

# Antimicrobial Resistance & Pandemics: emerging threats

---

Madhukar Pai, MD, PhD  
Director, McGill Global Health Programs



McGill



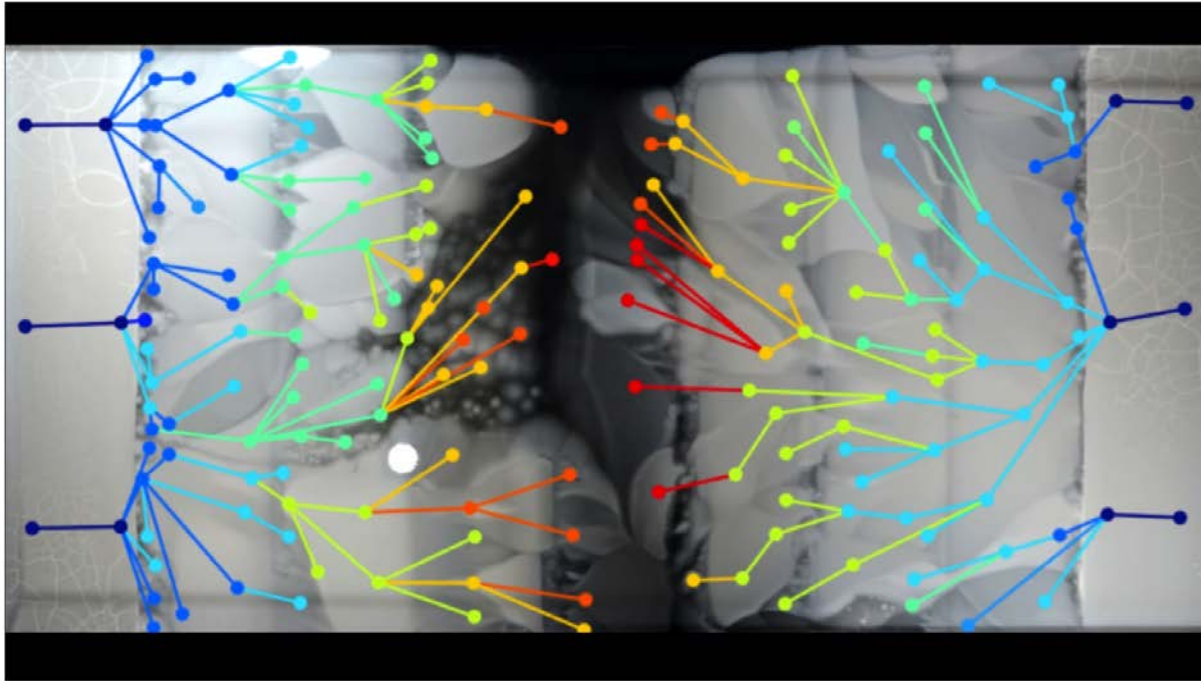
GLOBAL  
HEALTH  
PROGRAMS

# AMR

---



# Biology



The Evolution of Bacteria on a “Mega-Plate” Petri Dish (Kishony Lab)

