The AMR situation in the context of the COVID19 pandemic

Ramanan Laxminarayan

2nd AMR Course

Fondation Mérieux and University of Paris

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

PRINCETON UNIVERSITY

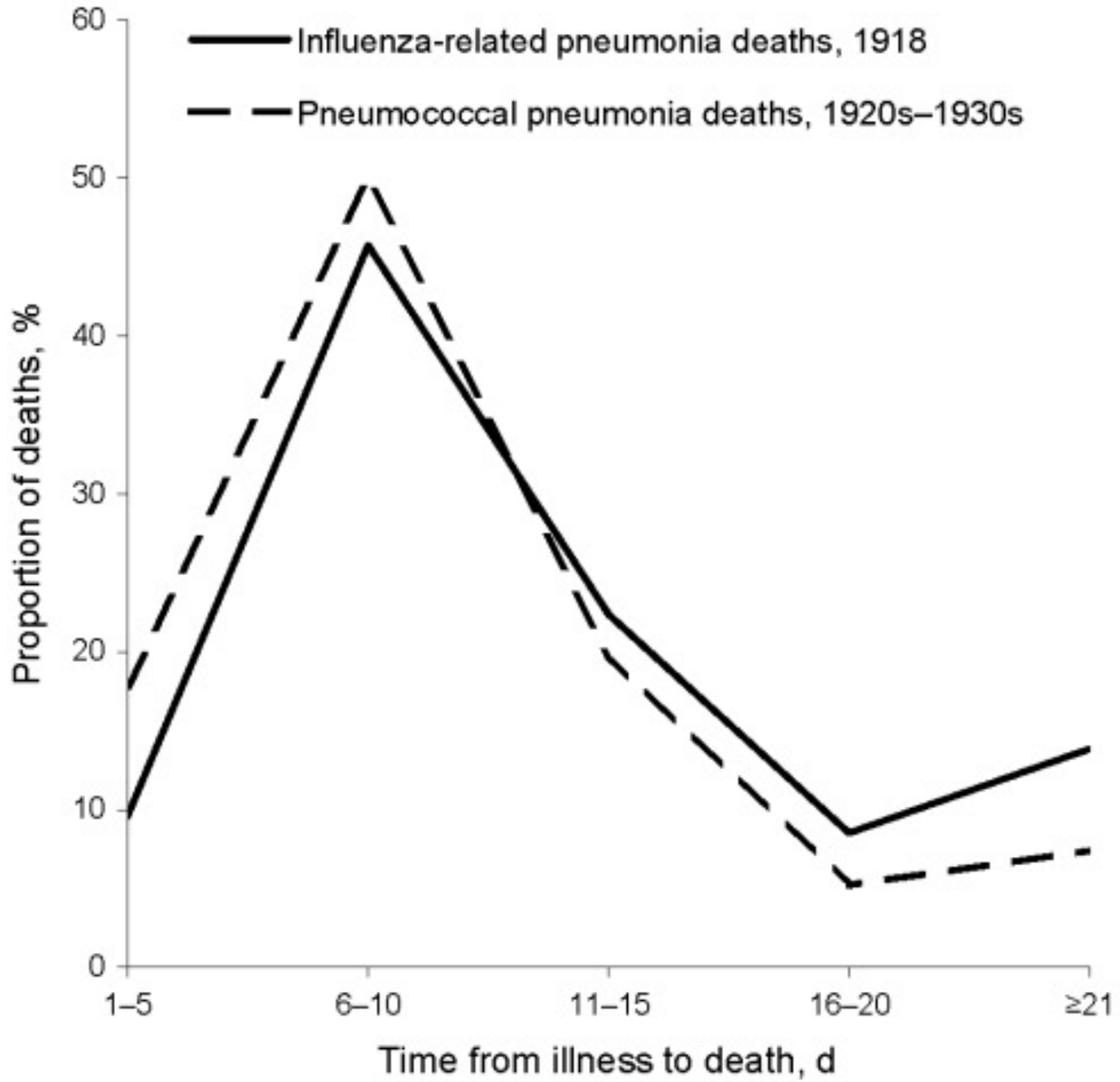
Pneumococcal infections, were a major cause of influenza-associated pneumonia and death among both military personnel and civilians in 1918–1919

Table 1. Culture Results for Patients during the 1918 Pandemic, According to Type of Culture and Pneumonia Status at the Time of Culture.*

Type of Culture and Population	No. of Studies	Positive Cultures	No. Positive for Pneumococci	No. Positive for Hemolytic Streptococci	No. Positive for *Staphylococcus aureus*	No. Positive for Other or Undetermined Bacteria
		no./total no. (%)				
Antemortem blood cultures						
Patients without pneumonia						
Military	5	0/323	0	0	0	0
Civilian	5	1/86 (1)	0	1	0	0
Total	10	1/409 (<1)	0	1	0	0
Patients with pneumonia						
Military	16	290/2042 (14)	238	49	2	3
Civilian	8	81/323 (25)	36	32	2	11
Total	24	371/2365 (16)	274	81	4	14
Patients with documented, subsequently fatal pneumonia						
Civilian	3	18/45 (40)	8	1	0	9
Antemortem pleural-effusion and lung cultures						
Military	5	182/224 (81)	140	55	0	10
Civilian	2	45/61 (74)	9	31	1	5
Total	7	227/285 (80)	149	86	1	15

* Results for individual studies are given in the Supplementary Appendix, available with the full text of this article at NEJM.org.

Chien et al, N Engl J Med 2009; 361:2582-2583



CDDEP TH Di Ec WA

PRINCETON UNIVERSITY

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Incidence of co-infections and superinfections in hospitalized patients with COVID-19: a retrospective cohort study

Carolina Garcia-Vidal [1,*,†], Gemma Sanjuan [1,†], Estela Moreno-García [1], Pedro Puerta-Alcalde [1], Nicole Garcia-Pouton [1], Mariana Chumbita [1], Mariana Fernandez-Pittol [2], Cristina Pitart [2], Alexy Inciarte [1], Marta Bodro [1], Laura Morata [1], Juan Ambrosioni [1], Ignacio Grafia [1], Fernanda Meira [1], Irene Macaya [1], Celia Cardozo [1], Climent Casals [2], Adrian Tellez [3], Pedro Castro [3], Francesc Marco [2], Felipe García [1], Josep Mensa [1], José Antonio Martínez [1], Alex Soriano [1] for the COVID-19 Researchers Group[§]

[1] Department of Infectious Diseases, Hospital Clinic of Barcelona, IDIBAPS, Barcelona, Spain
[2] Department of Microbiology, Hospital Clinic, University of Barcelona, ISGLOBAL, Barcelona, Spain
[3] Medical Intensive Care Unit, Hospital Clinic of Barcelona, IDIBAPS, Barcelona, Spain

ARTICLE INFO

Article history:
Received 2 June 2020
Received in revised form
24 July 2020
Accepted 26 July 2020
Available online 31 July 2020

Editor: M. Paul

Keywords:
Co-infections
COVID-19
Mortality
SARS-CoV-2
Superinfections

ABSTRACT

Objectives: To describe the burden, epidemiology and outcomes of co-infections and superinfections occurring in hospitalized patients with coronavirus disease 2019 (COVID-19).

Methods: We performed an observational cohort study of all consecutive patients admitted for ≥48 hours to the Hospital Clinic of Barcelona for COVID-19 (28 February to 22 April 2020) who were discharged or dead. We describe demographic, epidemiologic, laboratory and microbiologic results, as well as outcome data retrieved from electronic health records.

Results: Of a total of 989 consecutive patients with COVID-19, 72 (7.2%) had 88 other microbiologically confirmed infections: 74 were bacterial, seven fungal and seven viral. Community-acquired co-infection at COVID-19 diagnosis was uncommon (31/989, 3.1%) and mainly caused by *Streptococcus pneumoniae* and *Staphylococcus aureus*. A total of 51 hospital-acquired bacterial superinfections, mostly caused by *Pseudomonas aeruginosa* and *Escherichia coli*, were diagnosed in 43 patients (4.7%), with a mean (SD) time from hospital admission to superinfection diagnosis of 10.6 (6.6) days. Overall mortality was 9.8% (97/989). Patients with community-acquired co-infections and hospital-acquired superinfections had worse outcomes.

