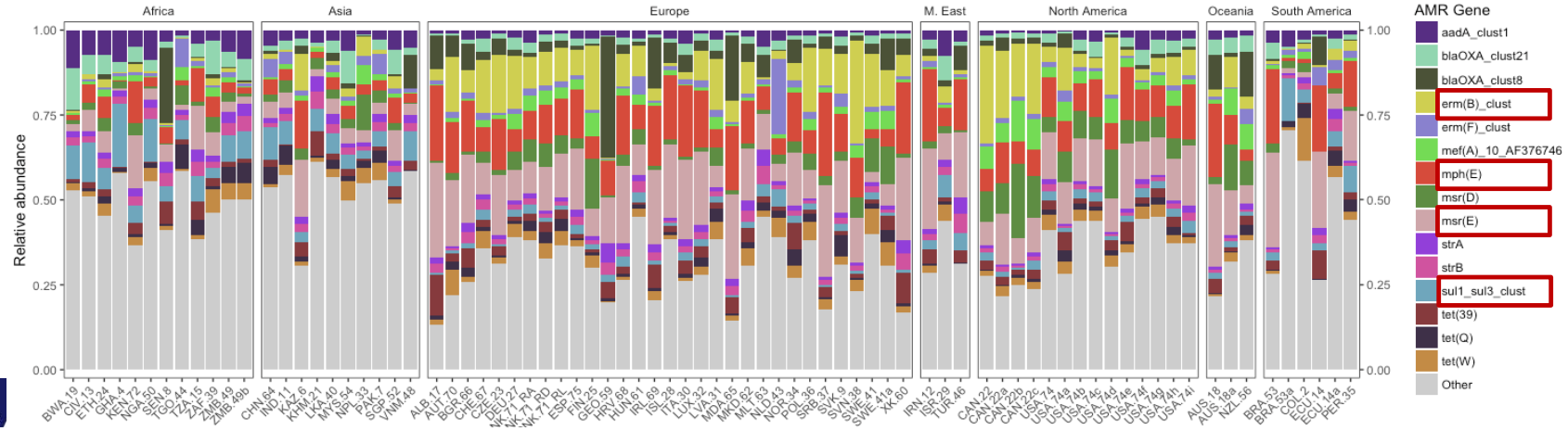
The structure of the project



Global sewage surveillance – 2016
AMR abundance per AMR class and gene



15 most common AMR genes –
Resistance genes depended on bacterial species



Developed by Patrick Munk

Hendriksen RS et al. Accepted NCOMMS

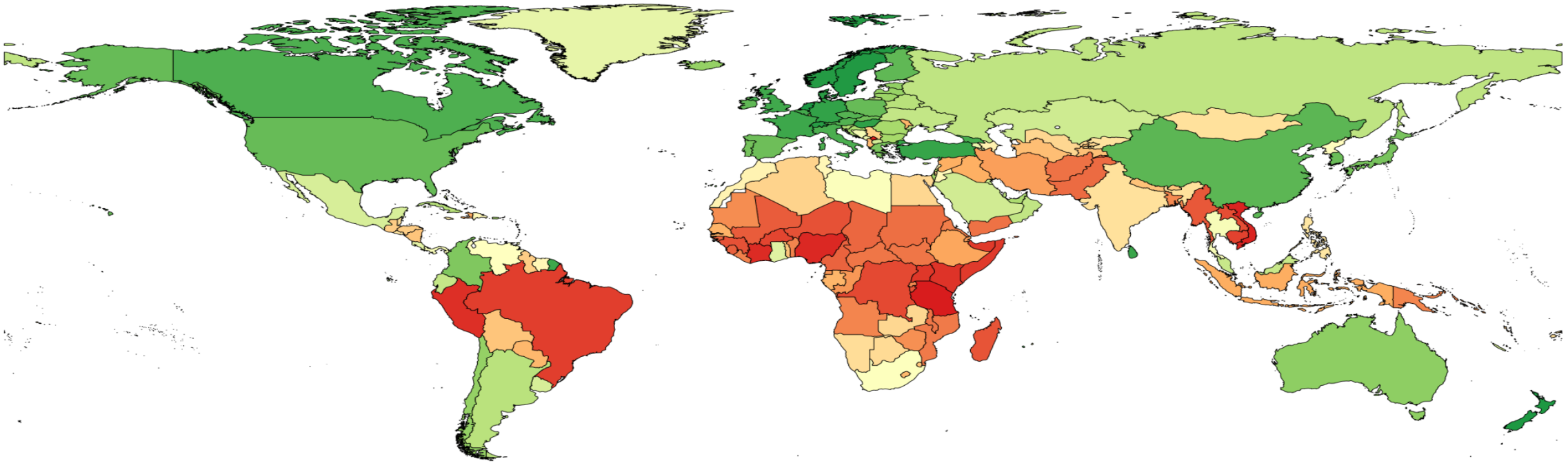
Global sewage surveillance – 2016
Applying artificial intelligence