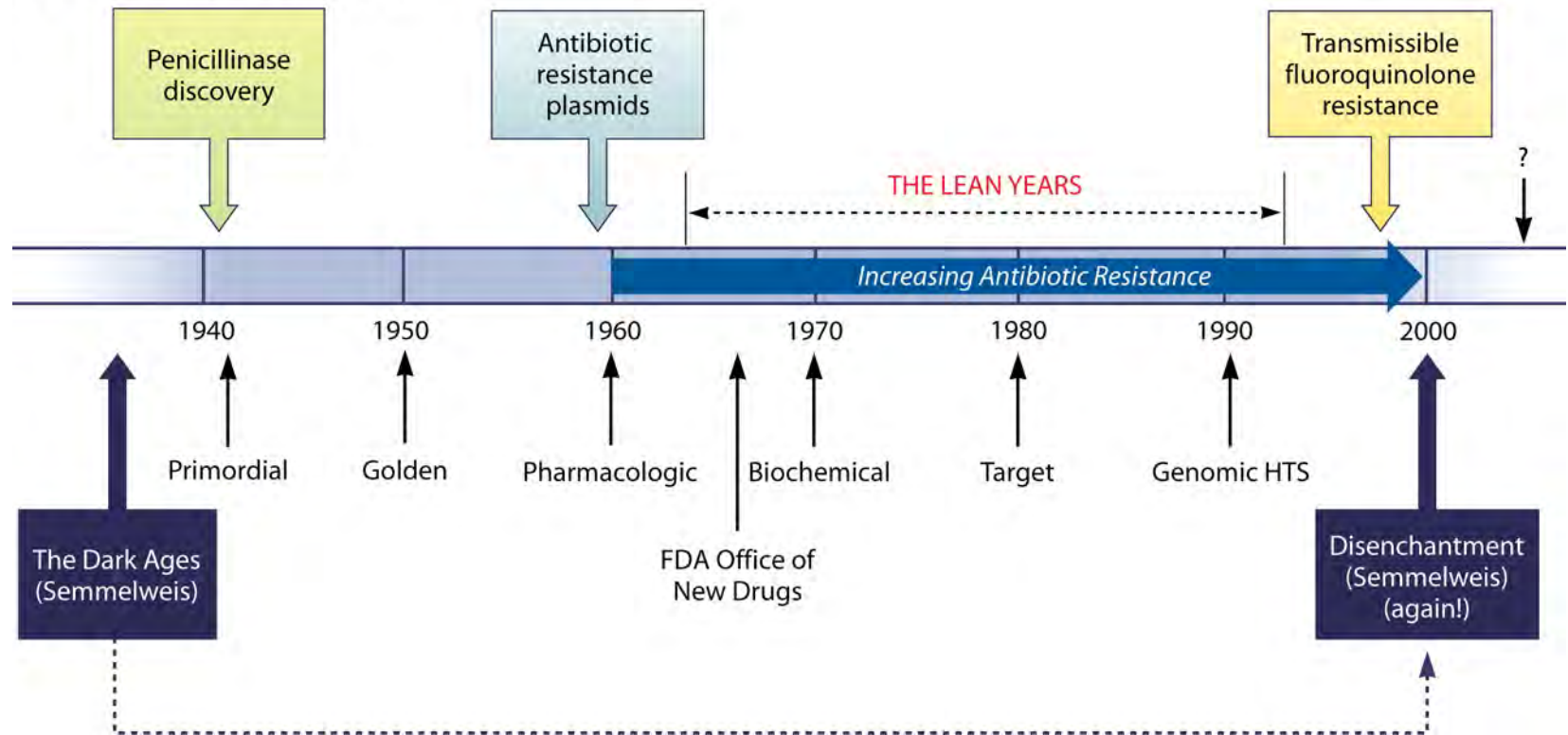
1,122,383 views

10K 141 SHARE

<https://www.youtube.com/watch?v=pIVk4NVIUh8>

# History of antibiotic discovery and concomitant development of antibiotic resistance.

## Events in the Age of Antibiotics

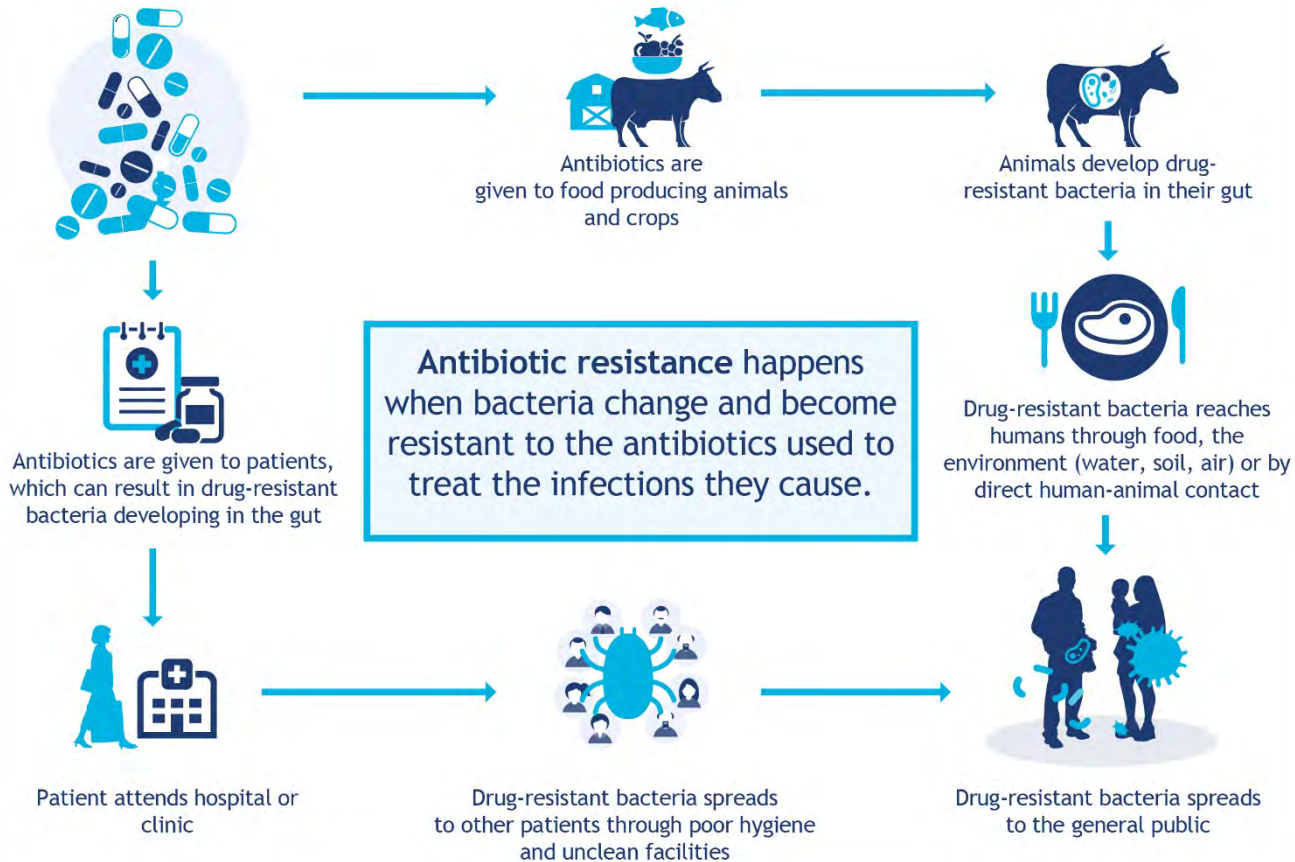


Julian Davies, and Dorothy Davies Microbiol. Mol. Biol. Rev.  
2010;74:417-433

Microbiology and Molecular Biology Reviews

# ANTIBIOTIC RESISTANCE

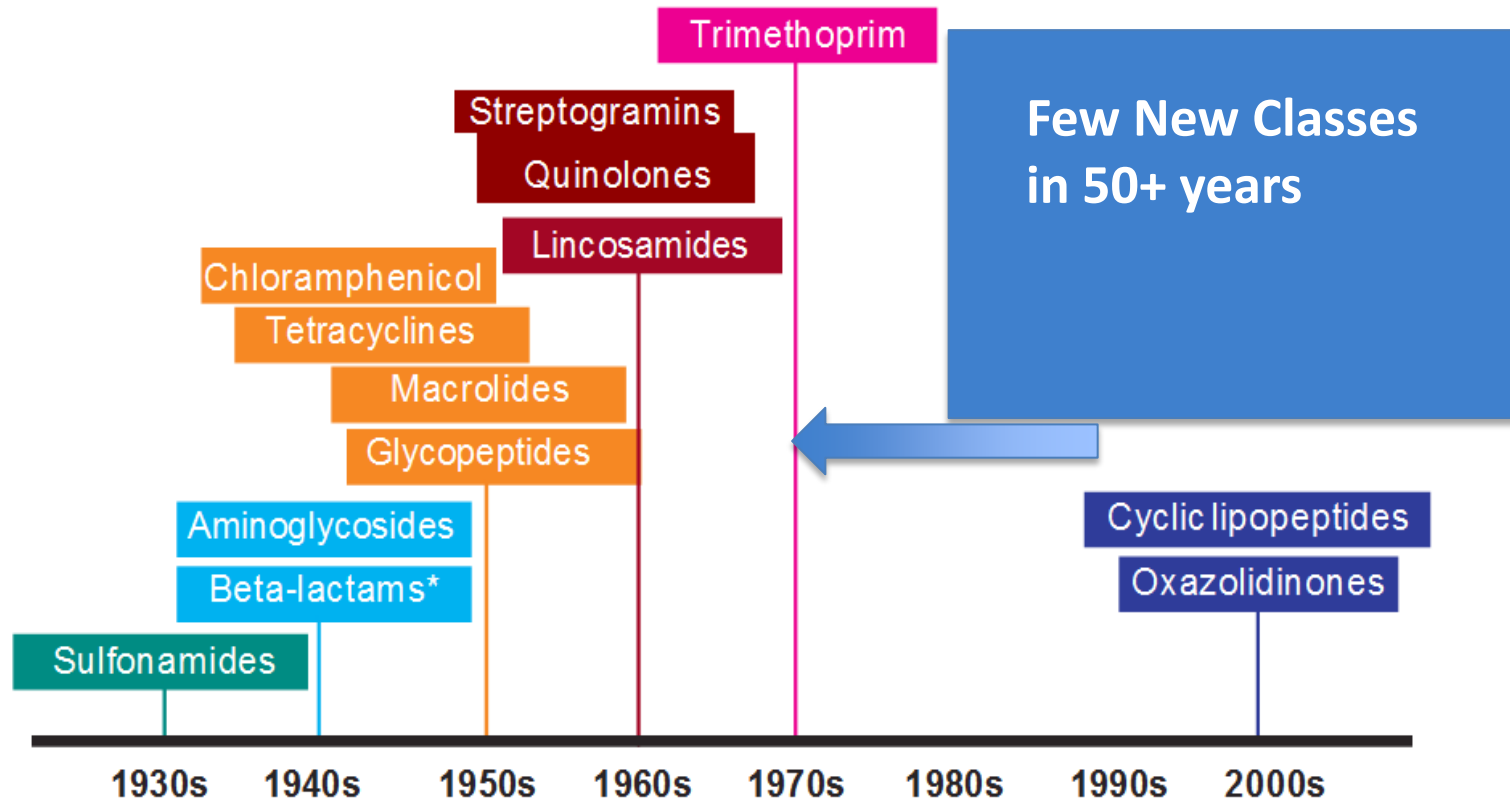
## HOW IT SPREADS



[www.who.int/drugresistance](http://www.who.int/drugresistance)

**#AntibioticResistance**

# Bad Bugs, Few Drugs



Adapted from Monnet DL, 2004





## Drug companies aren't making new antibiotics. Is there an economic cure?

Aug 4, 2017 8:03 pm EDT

<https://www.pbs.org/newshour/show/drug-companies-arent-making-new-antibiotics-economic-cure>

# AMR is now getting a lot of attention



## PRESS RELEASE: High-Level Meeting on Antimicrobial Resistance

21 September 2016 in Media, PGA Press Releases

OPGA/WHO/FAO/OIE Joint News Release



## HIGH-LEVEL MEETING ON ANTIMICROBIAL RESISTANCE



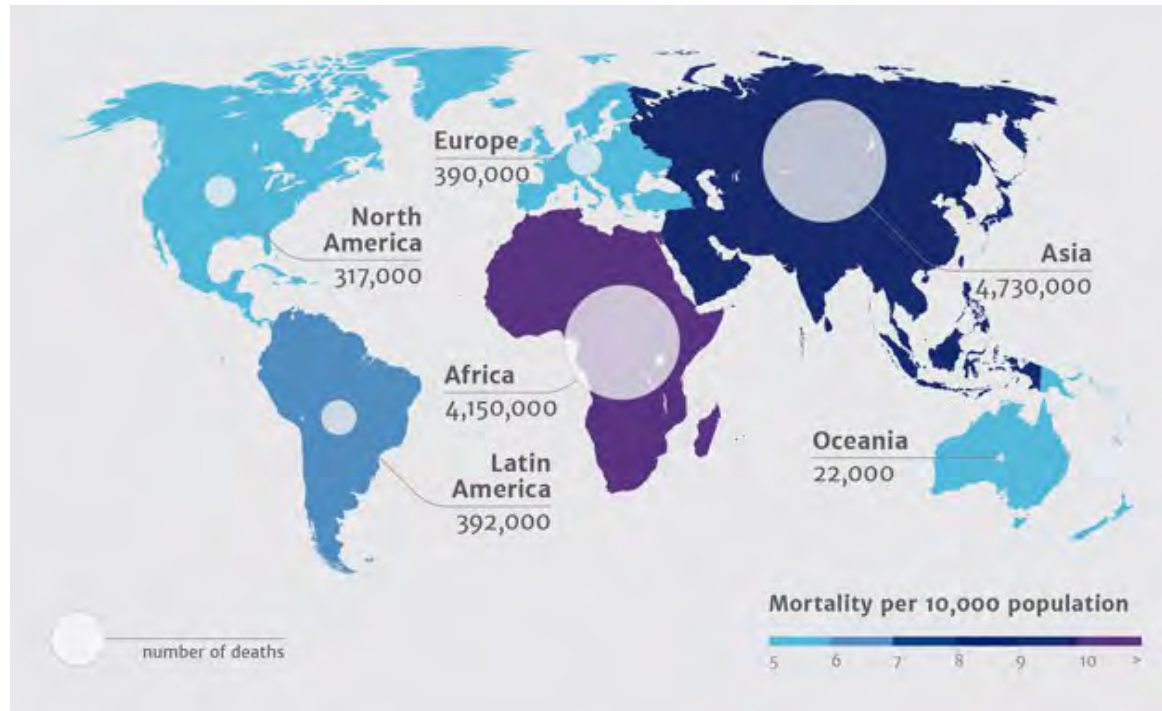
21 SEPTEMBER 2016, UN HEADQUARTERS, NEW YORK





**HOW BIG IS THE PROBLEM?**

# Antimicrobial Resistance burden in 2050



We estimate that by 2050, 10 million lives a year and a cumulative 100 trillion USD of economic output are at risk due to the rise of drug-resistant infections if we do not find proactive solutions now to slow down the rise of drug resistance. Even today, 700,000 people die of resistant infections every year.

