

New horizons in EID detection: the era of next generation sequencing and bioinformatics

A global platform for the sequence-based rapid identification of pathogens

Prof. Frank M. Aarestrup, coordinator, microbiology (Technical University of Denmark) Prof. Marion Koopmans, deputy coordinator, virology (Erasmus Medical Center, the Netherlands)





Infectious diseases in the current era

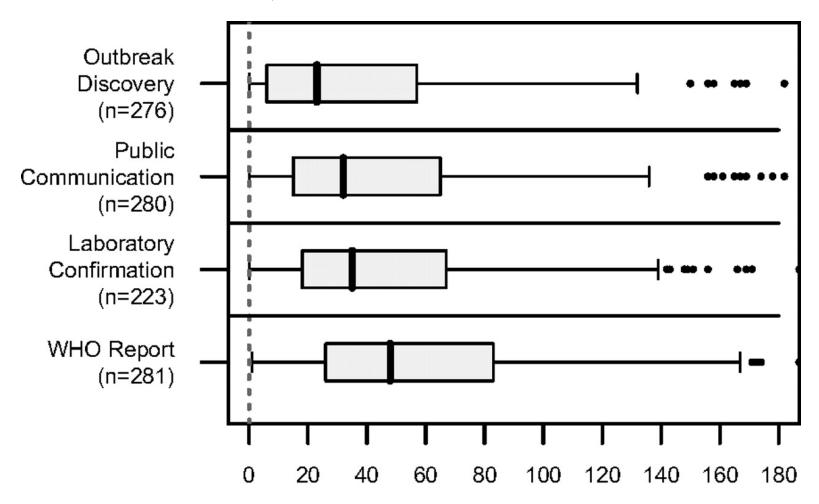
- Dynamics of <u>common</u> infectious diseases are <u>changing</u>
 - Demographic change, population density, anti vaccine, AMR, etc.
- New diseases emerge frequently
 - Deforestation, population growth, health system inequalities, travel, trade, climate change
- Effects are <u>difficult to predict</u> due to complexity of problems
 - Rapid flexible response
- Public health and clinical response depend on global capacity for disease surveillance
 - Rapid sharing, comparison and analysis of data from multiple sources and using multiple methodologies





Current performance

late detection, human disease first



Emily H. Chan et al. PNAS 2010;107:21701-21706 Days Since Outbreak Start

Priority research questions EID <u>after</u> disease emergence

Clinic/public health

How to diagnose/rule out?

Basic

Comparison with other

How to
 When

r species jump

Source

Modes

Role o⁻

Risk fa

Potent

interventions/prevention

SS

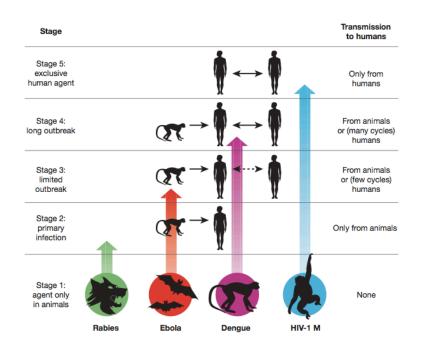
hancement

virals

Potential vaccines

Main aspects

- Increased likelihood of new (zoonotic) pathogens
- Increased opportunity for global spread

