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
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José Siri, PhD, MPH

Research Fellow in Urban Health

UNU International Institute for Global Health (UNU-IIGH)

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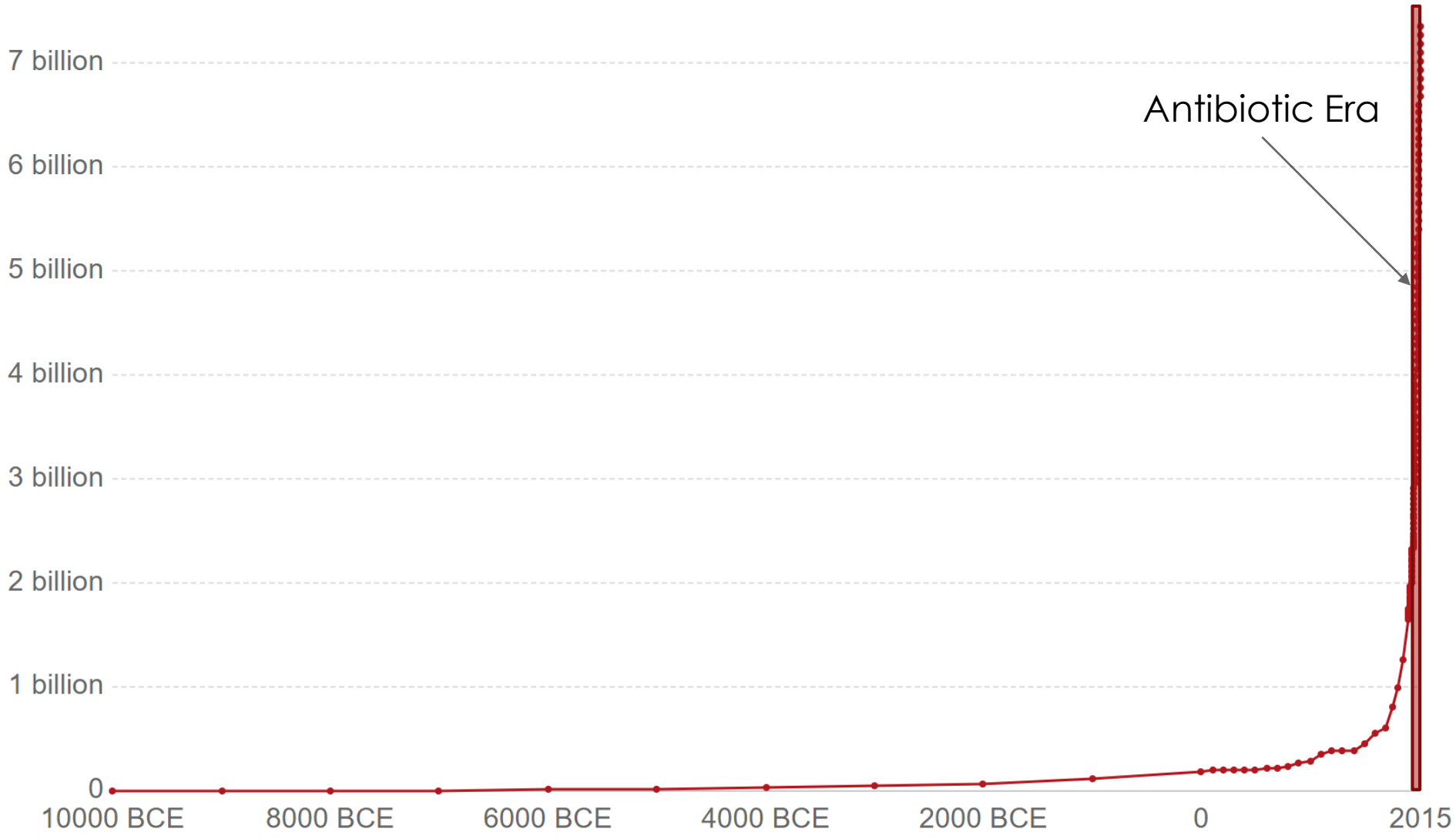
World population since 10,000 BCE (OurWorldInData series)



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)

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

World Health Organization

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The WHO priority list

PRIORITY: CRITICAL	PRIORITY 2: HIGH	PRIORITY 3: MEDIUM
Acinetobacter baumannii carbapenem-resistant	**Enterococcus faecium** vancomycin-resistant	**Streptococcus pneumoniae** penicillin-non-susceptible
Pseudomonas aeruginosa carbapenem-resistant	**Staphylococcus aureus** methicillin-resistant vancomycin-intermediate and resistant	**Haemophilus influenzae** ampicillin-resistant
Enterobacteriaceae carbapenem-resistant, ESBL-producing	**Helicobacter pylori** clarithromycin-resistant	**Shigella spp.** fluoroquinolone-resistant
	Campylobacter spp. fluoroquinolone-resistant	
	Salmonellae fluoroquinolone-resistant	
	Neisseria gonorrhoeae cephalosporin-resistant 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

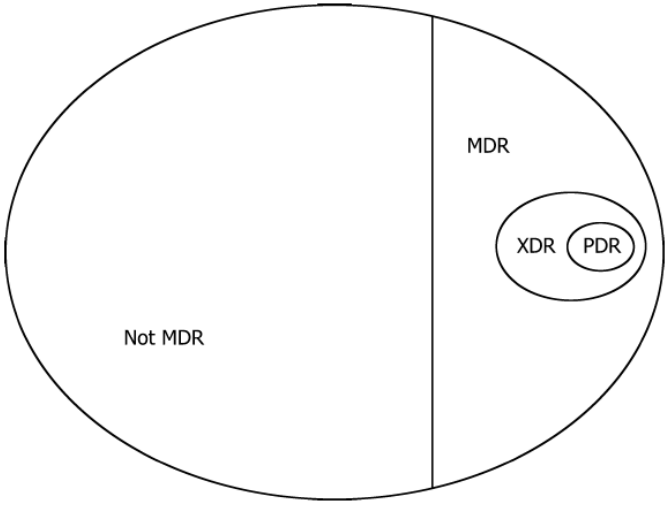

FIG. 1. Diagram showing the relationship of MDR, XDR and PDR to each other.

