

The emerging threat of multi-drug resistant microorganisms

Source: Jorge Láscar, <https://www.flickr.com/photos/jlascar/18794580599>



Infection Control: Old Problems and New Challenges
Asian Medical Student's Conference (AMSC) 2018
Kuala Lumpur, July 2018

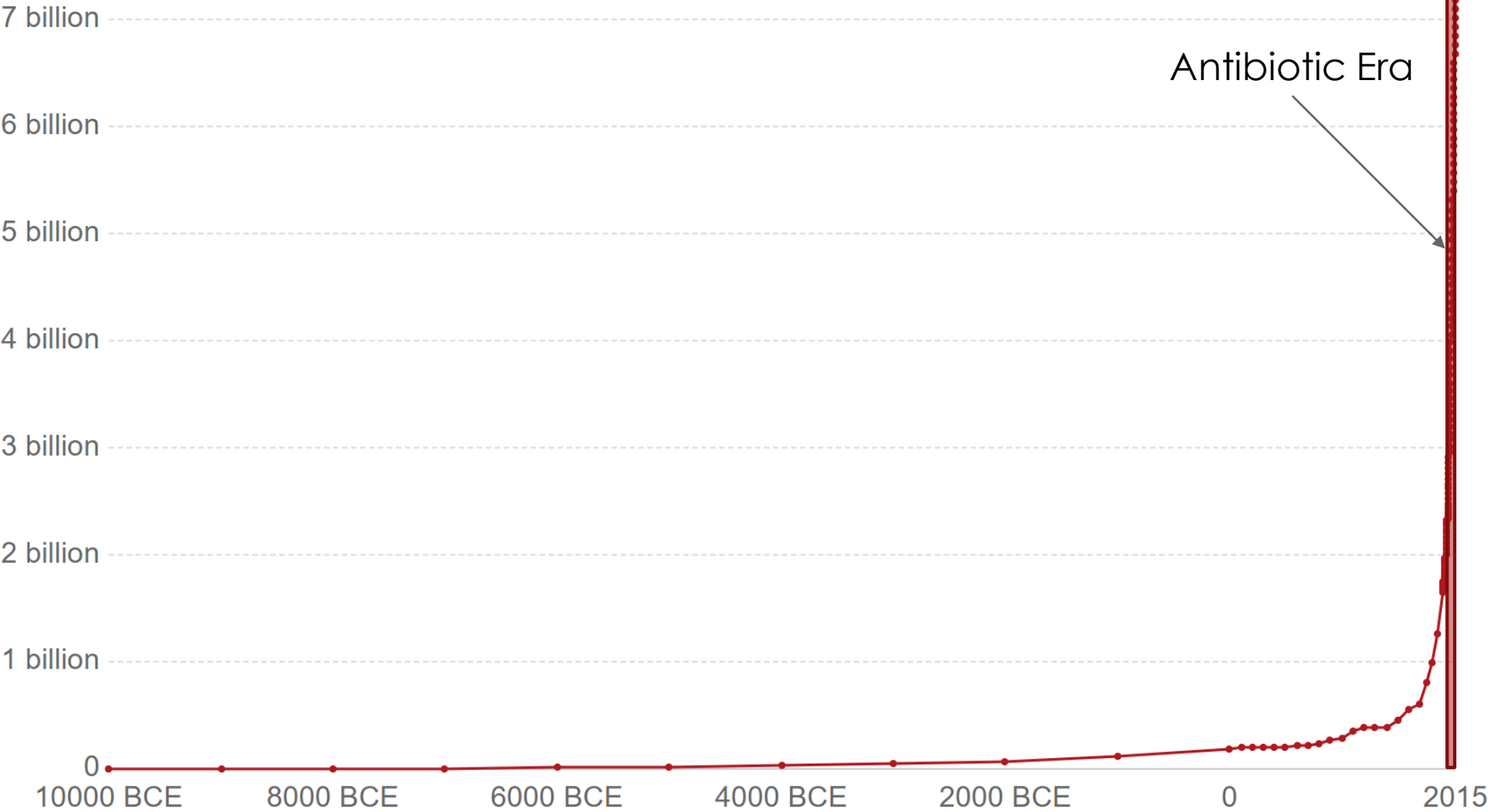
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Research Fellow in Urban
Health



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UNU International Institute for
Global Health (UNU-IIGH)

World population since 10,000 BCE (OurWorldInData series)

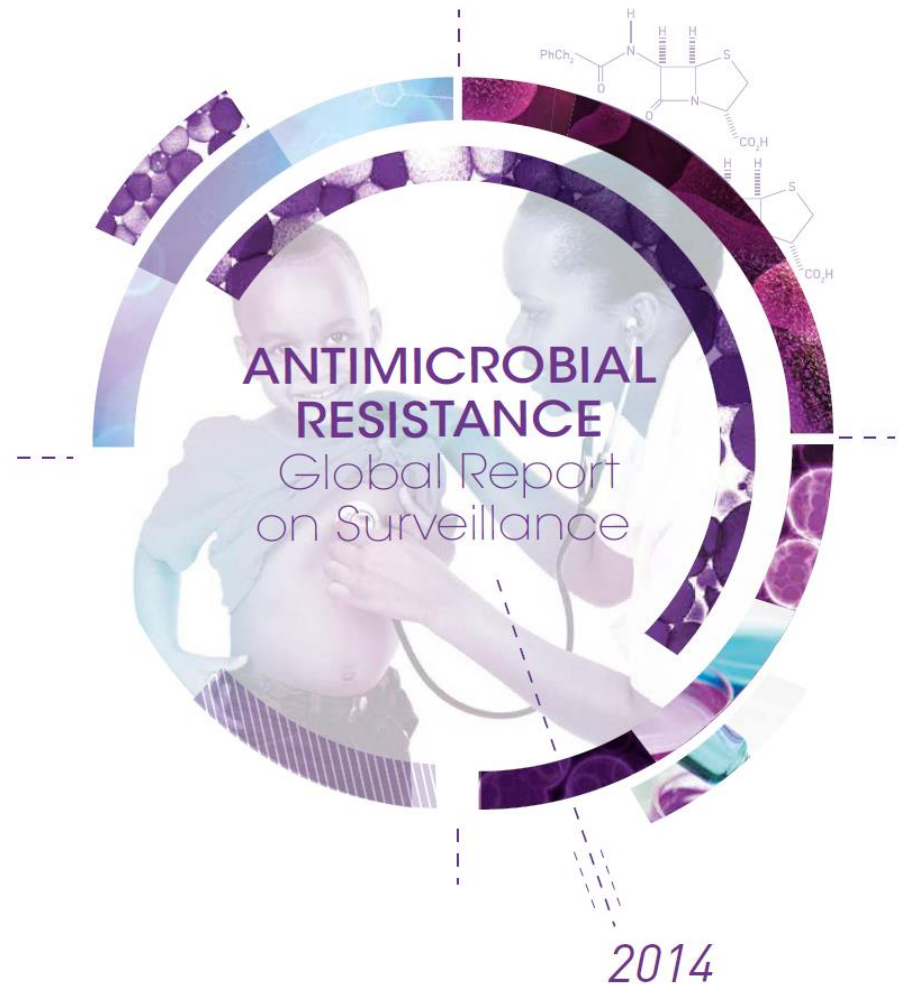


Source: History Database of the Global Environment (HYDE) (before 1900), UN Publication "The World at Six Billion" (1900-1940), UN World Population Prospects: 2015 Revision (1950-2015)
OurWorldInData.org/world-population-growth/ • CC BY-SA