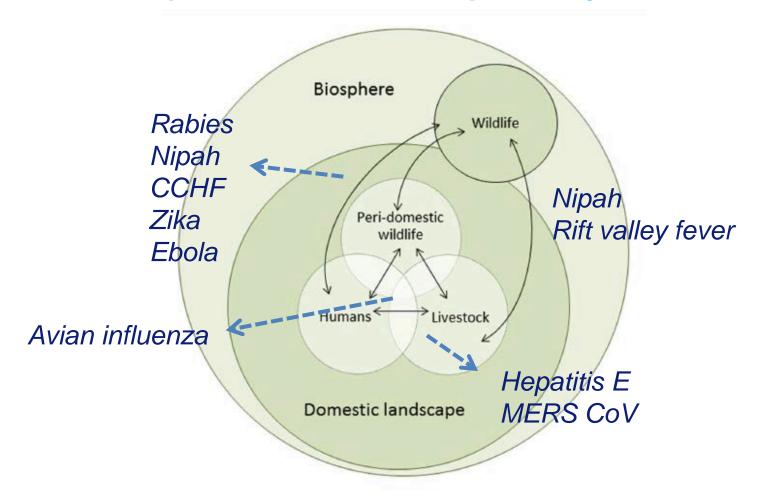




Challenges

- Competing priorities
- Inequality in health care systems
- Clinician knowledge of EID
- Privacy laws
- Poor prediction

EID require multidisciplinary research



COMPARE: developing an enabling system and tools for collaborative preparedness and outbreak research

- Collaboration between "users" of NGS and bio-informaticians
- Develop validated workflows for top 5 questions in disease preparedness research and outbreak research
- sector-, domain- and pathogen-independent (ONE HEALTH)
- Flexible, scalable and open-source based
- Data and information-sharing platforms
- building from sustainable infrastructure







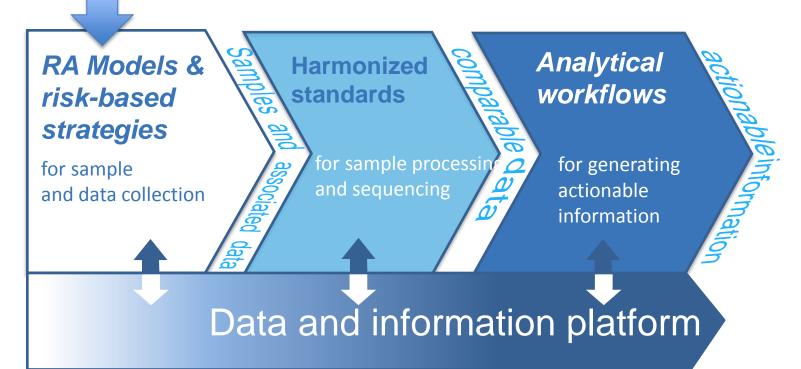
What to sample?

Where?

When?

How?

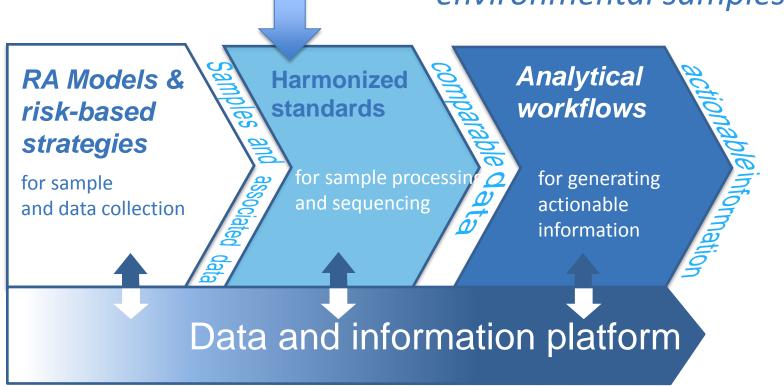
Humans, livestock, wildlife, food, environmental samples



How to sequence?
Pathogen targeted
Metagenomic, Deep sequencing
Viruses, bacteria, parasites
QUALITY ASSURANCE