## WHO PRIORITY PATHOGENS LIST FOR R&D OF NEW ANTIBIOTICS

### Priority 1: CRITICAL<sup>#</sup>

*Acinetobacter baumannii*, carbapenem-resistant

*Pseudomonas aeruginosa*, carbapenem-resistant

*Enterobacteriaceae*<sup>\*</sup>, carbapenem-resistant, 3<sup>rd</sup> generation  
cephalosporin-resistant

### Priority 2: HIGH

*Enterococcus faecium*, vancomycin-resistant

*Staphylococcus aureus*, methicillin-resistant, vancomycin  
intermediate and resistant

*Helicobacter pylori*, clarithromycin-resistant

*Campylobacter*, fluoroquinolone-resistant

*Salmonella* spp., fluoroquinolone-resistant

*Neisseria gonorrhoeae*, 3<sup>rd</sup> generation cephalosporin-resistant,  
fluoroquinolone-resistant

### Priority 3: MEDIUM

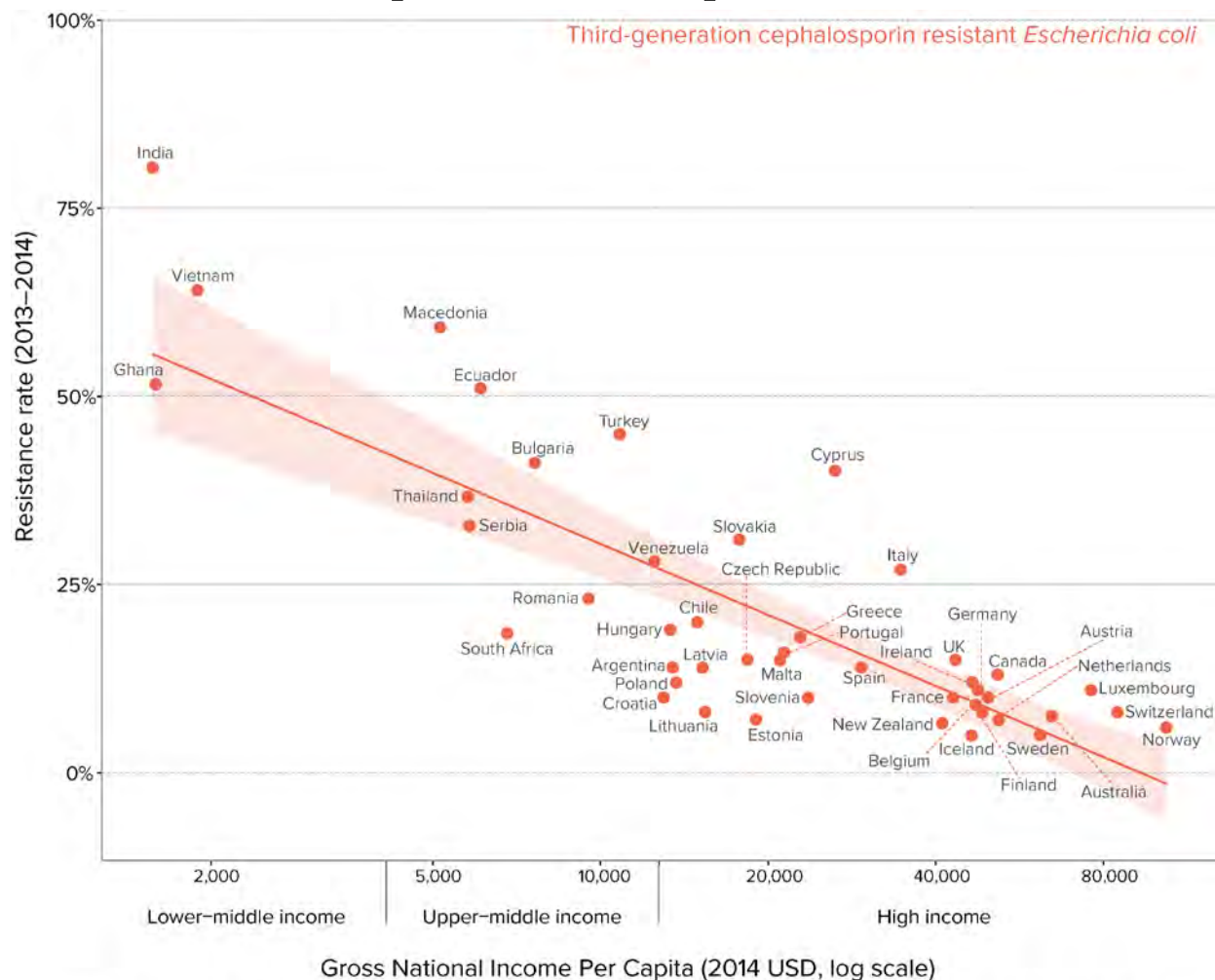
*Streptococcus pneumoniae*, penicillin-non-susceptible

*Haemophilus influenzae*, ampicillin-resistant

*Shigella* spp., fluoroquinolone-resistant

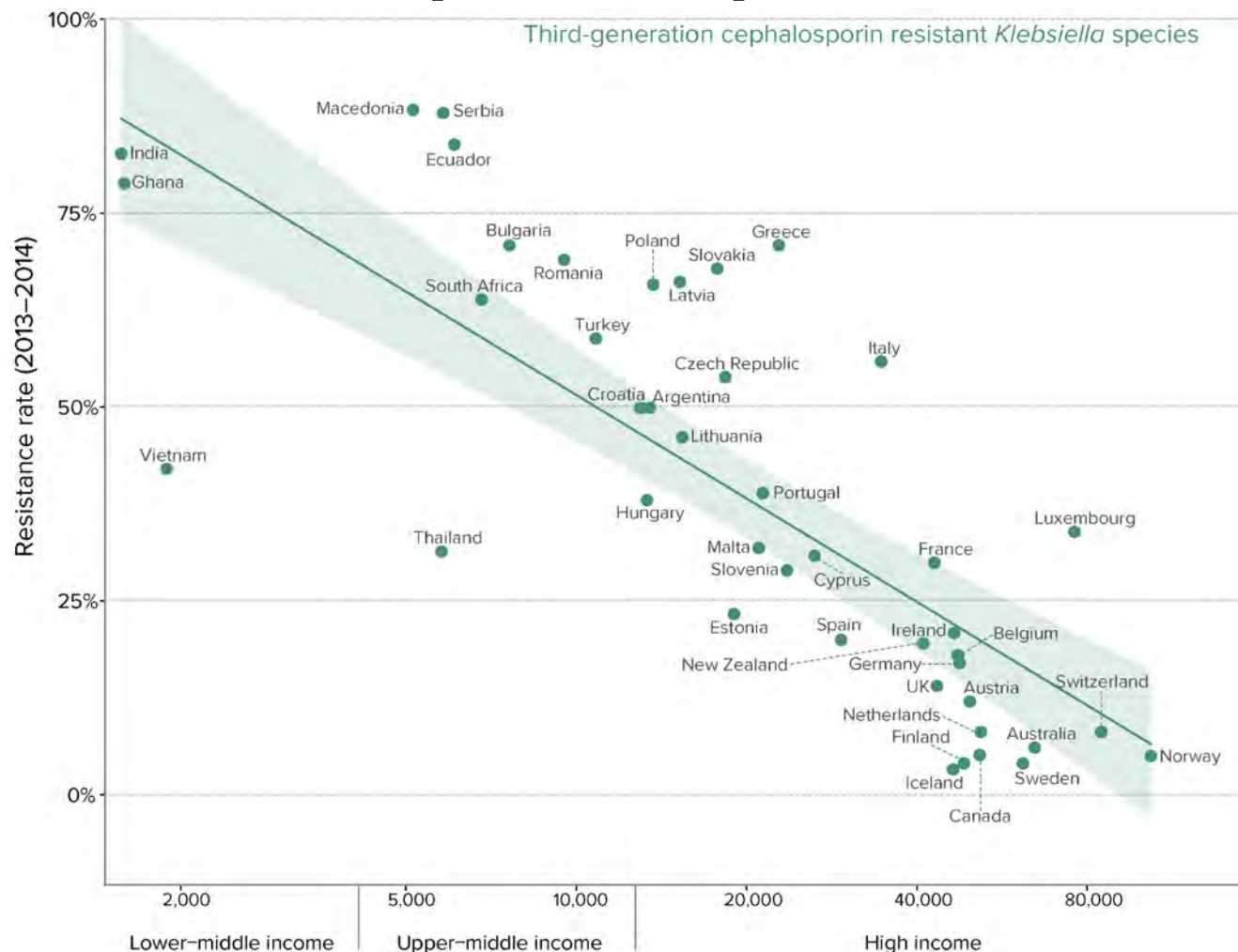
<sup>#</sup> *Mycobacteria* (including *Mycobacterium tuberculosis*, the cause of human tuberculosis), was not subjected to review for inclusion in this prioritization exercise as it is already a globally established priority for which innovative new treatments are urgently needed.

# Antibiotic resistance prevalence and national per-capita income



Lines represent predicted values with shaded regions showing 95% confidence intervals according to a linear regression model.

# Antibiotic resistance prevalence and national per-capita income





# CAUSES OF ANTIBIOTIC RESISTANCE



Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.