Conclusions: Co-infection at COVID-19 diagnosis is uncommon. Few patients developed superinfections during hospitalization. These findings are different compared to those of other viral pandemics. As it relates to hospitalized patients with COVID-19, such findings could prove essential in defining the role of empiric antimicrobial therapy or stewardship strategies. **Carolina Garcia-Vidal, Clin Microbiol Infect 2021;27:83**

Summary of published data describing secondary infections in COVID-19 patients.

Country	Total no. of patients	Secondary infections				Ref.
		No. of patients (%)	Identified organisms (No. of patients)			Clinical Outcome
			Viral	Bacterial	Fungal	
USA	5700	42 (2.1%)	Rhinovirus/enterovirus (22), other coronaviridae (7), RSV (4), parainfluenza (3), metapneumovirus (2), and influenza A (1)	*Chlamydophila pneumoniae* (2), *M. pneumoniae* (1)	NA	21% died	[12]
USA	338	19 (5.6%)	NA			NA	[13]
China	201 (ARDS)	1 (0.6%)	Influenza A virus (1)	NA		NA	[14]
China	191	27 (50%) of 54 non-survivors	NA			96% died	[2]
USA	116	24 (20.7%)	Rhinovirus/enterovirus (8), RSV (6), other coronaviridae (5), parainfluenza (3), metapneumovirus (2), and influenza A (1)	NA		NA	[15]
China	115	5 (4.3%)	Influenza A virus (3) Influenza B virus (2)	NA		NA	[16]
China	99	5 (5%)	NA	*Acinetobacter baumannii, Klebsiella pneumoniae*, and *Aspergillus flavus* in respiratory samples (1)	*Candida albicans* (3) *Candida glabrata* (1)	NA	[17]
Italy	73 (ARDS)	*Bacterial pneumonia (9, 17.2%)* *Secondary bacteremia (27, 37.0%)* Other secondary infection (3, 4.1%)				23.3% died	[18]
China	41	4 (9.8%)	NA			NA	[19]
China	40*	18 (45%)	Influenza A or B virus (3), Adenovirus (1)	*M. pneumoniae* (13), *Streptococcus pneumoniae* (1)	NA	NA	[20]
China	29	5 (17.24%)	NA	*Enterobacter cloacae* (2), *Acinetobacter baumannii* (1)	*Candida albicans* (2)	NA	[21]
China	29	1 (3.4%)	NA			3.4% died	[22]
USA	21	4 (19.0%)	NA			NA	[23]
China	11	1 (9%)	NA	Mixture seen (1)	NA	NA	[24]
China	7	1 (14%)	NA	*Legionella pneumophillia* (1)	NA	Favorable outcomes, no ICU admission	[25]

NA; Data not available/Not mentioned, ARDS; acute respiratory distress syndrome, *; paediatric population.

Khurana et al, Indian J. Med. Micro. 29 (2021), 147-53

Resistance profile of clinical isolates causing secondary infections in COVID-19 patients.

Sample Type Number of samples (%)		Blood 39 (37.1%)	Urine 18 (17.1)	Respiratory samples 32 (30.5%)	Pus 12 (11.4%)	Others 4 (3.8%)	Total 105
Antimicrobials	Amikacin	29 (74.4%)	0 (0%)	16 (50%)	2 (16.7%)	1 (25%)	48 (46%)
	Amoxicillin/Clavulanic Acid	39 (100.0%)	18 (100%)	21 (65.6%)	6 (50%)	4 (100%)	88 (84%)
	Ampicillin	39 (100.0%)	18 (100%)	0	9 (75%)	4 (100%)	70 (67%)
	Caspofungin#	NT	0	NT	NT	NT	0
	Cefepime	37 (94.9%)	0	26 (81%)	5 (41.7%)	4 (100%)	72 (69%)
	Cefoperazone/Sulbactam	36 (92.3%)	5 (25%)	22 (69%)	5 (41.7%)	4 (100%)	72 (69%)
	Ceftazidime	36 (92.3%)	0	27 (84.4%)	0	4 (100%)	67 (64%)
	Ciprofloxacin	38 (97.4%)	3 (16.70%)	28 (88%)	10 (83.3%)	4 (100%)	83 (79%)
	Colistin*	3 (7.7%)	0	3 (9.37%)	3 (25%)	0	9 (9%)
	Fluconazole#	NT	0	NT	NT	NT	0
	Imipenem	36 (92.3%)	0	24 (75%)	5 (41.7%)	2 (50%)	67 (64%)
	Levofloxacin	36 (92.3%)	5 (25%)	30 (94%)	12 (100%)	4 (100%)	87 (83%)
	Meropenem	37 (94.9%)	3 (14.30%)	26 (81%)	4 (33.3%)	2 (50%)	72 (69%)
	Nitrofurantoin	28 (71.8%)	9 (50%)	0	8 (66.7%)	4 (100%)	49 (47%)
	Piperacillin/Tazobactam	38 (97.4%)	3 (16.70%)	29 (91%)	7 (58.3%)	4 (100%)	81 (77%)
	Tigecycline	14 (35.9%)	0	17 (53%)	3 (25%)	1 (25%)	35 (33%)
	Trimethoprim/Sulfamethoxazole	37.00% (94.9%)	6 (33.30%)	24 (75%)	8 (66.7%)	4 (100%)	79 (75%)

#; Antifungal., NT; Not Tested, *; The minimum inhibitor concentration for colistin was tested by the broth microdilution method as per the joint guidelines of EUCAST-CLSI. The resistance profile is depicted as the number of resistant isolates and percentages.

Infection and Drug Resistance

Dovepress
open access to scientific and medical research

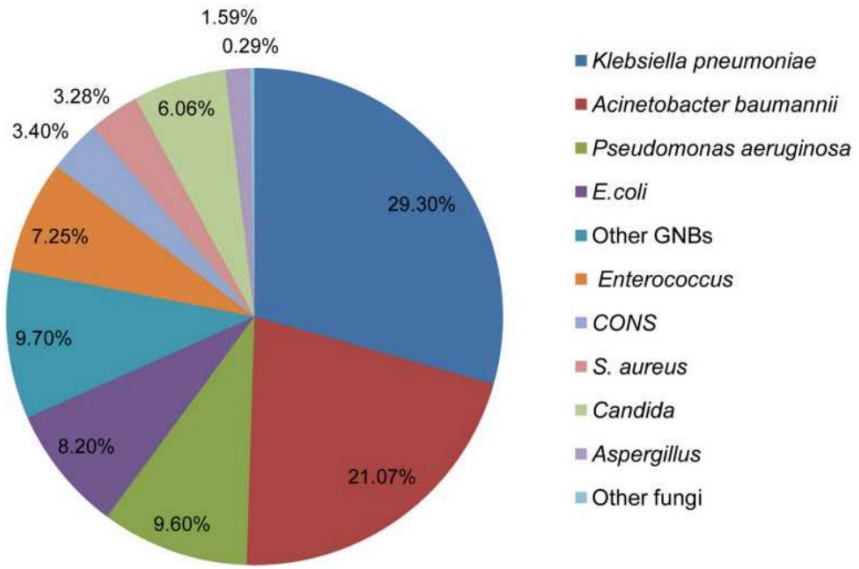
Open Access Full Text Article

ORIGINAL RESEARCH

Secondary Infections in Hospitalized COVID-19 Patients: Indian Experience

Sonam Vijay[1]
Nitin Bansal[1]
Brijendra Kumar Rao[2]
Balaji Veeraraghavan[3]
Camilla Rodrigues[4]
Chand Wattal[5]
Jagdish Prasad Goyal[6]
Karuna Tadepalli[7]

Purpose: Critically ill coronavirus disease 2019 (COVID-19) patients need hospitalization which increases their risk of acquiring secondary bacterial and fungal infections. The practice of empiric antimicrobial prescription, due to limited diagnostic capabilities of many hospitals, has the potential to escalate an already worrisome antimicrobial resistance (AMR) situation in India. This study reports the prevalence and profiles of secondary infections (SIs) and clinical outcomes in hospitalized COVID-19 patients in India.