Emerging crisis

“Without urgent, coordinated action by many stakeholders, the world is headed for a post-antibiotic era, in which common infections and minor injuries which have been treatable for decades can once again kill...”

*- Dr. Keiji Fukuda, WHO
Assistant Director-General
for Health Security, 2014*





The WHO priority list

PRIORITY: CRITICAL	PRIORITY 2: HIGH	PRIORITY 3: MEDIUM
<ul style="list-style-type: none">◆ Acinetobacter baumannii carbapenem-resistant◆ Pseudomonas aeruginosa carbapenem-resistant◆ Enterobacteriaceae carbapenem-resistant, ESBL-producing	<ul style="list-style-type: none">◆ Enterococcus faecium vancomycin-resistant◆ Staphylococcus aureus methicillin-resistant vancomycin-intermediate and resistant◆ Helicobacter pylori clarithromycin-resistant◆ Campylobacter spp. fluoroquinolone-resistant◆ Salmonellae fluoroquinolone-resistant◆ Neisseria gonorrhoeae cephalosporin-resistant fluoroquinolone-resistant	<ul style="list-style-type: none">◆ Streptococcus pneumoniae penicillin-non-susceptible◆ Haemophilus influenzae ampicillin-resistant◆ Shigella spp. fluoroquinolone-resistant

Source: WHO

But also, e.g., Malaria (protozoan), HIV & influenza (viral), TB (mycobacterial), *Candida* (fungal)

Levels of drug resistance

► Categories

- Multidrug-resistant (MDR): acquired non-susceptibility to at least one agent in three or more antimicrobial categories
- Extensively drug-resistant (XDR): non-susceptibility to at least one agent in all but two or fewer antimicrobial categories
- Pandrug-resistant (PDR): non-susceptibility to all agents in all antimicrobial categories

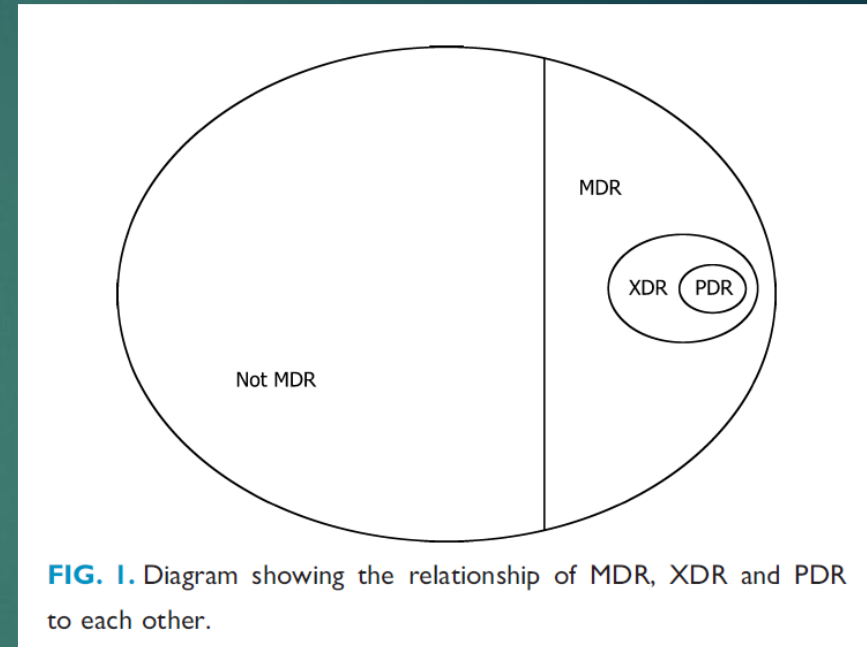


FIG. 1. Diagram showing the relationship of MDR, XDR and PDR to each other.

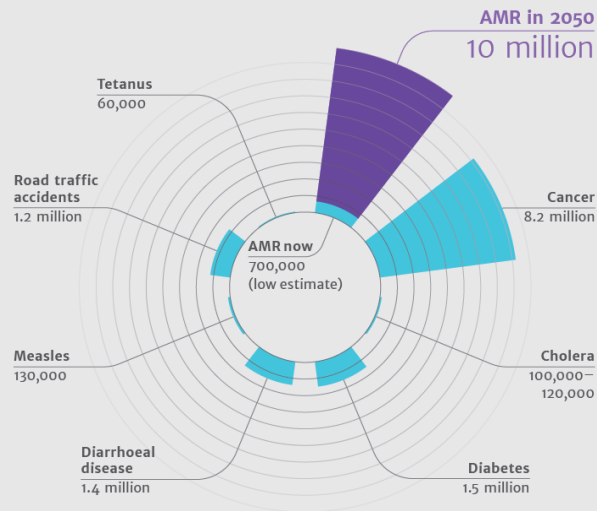
Source: Magoriakos et al, 2012. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance.



A post-antibiotic era

Source: 'Review on Antimicrobial Resistance. *Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations*. 2014.

