



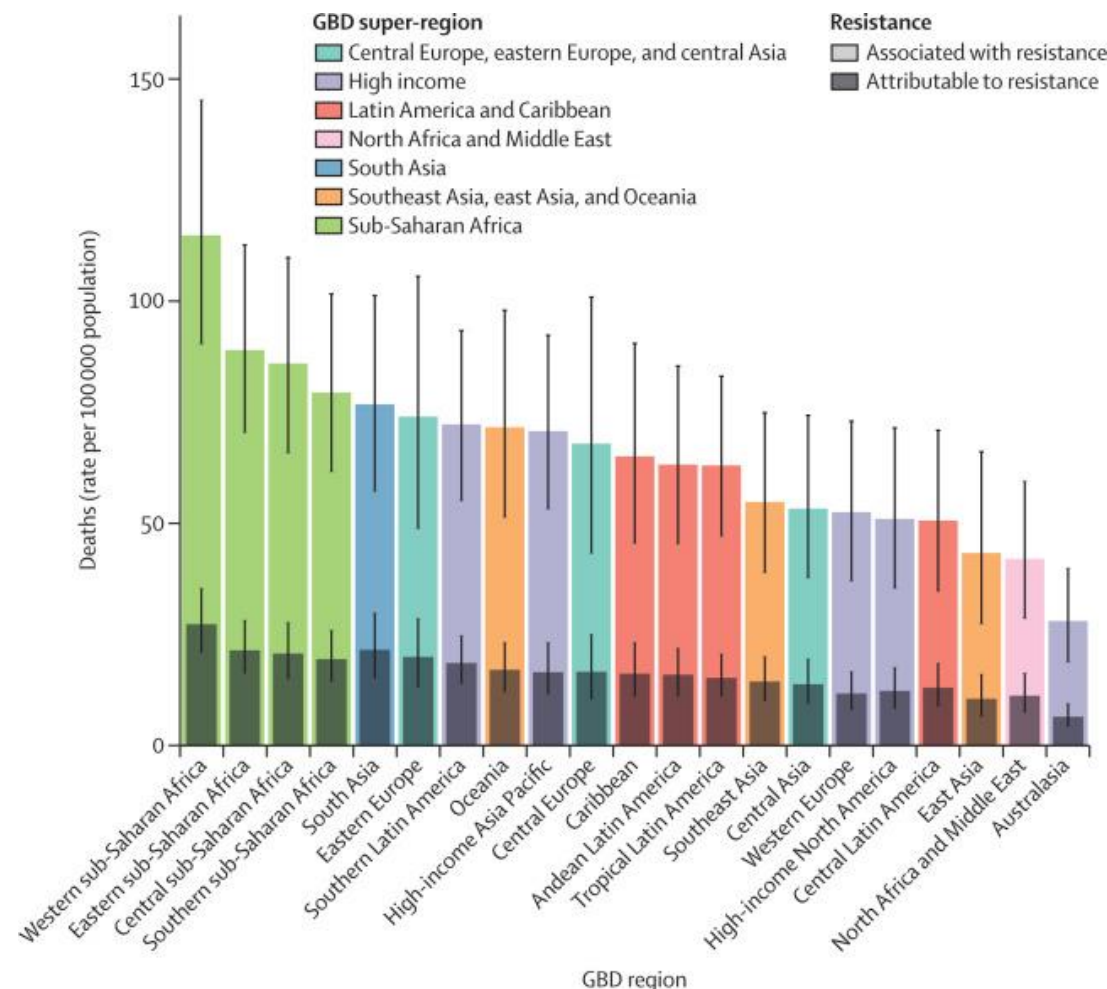
ONE HEALTH AMR ISSUES FROM A PUBLIC HEALTH PERSPECTIVE

Robert Skov, MD
Statens Serum Institut
Copenhagen, Denmark



DEATH TOLL OF AMR

- ❖ 4.95 million deaths were associated with drug resistant bacterial infections in 2019
- ❖ Resistant infections were the direct cause of 1.27 million deaths
 - Almost as many as HIV and malaria combined
- ❖ If nothing is done by 2050
 - 10 million AMR-related deaths
 - 9 million in LMICs
 - 400-1000 billion \$ extra cost for healthcare



Murray, The Lancet 2022 Global burden of bacterial antimicrobial resistance in 2019

Jim O' Neill (2016), Tackling Drug-Resistant Infections Globally

World Bank (2017): Drug-resistant infections A threat to our economic future.