Over-prescribing  
of antibiotics



Patients not finishing  
their treatment



Over-use of antibiotics in  
livestock and fish farming



Poor infection control  
in hospitals and clinics



Lack of hygiene and poor  
sanitation



Lack of new antibiotics  
being developed

[www.who.int/drugresistance](http://www.who.int/drugresistance)

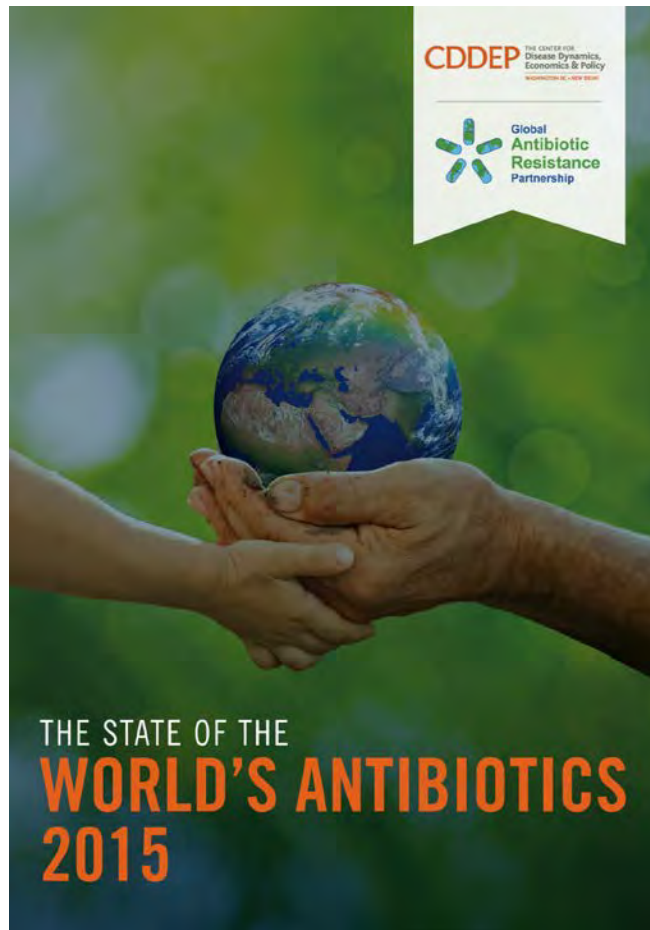
**#AntibioticResistance**



**World Health  
Organization**

# ANTIBIOTIC USE IN HUMANS

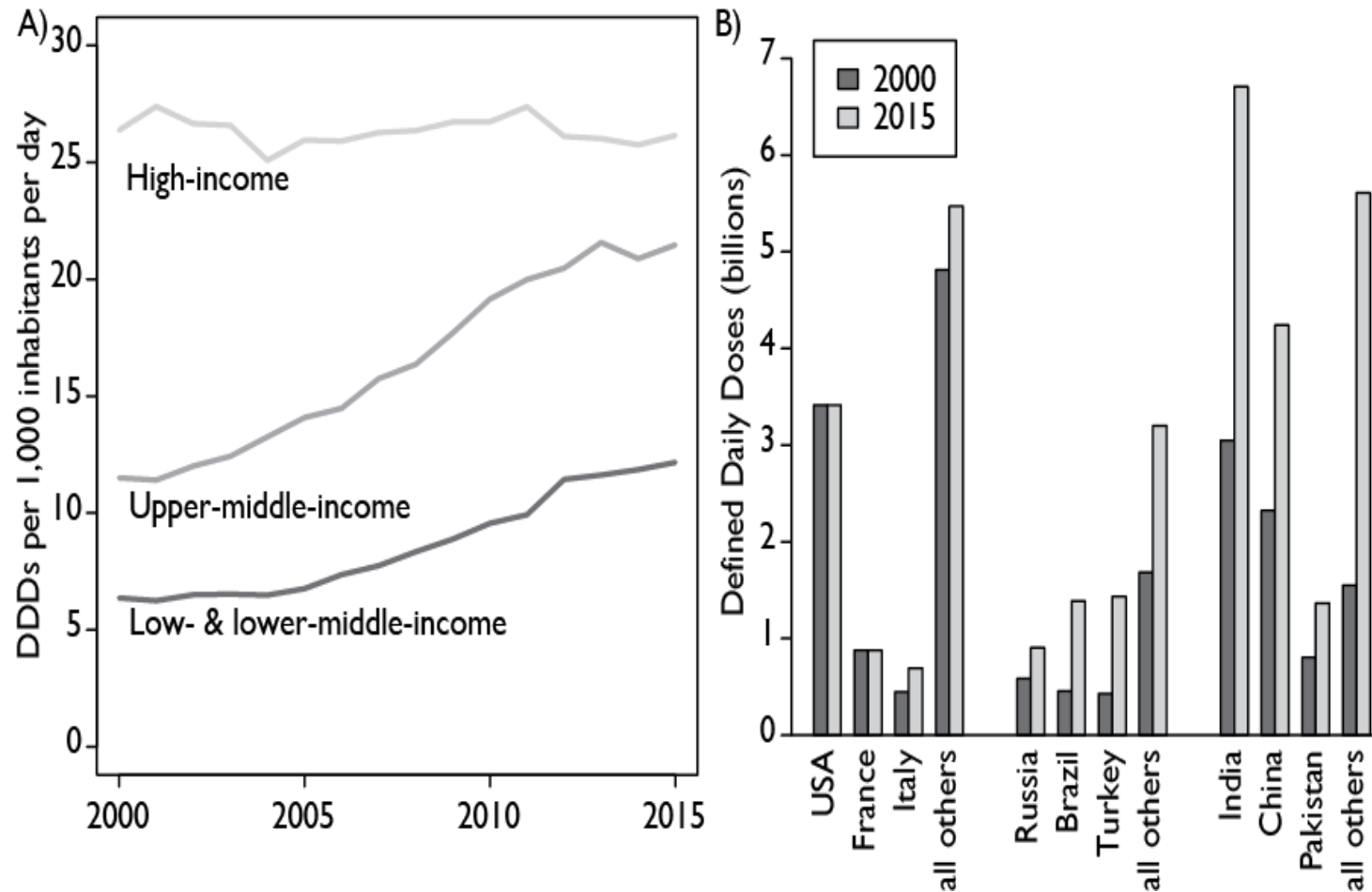




The greater the volume of antibiotics used, the greater the chances that antibiotic-resistant populations of bacteria will prevail in the contest for survival of the fittest at the bacterial level.

Evidence from around the world indicates an overall decline in the total stock of antibiotic effectiveness: resistance to all first-line and last-resort antibiotics is rising.