Deaths attributable to AMR every year compared to other major causes of death



Sources

Diabetes www.who.int/mediacentre/factsheets/fs312/en/

Cancer www.who.int/mediacentre/factsheets/fs304/en/

Cholera www.who.int/mediacentre/factsheets/fs03/en/

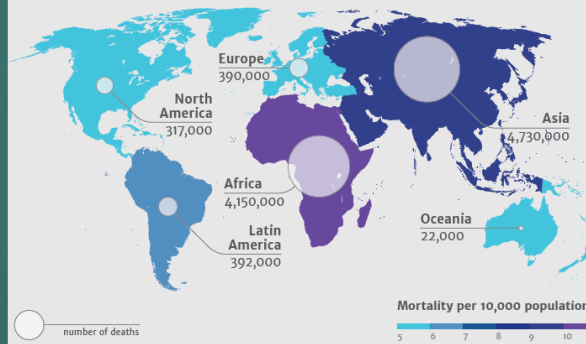
Diarrhoeal disease www.sciencedirect.com/science/article/pii/S1473167617280

Measles www.sciencedirect.com/science/article/pii/S014067361617280

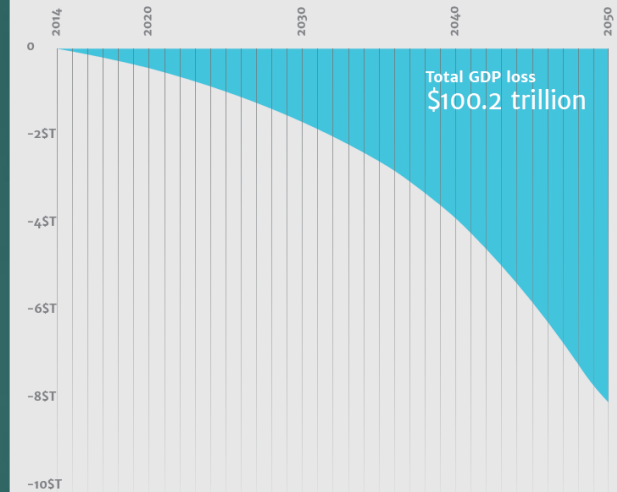
Road traffic accidents www.who.int/mediacentre/factsheets/fs304/en/

Tetanus www.sciencedirect.com/science/article/pii/S014067361617280

Deaths attributable to AMR every year by 2050



AMR's impact on World GDP in trillions of USD

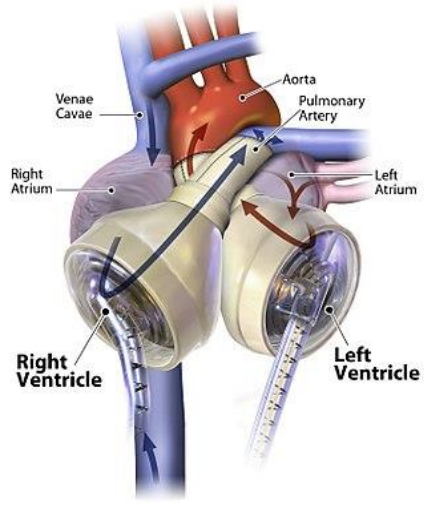


But see, e.g., de Kraker et al. (2016). Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050?

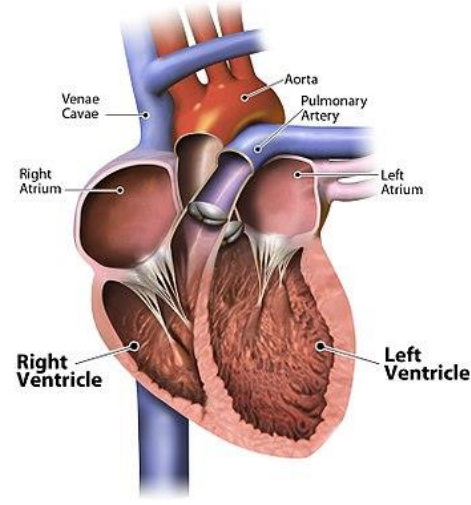


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Source: SynCardia Systems, https://commons.wikimedia.org/wiki/File:Graphic_of_the_SynCardia_temporary_Total_Artificial_Heart_beside_a_human_heart.jpg



Total Artificial Heart



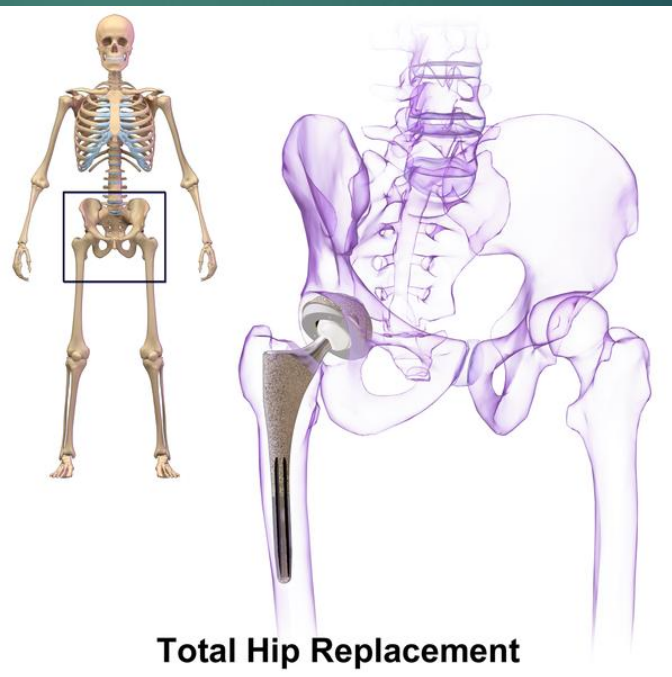
Human Heart



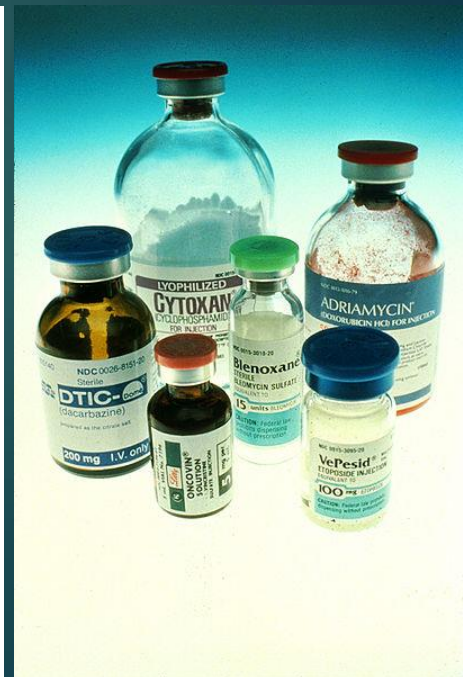
Impacts on medical practice

- ▶ Organ transplants
- ▶ C-sections
- ▶ Joint replacement
- ▶ Chemotherapy
- ▶ Childbirth

Source: Blausen Medical Communications, https://commons.wikimedia.org/wiki/File:Hip_Replacement.png



