FEAM
Federation of European Academies of Medicine

Active Citizenship Network Conference, 4th February 2019 - Brussels

Infections and antimicrobial resistance and their impact on public health

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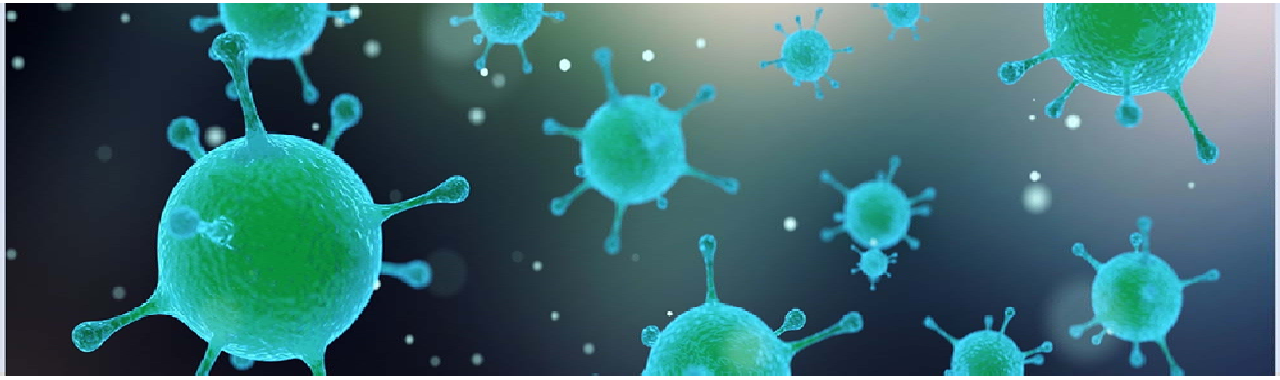
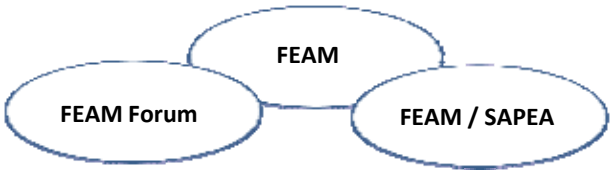


***FEAM**, European umbrella group of National Medical Academies*

- Representing **19 national Academies** in Europe : Medicine, Medical Sections of Academies of Sciences and now also Pharmacy
- **Elected Fellowships of FEAM Academies -** thousands of the best researchers and scholars from across Europe and the whole biomedical spectrum
- Providing **independent** (commercial, political, ideological) and **evidence-based** science policy advice, with a European dimension, on human and animal medicine, biomedical research, education and health priorities
- Academies' Fellows also serve as individual expert – able to engage in a **national/European agenda**

What are the distinctive strengths of FEAM:

- ✓ Providing **excellent and independent scientific advice** to policy-makers on European topical biomedical issues
- ✓ Dual capacity to Inform the **EU decision policy making process** at European and national level, with its Academies
- ✓ **Multidisciplinary cooperation** with other European and global academy networks – via EU-funded SAPEA project and bilateral projects
- ✓ **Cross-sectoral cooperation** with other European biomedical stakeholders via its European Biomedical Policy Forum



FEAM European Biomedical Policy Forum FEAM's involvement in the EU-funded SAPEA project

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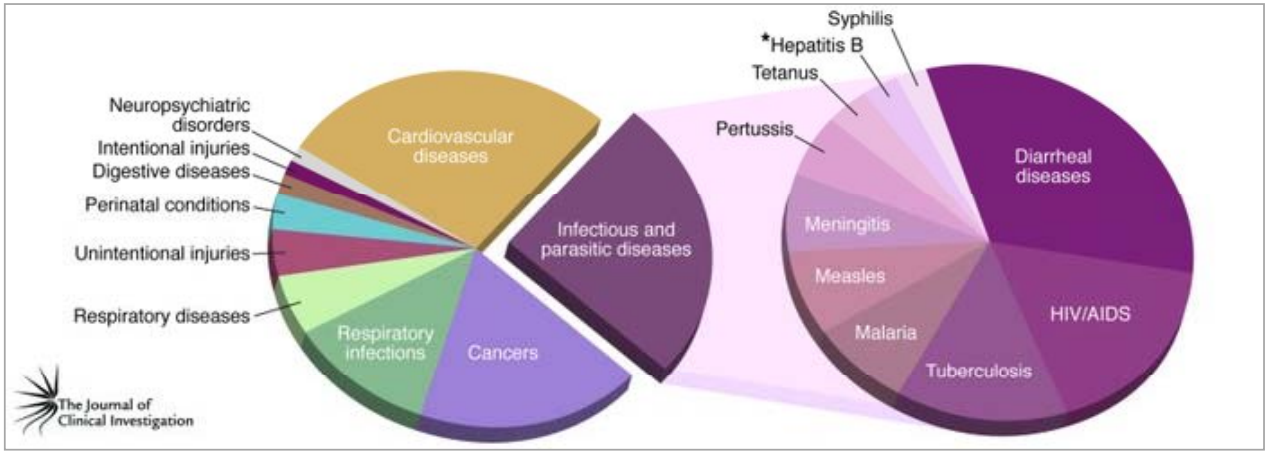
Infectious diseases: a natural emerging danger