RESISTANCE IS A NATURAL COMPLEX PHENOMENON

- ❖ AMR is a natural mechanism that allows microorganisms to survive.
 - It is present in ALL bacterial communities (human, agricultural, environment) both in pathogenic and non-pathogenic/commensal bacteria
 - Intrinsic – (the bacteria is born with the R)
 - Acquired
 - De novo “creation” i.e. mutations
 - Uptake of antimicrobial resistance genes (ARG) – also called horizontal gene transfer (HGT)
- ARG can be part of mobile genetic elements harboring other genes favoring its spread also between different bacterial species
- Exchange of resistance genes and antibiotic resistant bacteria do not respect borders or sectors!

RESISTANCE IS A NATURAL COMPLEX PHENOMENON

- ❖ AMR is a natural mechanism that allows microorganisms to survive.
 - It is present in ALL bacterial communities (human, agricultural, environment) both in pathogenic and non-pathogenic/commensal bacteria

- Intrinsic – (the bacteria is born with the R)

- Acquired

- De novo “creation”

- Uptake of a resistance gene (HGT)

Antimicrobials

- SPEED UP both creation and uptake of ARGs.

- Kill the sensitive bacterial flora (normal flora)

Leads to selection of R-microorganisms

- ARG can be part of mobile genetic elements that can be transferred between different bacterial species

horizontal gene transfer

can spread also

- Exchange of resistance genes and antibiotic resistant bacteria do not respect borders or sectors!

RESISTANCE IS A NATURAL COMPLEX PHENOMENON

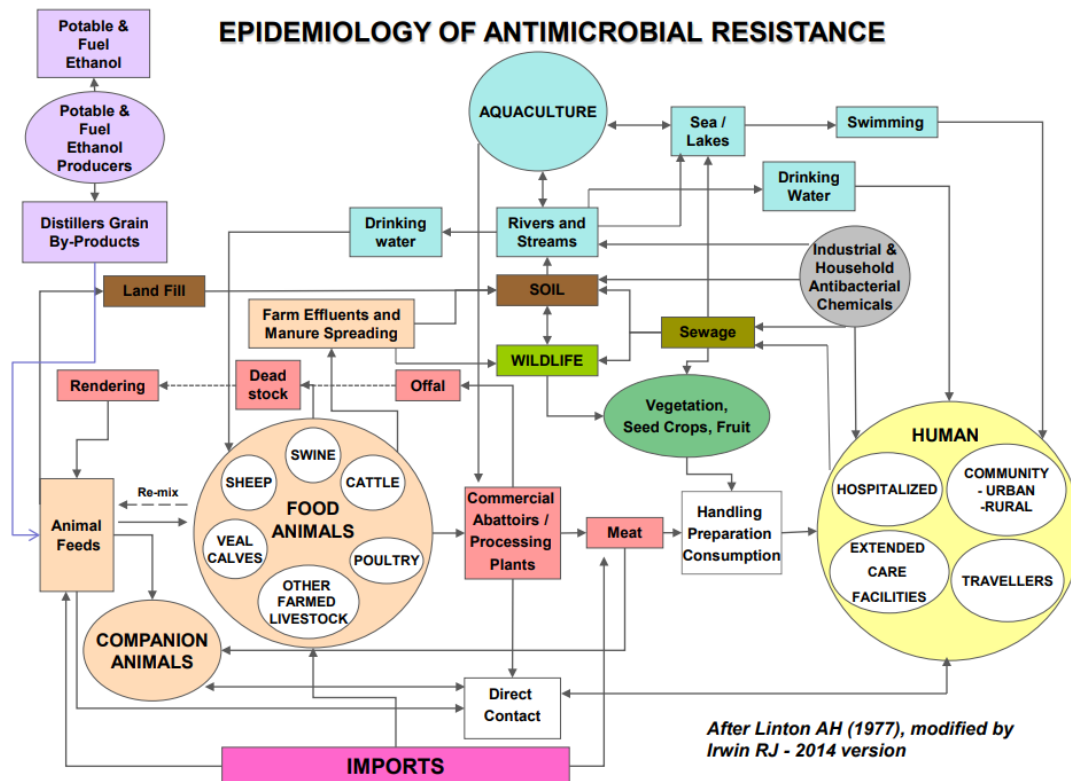
- ❖ AMR is a natural mechanism that allows microorganisms to survive.
 - It is present in ALL bacterial communities (human, agricultural, environment) both in pathogenic and non-pathogenic/commensal bacteria
 - Intrinsic – (the bacteria is born with the R)
 - Acquired
 - De novo
 - Uptake of DNA (HGT)
- ARG can be part of the resistance repertoire of a bacterial species and can spread also between different bacterial species
- Exchange of resistance genes and antibiotic resistant bacteria do not respect borders or sectors!