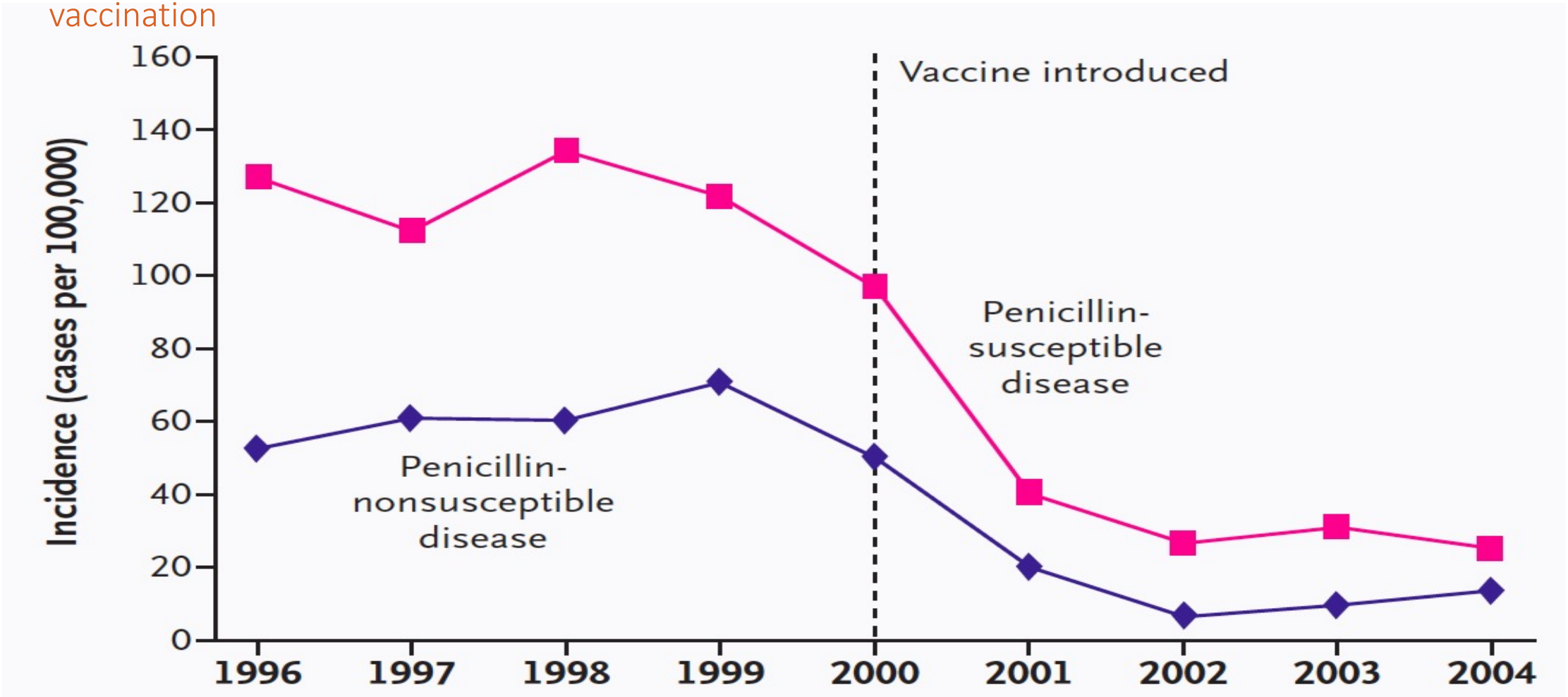


Results: Out of 17,534 admitted patients, 3.6% of patients developed secondary bacterial or fungal infections. The mortality among patients who developed secondary infections was 56.7% against an overall mortality of 10.6% in total admitted COVID-19 patients. Gram-negative bacteria were isolated from 78% of patients. *Klebsiella pneumoniae* (29%) was the predominant pathogen, followed by *Acinetobacter baumannii* (21%). Thirty-five percent of patients reported polymicrobial infections, including fungal infections. High levels of carbapenem resistance was seen in *A. baumannii* (92.6%) followed by *K. pneumoniae* (72.8%).

Conclusion: Predominance of Gram-negative pathogens in COVID-19 patients coupled with high rates of resistance to higher generation antimicrobials is an alarming finding. A high rate of mortality in patients with secondary infections warrants extra caution to improve the infection control practices and practice of antimicrobial stewardship interventions not only to save patient lives but also prevent selection of drug-resistant infections, to which the current situation is very conducive.

Vaccines can be effective

Invasive disease caused by Pneumococci in children under two declined in the US post pneumo vaccination



CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy WASHINGTON DC • NEW DELHI

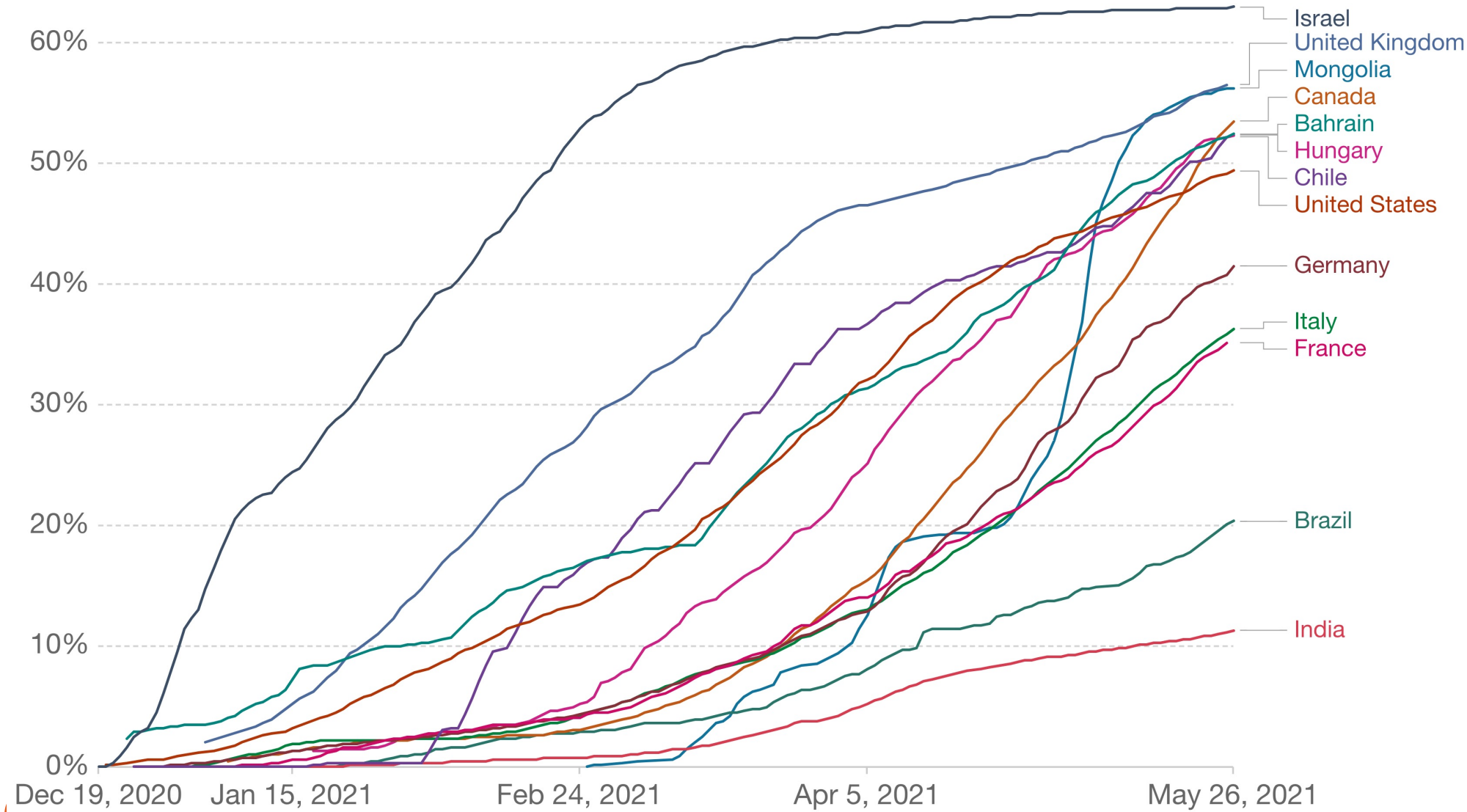
Kyaw MH et al. N Engl J Med 2006;354:1455-1463.

