Antimicrobial Resistance (AMR)

- Long-term economic burden
- Action to reduce use

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Deaths due to Antimicrobial resistance (AMR)

From Tillotson & Zinner, 2017)
AMR - A global emerging threat

Yet, in 2013 an estimated 5.6 mio people died because they did not have access to antibiotics!

The use of antimicrobials

Common use of antimicrobials in human and animals:
– to control diseases,
– to prevent disease
– to promote growth of animals in confined systems

All antimicrobial use generates significant risks to public health through development and spread of AMR microorganisms

AMR microorganisms can cause human disease directly and/or transfer AMR genes to the human microbiota
Where do we (mostly) use our antimicrobials?

- Sick humans: 15 - 25%
- Sick animals: 15 - 25%
- To grow healthy animals faster: 50 - 70%

(Estimated figures from USA)
Surely the problems mainly relate to human use of antimicrobials, no?
Fluoquinolone use and Fluoquinolone resistance in human infections in USA
Economic costs attributable to AMR

negative impact on the labour supply through two mechanisms.

1) Increased mortality – deaths attributable to AMR permanently reduces the size of the working age population

2) Increased morbidity – prolonged periods of sickness temporarily reduce the size of the global workforce and may, in severe cases, lead to permanent reductions in labour efficiency (productivity)

Other costs typically not included in monetising AMR costs
## Minimum Estimates of Morbidity/Mortality from AMR Infections – USA 2013*

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<tbody>
<tr>
<td>Carbapenem-resistant Enterobacteriaceae (CRE)</td>
<td>9,300</td>
<td>610</td>
</tr>
<tr>
<td>Drug-resistant <em>Neisseria gonorrhoeae</em> (any drug)</td>
<td>246,000</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Multidrug-resistant <em>Acinetobacter</em> (three or more drug classes)</td>
<td>7,300</td>
<td>500</td>
</tr>
<tr>
<td>Drug-resistant <em>Campylobacter</em> (azithromycin or ciprofloxacin)</td>
<td>310,000</td>
<td>28</td>
</tr>
<tr>
<td>Drug-resistant <em>Candida</em> (fluconazole)</td>
<td>3,400</td>
<td>220</td>
</tr>
<tr>
<td>ESBL producing Enterobacteriaceae (ESBLs)</td>
<td>26,000</td>
<td>1,700</td>
</tr>
<tr>
<td>Methicillin-resistant <em>Staphylococcus aureus</em> (MRSA)</td>
<td>80,000</td>
<td>11,000</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em> (full resistance)</td>
<td>1,200,000</td>
<td>7,000</td>
</tr>
<tr>
<td>Drug-resistant tuberculosis (any clinically relevant drug)</td>
<td>1,042</td>
<td>50</td>
</tr>
<tr>
<td>Erythromycin-resistant Group A <em>Streptococcus</em></td>
<td>1,300</td>
<td>160</td>
</tr>
<tr>
<td>Clindamycin-resistant Group B <em>Streptococcus</em></td>
<td>7,600</td>
<td>440</td>
</tr>
</tbody>
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**Summary Totals for Antibiotic-Resistant Infections**  
2,049,442  
23,488

*(Clostridium difficile Infections*  
250,000  
14,000)

*ANTIBIOTIC RESISTANCE THREATS in the United States, 2013, USCDC.*
Indirect Economic costs attributable to AMR
(not included in the studies cited here)

With dramatic AMR increase, there could be further indirect costs:

- People may choose not to undergo certain medical procedures because of the heightened risks involved
- People may also refrain from undertaking certain economic activities, such as travel and trade,
- People may experience general negative psychological effects, such as panic.
Cost of AMR (human health cost)

The cost of AMR in USA is estimated at:

**US$ 20 billion** in excess direct health care costs,
additional lost productivity cost **$ 35 billion** a year

**Total cost USA: US$ 55 billion**

Corresponding to **US$ 157 million per 1 million inhabitants**

† *US CDC: Antibiotic resistance threats in the United States, 2013*
Cost of AMR (human health cost)  
(does not include foodborne disease or trade costs)