Predicting global AMR significance for persistence in metagenomics sewage samples by applying artificial intelligence using explanatory variables, social demographics

Database	Source
Antimicrobial usage	MIDAS, Xponent, ECDC
Human Development Index	World Bank
Health, Nutrition and Population	World Bank
GEMS/Food consumption database	World Health Organization
FAOSTAT Food security and agriculture	Food and Agriculture Organization UN
Global Livestock Production and Health Atlas	Food and Agriculture Organization UN
Antimicrobial resistance	Sewers, ECDC
Flight data	
Labor data	International Labor organization
Environment	CDIAC (Carbon Dioxide Information Analysis Center)

Global sewage surveillance – 2016
Predicting resistance

Map showing predicted prevalence of AMR



Developed by Frank Aarestrup

Hendriksen RS et al. Accepted NCOMMS

Global sewage surveillance – 2016
Important predictors

Predictors of higher AMR

- Mortality rate
- Informal employment
- Time to import
- Death, by communicable diseases and maternal, prenatal and nutrition conditions
- Risk of maternal death
- Open defecation
- Diarrhoea prevalence in children
- Risk of impoverishing expenditure for surgical care

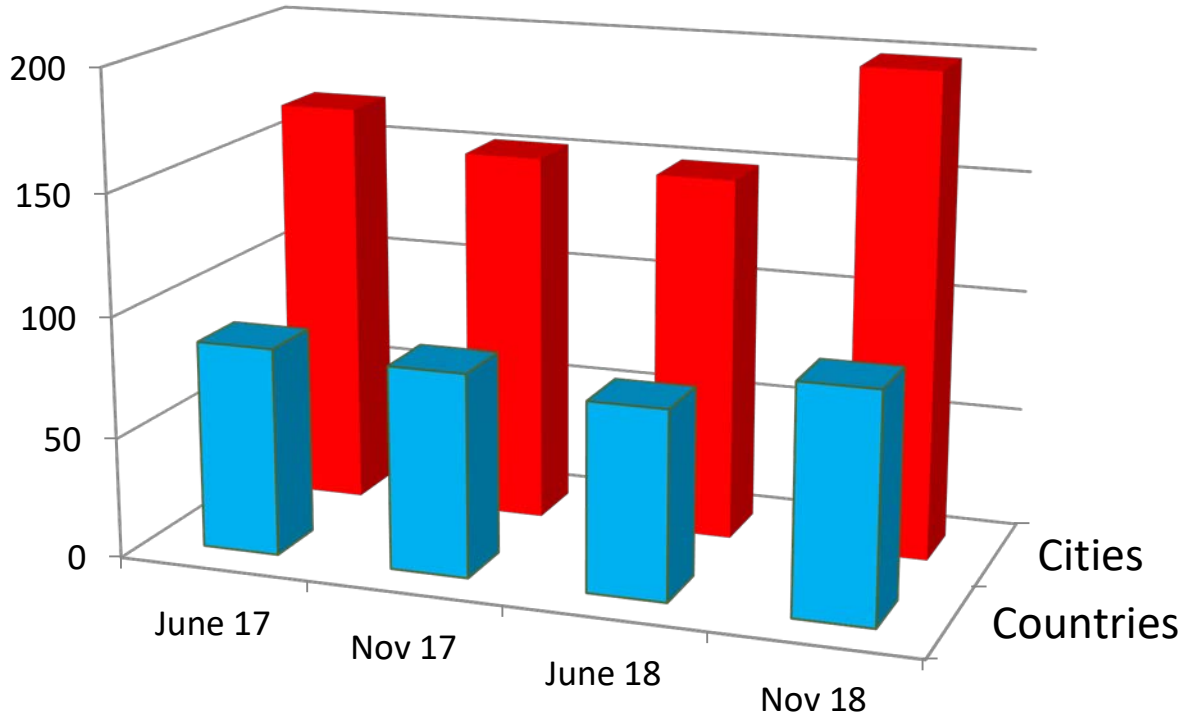
Predictors of lower AMR