PRINCETON UNIVERSITY

Share of people who received at least one dose of COVID-19 vaccine

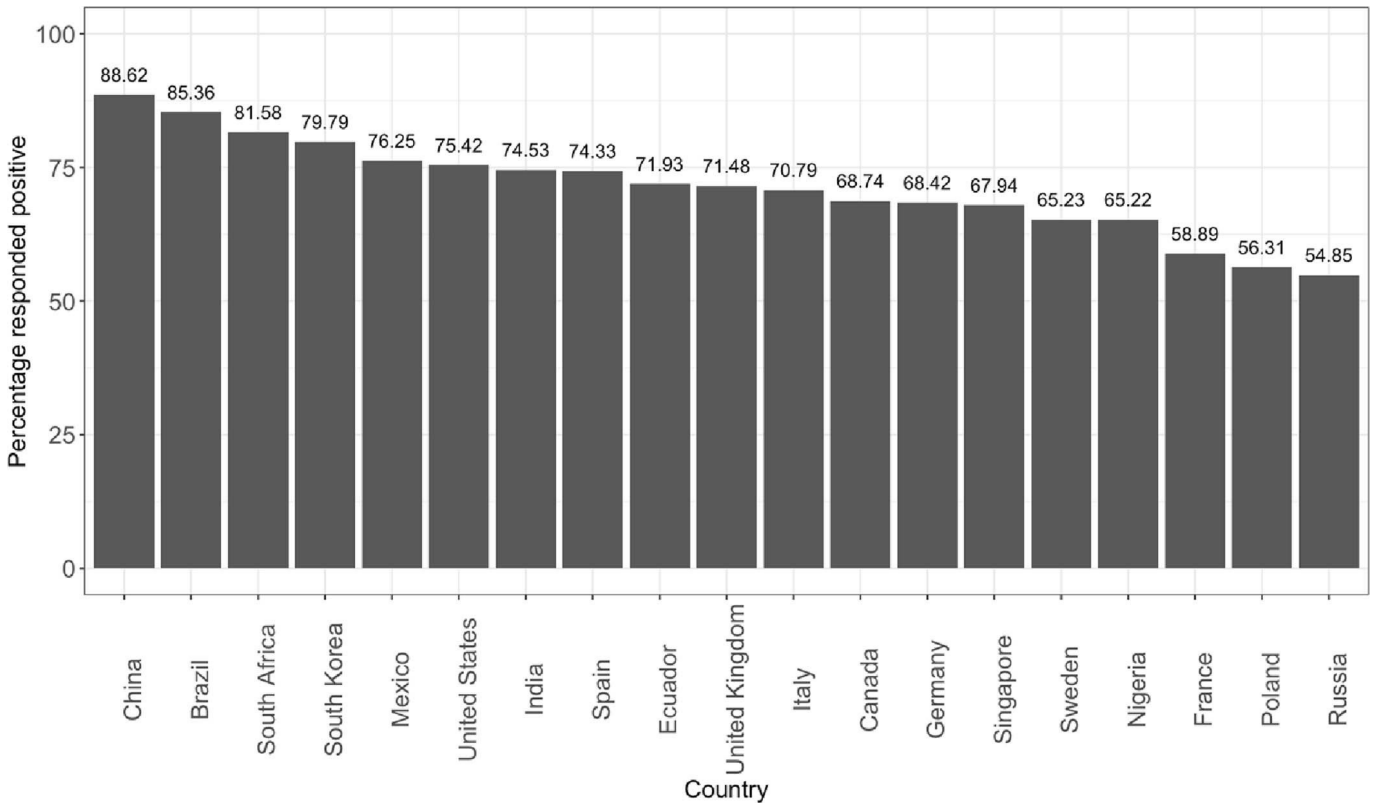
Share of the total population that received at least one vaccine dose. This may not equal the share that are fully vaccinated if the vaccine requires two doses.

Our World in Data



Source: Official data collated by Our World in Data

Numbers above the bars represent the percent of respondents in each country who responded positively to the question ‘If a COVID-19 vaccine is proven safe and effective and is available, I will take it’.

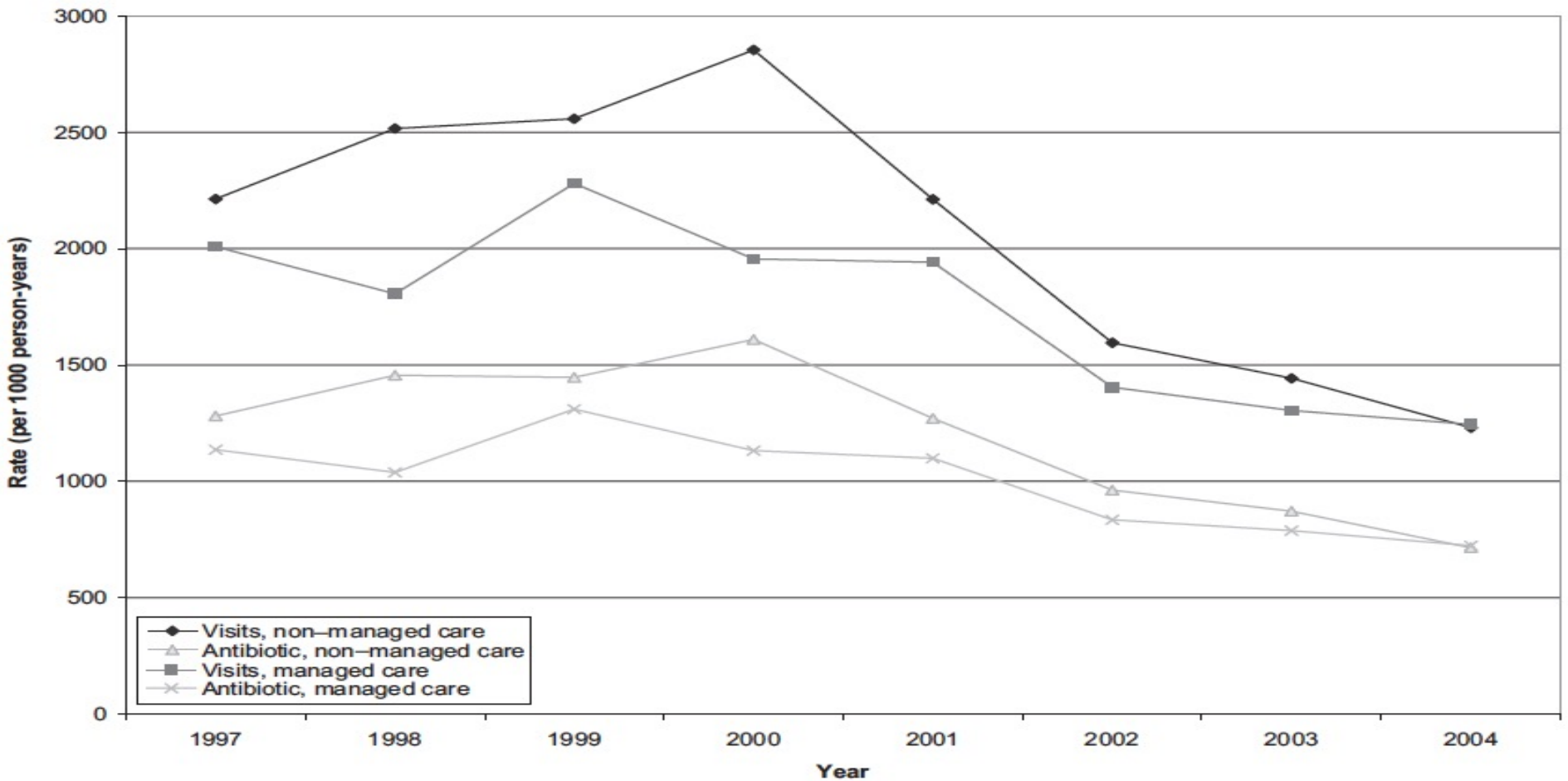


Lazarus et al, Nature Medicine volume 27, pages225–228 (2021)