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

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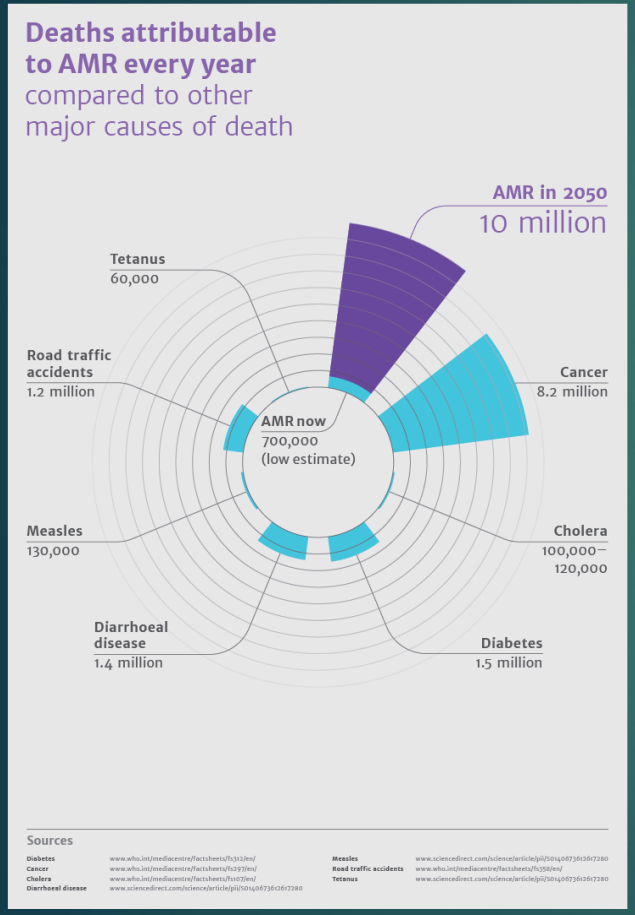
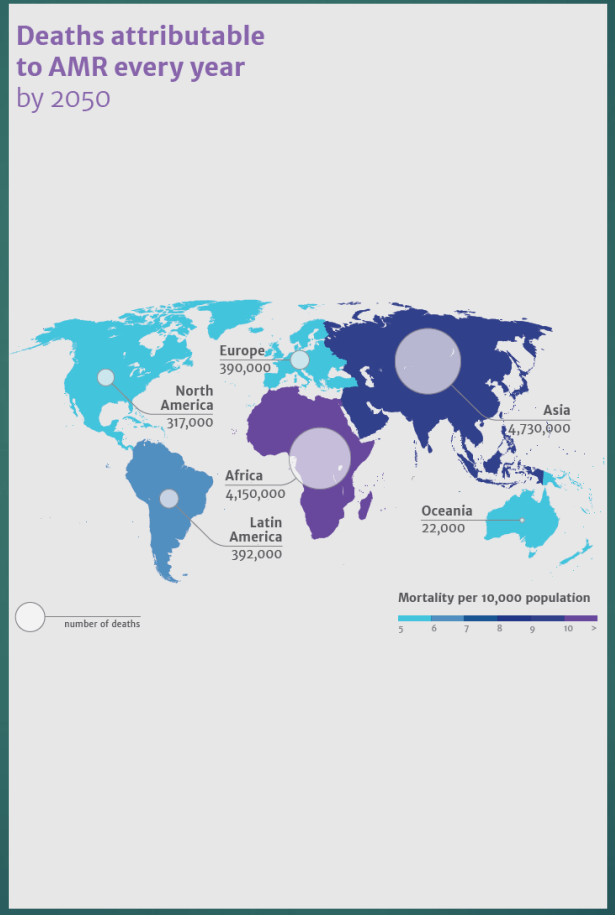
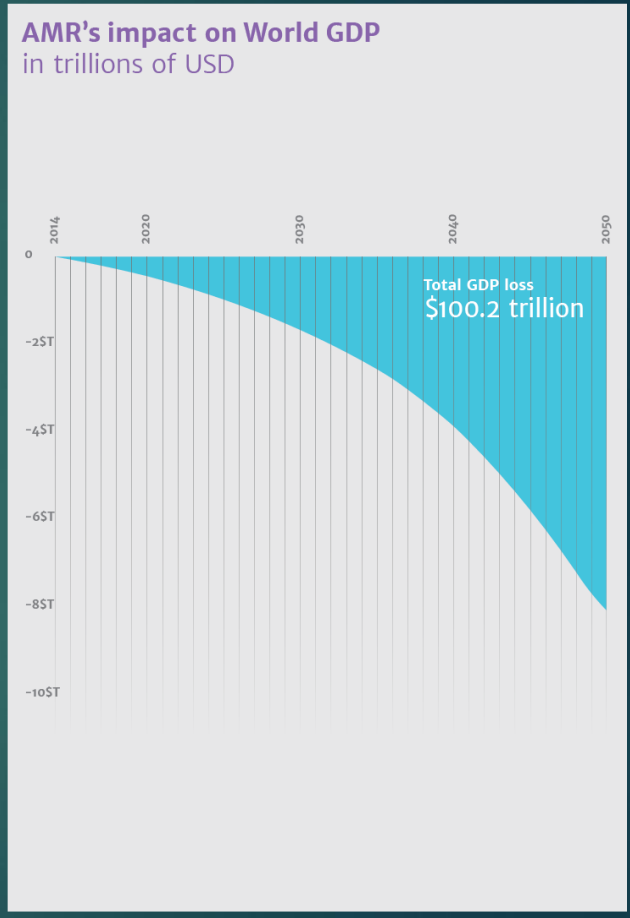
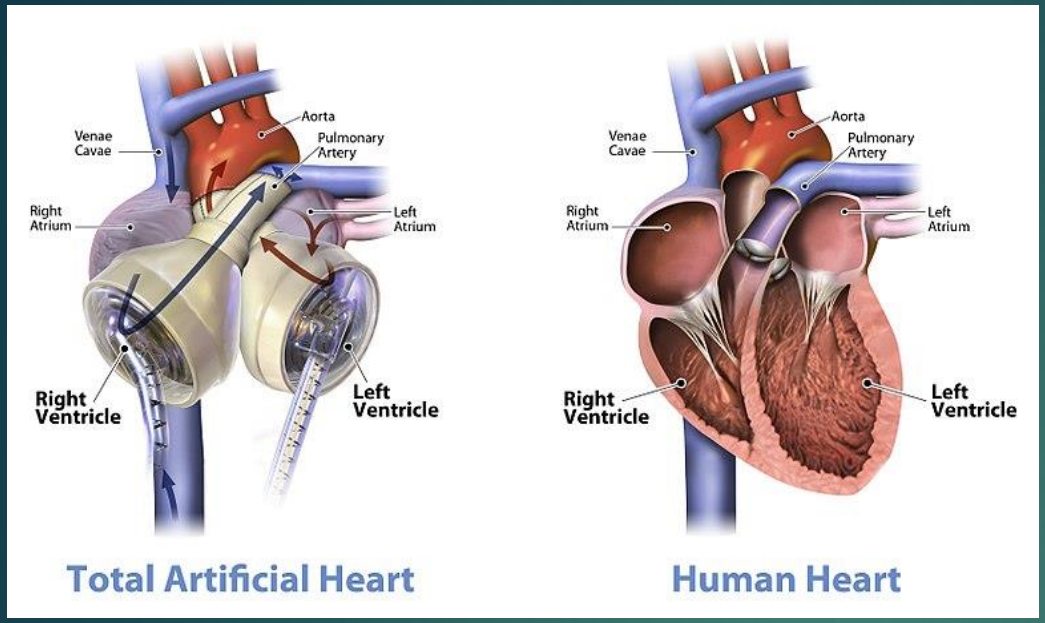
Source: 'Review on Antimicrobial Resistance. *Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations.* 2014.