- Infectious diseases are disorders caused by organisms, such as **bacteria**, **viruses**, **fungi** or **parasites**
- Many organisms live in and on our bodies. They're normally harmless or even helpful, but under certain conditions, some organisms may cause disease
- Infectious diseases can also be the result of transmission that occurs in a direct or indirect contact (from person to person, from bites of insects or animals, through the ingestion of contaminated food/water or exposure to organisms in the environment)



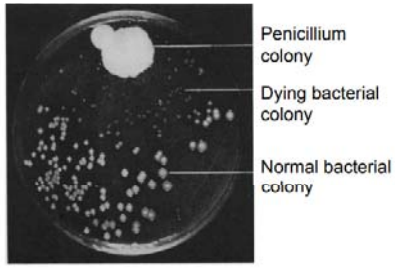
- Second leading cause of death in the world in 2004
- 9.5 million deaths, after cardiovascular diseases

The 2004 worldwide ten leading causes of death and ten leading causes of death from infectious and parasitic diseases.
The global burden of disease: 2004 update, published by the WHO in 2008. The data indicate that infectious and parasitic diseases were the second leading cause of death in the world in 2004, after cardiovascular diseases. Specifically, approximately 17 million and 9.5 million deaths were a result of cardiovascular diseases and infectious and parasitic diseases, respectively. Among those who died of infectious and parasitic diseases, diarrheal diseases were the leading cause of death, closely followed by HIV/AIDS. *These numbers exclude deaths from liver cancer and cirrhosis resulting from chronic HBV infection.

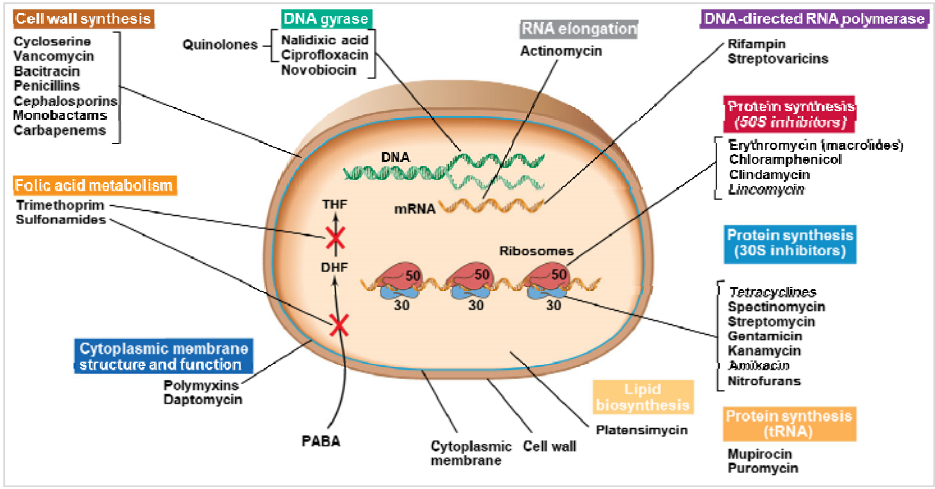
Source: Tales from the gene pool: a genomic view of infectious disease.
Karen Honey. *Published September 1, 2009. J Clin Invest.* 2009;119(9):2452 2454. https://doi.org/10.1172/JCI40662

Treatment for infectious diseases: Anti-microbial agents

- An **anti-microbial agent** is a chemical compound capable to destroy microorganisms or prevent their development
- Anti-microbial agents are some of the most widely, and often injudiciously, used therapeutic drugs worldwide
- The antibiotic penicillin was the first compound discovered in the early 1928. Streptomycin was then discovered in 1944, and since then many other antibiotics and other types of antimicrobials have been found and put into use
- Anti-microbial drugs are generally classified on the basis of:
  - Molecular structure
  - Mechanism of action
  - Spectrum of antimicrobial activity



Sir Alexander Fleming, a Scottish physician, microbiologist, and pharmacologist that discoveries the world's first antibiotic substance benzylpenicillin (Penicillin G) in 1928. He shared the Nobel Prize in Medicine in 1945 with Howard Florey and Ernst Boris Chain