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

PRINCETON UNIVERSITY

Effect of PCV7 introduction in 2000 on antibiotic prescriptions and ambulatory care visits

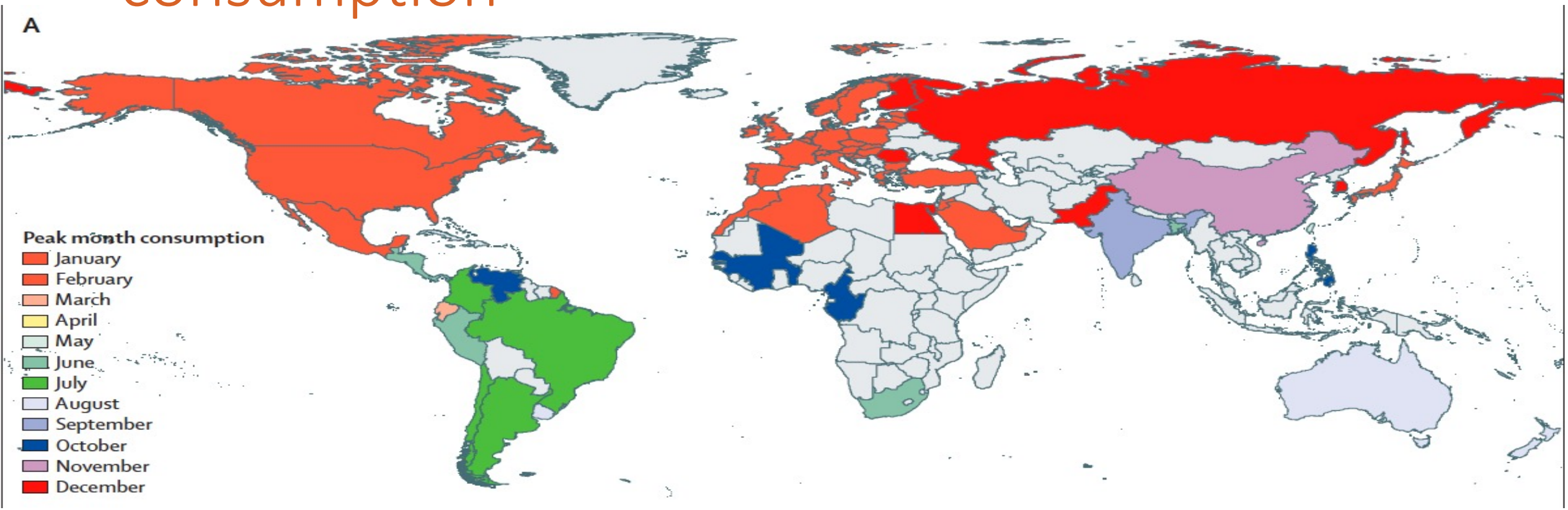


CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy WASHINGTON DC • NEW DELHI

Zhou et al, Pediatrics 2008

PRINCETON UNIVERSITY

The flu season is a key driver of antibiotic consumption



Van Boeckel et al, Lancet Inf Dis, 2014

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

PRINCETON UNIVERSITY

Influenza in the United States is nearly perfectly predicted by antibiotic sales data

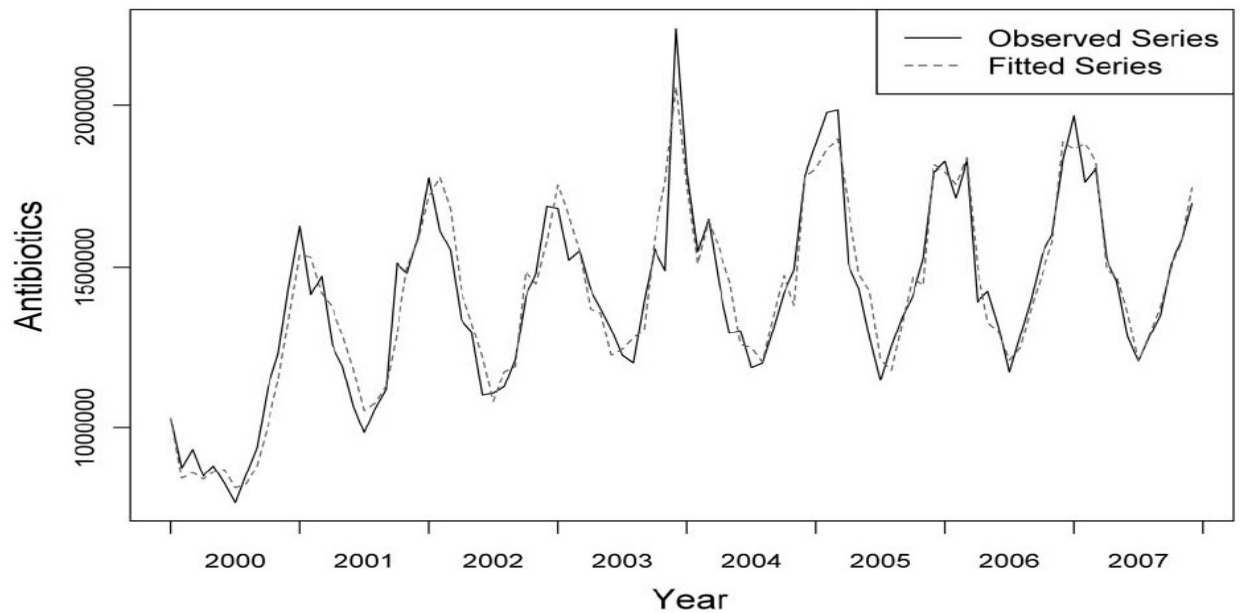


FIGURE 1. Observed and fitted antibiotics series from 2000 to 2007. The solid line represents the actually observed antibiotics series; the dashed line represents the fitted antibiotics series from the time series regression model that uses influenza-like illness as an explanatory series.

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy WASHINGTON DC • NEW DELHI

PRINCETON UNIVERSITY

Polgreen et al Inf Cont Hosp Epi, 20

Open Forum Infectious Diseases

MAJOR ARTICLE

The Impact of Influenza Vaccination on Antibiotic Use in the United States, 2010–2017

Eili Y. Klein,[1,2] Emily Schueller,[1,*] Katie K. Tseng,[1] Daniel J. Morgan,[3] Ramanan Laxminarayan,[1,4,5] and Arindam Nandi[1]

[1]Center for Disease Dynamics, Economics & Policy, Washington, DC, USA, [2]Johns Hopkins University, Baltimore, Maryland, USA, [3]University of Maryland School of Medicine, Baltimore, Maryland, USA, [4]Princeton University, Princeton, New Jersey, USA, and [5]University of Washington, Seattle, Washington, USA

Background. Influenza, which peaks seasonally, is an important driver for antibiotic prescribing. Although influenza vaccination has been shown to reduce severe illness, evidence of the population-level effects of vaccination coverage on rates of antibiotic prescribing in the United States is lacking.

Methods. We conducted a retrospective analysis of influenza vaccination coverage and antibiotic prescribing rates from 2010 to 2017 across states in the United States, controlling for differences in health infrastructure and yearly vaccine effectiveness. Using data from IQVIA's Xponent database and the US Centers for Disease Control and Prevention's FluVaxView, we employed fixed-effects regression analysis to analyze the relationship between influenza vaccine coverage rates and the number of antibiotic prescriptions per 1000 residents from January to March of each year.