# Antibiotic consumption trends by income: 2000–2015

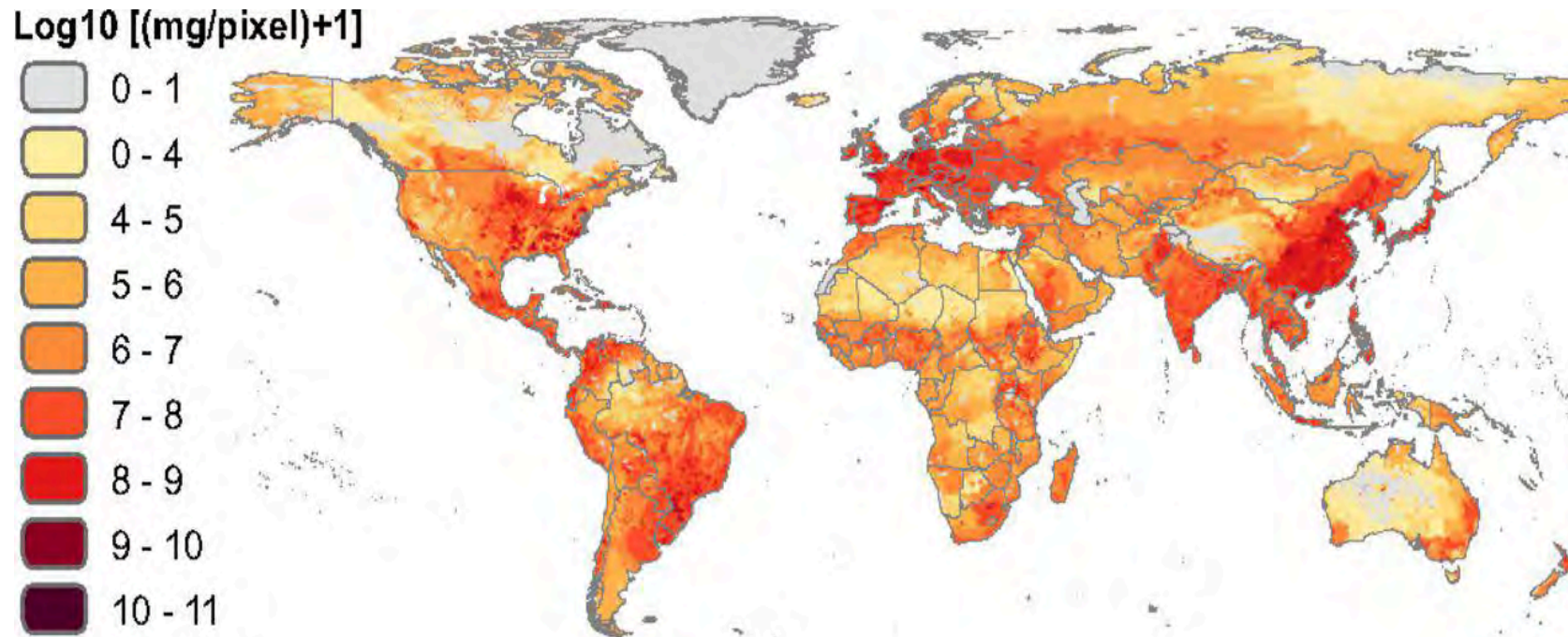


# ANTIBIOTIC USE IN ANIMALS





# Global Antimicrobial Consumption in Food Animals

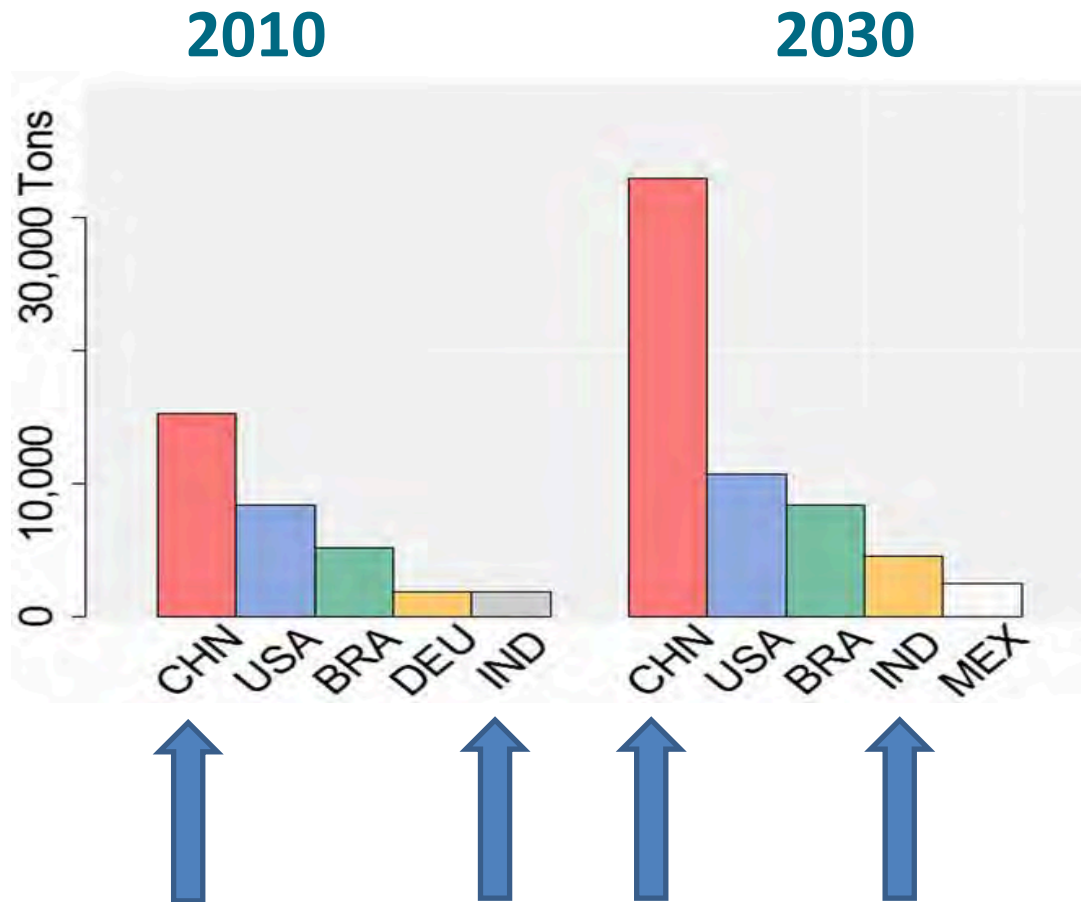


## Some Hot spots:

Southeast coast China

South coast of India, Mumbai, Delhi

# Countries with Highest Antimicrobial consumption in Food Animals



# **WHAT ARE THE DRIVERS OF AMR? EXAMPLE OF INDIA**



# Social Aspects in India

- **Reasons for prescribing antibiotics:**

- Private Sector**

- patient demand
    - fear of clinical failure
    - fear of losing patients
    - economic incentives
    - varying knowledge on antibiotics and antibiotic resistance

- Public Sector**

- Huge workload
    - Lack of diagnostic facilities
    - Pressure to use short-dated medicines

# Social Aspects in India

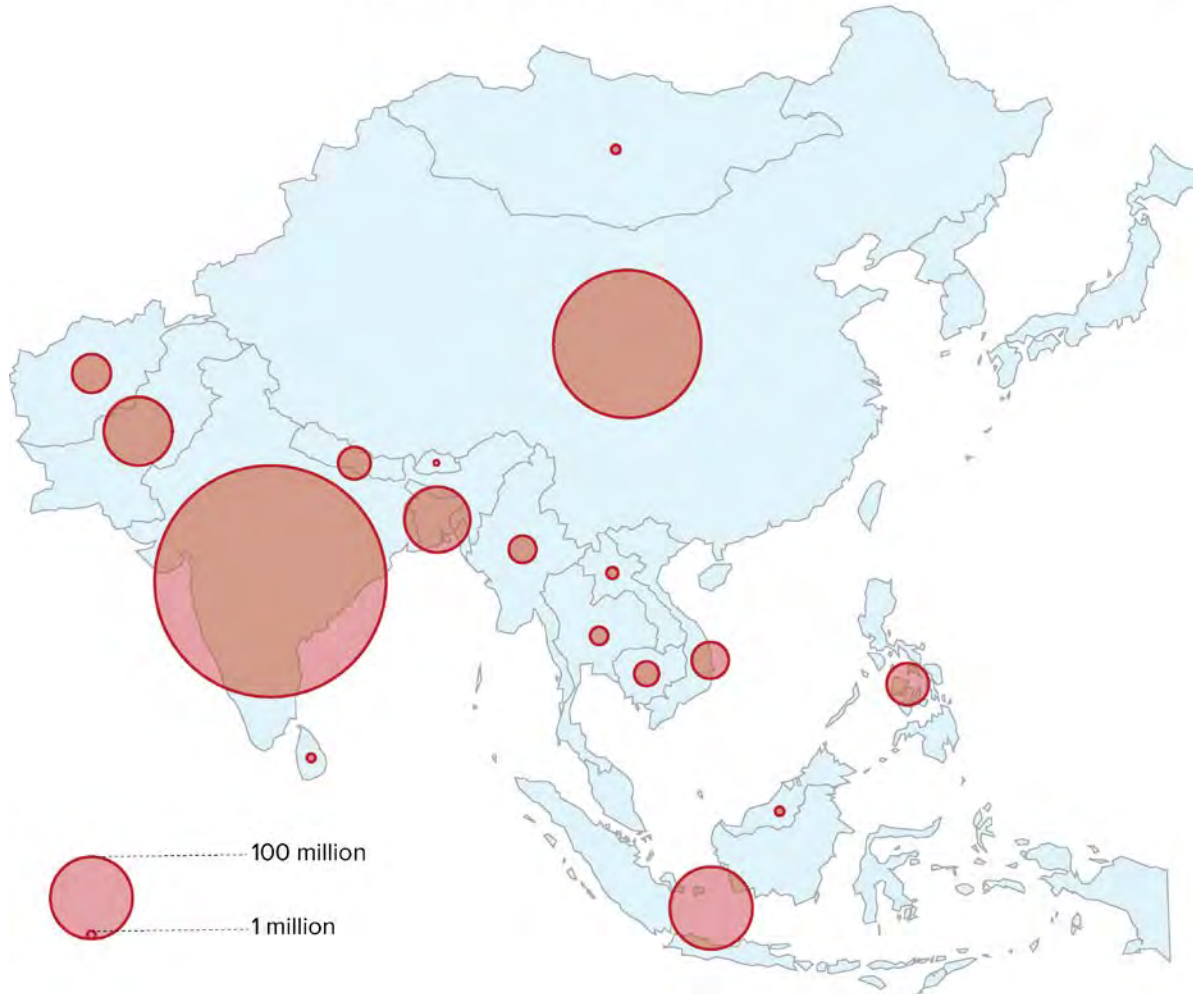
## General Public:

- self-medication
- access to antibiotics without prescription
- Utilizing pharmacies as source of healthcare
- lack of awareness of antibiotic resistance



# Poor Environmental Sanitation

Population without access to improved sanitation facilities, 2015



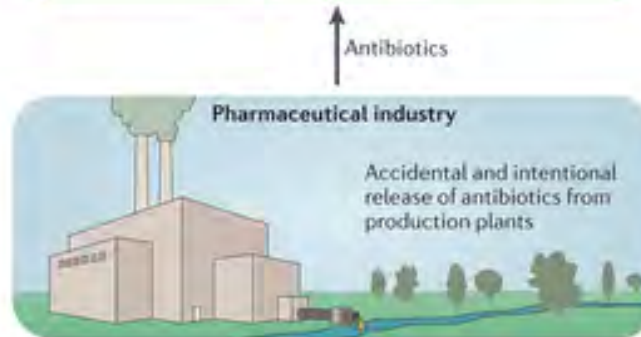
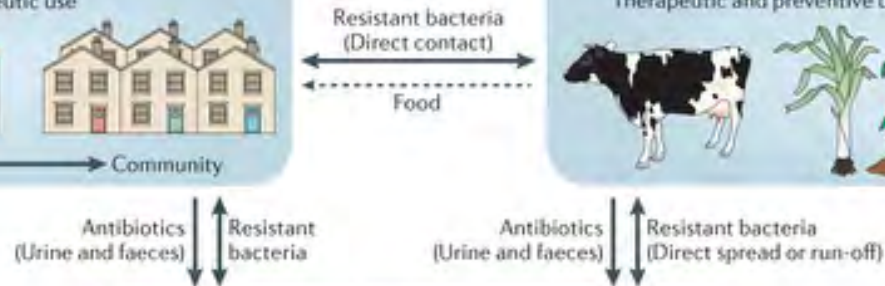
World Bank 2016

# Perfect conditions for emergence of Superbugs

## HUMAN SECTOR



## ANIMAL/AGRI SECTOR



## PHARMA SECTOR

Inadequate waste management from human, agriculture, and pharma sector

# **DRUG-RESISTANT TB AS A CASE STUDY**

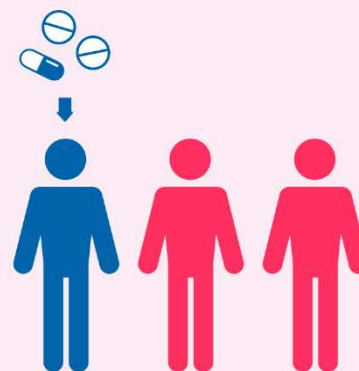


# DRUG-RESISTANT TUBERCULOSIS REMAINS A PUBLIC HEALTH CRISIS

IN 2018

**ABOUT 0.5 MILLION  
PEOPLE FELL ILL WITH  
DRUG-RESISTANT TB\***

**ONLY ONE IN THREE  
PEOPLE ACCESSED  
TREATMENT**



OF THOSE TREATED, ONLY  
**56% WERE TREATED SUCCESSFULLY**

\*The 95% uncertainty interval for the incidence of rifampicin-resistant TB is 420 000 - 560 000.  
About 80% of these cases had multidrug-resistant TB.