Classes of antibiotics/antibacterial agents and their modes of action on bacteria (Adopted from Labnotesweek4, 2013)

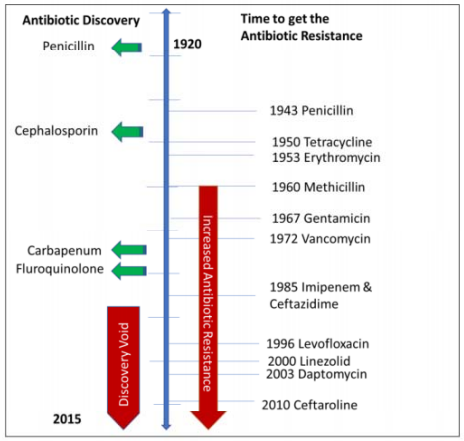
Anti-microbial Resistance (AMR): a growing public health issue

The anti-microbial drug resistance is defined as the acquired ability of a microorganism to resist at the effects of a chemotherapeutic agent to which it is normally sensitive

Anti-microbial resistance happens when microorganisms (bacteria, fungi, viruses, and parasites) change when they are exposed to antimicrobial drugs (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics)

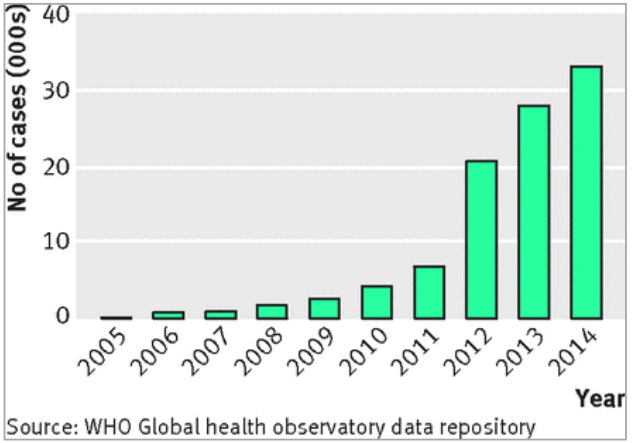
Medicines become ineffective and infections persist in the body, increasing the risk of spread to others

In recent times, the emergence and dissemination of drug-resistant pathogens has accelerated, proving to be global, extremely dangerous



Graphical representation of onset of antibiotic resistance versus time to get antibiotic resistance

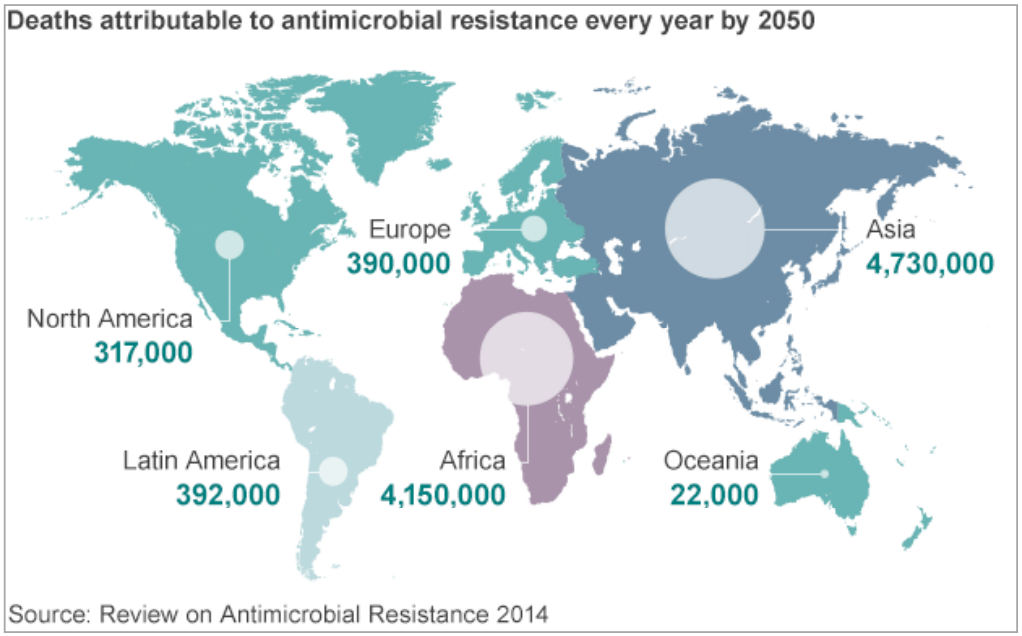
Adapted from A Review on Antibiotic Resistance: Alarm Bells are Ringing Sojib Bin Zaman , Muhammed Awlad Hussain , Rachel Nye , Varshil Mehta , Kazi Taib Mamun , Naznin Hossain