Total Hip Replacement



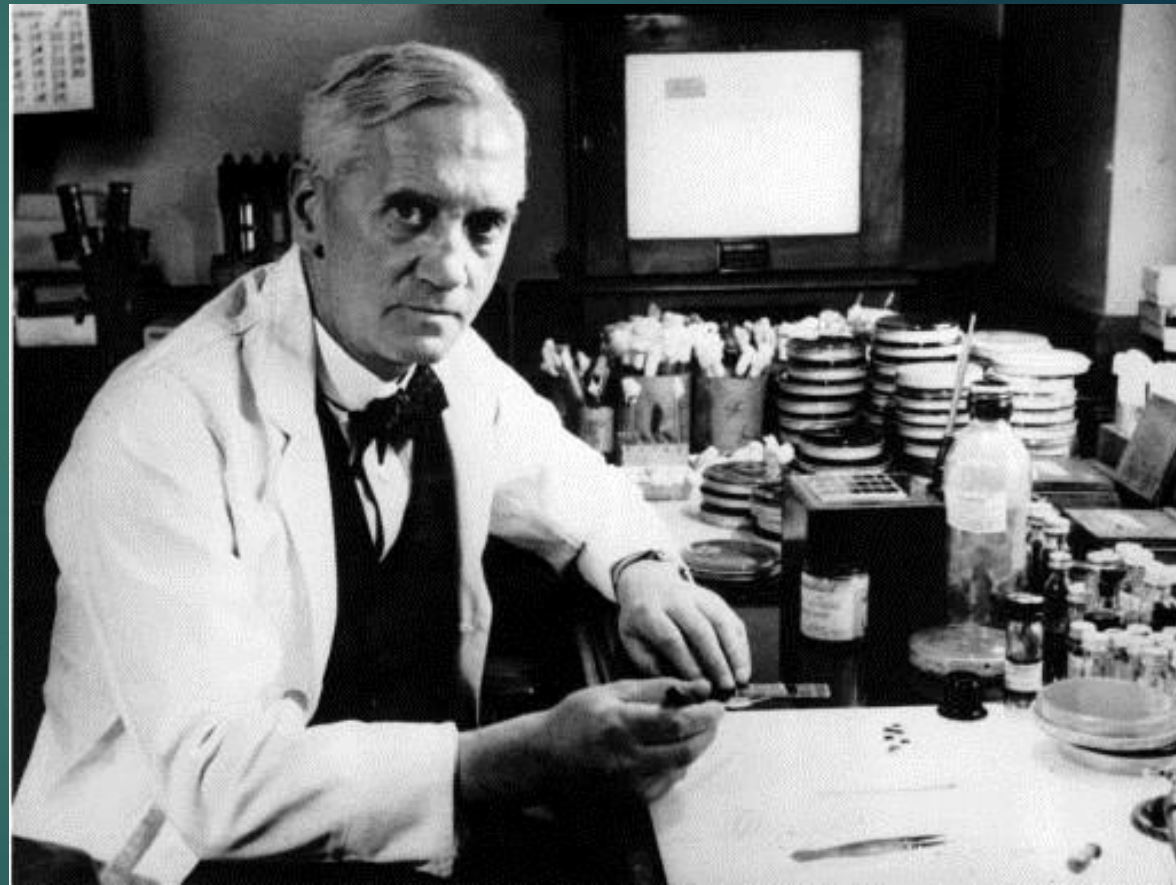


Source: Wellcome Library/London

Plague in Florence, 1348. L. Sabatelli.

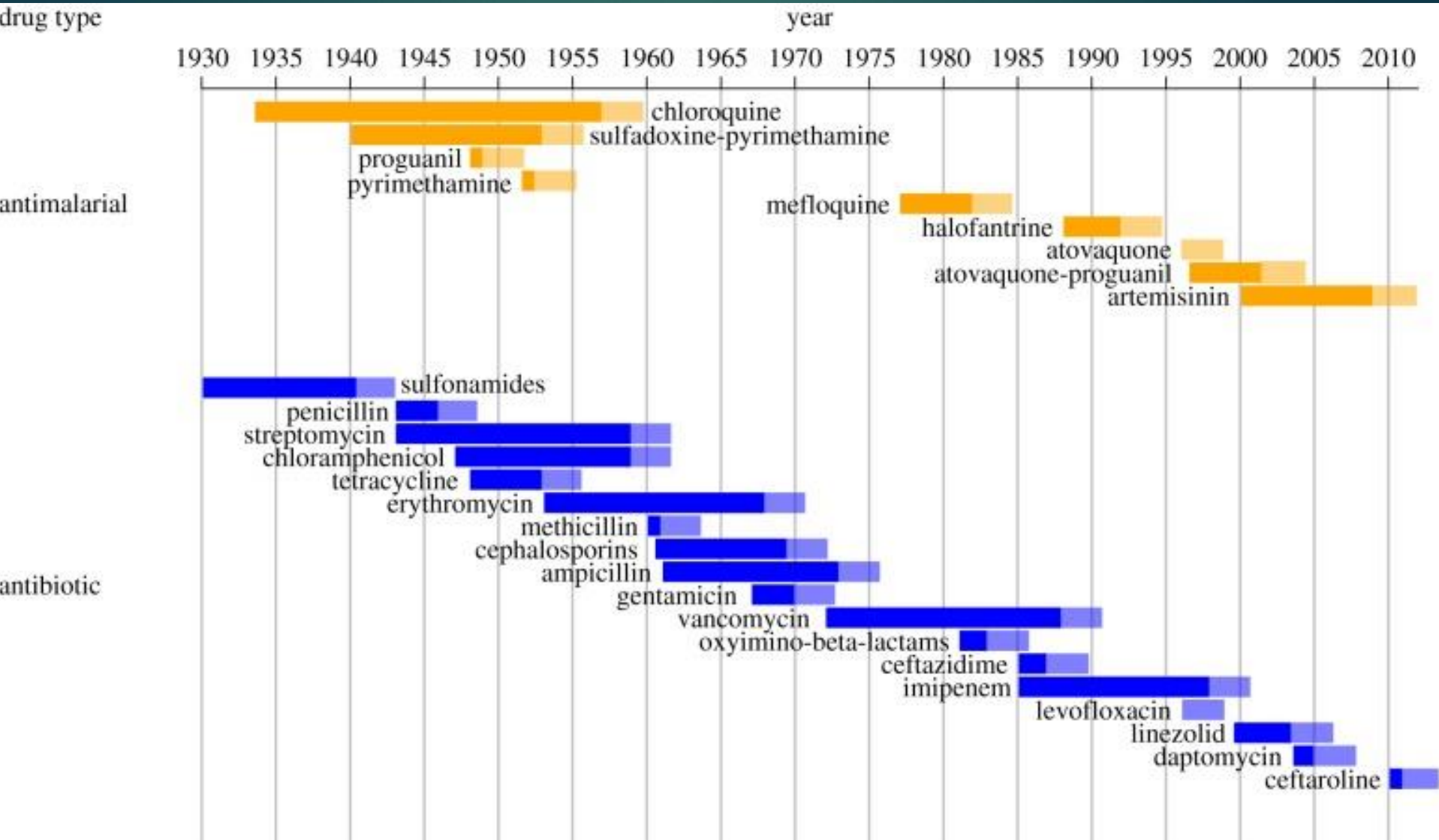


- ▶ First antibiotics
 - ▶ 1907: Salvarsan (arsphenamine), anti-syphilis
 - ▶ From ~1932: sulfonamides (sulfa)
 - ▶ 1942: Penicillin (first natural antibiotic)