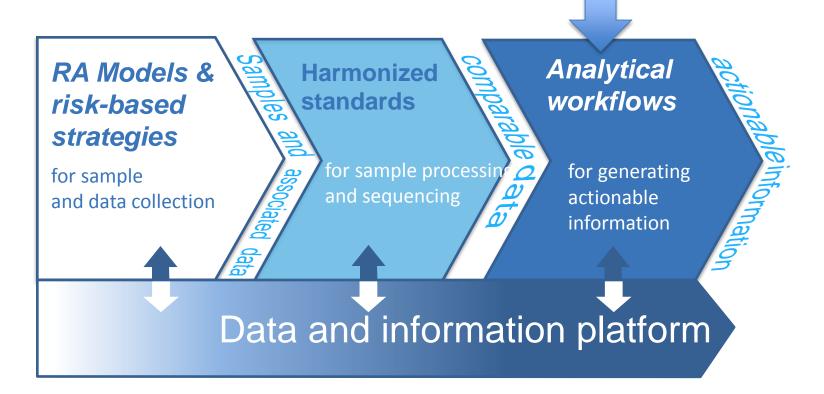
Clinical, tissue, food, environmental samples





Clinical, public health, research Human, veterinary Ecology, food

How to analyze?
What does the analysis mean?
How do I use it?



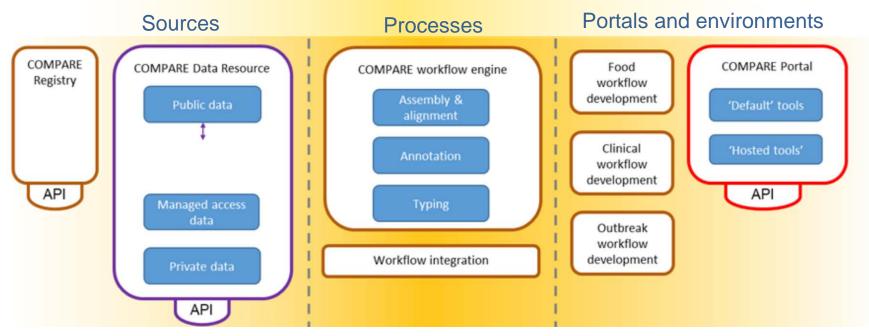
WP9 Information sharing platform





Ole Lund







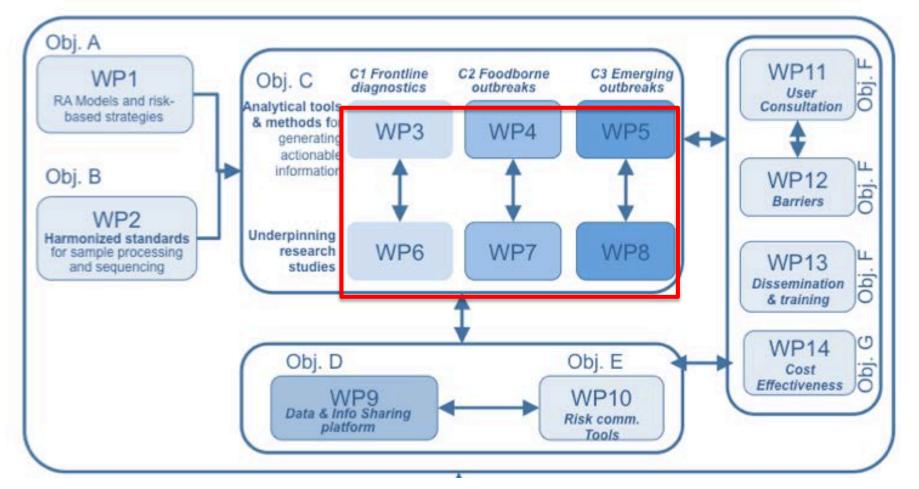




Building on the EU ESFRI Elixir, EMBL and DTU infrastructures



Develop a "catch all" metagenomics approach for surveillance of pathogens transmitted via fecal-oral and environmental, and respiratory routes with user friendly data analysis