Confirmed cases of rifampicin resistant or multidrug resistant tuberculosis in the WHO South East Asia region, 2005-14

AMR is increasingly recognized by many international health organizations as a global public health issue and a threat to the modern health-care system

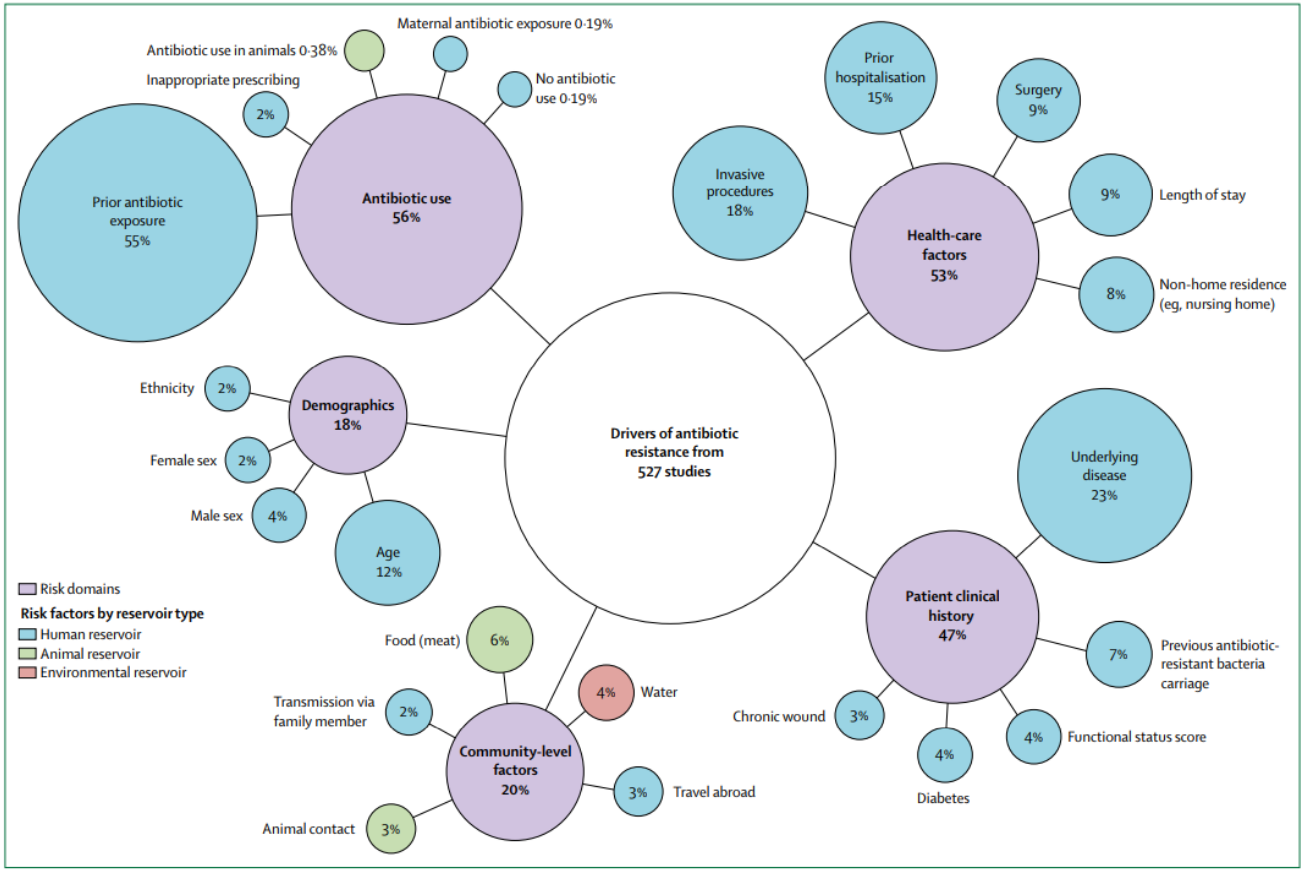
- The growing worldwide AMR phenomenon is generally associated to the "selective pressure" caused by the improper use, overuse, or misuse of anti-microbials in humans and animals
- The G8 Summit in June 2013 discussed about the AMR. In this occasion, science ministers identified AMR as the "major health security challenge of the 21st century" requiring intensive international collaboration
- The Health-care costs represent one of the issues related to AMR (higher costs due to extended hospital stays and the use of more expensive drugs)