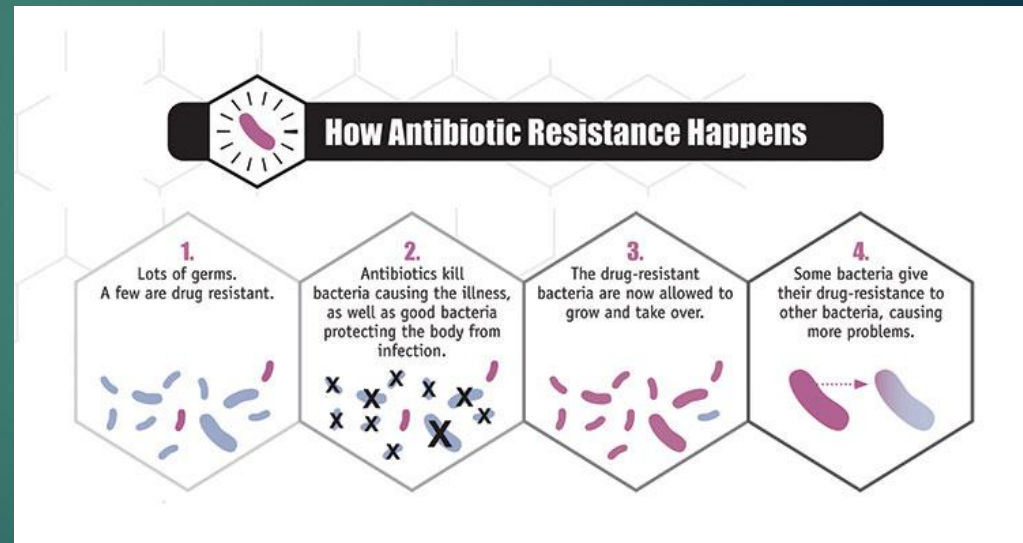
Emergence of AMR





What is driving MDR emergence and risk?

- ▶ Use of antibiotics in medicine
- ▶ Use of antibiotics in food systems
- ▶ Human population growth/demographics
- ▶ Urbanization
- ▶ Antibiotic discovery void



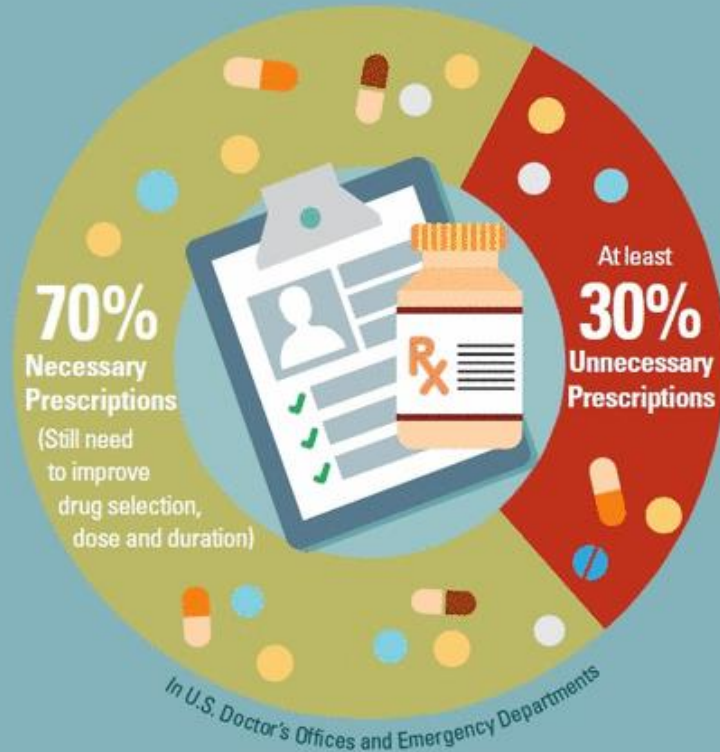
Improve Antibiotic Use to Combat Antibiotic Resistance



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Drivers: medical use

- ▶ Overprescription (duration)
- ▶ Inappropriate prescription (e.g., for viral infection or prophylaxis)
- ▶ Non-compliance or self-medication
- ▶ Nosocomial infection



CDC is working to reduce unnecessary antibiotic use

White House National Action Plan to Combat Antibiotic-Resistant Bacteria (CARB)

Goal: By 2020, reduce inappropriate outpatient antibiotic use by 50%

Find out when antibiotics are necessary.

Visit: <http://www.cdc.gov/getsmart>

Centers for Disease Control and Prevention (2012).
Flaming-Dutra, K et al. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010-2011. Journal of the American Medical Association. May 2016. CD201112-02



Centers for Disease
Control and Prevention
National Center for Emerging and
Zoonotic Infectious Diseases



ANTIBIOTIC RESISTANCE

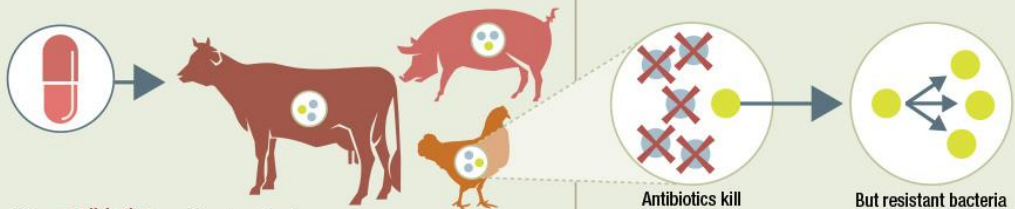
from the farm to the table



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RESISTANCE

Animals can carry harmful **bacteria** in their intestines



When **antibiotics** are given to animals...