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



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

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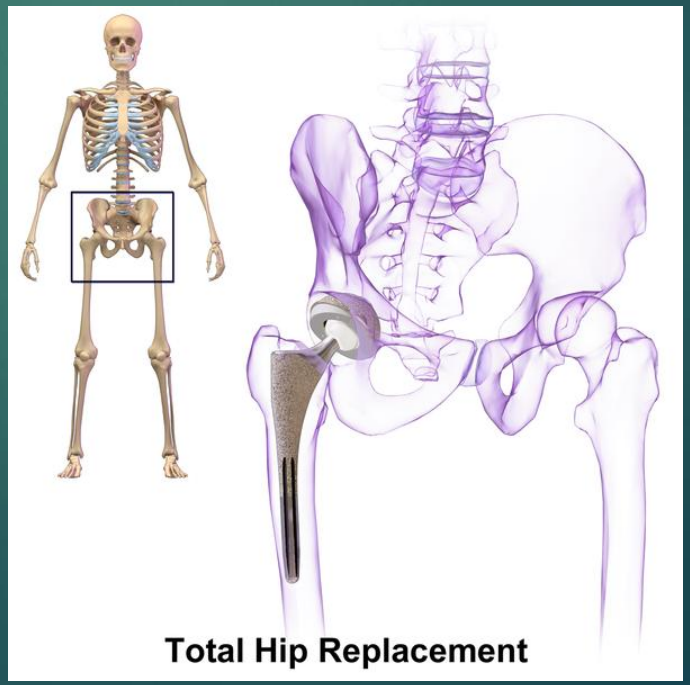
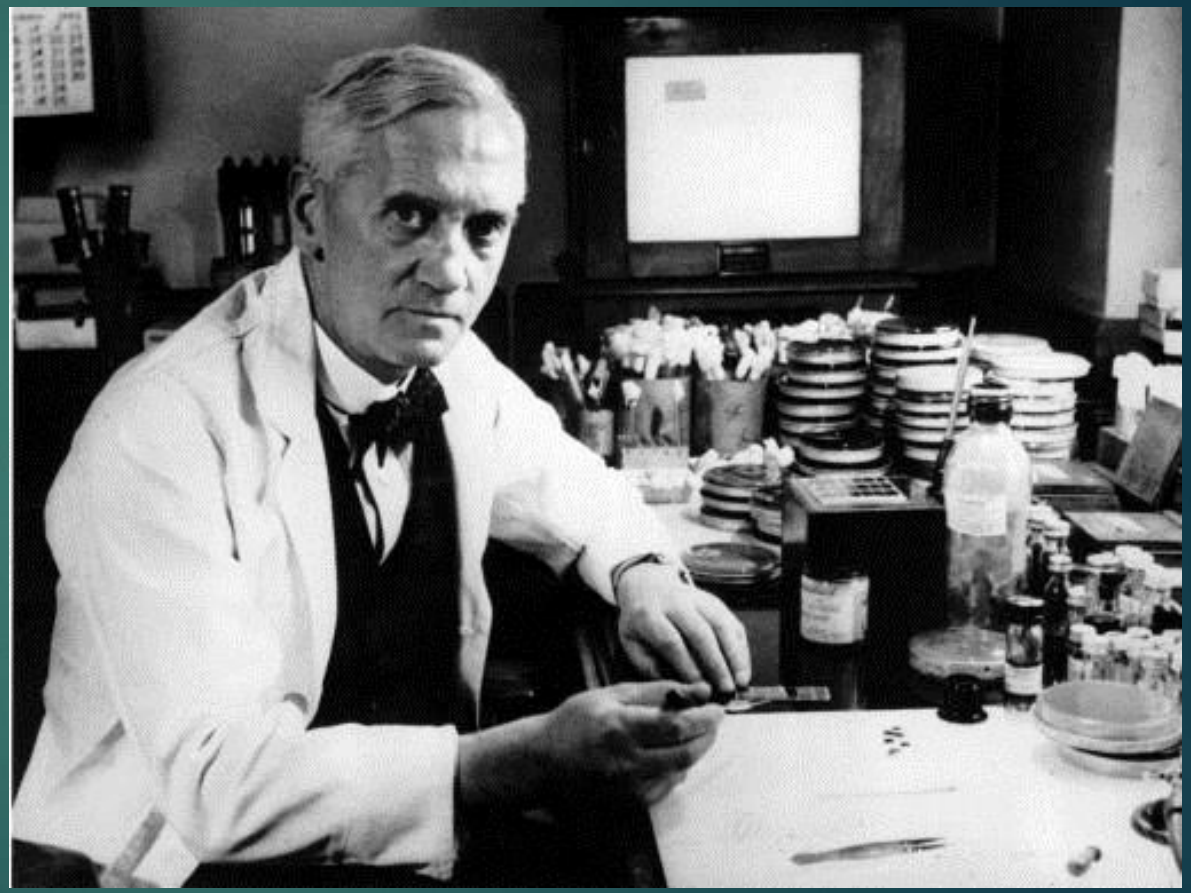
- Impacts on medical practice
  - Organ transplants
  - C-sections
  - Joint replacement
  - Chemotherapy
  - Childbirth