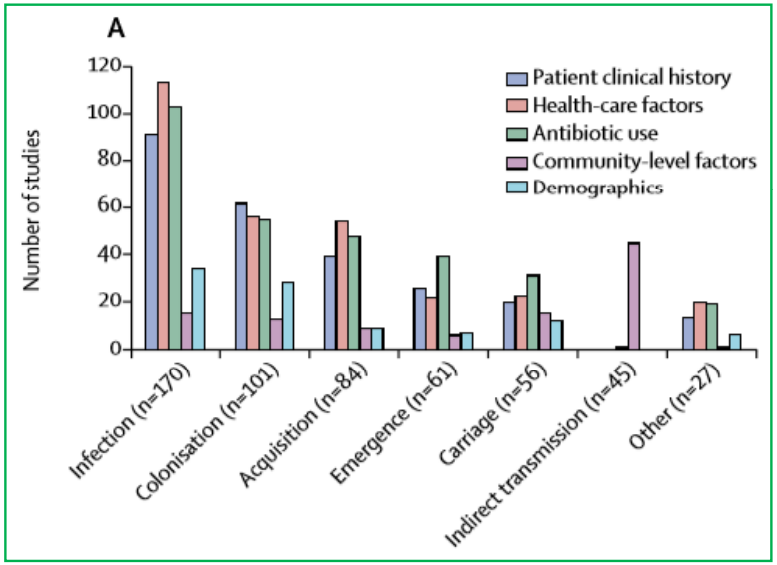


AMR is responsible for an estimated **33,000 deaths per year in the EU**. It is also estimated that AMR costs the EU **EUR 1.5 billion per year in healthcare costs and productivity losses.**

European Commission

Drivers of antibiotic resistance in humans





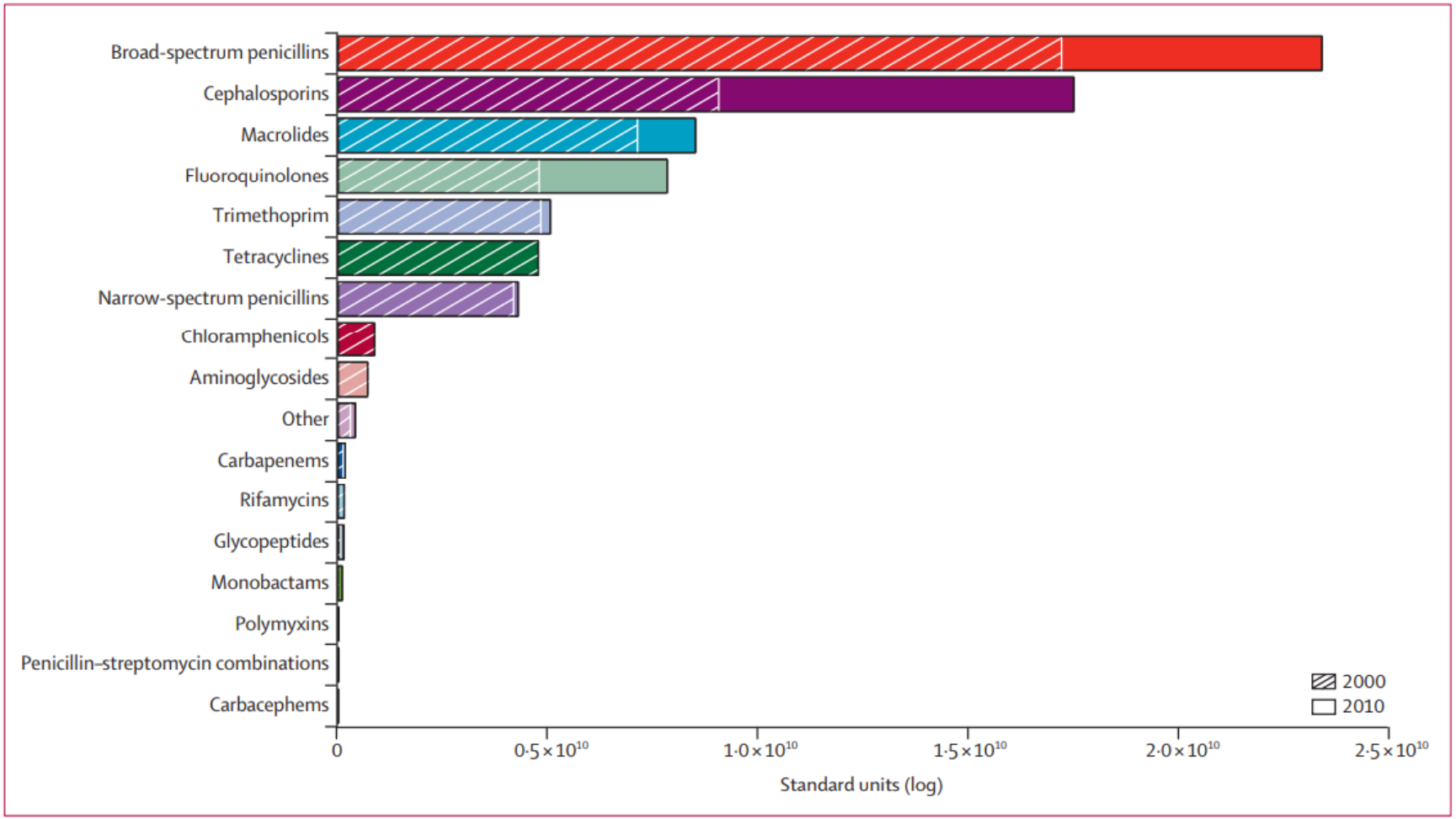
Overview of the risk factor domains stratified by outcomes of antibiotic resistance. Total number of studies by type of outcome for antibiotic resistance across the five risk domains.