Results. We observed that, controlling for socioeconomic differences, access to health care, childcare centers, climate, vaccine effectiveness, and state-level differences, a 10–percentage point increase in the influenza vaccination rate was associated with a 6.5% decrease in antibiotic use, equivalent to 14.2 (95% CI, 6.0–22.4; $P = .001$) fewer antibiotic prescriptions per 1000 individuals. Increased vaccination coverage reduced prescribing rates the most in the pediatric population (0–18 years), by 15.2 (95% CI, 9.0–21.3; $P < .001$) or 6.0%, and the elderly (aged 65+), by 12.8 (95% CI, 6.5–19.2; $P < .001$) or 5.2%.

Conclusions. Increased influenza vaccination uptake at the population level is associated with state-level reductions in antibiotic use. Expanding influenza vaccination could be an important intervention to reduce unnecessary antibiotic prescribing.

Keywords. antibiotic consumption; antimicrobial resistance; ecological study; influenza vaccination; upper respiratory tract infections.

Article

Childhood vaccines and antibiotic use in low- and middle-income countries

https://doi.org/10.1038/s41586-020-2238-4

Received: 3 December 2019

Accepted: 5 March 2020

Published online: 29 April 2020

Open access

Check for updates

Joseph A. Lewnard[1,2,3]✉, Nathan C. Lo[4], Nimalan Arinaminpathy[5], Isabel Frost[5,6] & Ramanan Laxminarayan[6,7]

Vaccines may reduce the burden of antimicrobial resistance, in part by preventing infections for which treatment often includes the use of antibiotics[1–4]. However, the effects of vaccination on antibiotic consumption remain poorly understood—especially in low- and middle-income countries (LMICs), where the burden of antimicrobial resistance is greatest[5]. Here we show that vaccines that have recently been implemented in the World Health Organization's Expanded Programme on Immunization reduce antibiotic consumption substantially among children under five years of age in LMICs. By analysing data from large-scale studies of households, we estimate that pneumococcal conjugate vaccines and live attenuated rotavirus vaccines confer 19.7% (95% confidence interval, 3.4–43.4%) and 11.4% (4.0–18.6%) protection against antibiotic-treated episodes of acute respiratory infection and diarrhoea, respectively, in age groups that experience the greatest disease burden attributable to the vaccine-targeted pathogens[6,7]. Under current coverage levels, pneumococcal and rotavirus vaccines prevent 23.8 million and 13.6 million episodes of antibiotic-treated illness, respectively, among children under five years of age in LMICs each year. Direct protection resulting from the achievement of universal coverage targets for these vaccines could prevent an additional 40.0 million episodes of antibiotic-treated illness. This evidence supports the prioritization of vaccines within the global strategy to combat antimicrobial resistance[8].

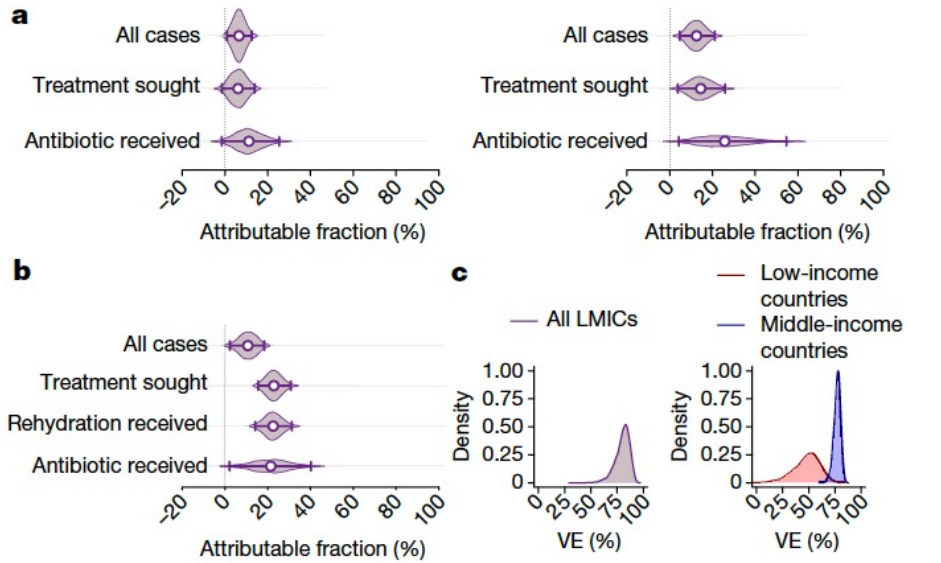


Fig. 2 | Estimates of the attributable fraction for vaccine-preventable infections. a, b, We illustrate estimates of pathogen-specific attributable

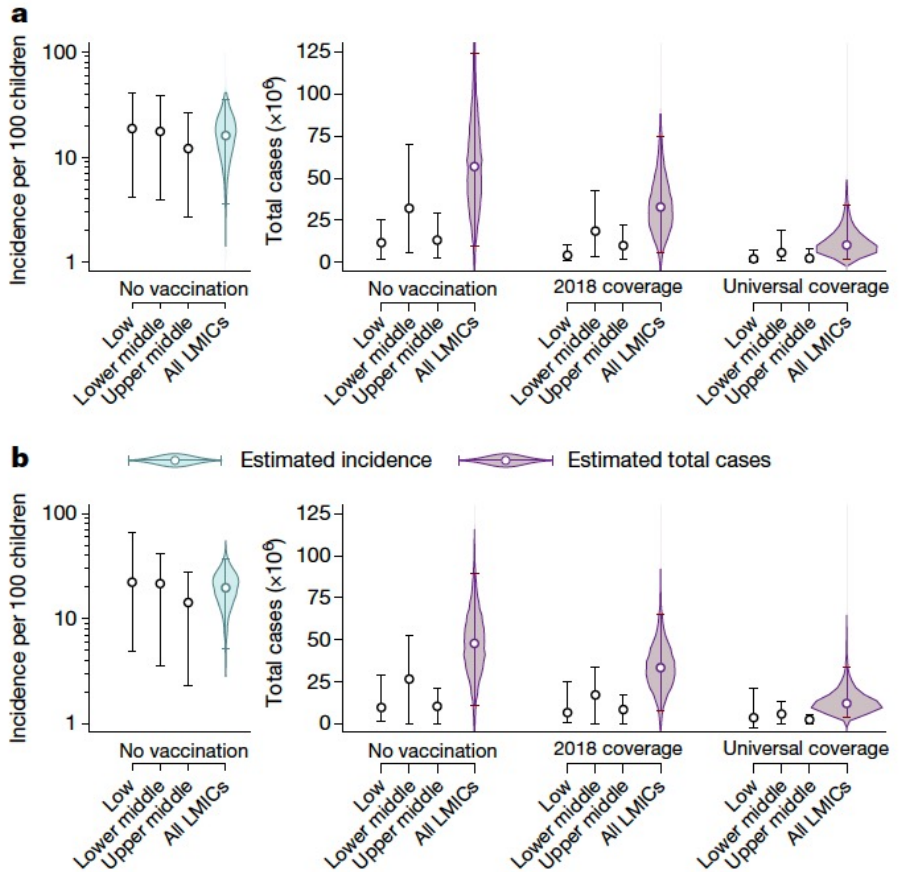


Fig. 4 | Total vaccine-preventable antibiotic consumption and incidence per 100 children. a, b, We estimated the incidence and total number of antibiotic-treated ARI and diarrhoea episodes attributable to PCV10/13-serotype pneumococci in children aged 24–59 months (**a**) and rotavirus in children aged 0–23 months (**b**), respectively. Left, incidence in the absence of vaccination. Right, the corresponding total number of cases, the

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

PRINCETON UNIVERSITY

nature COMMUNICATIONS

ARTICLE

https://doi.org/10.1038/s41467-020-20731-x OPEN

Check for updates

Modelling the global burden of drug-resistant tuberculosis avertable by a post-exposure vaccine

Han Fu [1✉], Joseph A. Lewnard [2], Isabel Frost [3,4], Ramanan Laxminarayan [3,5] & Nimalan Arinaminpathy [1]

There have been notable advances in the development of vaccines against active tuberculosis (TB) disease for adults and adolescents. Using mathematical models, we seek to estimate the potential impact of a post-exposure TB vaccine, having 50% efficacy in reducing active disease, on global rifampicin-resistant (RR-) TB burden. In 30 countries that together accounted for 90% of global RR-TB incidence in 2018, a future TB vaccine could avert 10% (95% credible interval: 9.7–11%) of RR-TB cases and 7.3% (6.6–8.1%) of deaths over 2020–2035, with India, China, Indonesia, Pakistan, and the Russian Federation having the greatest contribution. This impact would increase to 14% (12–16%) and 31% (29–33%) respectively, when combined with improvements in RR-TB diagnosis and treatment relative to a scenario of no vaccine and no such improvements. A future TB vaccine could have important implications for the global control of RR-TB, especially if implemented alongside enhancements in management of drug resistance.