Average GDP annual loss has been estimated as high as

**US$ 100 billion to US$ 3 trillion** for the world
(depending on AMR development scenario chosen)

Global GDP in 2018 is US$ 90 trillion
(thus 0.1 – 3.3% of GDP annually lost to AMR)

※ The Rand Report, 2014, The Wellcome Trust: a study, commissioned in the framework of the independent review led by Jim O’Neill
Patients at especially high risk

- CANCER CHEMOTHERAPY
- COMPLEX SURGERY
- RHEUMATOID ARTHRITIS
- DIALYSIS FOR END-STAGE RENAL DISEASE
- ORGAN AND BONE MARROW TRANSPLANTS
Overall Resistance / Multiple Drug Resistance from food

<table>
<thead>
<tr>
<th>Salmonella</th>
<th>Overall resistant rate (%)</th>
<th>Overall MDR rate (%)</th>
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<tbody>
<tr>
<td></td>
<td>China (2000-2016)</td>
<td>EU (^a)</td>
</tr>
<tr>
<td>recovered from broiler meat (retail chicken)</td>
<td>81.3</td>
<td>63.8</td>
</tr>
<tr>
<td>recovered from pork</td>
<td>40.6</td>
<td>64.1</td>
</tr>
<tr>
<td>Recover from overall retail foods</td>
<td>82.6</td>
<td>-</td>
</tr>
</tbody>
</table>

\(^a\): broiler data-year 2016, 2012-2014; pork data-year 2015, 2011-2013. \(^b\) estimated from single-antimicrobial resistance figures

Source:
USA NARMS interactive data:
https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm416741.htm
Risk mitigation for AMR risk (re. food production)

• A number of initiatives, including regulatory initiatives, have been taken in recent years
• The EU have banned the use of antimicrobials for animal growth promotion since 2006
• USA is moving (slowly) in the same direction
• China will ban use of antimicrobials for animal growth promotion (in aquaculture) by 2020
• Most countries have yet to impose a ban, although most countries are drafting action plans – till now mostly words, no action

In many cases food producers are concerned over potential reduction in production efficiency when abandoning antimicrobial growth promoters
So –

can we have efficient animal production without antimicrobial growth promoters?

and

Where is the evidence it works?
DANMAP Data Collection

*Diagram showing the data collection process involving Regional Food Control Laboratory, Slaughter Plants, Private Laboratories, Veterinary Practice, Departments of Clinical Microbiology, Danish Veterinary and Food Administration, Technical University of Denmark, National Food Institute & National Vet Institute, and Statens Serum Institut.*
Antimicrobial consumption in Denmark 1994-2017

No prophylactic use
Restrictions on sales
Health Advisory Contracts

Yellow card

Antimicrobial agents (tonnes)

Prescribed human antibacterials
Prescribed veterinary antimicrobials
Antimicrobial growth promoters

04.12.2018
BACON BOOST

Denmark’s actions to stop using antibiotics as growth promoters (AGP) in livestock has reduced antibiotic consumption but not pig production.

Milligrams antibiotic per kg meat produced

No sales profit for vets. Avoparcin banned.

Virginiamycin banned.
No AGP in older pigs.

No AGP in piglets.

“Yellow card” scheme began.

Next Generation Sequencing (NGS) and Whole Genome Sequencing (WGS) - The next Milestone

**NOTEWORTHY MILESTONES IN MICROBIOLOGY**

- **Leeuwenhook** – 1676 – Bacteria/Microscopy
- **Pasteur** – 1861 – Proves Germ Theory
- **Invents pure culture technique (+ Koch)**
- **Schwann** – 1839 – Cell Theory
- **Fleming** – 1928 – Discovers Antibiotics
- **2005 – WGS of microorganisms**
**FUTURE** Global Microbial Identifier: GMI
1st global tool to identify Microorganisms and Antimicrobial Resistance

Still just an idea !!
Monitoring large healthy populations using a metagenomic approach
Global sewage surveillance – 2017

• 170 samples from 88 countries collected in June 2017
• 10 cities running longitudinal
• 15 new countries for November 2017
• More countries and cities in 2018
• 103 countries have signed up
Global sewage surveillance – 2016 AMR abundance (collective pool of AMR genes) per sample and region

Developed by Patrick Munk
Tech. University of Denmark

Preliminary results, Hendriksen RS et al. In prep