Percentage of studies quantifying drivers of antibiotic resistance in humans

Adapted from: *Quantifying drivers of antibiotic resistance in humans: a systematic review*

Anuja Chatterjee, Maryam Modarai, Nichola R Naylor, Sara E Boyd, Rifat Atun, James Barlow, Alison H Holmes, Alan Johnson, Julie V Robotham

Increased antibiotic consumption over the time



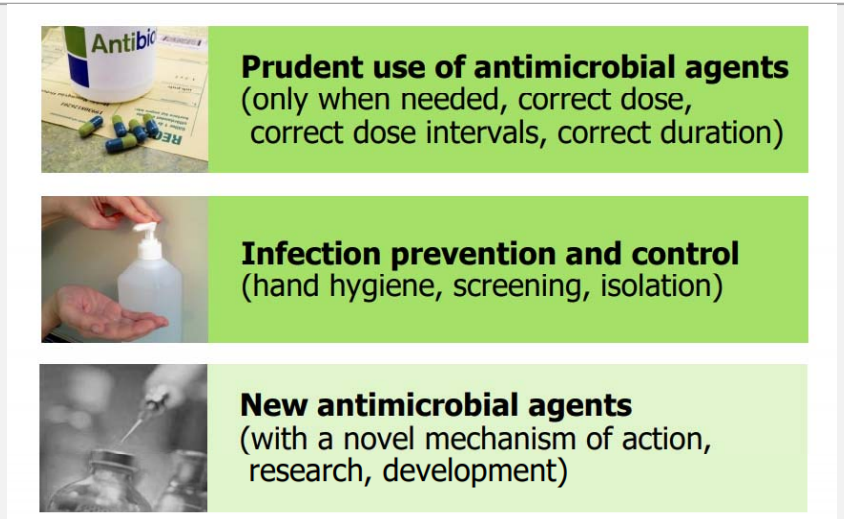
Global antibiotic consumption by class in 2000 and 2010.
Standard units are defined as a single dose unit (ie, pill, capsule, or ampoule).

Source: Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. Van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, Laxminarayan R. Lancet Infect Dis. 2014 Aug;14(8):742-750. doi: 10.1016/S1473-3099(14)70780-7. Epub 2014 Jul 9.

The European Commission under the EU's Seventh Framework Programme for Research and Technological Development - as well as the program Horizon 2020 and the Innovative Medicines Initiative (IMI) - financed more than 140 AMR-related research projects with a budget of euro 130 million (European Commission, 2015)

In 2011, the European Parliament approved a resolution to implement AMR national strategies both in animals and human medicine:

- Prudent use of antimicrobial agents
- Monitoring and surveillance of AMR
- Need for research and development of new antimicrobial agents and alternatives holistic approach
- International cooperation



Main actions to prevent and control anti-microbial resistance

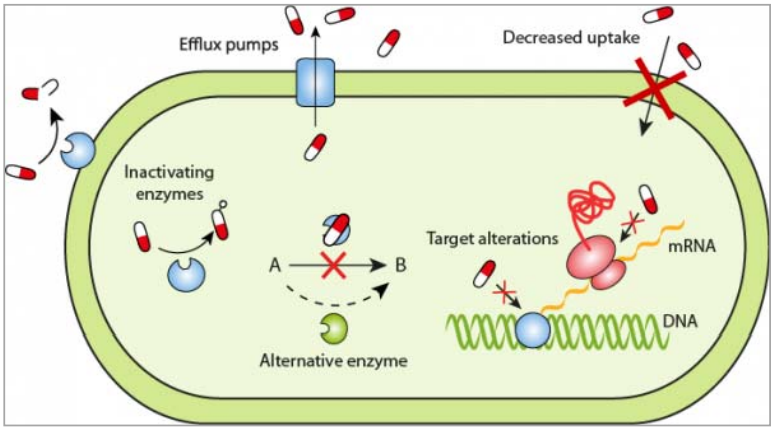
ecdc
EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Anti-microbial Resistance: Mechanisms of action

Anti-microbial agents disrupt essential structures or processes in microbes.