Spread of resistance is thus heavily affected of

- Use of antimicrobials (AMU)
- Transmission of ARB/ARGs

gene transfer

spread also



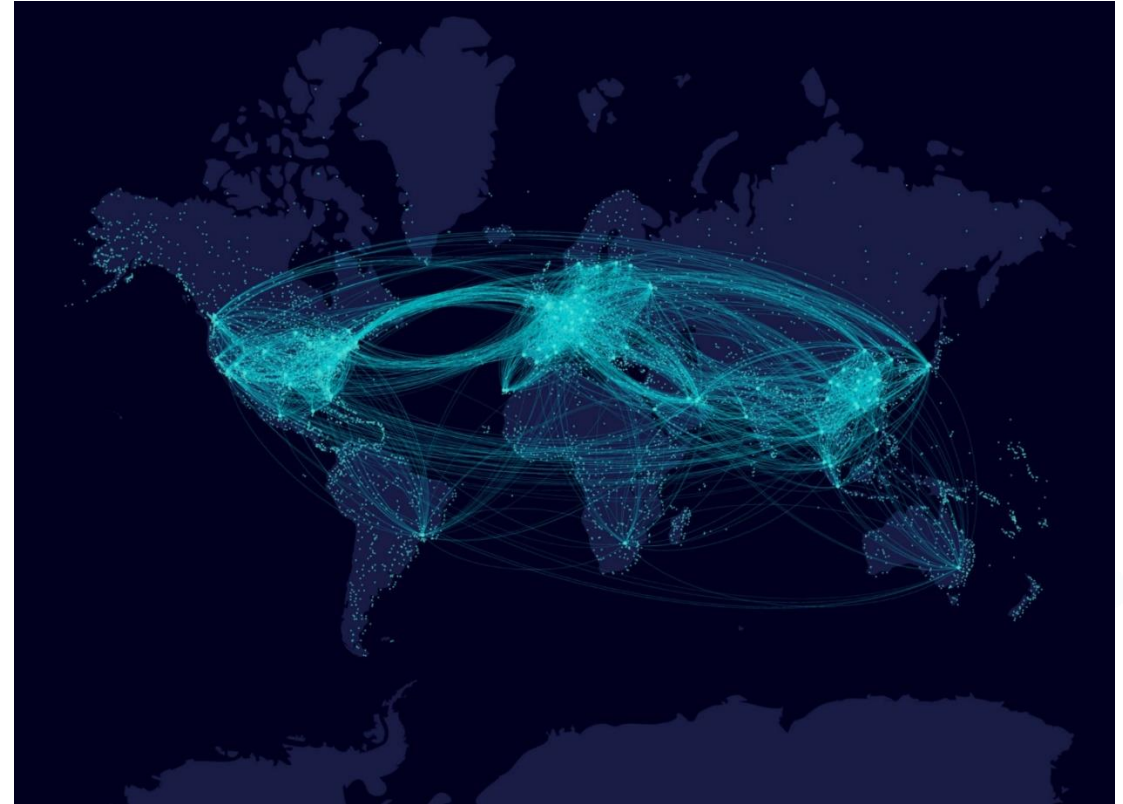
One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems.

It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent.

The approach mobilizes multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for clean water, energy and air, safe and nutritious food, taking action on climate change, and contributing to sustainable development.