Antibiotics kill most bacteria

But resistant bacteria can survive and multiply

SPREAD

Resistant bacteria can spread to...



animal products



produce through contaminated water or soil



prepared food through contaminated surfaces



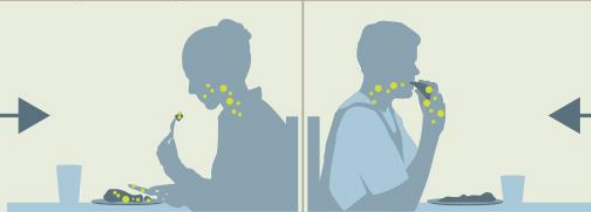
the environment when animals poop

EXPOSURE

People can get sick with resistant infections from...



contaminated food



contaminated environment

Learn 4 steps to prevent food poisoning at www.foodsafety.gov

IMPACT

Some resistant infections cause...



mild illness



severe illness and may lead to death

About **1 in 5** resistant infections are caused by germs from food and animals.

Source: *Antibiotic Resistant Threats in the United States, 2013*

Drivers: food systems

- ▶ Up to 80% of antibiotics go to animals
- ▶ Little evidence of efficacy: up to 90% excreted
- ▶ Spread to humans through contact or ingestion
- ▶ Environmental contamination

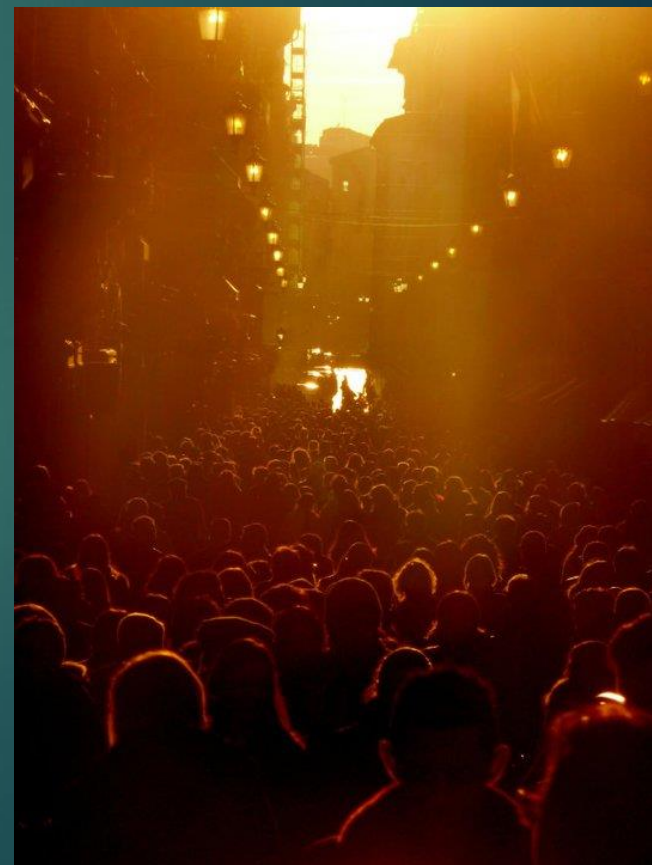
Learn more about antibiotic resistance and food safety at www.cdc.gov/foodsafety/antibiotic-resistance.html

Learn more about protecting you and your family from resistant infections at www.cdc.gov/drugresistance/protecting_yourself_family.html



Drivers: population/demographics

- ▶ Greater population = more opportunities for evolution of resistance and human-human transmission
- ▶ More elderly population = more opportunities for nosocomial spread





Drivers: urbanization

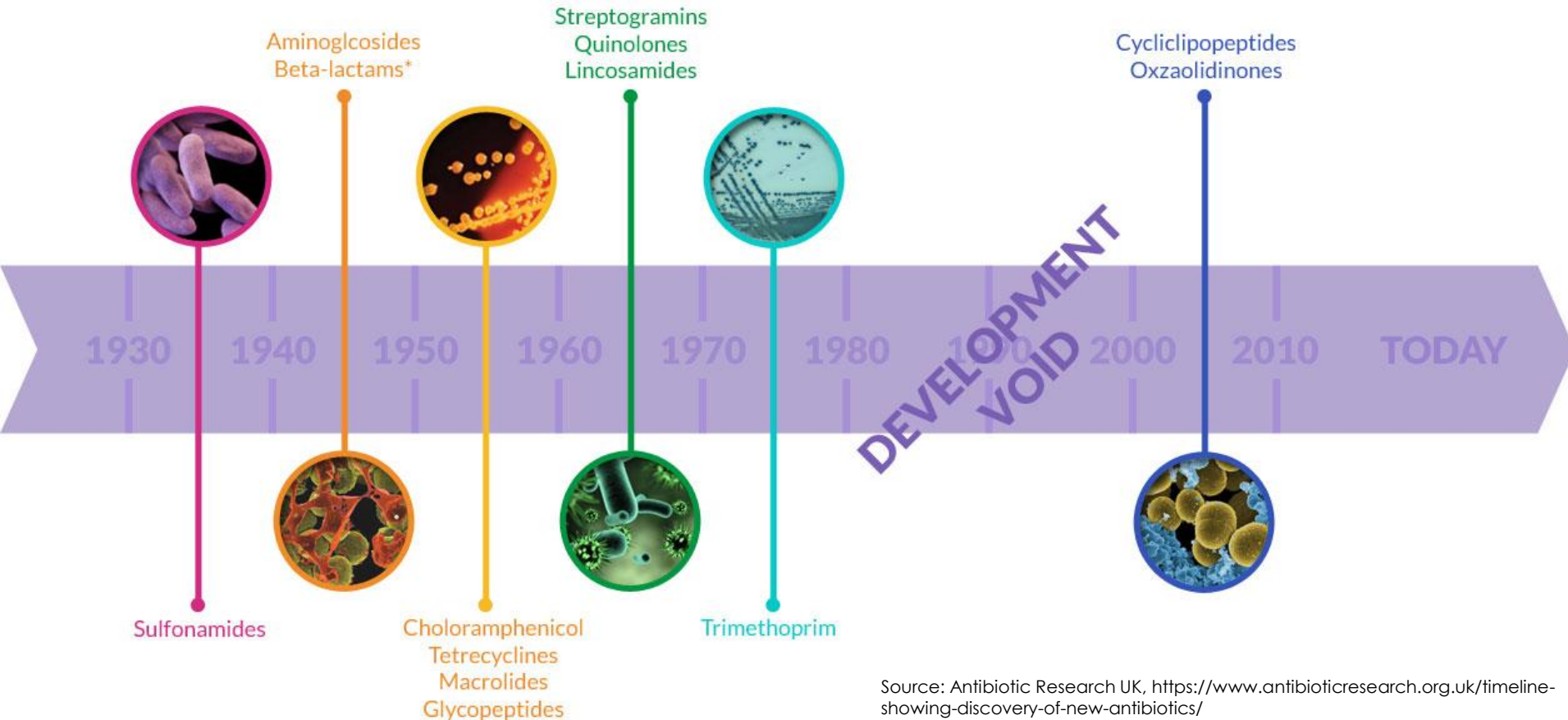
- ▶ Patterns of human-human (and sometimes human-animal) contact
- ▶ Density of people
- ▶ Health system structure and function
- ▶ Food system structure and function