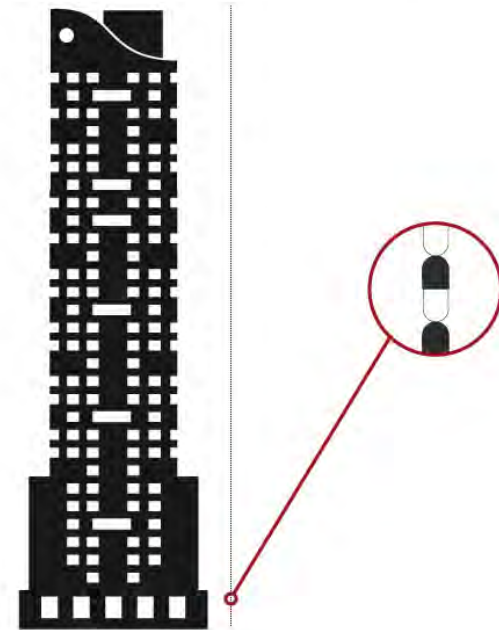
# Drug-resistant TB: hard to treat with low cure rates



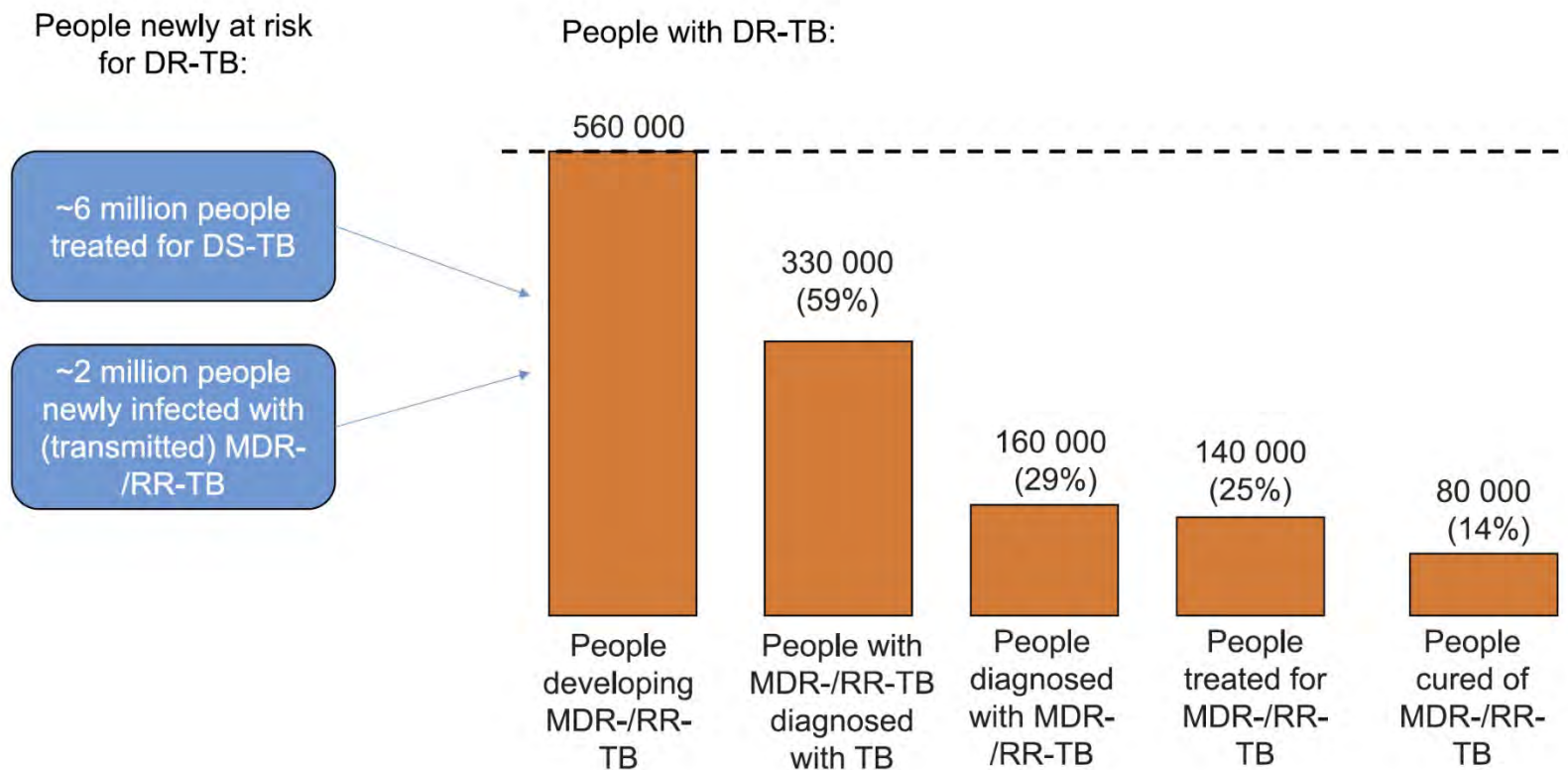
A patient with MDR-TB must take

**14,600 pills in two years.**

If you stack that many pills end-to-end, the line would be as tall as a 30-story building.



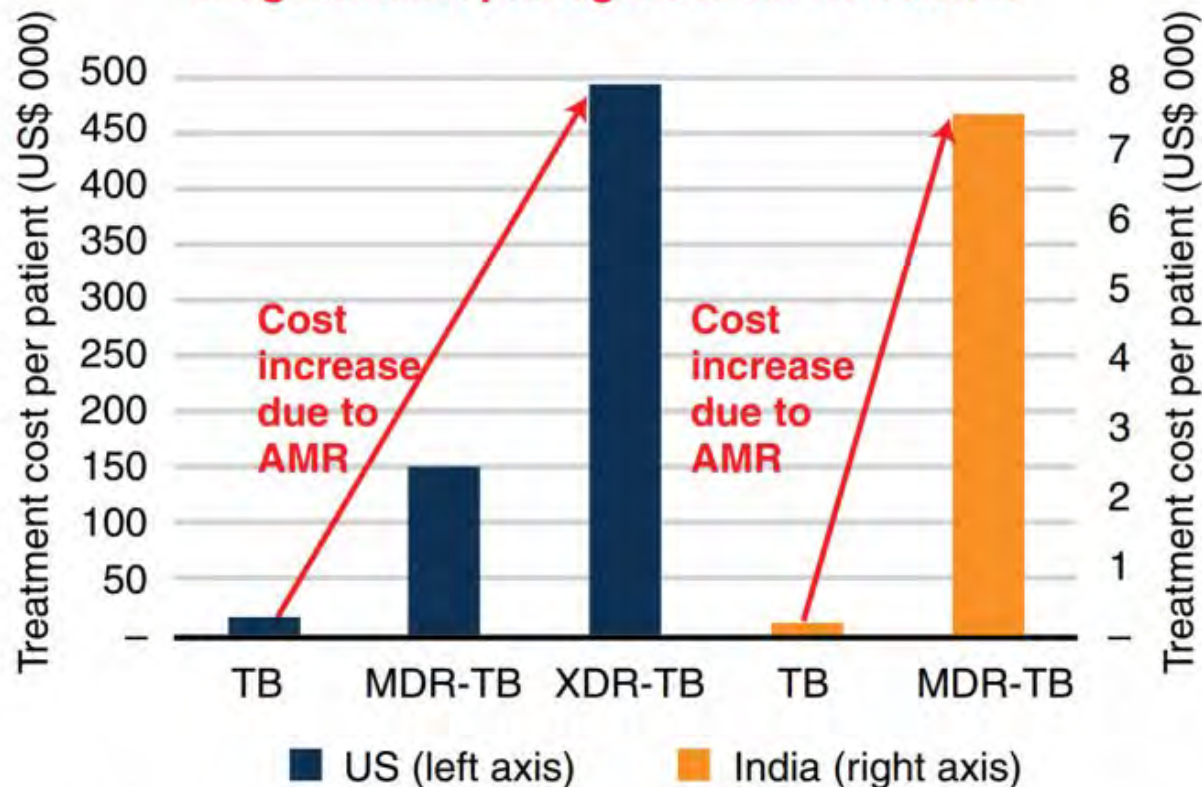




## TB treatments costs rise dramatically due to AMR

Treatment costs are much higher in HICs than in LMICs  
(e.g., 80x higher for TB—and 20x higher for MDR-TB—in the U.S. than in India)

**Drug-resistant pathogens know no borders**



TB = Tuberculosis (infectious disease caused by bacteria)  
MDR = Multidrug-resistant  
XDR = Extensively drug-resistant; TB caused by bacteria that are resistant to some of the most effective anti-TB drugs

# SOLUTIONS & STRATEGIES



# TACKLING ANTIMICROBIAL RESISTANCE ON TEN FRONTS

---



**Public awareness**



**Sanitation and hygiene**



**Antibiotics in agriculture and the environment**



**Vaccines and alternatives**



**Surveillance**



**Rapid diagnostics**



**Human capital**



**Drugs**



**Global Innovation Fund**



**International coalition for action**



**LONGITUDE PRIZE**

The Challenge Applying & Support Blog Teams Antimicrobial resistance About us & Governance

**ANTIBIOTIC DIAGNOSTICS: REPORT SHOWS DOWNWARD TREND IN INNOVATION**

Our new patent report has pointed to a decline in the number of new point-of-care technologies being created to diagnose infectious disease and identify pathogens and antimicrobial resistance (AMR), amid a concerning lack of industry and investment.