- ❖ Human, live animals food and goods travels all over the world
 - Spread of resistance not only across sectors but also across continents and borders

Human travel in 2019



ACI insights

❖ >70% of Antibiotics is used to food producing animals

- < 5 mg/PCU in Norway and Iceland
- > 300 mg/PCU in China and Cyprus

Average EU/EAA countries: 89 mg/PCU in 2020

PCU:per 1 kilo animal produce

❖ In 2013 globally use was estimated to 130.000 tons. Forecasted to increase by 50% by 2030

- In 2019 AB for growth promotion was reported in 26% of countries worldwide!
- Resistance of ARB resistant to 50% of antibiotics increased with 160-170% for chickens and pigs between 2000-2018 in LMICs

❖ In humans (2000-2015): In HICs DDDs/1,000 inhabitants increased slowly or even declined. In LMICs significant increases especially for the WATCgroup

- Use in humans keeps the selection pressure on resistance genes!

CDDEP (2021): The State of The World's Antibiotics 2021
ESVAC 2019-2020 report; [OIE Annual Report on Antimicrobial Agents Intended for Use in Animals \(2021\)](#), Van Boeckel. Global trends in antimicrobial resistance in animals in low- and middle-income countries(Science, 2019).



❖ The BioHAZ panel identified the following antibiotic resistant bacteria as those of highest priority for public health

- Non-typhoidal *S. enterica* serovars, R to 3rd-generation cephalosporins (3rd-GC), carbapenems (CARB) and fluoroquinolones (FQ) – Zoonosis
- *Campylobacter* spp, R to Macrolides, FQ, Aminoglycosides or CARB – Zoonosis
- Enterobacterales (*E. coli*, *K. pneumoniae*), R to 3rd, 4th, 5th-GC, CARB, FQ, Colistin, plazomycin or Glycocyclines
- *S. aureus*, R to methicillin (MRSA), glycopeptides (VRSA), Oxazolidinones (OXAZ), lipopeptides or glycocyclines
- *E. faecium/faecalis*, R to Glycopeptides (VRE), OXAZ, lipopeptides or glycocyclines
- *A. baumannii*, *P. aeruginosa*, R to CARB and colistin

LEVELS OF RESISTANCE IN HUMANS



MRSA

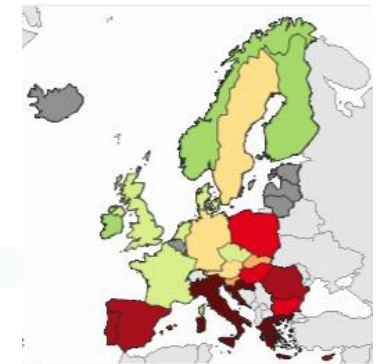
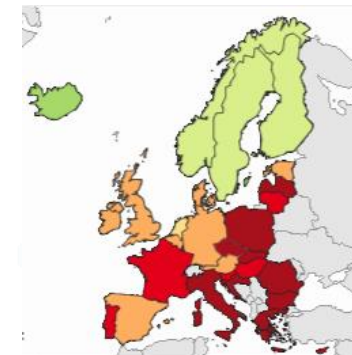
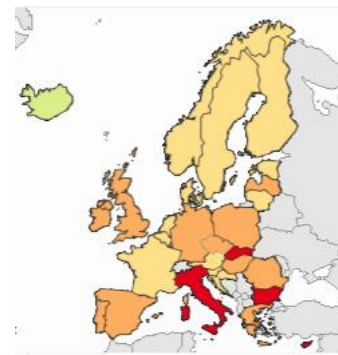
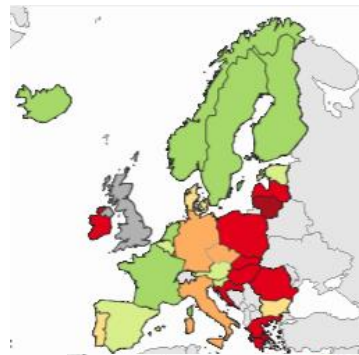
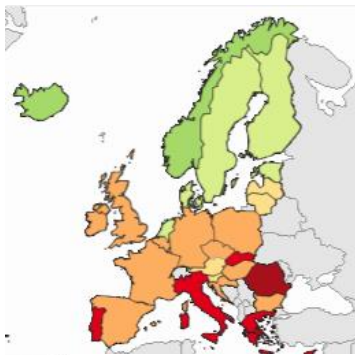
E. faecium
VRE