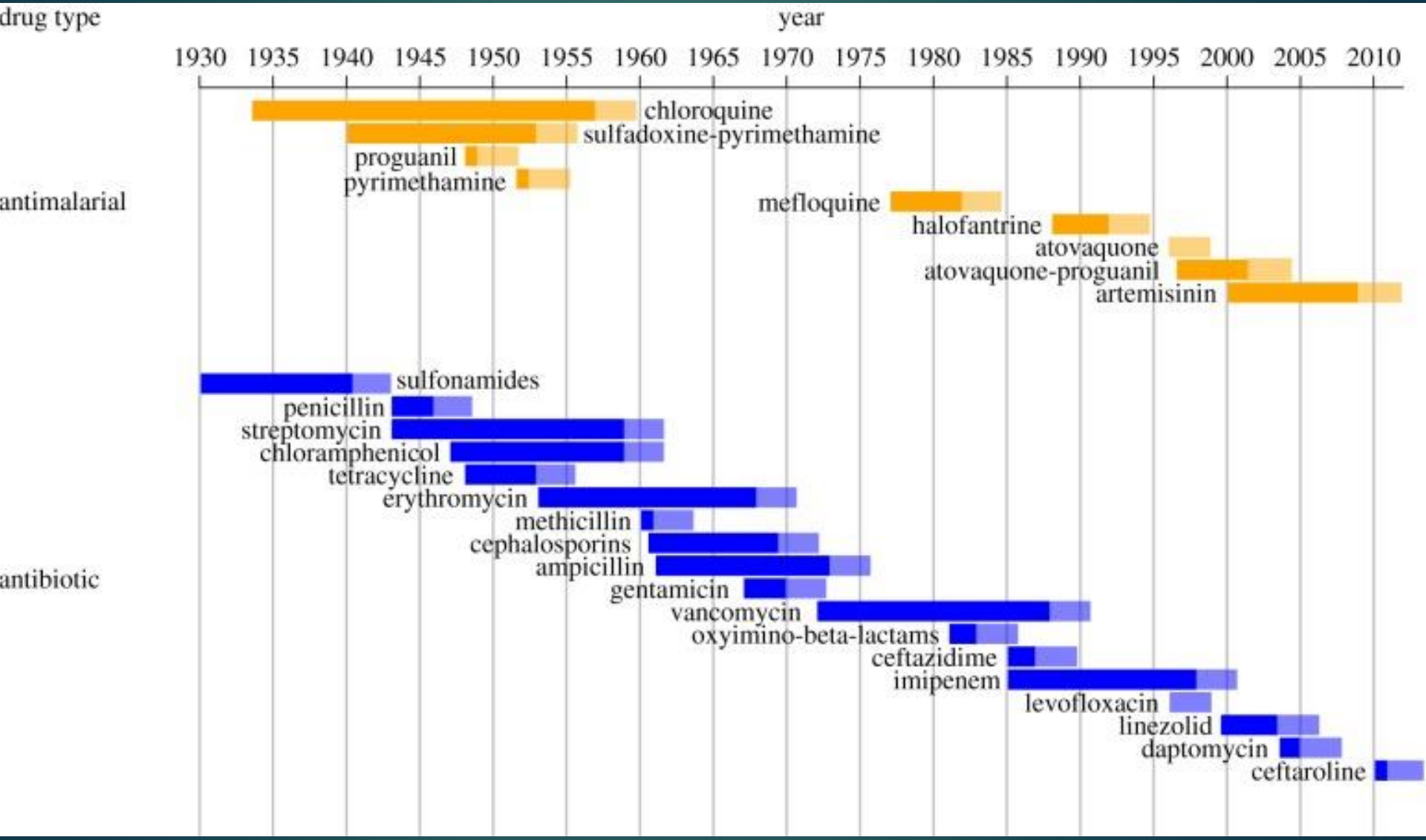
Source: Blausen Medical Communications, https://commons.wikimedia.org/wiki/File:Hip_Replacement.png

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



Source: McClure and Day (2014). A theoretical examination of the relative importance of evolution management and drug development for managing resistance