- Investment in water and sanitation
- Completeness of death reporting
- Grace period on external debt
- Educational attainment
- Number of surgical procedures
- Life expectancy at birth
- Number of Physicians
- Births attended by skilled health staff

Developed by Patrick Njage

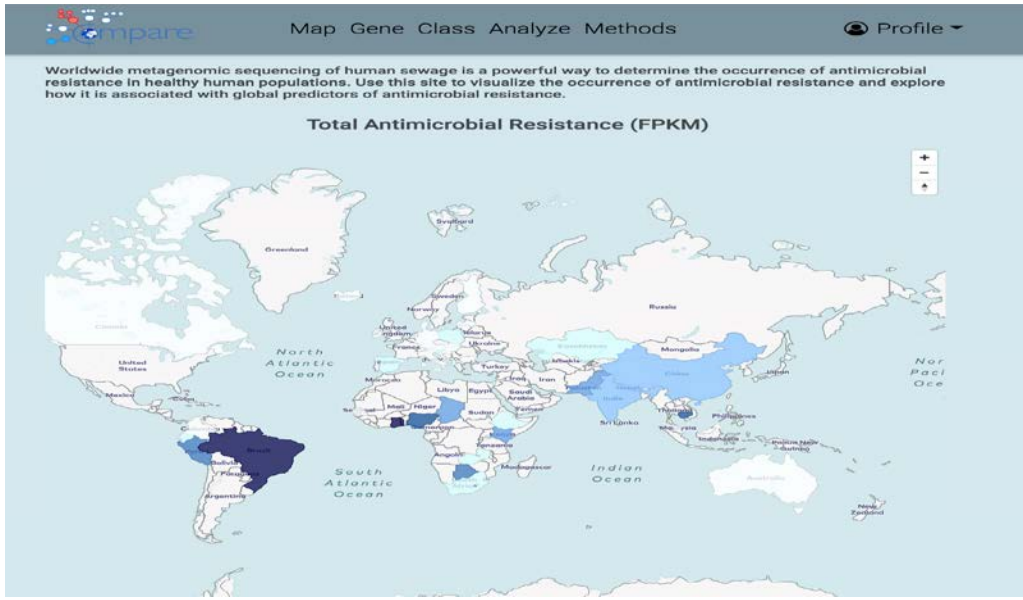
Hendriksen RS et al. Accepted NCOMMS

Global sewage surveillance – 2017 - 2018



On average 85 countries and 160 cities per round

- 620 samples in total
- App 100 countries



Collected by Rene Hendriksen / Jette Kjeldsen

Conclusions – sewage studies

- Metagenomic sequencing is potential superior to conventional and other genomic methods for quantification of AMR and pathogens

  - Powerful way to **determine prevalence and differences of all genes**
  - A realistic **alternative to conventional surveillance**
    - urban sewage is a proxy for clinical or individual human samples for population based surveillance?
    - Potential to use the same data for other surveillance topics
    - Some challenges still to overcome

- **Sanitation and health seems to be the main drivers of resistance** in healthy humans / usage in animals but other explanatory variables might also explain the occurrence of AMR

- Sustainability!