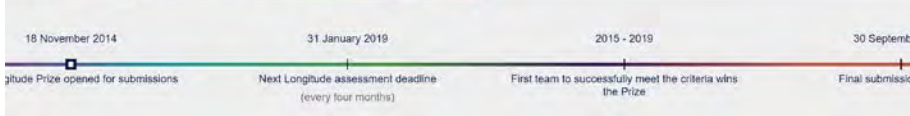
Read more

Crafting the uncrafterable: Designing "diagnostics"

Q&A: Diagnostic advice for low-resource settings

Sting: A story from Infectious Futures

Sex, Drugs and Superbugs: Gonorrhoea and the post-antibiotic apocalypse



The Longitude Prize is a £10m prize fund, with an £8m payout, that will reward a team of researchers who develop a point-of-care diagnostic test that will conserve antibiotics for future generations and revolutionise the delivery of global healthcare.

<https://longitudeprize.org>

CONTACT

**CARB-X**  
Combating Antibiotic Resistant Bacteria

ABOUT CARB-X • PORTFOLIO • PARTNERS • APPLY • RESOURCES • NEWS • EVENTS

WINNING THE RACE AGAINST SUPERBUGS

**Growing resistance**

Antibiotic resistance is growing and we are fast running out of treatment options.

CARB-X is investing more than \$500 million between 2016 and 2021 into the research and development of new antibiotics, vaccines, rapid diagnostics and other life-saving products to tackle the global threat of drug-resistant bacteria

<https://carb-x.org/>

# Pandemics





# THE TERRIFYING LESSONS OF A PANDEMIC SIMULATION



By Nicola Twilley June 1, 2018



Among one do

☐ Sunwi

☐ Porter

☐ Westje

☐ Air Ca

☐ Air Tra

Powered By  
View Privacy

*A recent outbreak exercise held by the Johns Hopkins Center for Health Security revealed vulnerabilities that are hardwired into the American system.*



JOHNS HOPKINS  
BLOOMBERG SCHOOL  
of PUBLIC HEALTH

Center for  
**Health Security**

[ABOUT](#) | [PLAYERS](#) | [RESOURCES](#) | [CONTACT](#)



[http://www.centerforhealthsecurity.org/our-work/events/2018\\_clade\\_x\\_exercise/media](http://www.centerforhealthsecurity.org/our-work/events/2018_clade_x_exercise/media)

<https://academic.oup.com/jid/article/200/7/1018/903237>

**Antimicrobial-resistant threats**

- CRE
- MRSA
- *C. difficile*
- *N. gonorrhoeae*

**Newly emerging diseases (red dots):**

- Enterovirus D68
- Heartland
- West Nile virus
- Cryptosporidiosis
- Powassan virus
- E. coli* O104:H4
- Ebola virus disease
- Drug-resistant malaria
- Diphtheria
- MERS-CoV
- Akhmeta virus
- Rift Valley fever
- Typhoid fever
- SFTSV bunyavirus
- E. coli* O157:H7
- H10N8 influenza
- H7N9 influenza
- H5N1 influenza
- SARS
- Nipah virus
- Hendra virus
- Enterovirus 71
- Human monkeypox
- Ebola virus disease
- Zika virus

**Re-emerging/resurging diseases (blue dots):**

- H3N2v influenza
- Cyclosporiasis
- E. coli* O157:H7
- Measles
- Human monkeypox
- Listeriosis
- Bourbon virus
- 2009 H1N1 influenza
- Adenovirus 14
- Anthrax bioterrorism
- Chikungunya
- Hantavirus pulmonary syndrome
- Dengue
- Zika virus
- Yellow fever
- Human African trypanosomiasis
- Cholera
- Marburg hemorrhagic fever
- MDR / XDR tuberculosis
- Plague

**'Deliberately emerging' disease (black dot):**

- Lyme disease

**Other diseases shown:**

- Hepatitis C
- vCJD
- Lassa fever
- HIV

**Legend:**

- Newly emerging
- Re-emerging/resurging
- "Deliberately emerging"

September 2011

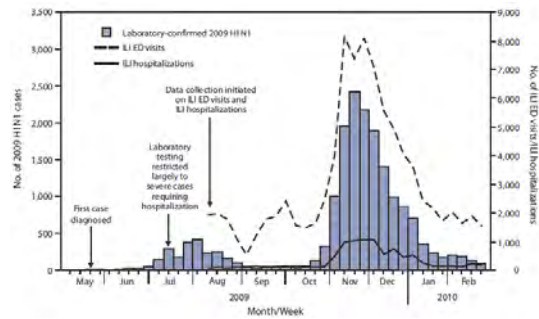
September 2017



# Famous, historic pandemics

- 1347 to 1351 Black Death: remade the landscape of Europe; in a time when the global population was an estimated 450 million, at least 75 million are believed to have perished throughout the pandemic
- 1918 Spanish flu: mortality rate as high as one in five and an estimated one-third of the world population afflicted, as many as 50 million people are believed to have died.

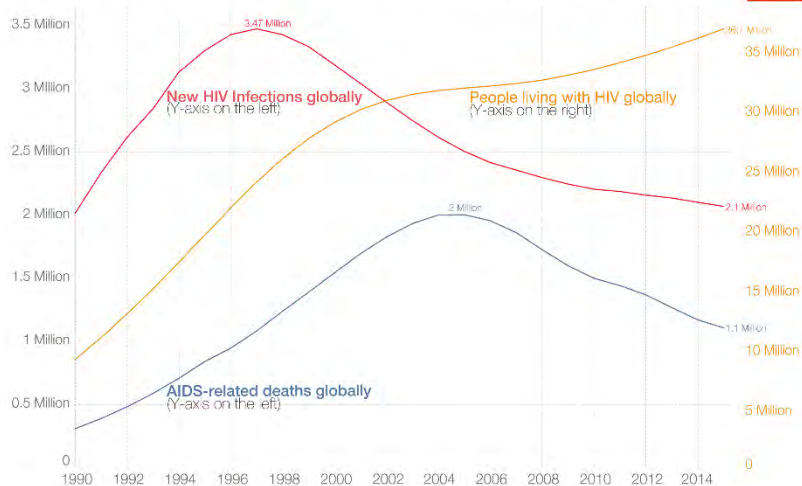




## Famous 'modern' plagues

- HIV: originated from non-human primates in the 1920s, recognized in humans in 1980s, and killed >35 million people
- Swine flu: One of the new strains was the H1N1 "swine flu" virus that originated in Mexico in 2009. The strain went on to kill more than 18,000 people around the world.

Global number of AIDS-related deaths, new HIV Infections, and People living with HIV (1990-2015) Our World in Data



Data source: UN AIDS (via [www.aidsinfoonline.org](http://www.aidsinfoonline.org))  
The data visualization is available at [OurWorldinData.org](http://OurWorldinData.org). There you find more visualizations and research on HIV/AIDS.

Licensed under CC-BY-SA by the author Max Roser.



Health » Food | Fitness | Wellness | Parenting | Live Longer

Live TV

U.S. Edition +



CNN FILMS

UNSEEN ENEMY

A WORLD HEALTH DAY PRESENTATION

# Seven reasons we're at more risk than ever of a global pandemic

By Meera Senthilingam, CNN

Updated 2:21 PM ET, Mon April 10, 2017



## More from CNN



All Blacks and England to wear poppies in 'special' match

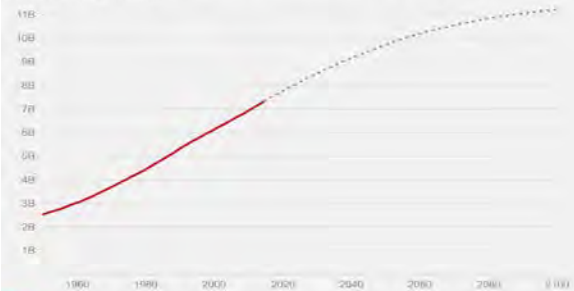


Bill Nelson's campaign sues Florida secretary of state as vote...



## Rising population increases epidemic risk

The world is getting more and more crowded. Our skyrocketing population makes us more at risk for spreading deadly epidemics amongst ourselves.



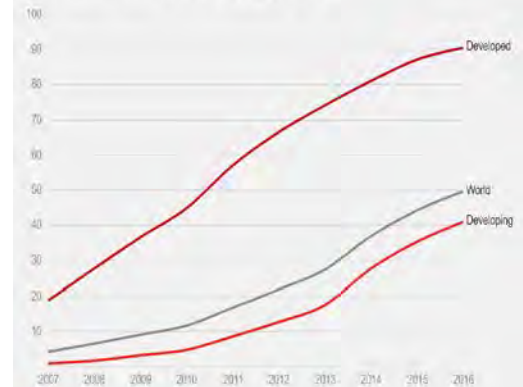
Source: United Nations, Department of Economic and Social Affairs



## Faster communication raises the risk of panic

More than 90% of the population will be covered by mobile broadband networks by 2021, according to the UN. Instant communication everywhere raises the possibility that false rumors will spread during a crisis. Worst case: Fearful rumors may trigger panic, which might hinder key institutions like stock markets and emergency responders.