E. coli
3CG

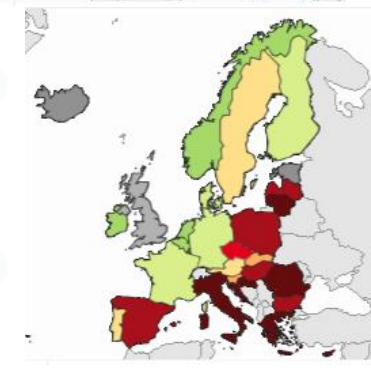
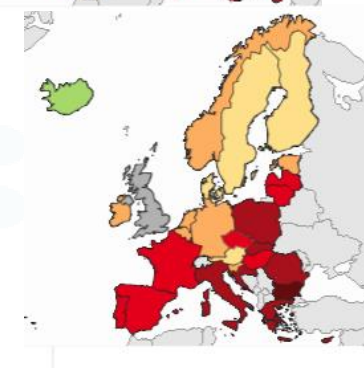
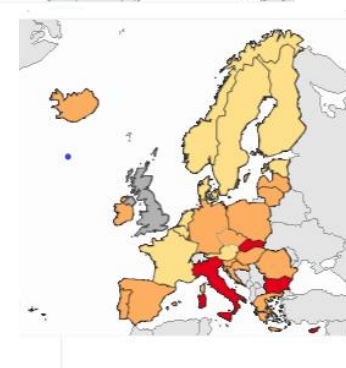
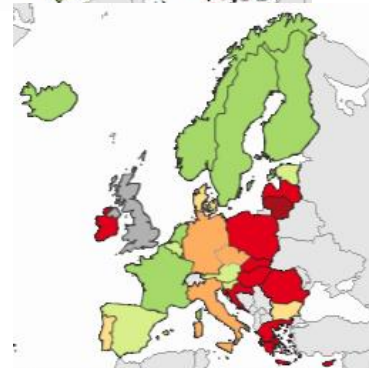
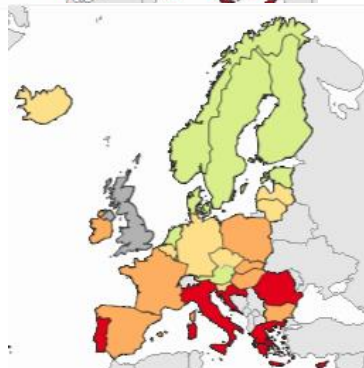
K. pneumoniae
3CG

A. baumannii
multiresistant

2013



2020



- ❖ What are the contribution of resistance from the food producing chain /environment?
 - Difficult to answer precisely
 - The ARB and ARGs of most importance are all found in all sectors (i.e. towards 3rd GC, CARB, FQ, methicillin, OZAZ, colistin)
 - BUT transmission of resistance is not necessarily linear!
 - » Transmit directly giving disease / not giving disease = carriage - these can transmit further
 - » Pass on ARG to other bacteria of the same or different spp.
 - Along the whole chain and from humans to other humans
 - ❖ New data from US looking at *E.coli* from urinary tract infections (UTI) in people identify genetic markers from poultry in 8% of the isolates – clearly indicating that they originate from poultry
 - equals 480-640.000 UTIs per year in US – more than any other non-*E. coli* uropathogen
- Lance Price, personal information
- What does this translate to in countries with less hygienic/biosecurity practices??

- ❖ AMR is a **silent evolving pandemic** and to a large extent **unrecognized** by civil society, policy makers and politicians
- ❖ Urgent need for action in all sectors
 - Both mono sectorial and cross sectorial (One Health)
 - Need to have policy and structures in place that ensure cross-sector mitigation of AMR
 - Locally, regional and globally
- ❖ Prudent use of antimicrobials (AMU) and co-selecting agents **in all sectors**
 - Antimicrobial AND Diagnostic stewardship
 - Rapid, user-near, affordable - innovation highly needed
 - Innovation of non antimicrobial treatment modalities
- ❖ Mitigation of transmission of ARB/ARGs
 - Good hygiene practices / biosecurity
 - Good management practices

SILENT EVOLVING PANDEMIC

ONE HEALTH

Acknowledgement: Lance Price, George Washington University, Milken school of Public Health of for unpublished data on *E. coli* from UTI in US likely stemming from poultry

.

THANK YOU FOR THE ATTENTION