Shotgun metagenomics

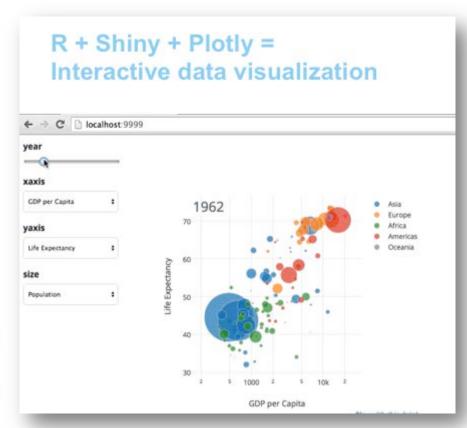
- "Sampling of all genetic material in all organisms present in a given complex sample"
- Sample preparation by filtering and centrifugation
- Nuclease treatment
- DNA+RNA extraction
- Random nucleic acid amplification
- Sequencing library preparation
- •High throughput sequencing (Roche 454/Illumina)

Metagenomics Analysis Workflow

Remove low quality Newbler QC reads Generate contigs Iterative assembly with Newbler assembler + CAP3 Map sequencing Newbler read mapper reads to contigs

Filter low quality +

off-target contigs



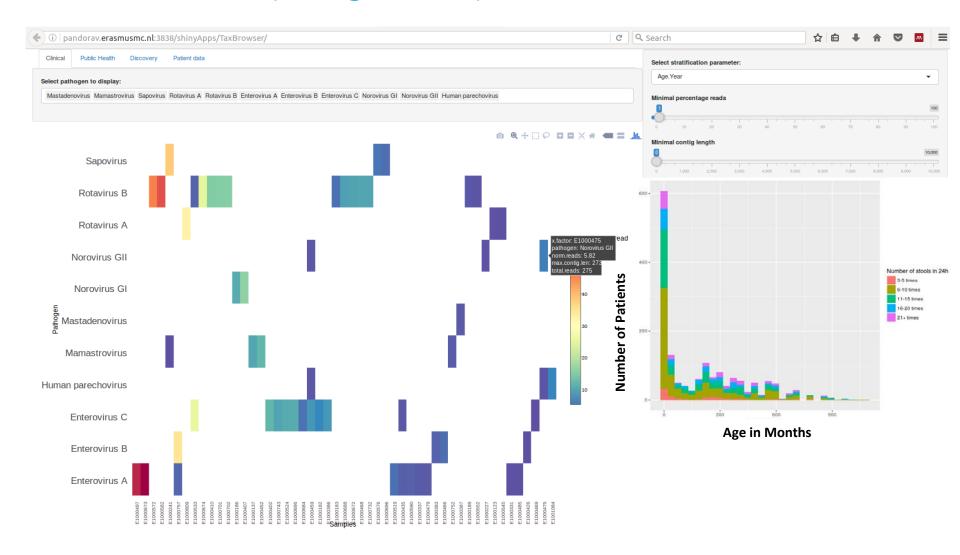
Taxonomically identify genomes

BLASTN + BLASTX

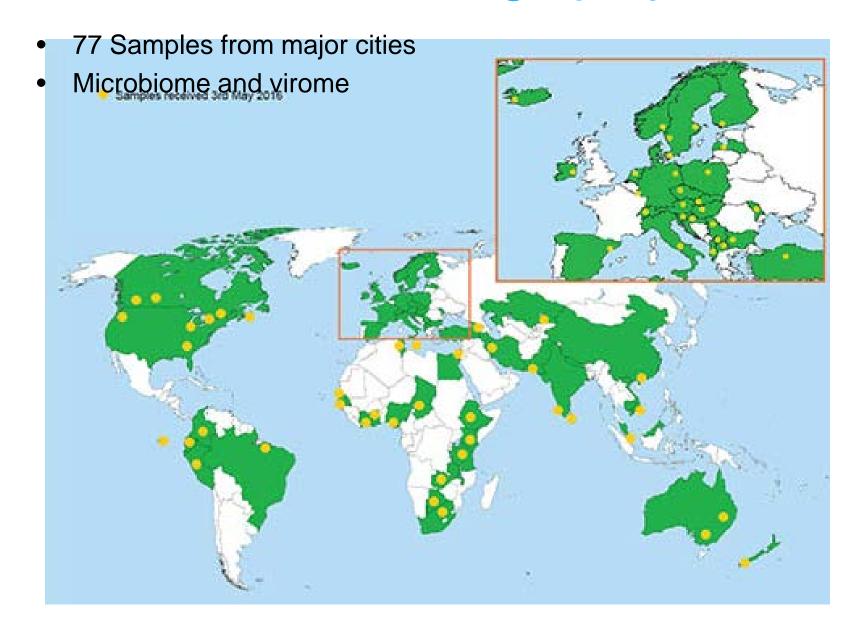


Dustmasker + HostBLAST

Analysis of samples from diarrheal disease surveillance (Bangladesh), virome



Global urban sewage project



Results sofar (>3 years to go)

- 1. Uniform protocols and workflows for NGS detection of a range of viruses, bacteria and parasites in different sample types
- 2. Pilot studies to develop customized analytical workflows for the top 6 food borne diseases
 - tracking of avian influenza outbreak in wildlife