This in turn either kills the microbes or stops them from multiplying. Microbes have in turn evolved many antibiotic resistance mechanisms to withstand the actions of anti-microbial drugs:

- By modification or inactivation of anti-microbial agents
- By alteration in the target site and reducing binding capacity
- By modification of metabolic pathways to avoid the anti-microbial effect
- By reducing intracellular anti-microbial assembly and decreasing porosity and/ or increasing drug active efflux



Antibiotic resistance strategies in bacteria

Common ways of acquiring resistance

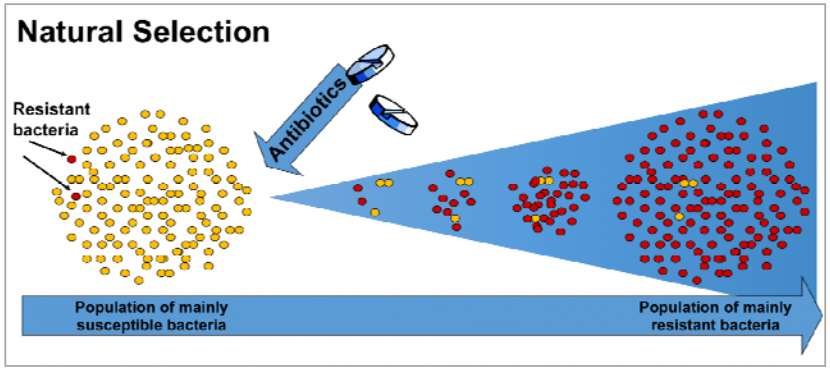
1) Intrinsic resistance properties (permeability cell membrane, lack of antimicrobial target)

2) Mutation (genetic changes)

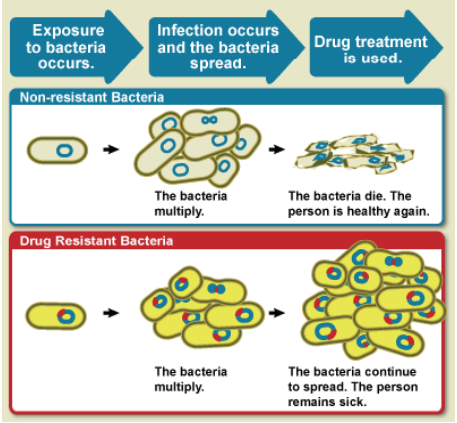
3) Inactivation of anti-microbial drugs (presence of degrading enzymes)

4) Horizontal gene transfer (transfer of antimicrobial-resistant genes)

5) Efflux pumps, biofilm resistance & quorum sensing (e.g. drug efflux pumps lower the level of antibiotics inside the cell)



Why antibiotic resistance is growing



Difference between non-resistant bacteria and drug resistant bacteria

Non-resistant bacteria multiply, and upon drug treatment, the bacteria die. Drug resistant bacteria multiply as well, but upon drug treatment, the bacteria continue to spread

How anti-microbial resistance can be prevented?

New classes of anti-microbial agents were discovered, existing antibiotics were modified, and synthetic components were constantly tailored to combat emerging AMR by improving the clinical qualities

The emergence and spreading of drug resistant pathogens, particularly zoonoses, has accelerated due to overuse, not following the prescribed length of use, misuse, and abuse of antimicrobials.

Guidelines & Suggestion

- Antibiotics should be the last line of defence NOT the first
- Most common infections will get better by themselves through time, bed rest, liquid intake and healthy living
- Only take antibiotics prescribed by a doctor
- If prescribed antibiotics, finish the course
- Do not use other peoples or leftover antibiotics

⇒ Resistance can be minimized by using anti-microbial agents correctly and only when needed
⇒ Resistance to a certain antibiotic can be lost if antibiotic is not used for several years

⇒ Long-term solution to anti-microbial resistance relies on the development of new anti-microbial compounds