Discovery void

- ▶ 40s-60s: “glory years of antibiotic discovery” (Hancock and Knowles 1998); numerous new classes of antibiotics
- ▶ Very little since; easy wins identified





Systems problems

▶ Characteristics

- ▶ Detail and dynamic complexity
- ▶ Multiple stakeholders
- ▶ Multiple scales
- ▶ Cross-sectoral/related to other problems
- ▶ Resistance to change
- ▶ Unanticipated outcomes

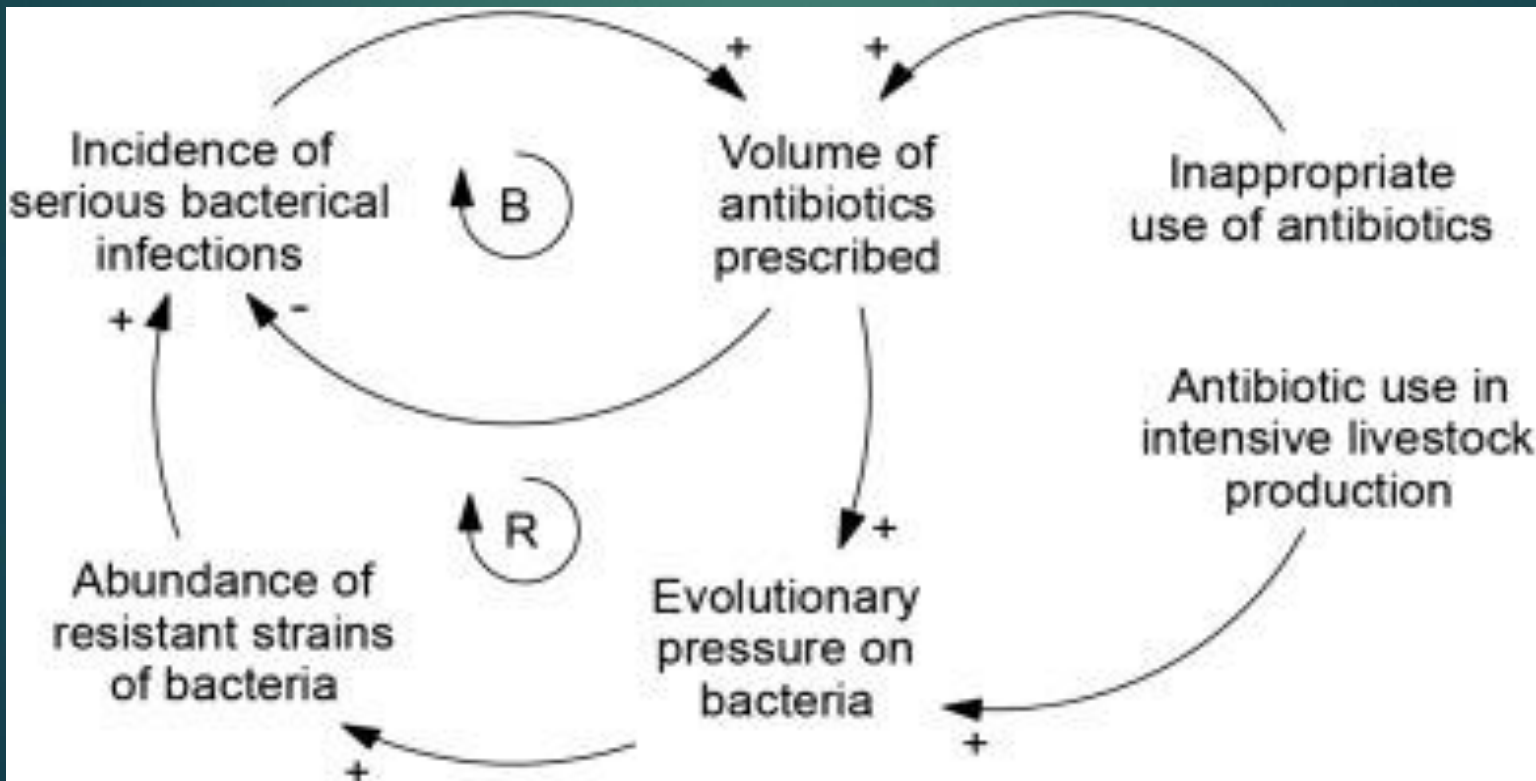




Complexity drives outcomes

- ▶ *Any use of antimicrobials, however appropriate and conservative, contributes to the development of resistance”*

- *Review on Antimicrobial Resistance, 2014*



SEAR's antibiotic challenge

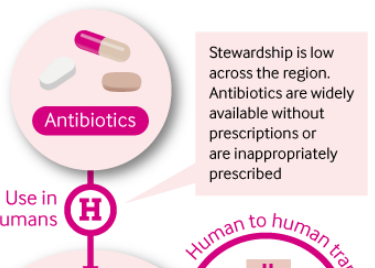
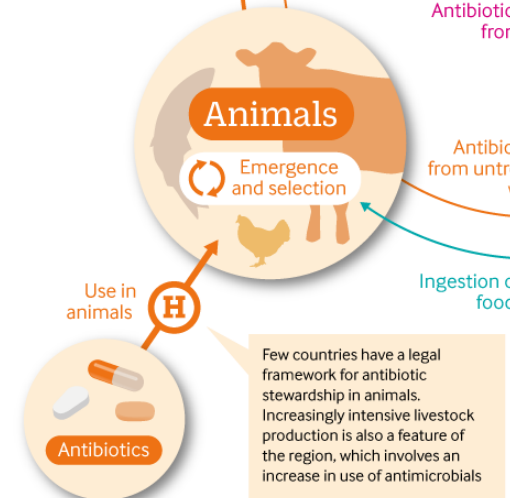
Risks of emergence and spread of antibiotic resistance in South East Asia

The WHO South East Asia Region (SEAR) has unique characteristics that contribute to the likelihood of increasing resistance to antibiotics developing in the region. In their 2017 model published in *The BMJ*, Chereau and colleagues use a risk assessment approach to characterise the likelihood of emergence and spread of antibiotic resistance in the region. They conclude that the overall risk for emergence and spread of antibiotic resistance among humans in South East Asia is high.