 - support of outbreaks (Ebola, H5N8 AIV, norovirus, AMR-colistine, Zika)
 - metagenomic analysis of a global urban sewage snapshot as experimental surveillance tool
- 3. First version of data sharing hubs for collaboration between data providers and data users

Mateneh Ebola Treatment Centre Makeni Sierra Leone



1 of 6 DfID-funded treatment centres

Part of network of diagnostic labs set up by EML, DML, PHE, many other groups Ian Goodfellow
Univ of Cambridge
Sequencing
Tent
Diagnostic
Lab







Sequencing Tent

Ian Goodfellow



My Phan



Clinical diagnostic sample Convert to cDNAamplification adapter ligation

Library preparation Sequencing run

Genome assembly preliminary analysis

6 hours

10 hours

4 hours

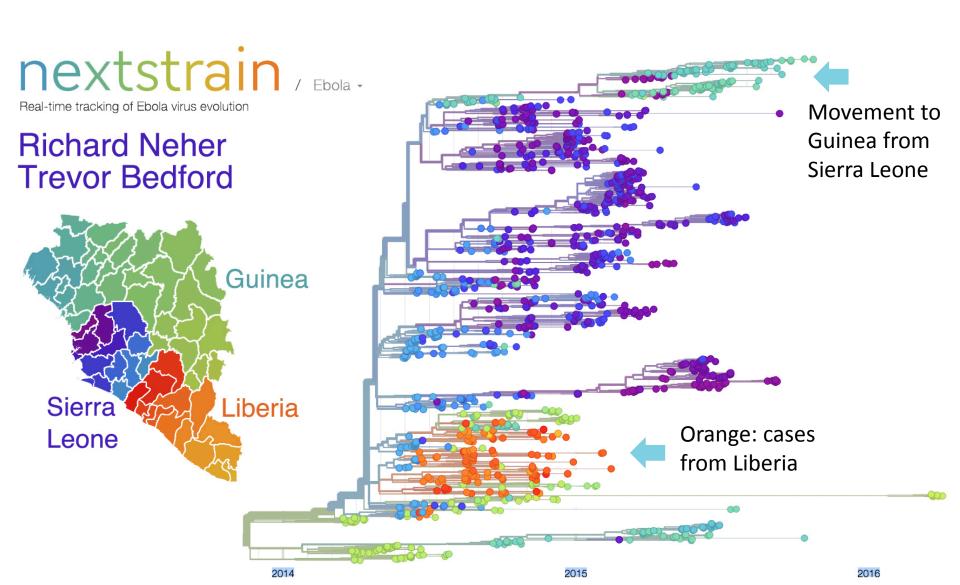
3 hours

24 hours





Rapid NGS of all Ebola cases to track source of new infections



Research needs

- 1. Affordable and robust technology
- 2. The translation of genetic information into properties that are important for risk assessment (virulence, transmissibility, susceptibility to population immunity).
- 3. Technological solutions for innovative surveillance (e.g. similar to air pollution technology)