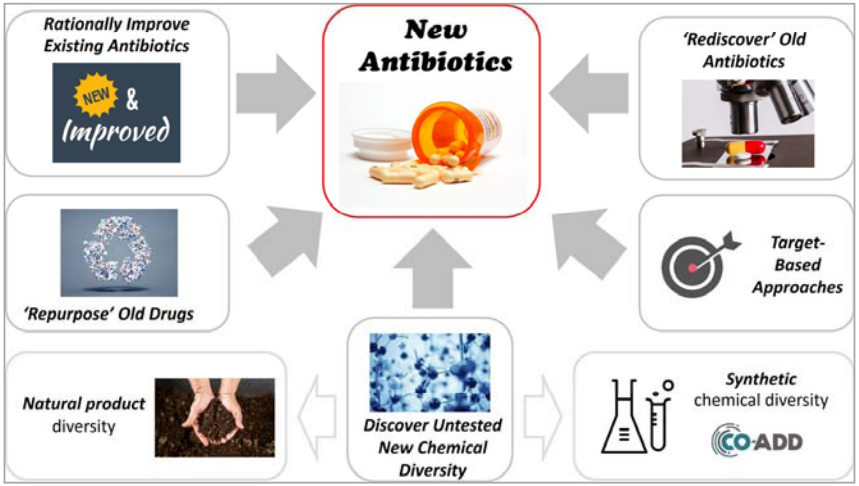
- Modification of current anti-microbial compounds is often productive
- Automated chemistry methods (combinatorial chemistry) has sped up drug discovery
- 7,000,000 compounds must be screened to find a single useful clinical drug

⇒ Computers can now be used to design molecules to interact with specific microbial structures

⇒ New methods of screening natural products have been used

⇒ Combinations of drugs can also be used (e.g., ampicillin and sulbactam)

⇒ Bacteriophage therapy



Different approaches to discover new antibiotics
Adapted from "*Polishing the tarnished silver bullet: the quest for new antibiotics*" Mark A.T. Blaskovich, Mark S. Butler, Matthew A. CooperEssays In Biochemistry Mar 03, 2017, 61(1) 103-114; DOI: 10.1042/EBC20160077

Conclusion

- Anti-microbial resistance has been recognized as a global health problem and considered by major health organizations as the top health challenge in the 21st century
- It is certain that the inappropriate therapeutic use and the nontherapeutic use of antimicrobials is considered to be one of the drivers for the development of resistance in human
- The EU has proved to be in the upfront in tackling the public health and environmental consequences of AMR by developing an action plan that provides a comprehensive and science-based strategy for the future

World Health Organization
Regional Office for South-East Asia

Regional Meeting on Antimicrobial Resistance
Jaipur, India 10 to 13 November 2014

Recommendations to Member States

⇒ Develop time bound action plan in accordance with Jaipur Declaration;
⇒ Estimate disease burden and trend of antibacterial resistance through national network of quality laboratory services;
⇒ Undertake operational research in AMR to find out practical solutions to local challenges/issues;
⇒ Involve professional bodies and civil society and improve awareness in prescribers, dispensers, and consumers;
⇒ Strengthen national regulations to ensure quality of drugs, preparation standard treatment guidelines, and ensure proper distribution sale, and utilization of antibiotics;
⇒ Develop mechanisms to test and assure quality of drugs;
⇒ Consider banning or restricting non therapeutic use of antibiotics in veterinary practices; and
⇒ Strategically use mass media, social media, community leaders, NGOs, CHW and practitioners of alternative systems of medicines to educate communities on compliance with prescribed regimen and avoiding self-medication.

References

- Emerging Infectious Diseases, Antimicrobial Resistance and Millennium Development Goals: Resolving the Challenges through One Health.
Asokan GV, Kasimanickam RK. Cent Asian J Glob Health. 2013 Oct 1;2(2):76. doi: 10.5195/cajgh.2013.76. eCollection 2013.

- Antimicrobial resistance: A global emerging threat to public health systems.
Ferri M, Ranucci E, Romagnoli P, Giaccone V. Crit Rev Food Sci Nutr. 2017 Sep 2;57(13):2857-2876. doi: 10.1080/10408398.2015.1077192.

- Polishing the tarnished silver bullet: the quest for new antibiotics.
Blaskovich MA, Butler MS, Cooper MA. Essays Biochem. 2017 Mar 3;61(1):103-114. doi: 10.1042/EBC20160077. Print 2017 Feb 28.

- Quantifying drivers of antibiotic resistance in humans: a systematic review.
Chatterjee A, Modarai M, Naylor NR, Boyd SE, Atun R, Barlow J, Holmes AH, Johnson A, Robotham JV. Lancet Infect Dis. 2018 Dec;18(12):e368-e378. doi: 10.1016/S1473-3099(18)30296-2. Epub 2018 Aug 29.

- Antimicrobial resistance mechanisms and potential synthetic treatments.
Ali J, Rafiq QA, Ratcliffe E. Future Sci OA. 2018 Feb 5;4(4):FSO290. doi: 10.4155/fsoa-2017-0109. eCollection 2018 Apr.

- Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data.
Van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, Laxminarayan R. Lancet Infect Dis. 2014 Aug;14(8):742-750. doi: 10.1016/S1473-3099(14)70780-7. Epub 2014 Jul 9.