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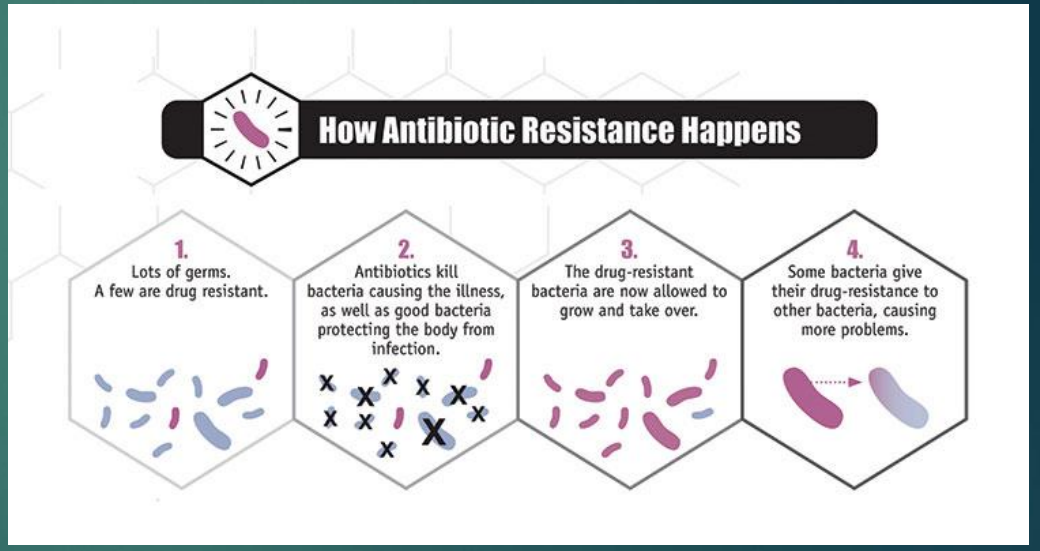
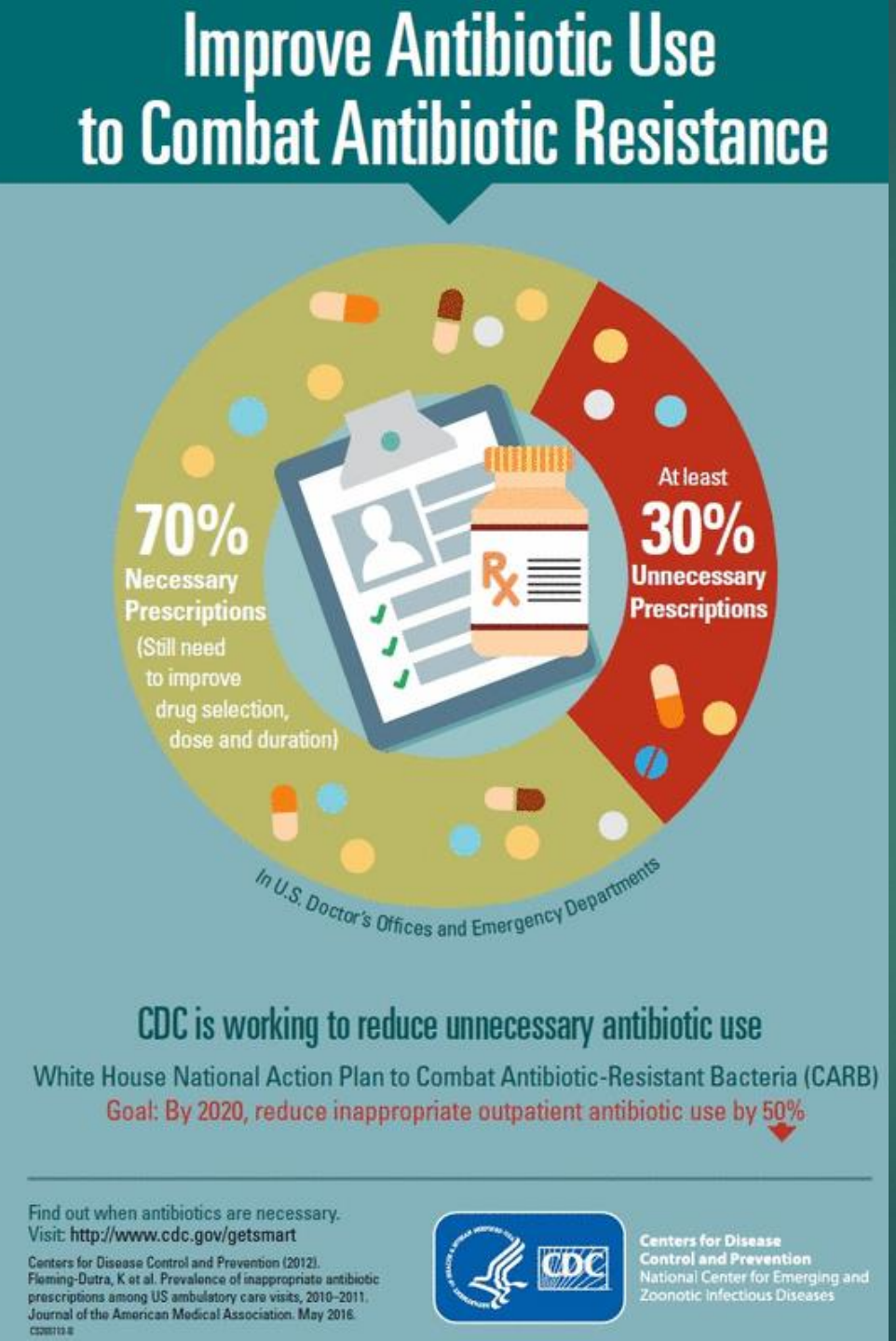
What is driving MDR emergence and risk?

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





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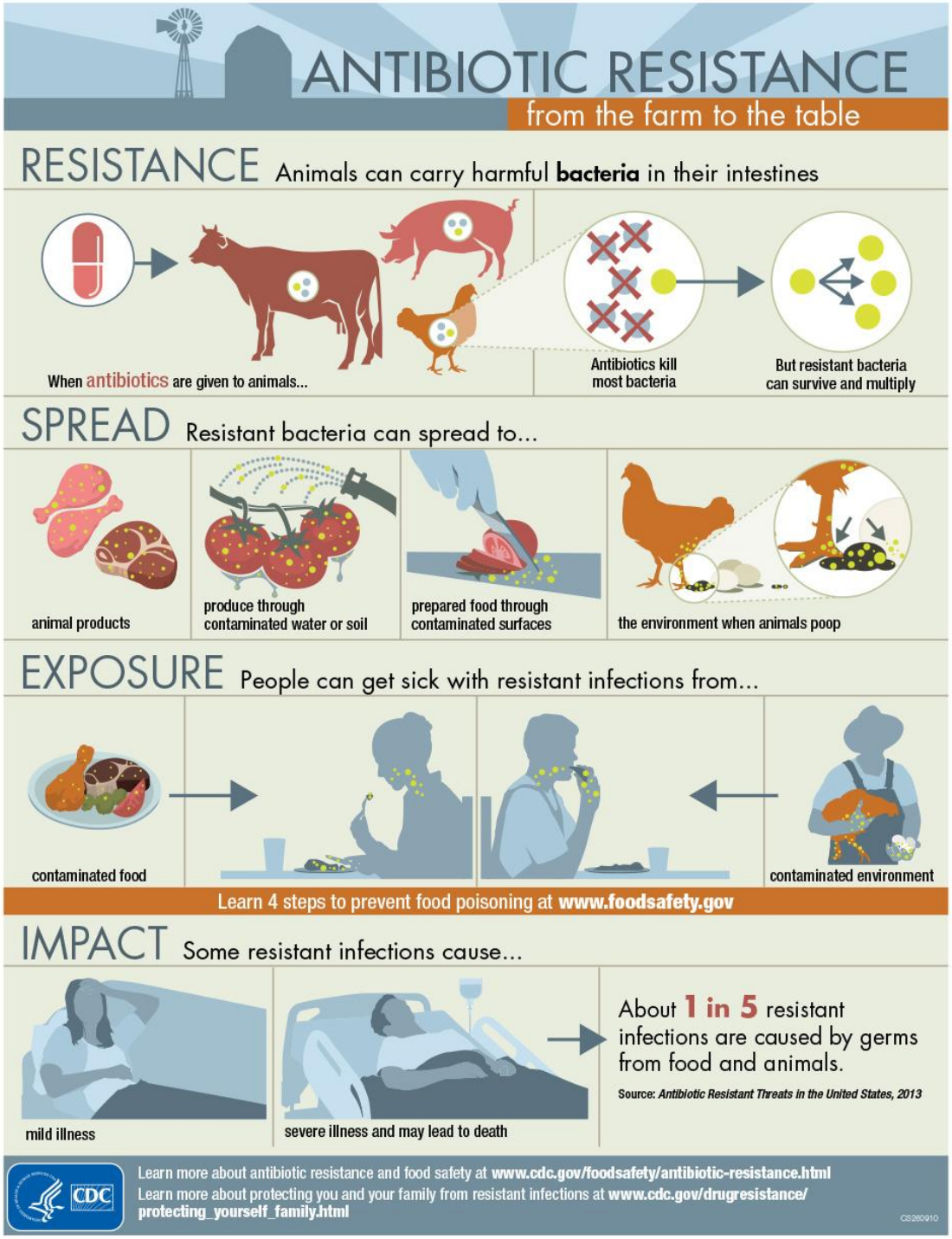
Drivers: medical use