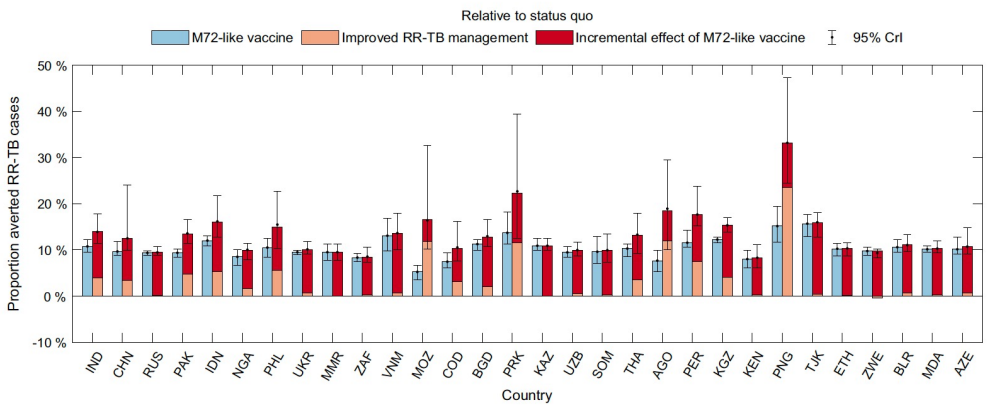


Fig. 3 Projected percent cases of RR-TB averted by an M72-like vaccine. Rectangular bars show median estimates and error bars show 95% Bayesian credible intervals (CrIs), both estimated from $n = 200$ posterior samples for each country. Blue bars show the vaccine-avertable proportions of rifampicin-resistant tuberculosis (RR-TB) cases relative to a 'status quo' scenario, while adjacent bars together show averted proportions in combination with 'improved RR-TB management', as outlined in the caption to Fig. 1. The latter bars are stratified to show: (i) the impact of improved management of RR-TB alone, i.e. in the absence of vaccination (orange segment), and (ii) the incremental impact of vaccination, acting in combination with these improvements (red segment). Error bars on the stacked orange and red bars show the 95% CrIs of the total impact of a vaccine combined with improved management of RR-TB. Countries are ranked in a descending order according to the number of RR-TB incident cases in 2018.

RR-TB. Countries are ranked in a descending order according to the number of RR-TB incident cases in 2018.

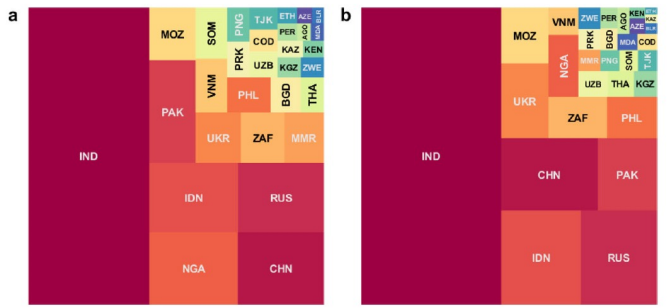


Fig. 4 Country-wise contribution to vaccine-avertable deaths from RR-TB. As for Fig. 2, the area of each square here is proportional to the median estimate from $n = 200$ posterior samples, for the absolute number of avertable rifampicin-resistant tuberculosis (RR-TB) deaths by a post-exposure, M72-like vaccine, between 2020 and 2035. Panel **a** shows deaths averted by a vaccine alone, while panel **b** shows deaths averted by a combination of a vaccine and measures to improve the management of RR-TB (both relative to a scenario of no vaccine, and no improvement in RR-TB, i.e. status quo). Countries are denoted by their ISO alpha-3 codes and their corresponding full names are listed in Table 1. Colours for each country are only for the purpose of display, and do not designate any quantitative scale.

Unlike antivirals, vaccines, etc, the value of effective antibiotics during a pandemic remains unexplored.