Access to water and soap in the household can be very limited. Combined with poor knowledge and education about hygiene, transmission of antibiotic resistant strains is a high risk

Ingestion of contaminated meat

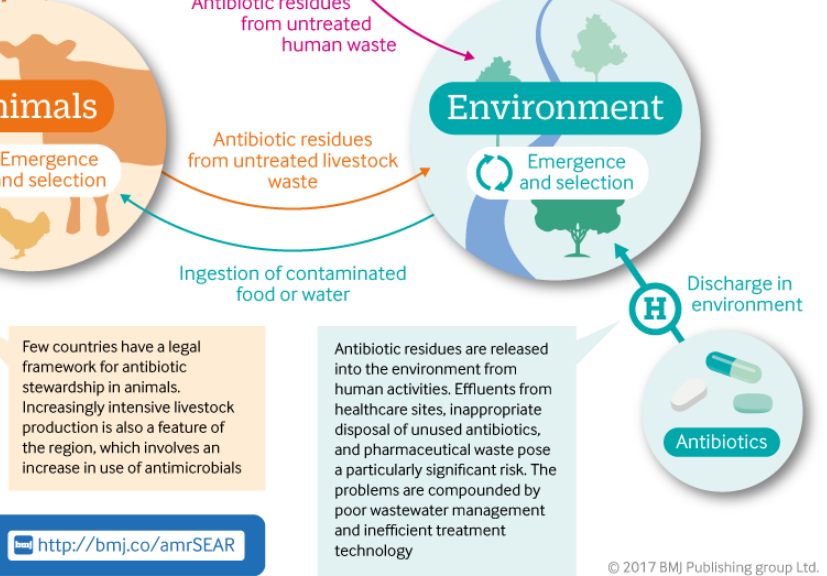
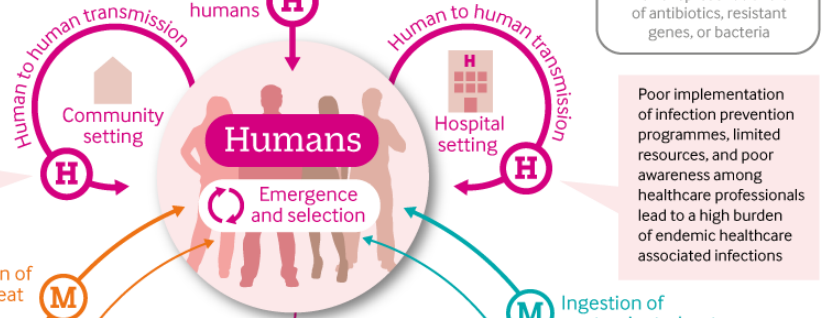
While some countries have food safety policies, these are often poorly enforced. Meat consumption remains limited across the region but is increasing



Level of risk

- High (H)
- Medium (M)
- Low (L)
- Negligible (N)

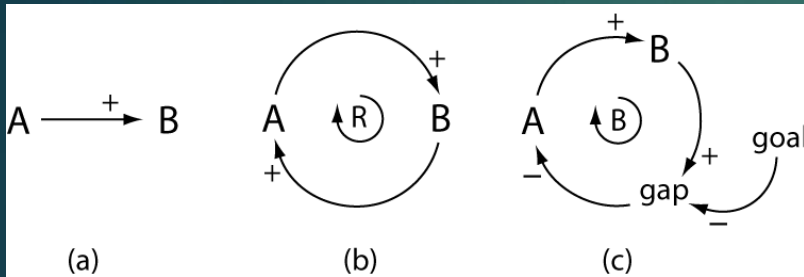
Arrows represent transfer of antibiotics, resistant genes, or bacteria



Complexity and engagement

- ▶ Real systems have many parts
- ▶ Understanding parts ≠ understanding system
- ▶ Silos lead to restricted focus

Systems approaches

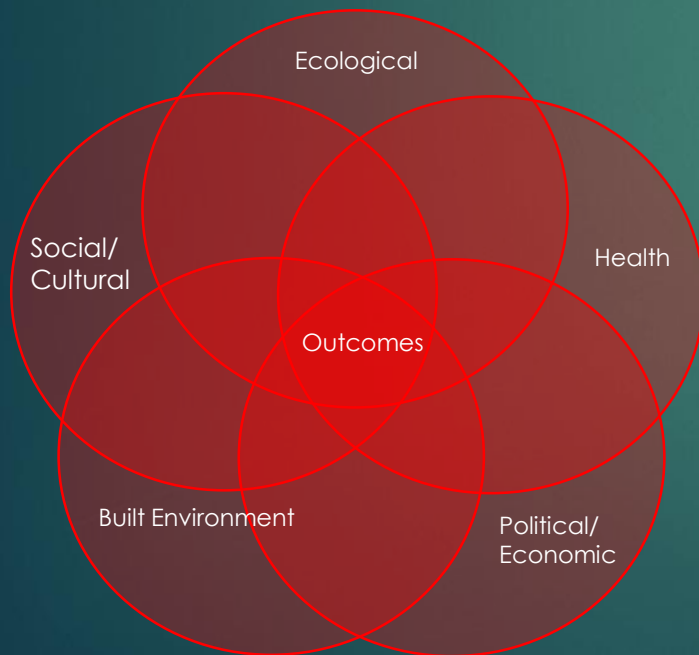


► Systems methods to:

- Characterize and measure feedback
- Identify leverage points for action
- Forecast likely outcomes and compare policy scenarios

► Collaborative work (co-production of knowledge/ inter- and trans-disciplinarity / stakeholder involvement) to:

- Improve communication
- Provide more complete understanding of systems
- Assess feasibility of actions
- Promote stakeholder ownership



Solutions



- ▶ New antibiotic development
- ▶ Stewardship of existing antibiotics
 - ▶ Reduce use in animal husbandry
 - ▶ Reduce human-animal contact
 - ▶ Reduce inappropriate prescriptions
 - ▶ Improve diagnosis and treatment choice
 - ▶ Improve compliance
 - ▶ Prevent nosocomial infections
- ▶ Promote systemic change
 - ▶ Grow cross-sectoral communication
 - ▶ Highlight feedback narratives
 - ▶ Change incentives for all actors
 - ▶ Make correct action convenient



Thank you!



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AMSC 2018

ASIAN MEDICAL STUDENTS' CONFERENCE MALAYSIA



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Source: Nick Kim, http://scienceandink.com/screen_res/nz083.jpg



Source: Ventura County Star, Steve Greenberg, http://blogs.venturacountystar.com/greenberg/archives/2007/11/drugresist_ant_s.html