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



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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

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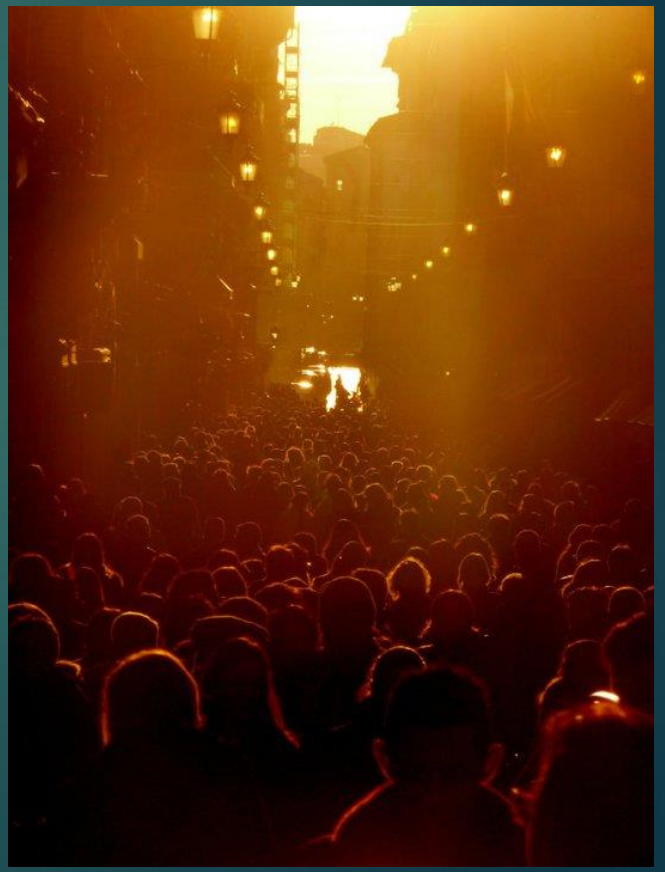
Drivers: population/demographics

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



Drivers: urbanization

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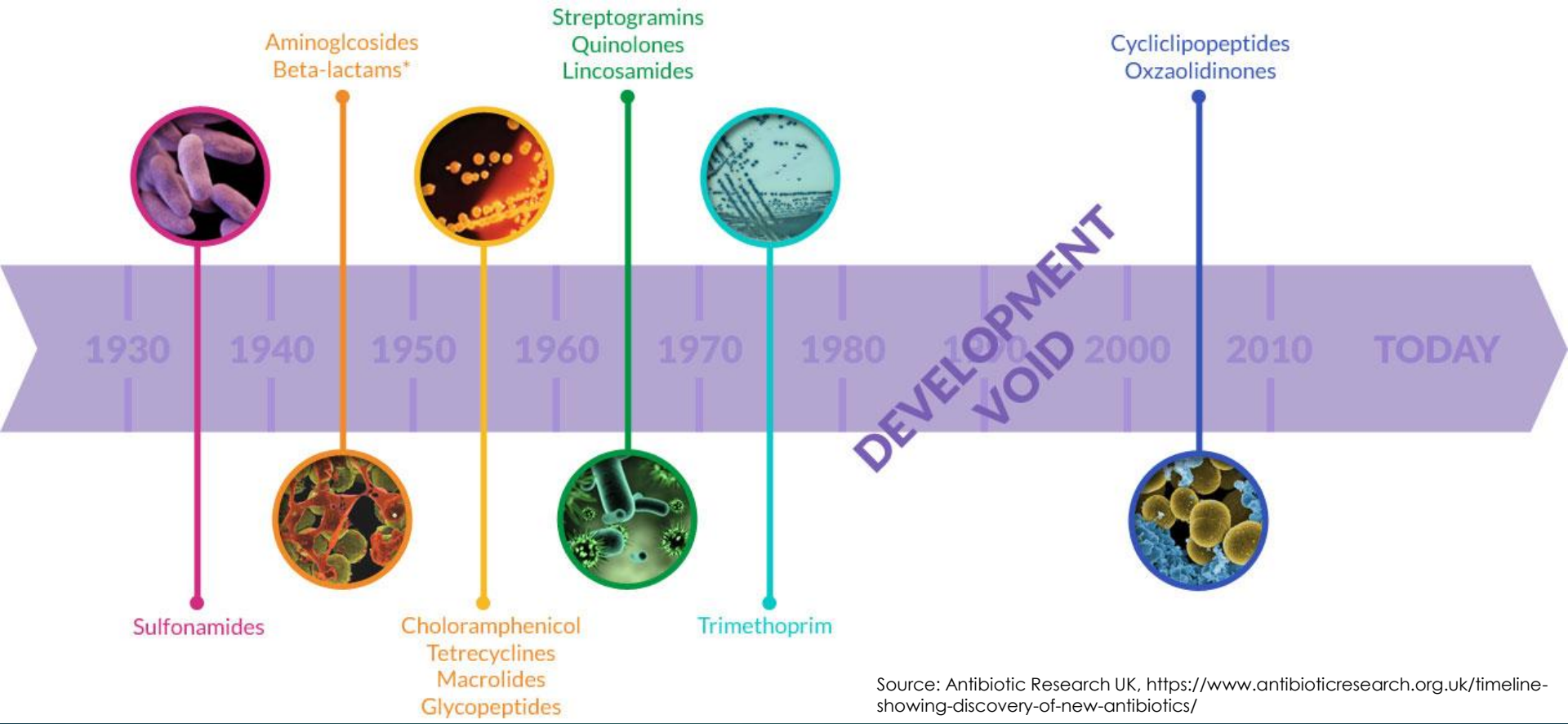
- Patterns of human-human (and sometimes human-animal) contact
- Density of people
- Health system structure and function
- Food system structure and function

Discovery void

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



Source: Antibiotic Research UK, https://www.antibioticresearch.org.uk/timeline-showing-discovery-of-new-antibiotics/