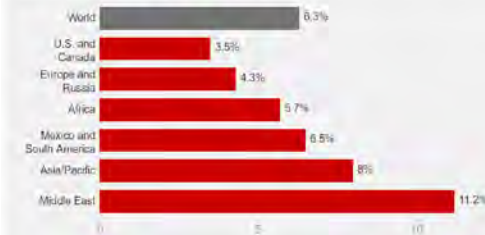
### Mobile broadband subscriptions per 100 people, 2007-2016



Source: United Nations, State of Broadband 2016

## International travel growth

International airline travel, measured in revenue passenger kilometers, rose 6.3% worldwide in 2016, with some regions seeing faster growth than others



Source: International Air Transport Association

Health • Seven reasons why we're more at risk than ever of a global pandemic

### Mega-cities have nearly tripled

More people live in densely-populated urban areas than ever before. The number of mega-cities, which have populations greater than 10 million, grew from 10 in 1990 to 26 in 2014.



### Countries with few doctors

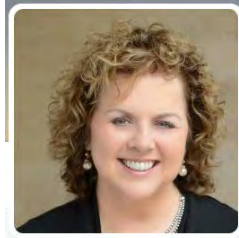
More than 75 countries have fewer than 1 physician per 1,000 population.



Source: World Health Organization



1. Growing populations and urbanization
2. Encroaching into new environments
3. Climate change
4. Global travel
5. Civil conflict
6. Fewer doctors and nurses in outbreak regions
7. Faster information



---

## Ebola's Lessons

---

How the WHO Mishandled the Crisis

---

*Laurie Garrett*

“the global response to the rise of new pathogens has continued to be limited, uncoordinated, and dysfunctional. From SARS to MERS, H5N1 to H1N1 to H7N9, the story has been similar. Poor nations are unable to detect new diseases quickly and bring them swiftly under control. Rich nations generally show only marginal interest in outbreaks until the microbes seem to directly threaten their citizens, at which point they hysterically overreact. Governments look after their own interests, cover up outbreaks, hoard scarce pharmaceutical supplies, prevent exports of life-saving medicines, shut borders, and bar travel.”

# Lessons from the Ebola Outbreak in West Africa



## POLICY FORUM

### Toward a Common Secure Future: Four Global Commissions in the Wake of Ebola

**Lawrence O. Gostin<sup>1\*</sup>, Oyewale Tomori<sup>2</sup>, Suwit Wibulpolprasert<sup>3</sup>, Ashish K. Jha<sup>4</sup>, Julio Frenk<sup>5</sup>, Suerie Moon<sup>6</sup>, Joy Phumaphi<sup>7</sup>, Peter Piot<sup>8</sup>, Barbara Stocking<sup>9</sup>, Victor J. Dzau<sup>10</sup>, Gabriel M. Leung<sup>11</sup>**

**1** O'Neill Institute for National and Global Health Law, Georgetown University, Washington, DC, United States of America, **2** Nigeria Academy of Sciences, Lagos, Nigeria, **3** Ministry of Public Health, Nonthaburi, Thailand, **4** Harvard T.H. Chan School of Public Health, Boston, Massachusetts, United States of America, **5** University of Miami, Coral Gables, Florida, United States of America, **6** Harvard Global Health Institute, Harvard University, Cambridge, Massachusetts, United States of America, **7** African Leaders Malaria Alliance, New York, New York, United States of America, **8** London School of Hygiene & Tropical Medicine, London, United Kingdom, **9** Murray Edwards College, University of Cambridge, United Kingdom, **10** National Academy of Medicine, Washington, DC, United States of America, **11** Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong, China



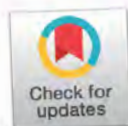


## Summary Points

- Four global commissions reviewing the recent Ebola virus disease epidemic response consistently recommended strengthening national health systems, consolidating and strengthening World Health Organization (WHO) emergency and outbreak response activities, and enhancing research and development.
- System-wide accountability is vital to effectively prevent, detect, and respond to future global health emergencies.
- Global leaders (e.g., United Nations, World Health Assembly, G7, and G20) should maintain continuous oversight of global health preparedness, and ensure effective implementation of the Ebola commissions' key recommendations, including sustainable and scalable financing.



# ANALYSIS



## Global epidemics: how well can we cope?

Although numerous initiatives have been launched to improve global capacity to respond to major outbreaks of disease, worrying gaps remain, report **Jennifer Leigh and colleagues**

Jennifer Leigh *DrPH candidate*<sup>1</sup>, Gabrielle Fitzgerald *chief executive officer*<sup>2</sup>, Elvis Garcia *DrPH candidate*<sup>1</sup>, Suerie Moon *director of research*<sup>3</sup>

<sup>1</sup>Harvard T H Chan School of Public Health, Boston, MA, USA; <sup>2</sup>Panorama Global, Seattle, Washington, USA; <sup>3</sup>Global Health Centre, Graduate Institute of Geneva, Switzerland

## Summary points

The west Africa Ebola outbreak in 2014-5 highlighted deficiencies in global capacity to respond

This year's Ebola outbreak in the Democratic Republic of Congo showed that some of those deficiencies have been addressed

However, more progress needs to be made related to preparedness, monitoring, and knowledge sharing

Overall leadership is lacking, leading to numerous unlinked initiatives rather than a functional global response

Stewardship beyond WHO is needed

Many funding promises have not been met as epidemics have fallen down the political agenda






Ring the alarm

## The next epidemic is coming. Here's how we can make sure we're ready.

By **Bill Gates** | April 27, 2018

 5799 SHARES

 666 SHARES

 SHARE

“The 2014 Ebola outbreak was a stark reminder of how vulnerable our society is to epidemics of infectious diseases. We weren’t ready then, and we’re still not ready now—but we can be. We don’t know when the next epidemic will strike, but I believe we can protect ourselves if we invest in better tools, a more effective early detection system, and a more robust global response system.”



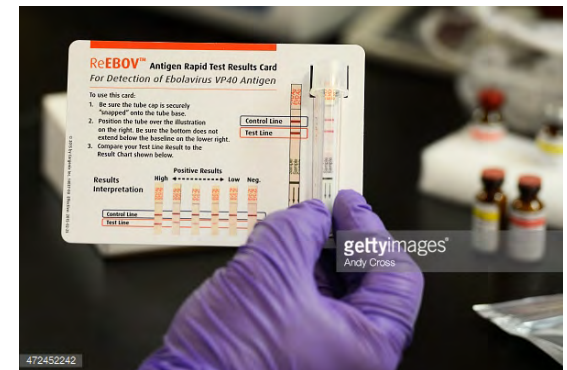
# Post Ebola, the world responded

- New tools (e.g. Ebola vaccine, diagnostics)
- Global Health Security Agenda
- CEPI
- Pandemic Emergency Financing Facility

# New tools for Ebola



Xpert Ebola on GeneXpert platform  
100% sensitivity & 96% specificity



Corgenix ReEBOV Antigen Rapid Test Kit  
100% sensitivity and 92% specificity

The Global Health Security Agenda (GHSA) was launched in February 2014 and is a growing partnership of over 64 nations, international organizations, and non-governmental stakeholders to help build countries' capacity to help create a world safe and secure from infectious disease threats and elevate global health security as a national and global priority.



<https://www.ghsagenda.org/home>



CEPI

About us

Get involved

Research & development

News & stories

Outbreaks

# New vaccines for a safer world

CEPI is a global alliance financing and coordinating the development of vaccines against infectious diseases.



<http://cepi.net/>

BRIEF

# Pandemic Emergency Financing Facility

July 27, 2017

## How the Pandemic Emergency Financing Facility (PEF) Works



Click [here](#) to zoom in.

The World Bank Group, with the support of Japan, Germany and the World Health Organization, has developed the [Pandemic Emergency Financing Facility](#) (PEF), a quick-disbursing financing mechanism that provides a surge of funds to enable a rapid and effective response to a large-scale disease outbreak. Eligible countries can receive timely, predictable, and coordinated surge financing if affected by an outbreak that meets PEF's activation criteria. The PEF breaks new ground by providing the first-ever insurance for pandemic risk, offering coverage to all low-income countries eligible for financing under [IDA](#).

## RELATED

FAQS

[Pandemic Emergency Financing Facility](#)

REPORT

[From Panic and Neglect to Investing in Health Security: Financing Pandemic Preparedness at a National Level](#)

FOCUS AREA

[Pandemic Preparedness and Health Systems Strengthening](#)

## MULTIMEDIA



**PANDEMIC EMERGENCY  
FINANCING FACILITY**

VIDEO

[What is the Pandemic Emergency Financing Facility?](#)

[Health](#)

## From Ebola to Zika: international emergencies and the securitization of global health

viewing the response to international emergencies only through the limited prism of security would condemn global health to an infinite succession of periods of “war” interspersed with “truces” focused on surveillance systems, rather than confronting the causes of the epidemics, rooted in the social determinants of health. If the immediate responses are not accompanied by structural changes capable of promoting a radical reduction in inequalities, the question remains: who will truly be safe at the end of each “war”?



**Deisy Ventura**



The NEW ENGLAND JOURNAL of MEDICINE

## Perspective

### Politics and Pandemics

Ron Klain, J.D.

1. Rising tide of isolationism and xenophobia — a turn inward — in many high-income nations, particularly the United States and European countries.
2. Growing tide of antiscientific thinking and resistance to Evidence-based medicine — often associated with surging populism and manifesting in the rise of the antivaccination movement.
3. Disease-related danger from change



If there really was a new  
pandemic, is the world unified  
enough to fight it??