Acknowledgement (for global sewage study)

Frank M. Aarestrup (PI)
Patrick Munk
Patrick M. K. Njage
Thomas Nordahl Petersen
Pimlapas Leekitcharoenphon
Håkan Vigre
Jette Sejer Kjeldgaard
Ole Lund
Philip Clausen
Rolf S. Kaas
Judit Szarvas
Marie Louise Jespersen
Jolene Pedersen
Markus Johansson
Sünje Johanna Pamp
Derya Aytan
Oksana Lukjancenko
Lukasz Dariusz Dynowski
Camilla Hundahl Johnsen
Christian Brinch
Jolene Pedersen

Tine Hald
Timo Röder
Saria Otani
Mark Woolhouse
Bram Van Bunnik
Luke McNally
Milou G. M. van de Schans
Simon Rasmussen
Bent Petersen
Clara Amid
Guy Cochrane
Thomas Sicheritz-Ponten
Ana Maria de Roda Husman
Heike Schmitt
Tina Zuidema
David Nieuwenhuijse
Heike Schmitt
Jorge Raul Matheu Alvarez
Awa Aidara-Kane
Marion Koopmans
the Global Sewage Surveillance project consortium and many many more…..

Funding and Support

World Health Organization

novo nordisk fonden

ompare

Building Global Capacity

http://cge.cbs.dtu.dk/services/all.php

Center for Genomic Epidemiology – DTU: Technical University of Denmark

Workflows

Bacterial Analysis Batch Upload Pipeline (Works)

Phenotyping

ResFinder (Works)
PathogenFinder (Works)
VirulenceFinder (Works)
Restriction-ModificationFinder (Works)

Typing

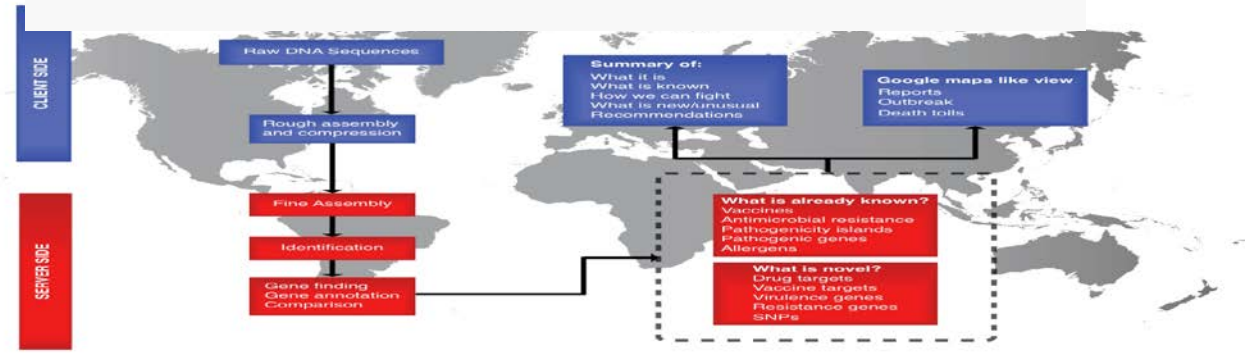
SeqSero (Works)
SerotypeFinder (Works)
PAst (in development)
VirusFinder (in development)
spaTyper (Works)
MLST (Works)
pMLST (Works)
PlasmidFinder (Works)
KmerFinder (Works)
SpeciesFinder (Works)
Read2Type (This service is not implemented on the new server)
TaxonomyFinder (This program is in development)
Tapir (This service is not implemented on the new server)

Phylogeny

snpTree (Works)
NDtree (Works)
CSIPhylogeny (Works)
TreeViewer (Works)

Other

Assembler (Works)
ENAUploader (in development)
PanFunPro (Works)
MGmapper (Works)
MyDbFinder (Works)
SPIFinder (Works)
HostPhinder (in development)
GeneticDiseaseProject (Not associated with CGE)
NetFCM (Not associated with CGE)



Future of Infectious Disease Control:
International – and National
Human - Animal

"Microbial molecular data are essential information for effective surveillance and proportional response to international Public Health Emergencies"
(EU/GESTURE Expert Meeting, 2009)

But we need same systems for:

- **Animal and Human strains**
- **Environmental, Food and Water strains**
- **National and International events**
- **Developing and Richer countries**