Systems problems

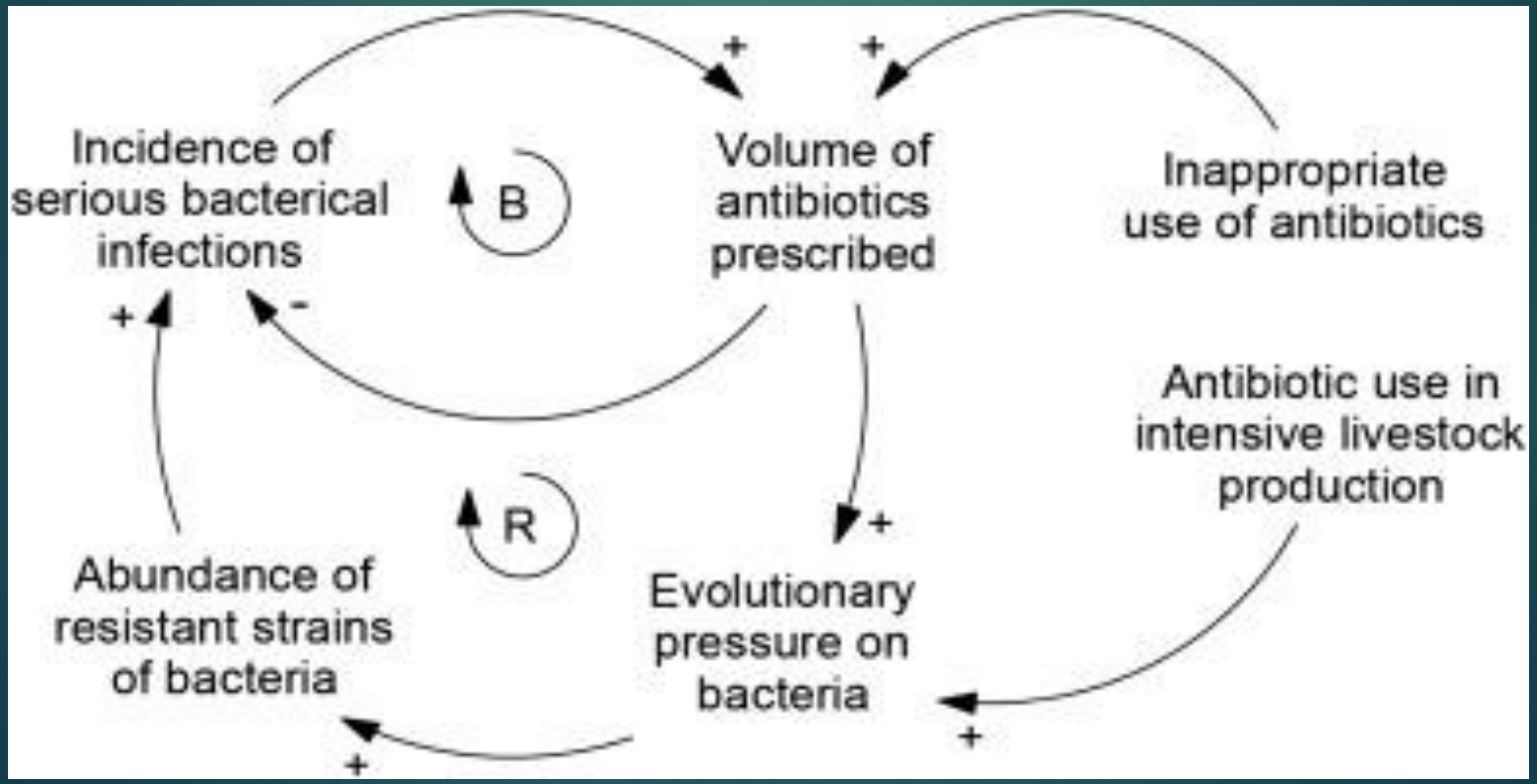
- Characteristics
  - Detail and dynamic complexity
  - Multiple stakeholders
  - Multiple scales
  - Cross-sectoral/related to other problems
  - Resistance to change
  - Unanticipated outcomes

Source: http://www.innovationmanagement.se/2010/06/14/complexity-science-and-innovation/