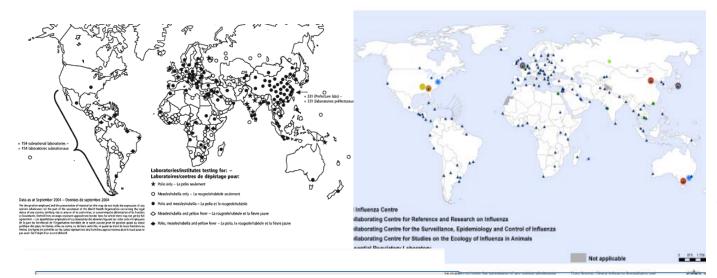
Other

- 2. Sustainability of COMPARE
- 3. Embedding of NGS technology in health systems strengthening programs, which can be across programs (polio, TB, HIV, malaria ao)





We could do things on the fly if capitalizing on existing networks



olo, FAO, WHO
networks
Polio, Measles,
Flu, TB, HIV,
VHF, malaria,
Dengue,
Salmonella, AMR,
Zika

PERSPECTIVES

Laboratory support during and after the Ebola virus endgame: towards a sustained laboratory infrastructure

I Goodfellow¹, C Reusken², M Koopmans (m.koopmans@erasmusmc.nl)^{2,3}

- 1. University of Cambridge, Department Virology, Cambridge, United Kingdom
- 2. Erasmus MC, Department Viroscience, Rotterdam, the Netherlands
- 3. Centre for Infectious Disease Control, Bilthoven, The Netherlands

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Frank Aarestrup, Ole Lund, Technical University of Denmark (DTU) Marion Koopmans, Ron Fouchier, Thiis Kuiken, Matt Cotton, Erasmus Medical Center (Erasmus MC) Eva Moller Nielssen, Tine Hald, Statens Serum Institut (SSI) Martin Beer, Anne Pohlmann, Dirk Hoper, Friedrich-Loeffler-Institute (FLI) Anne Brisabois. Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) Klaus Stark, Andres Nitsche, Robert Koch-Institut (**RKI**) Guy Cochrane, European Molecular Biology Laboratory (EMBL) Simone Caccio, Instituto Superiore di Sanita (ISS) Annelies Kroneman, George Haringhuizen, RijksInstituut voor Volksgezondheid en Milieu (RIVM) Amie Atkin, Emma Snary, Andrew Breed, Ian Brown, Animal Health and Veterinary Laboratories Agency (AHVLA) Marc Woolhouse, Andrew Rambaut, University of Edinburgh (UEDIN) Christian Drosten, Universitäts Klinikum Bonn (UK-Bonn) Menno de Jong, Academic Medical Center (AMC) Surbhi Malhothra, Universiteit Antwerpen (UA) Ab Osterhaus, Artemis Wildlife Health BV (Artemis) Derek Smith, Terry Jones, University of Cambridge (UCAM) Wolfgang Baumgaertner, Ab Osterhaus, Tierärztliche Hochschule Hannover (TIHO) Christian Cortazar, Universidad Castilla de la Mancha (UCLM) Hubert Endtz, Fondation Mérieux (FMER) Ana Papa, Aristotle University Thessaloniki (AUTH) Soizick LeGuyader, L'Institut Français de Récherche pour l'Exploitation de la Mer (IFREMER) Pieter van Baal, Erasmus Universiteit Rotterdam (EUR) Martyn Kirk, Australian National University (ANU) Istvan Csabai, Magyar Tudomanyos Akademia Wigner Fizikai kutatokozpont (Wigner RCP) Frank Alleweldt, Civic Consulting Alleweldt & Kara Gbr (CIVIC) Emilio Mordini, Responsible Technology (RT) University of Bologna (UNIBO) Ulbrecht Nubel, Leibniz-Institut DSMZ GmbH (**DSMZ**) Paul Kellam, David Aanensen, Wellcome Trust Sanger Institute (WTSI)