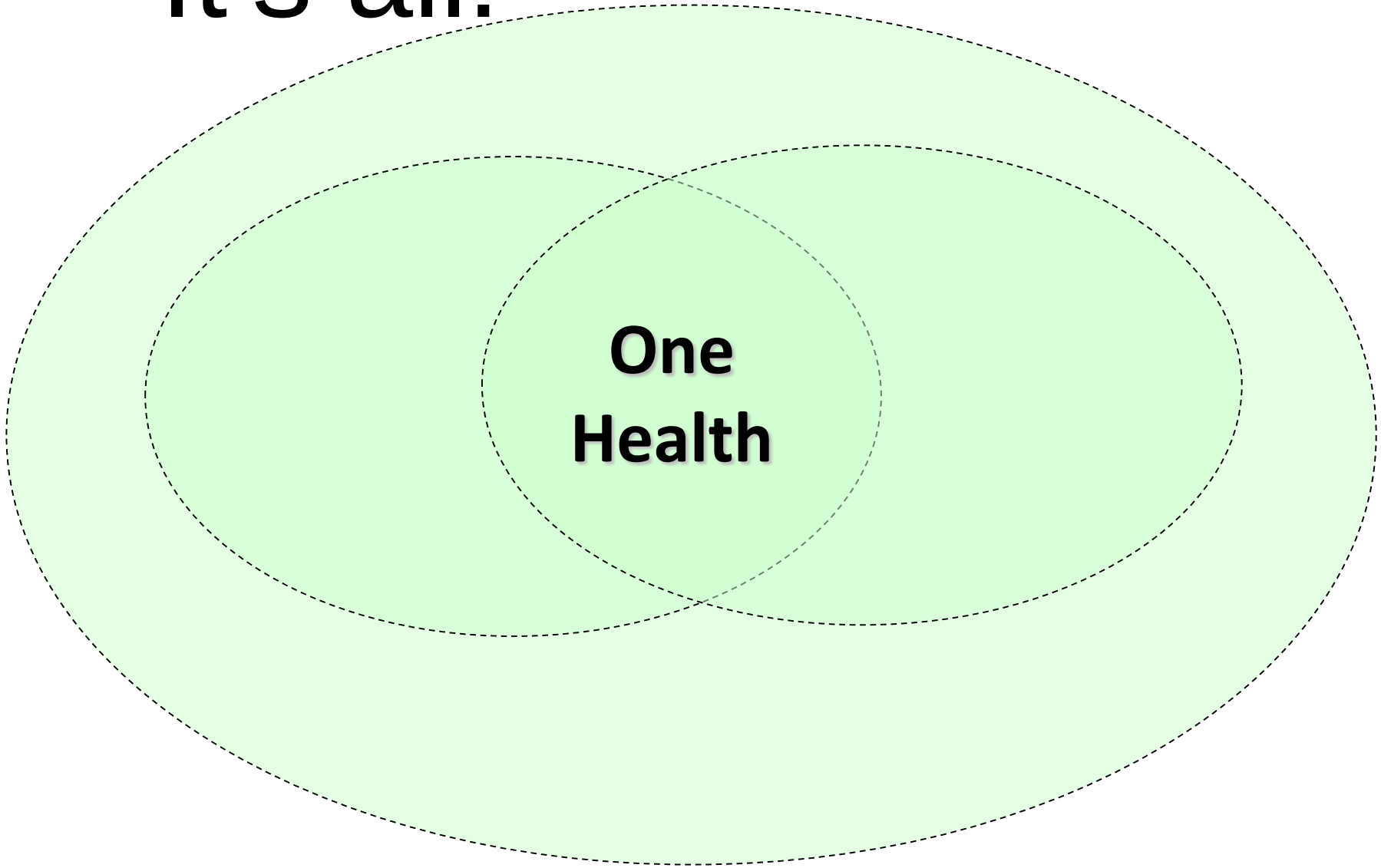
So, Why is WHO not driving this revolutionary potential for change: *too many players ??*

Food Safety
AMR
TB
Emergencies
Flu
Polio
Environment/Water
Sexual and reproductive health
Nagoya Protocol ?

However:
at World Health Assembly May 2020
There will be a **Food Safety Resolution**

Hopefully Member States will include strong statements about
the global use of NGS

It’s all:



Continuous improvement