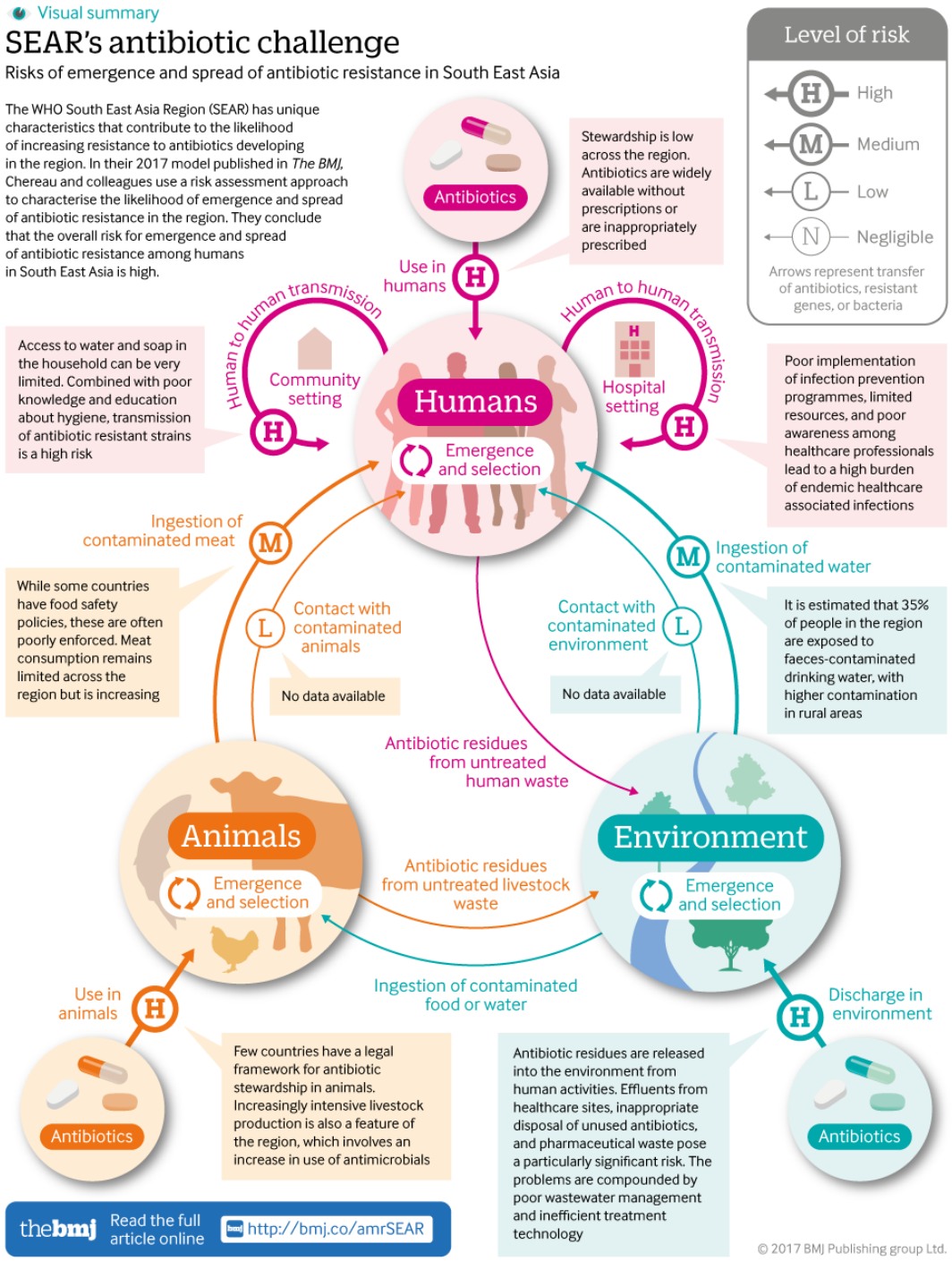
Complexity drives outcomes

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

- Review on Antimicrobial Resistance, 2014



Source: Newell and Siri, 2016. A role for low-order system dynamics models in urban health policy-making



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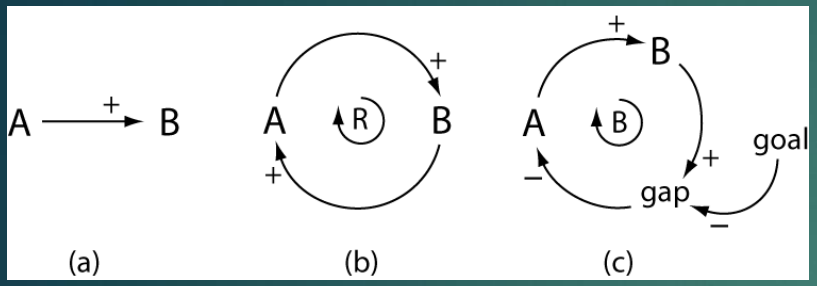
Complexity and engagement

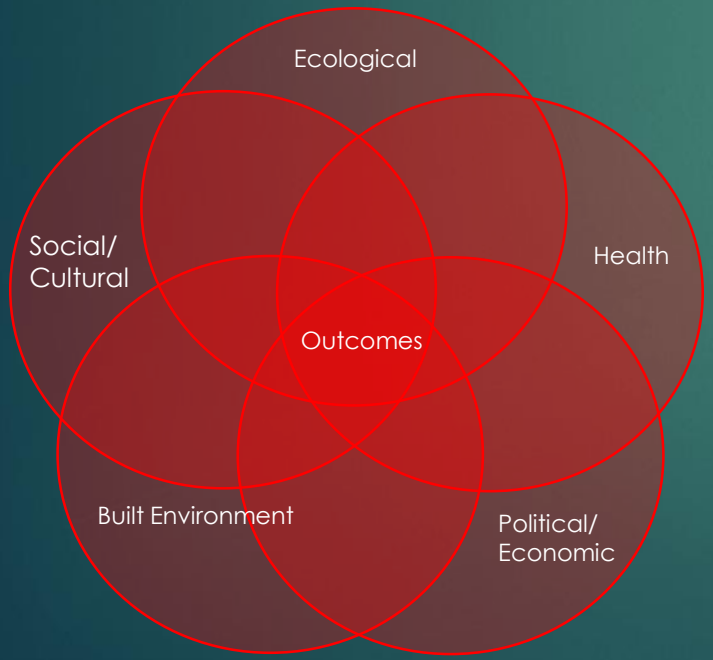
- Real systems have many parts
- Understanding parts ≠ understanding system
- Silos lead to restricted focus

Source: Cherau et al. (2017). Risk assessment for antibiotic resistance in South East Asia

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

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- 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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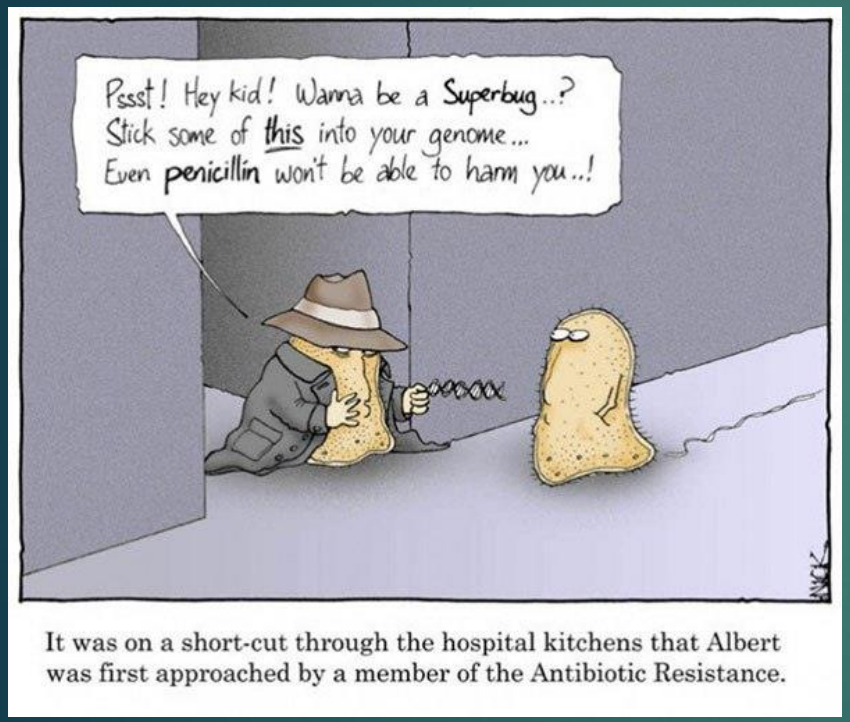

Source: Nick Kim, http://scienceandink.com/screen_res/nz083.jpg

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