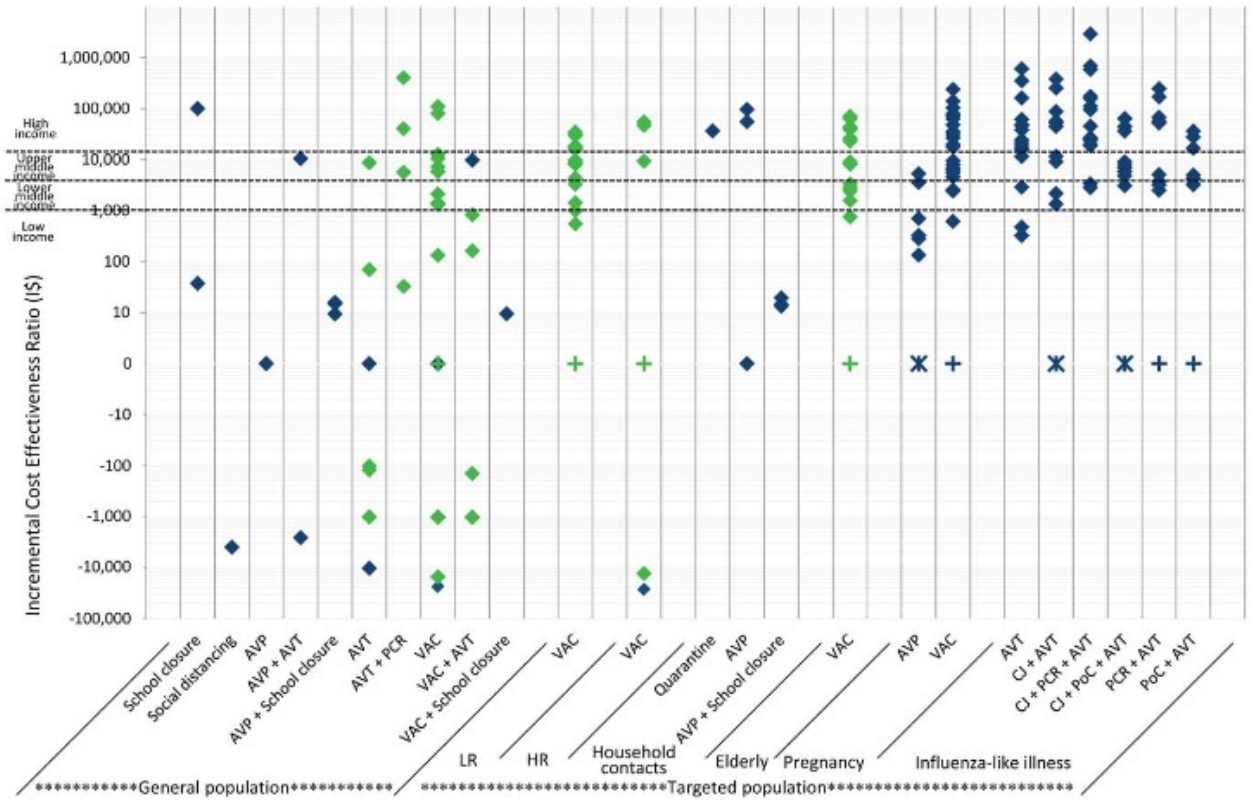


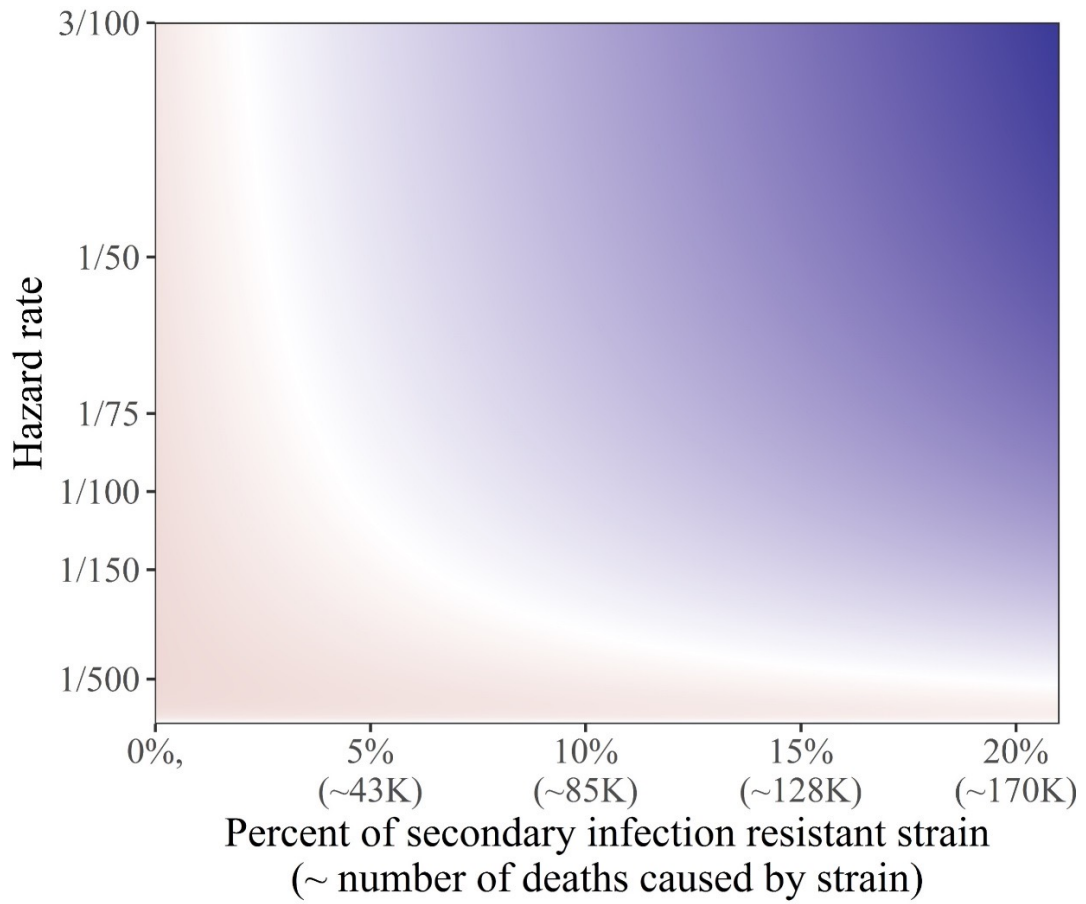
Figure 3. Incremental Cost Effectiveness Ratios (ICERs) for influenza pandemics according to type of intervention (I$/QALY). **AVP** = antiviral prophylaxis; **AVT** = antiviral treatment; **CJ** = clinical judgment; **PCR** = polymerase chain reaction; **PoC** = point of care test; **HR** = high risk for complications; **LR** = low risk for complications; **VAC** = vaccine; **Blue** = results of studies conducted before the 2009 H1N1 pandemic; **Green** = results of studies conducted after the 2009 H1N1 pandemic; ◆ = average incremental cost effectiveness ratio; ??? = cost saving intervention, ICER was not clearly stated; ★ = Cost saving/less effective intervention, ICER was not clearly stated.
doi:10.1371/journal.pone.0030333.g003

Velasco et al. (2012)

CDDEP THE Dis Economics & Policy
WASHINGTON DC • NEW DELHI

PRINCETON UNIVERSITY

Option value: Sensitivity to pandemic hazard rate and prevalence of resistant strain

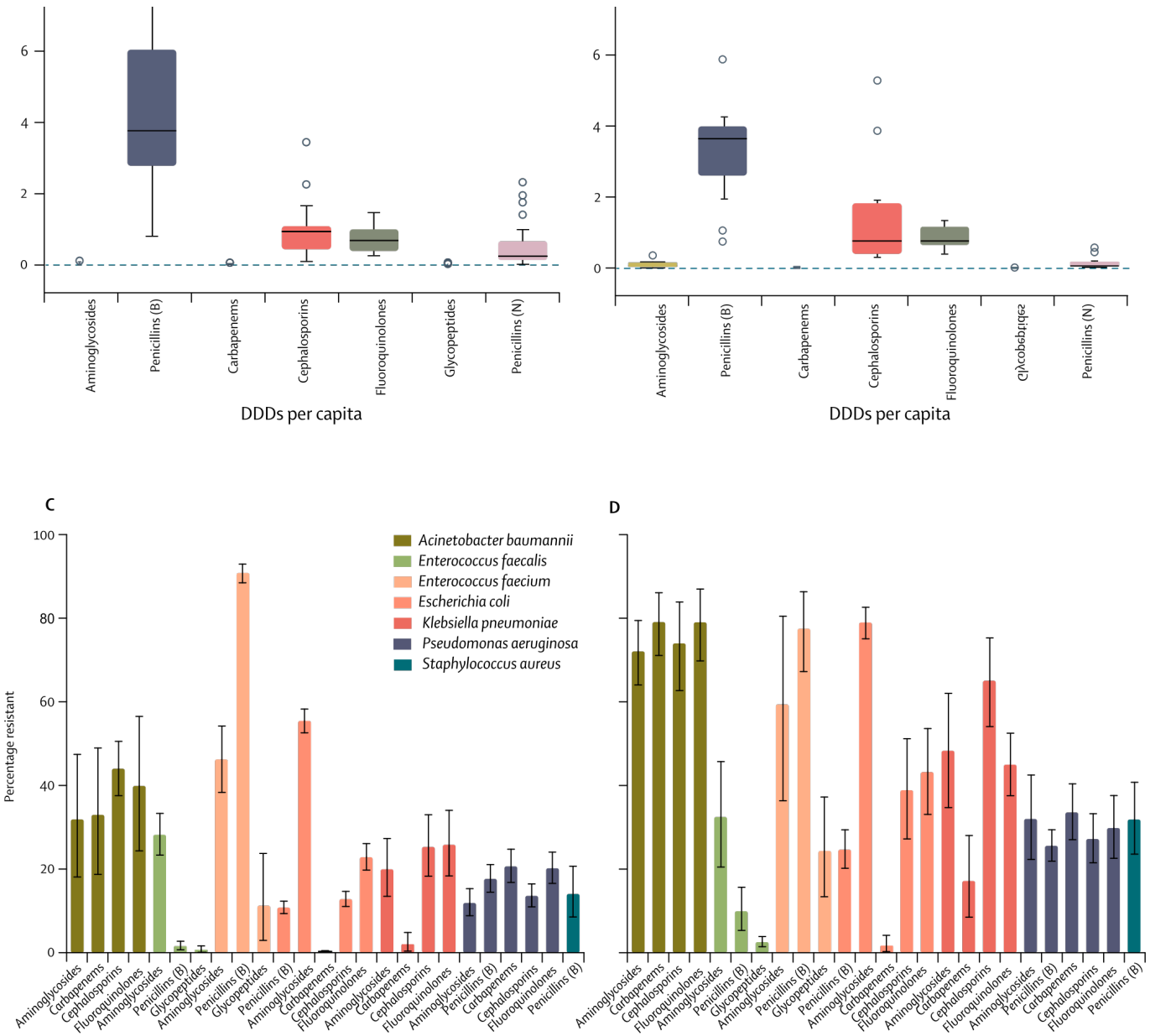


CDDEP THE CENTER FOR Disease Dyna Economics & WASHINGTON DC • NEW

PRINCETON UNIVERSITY

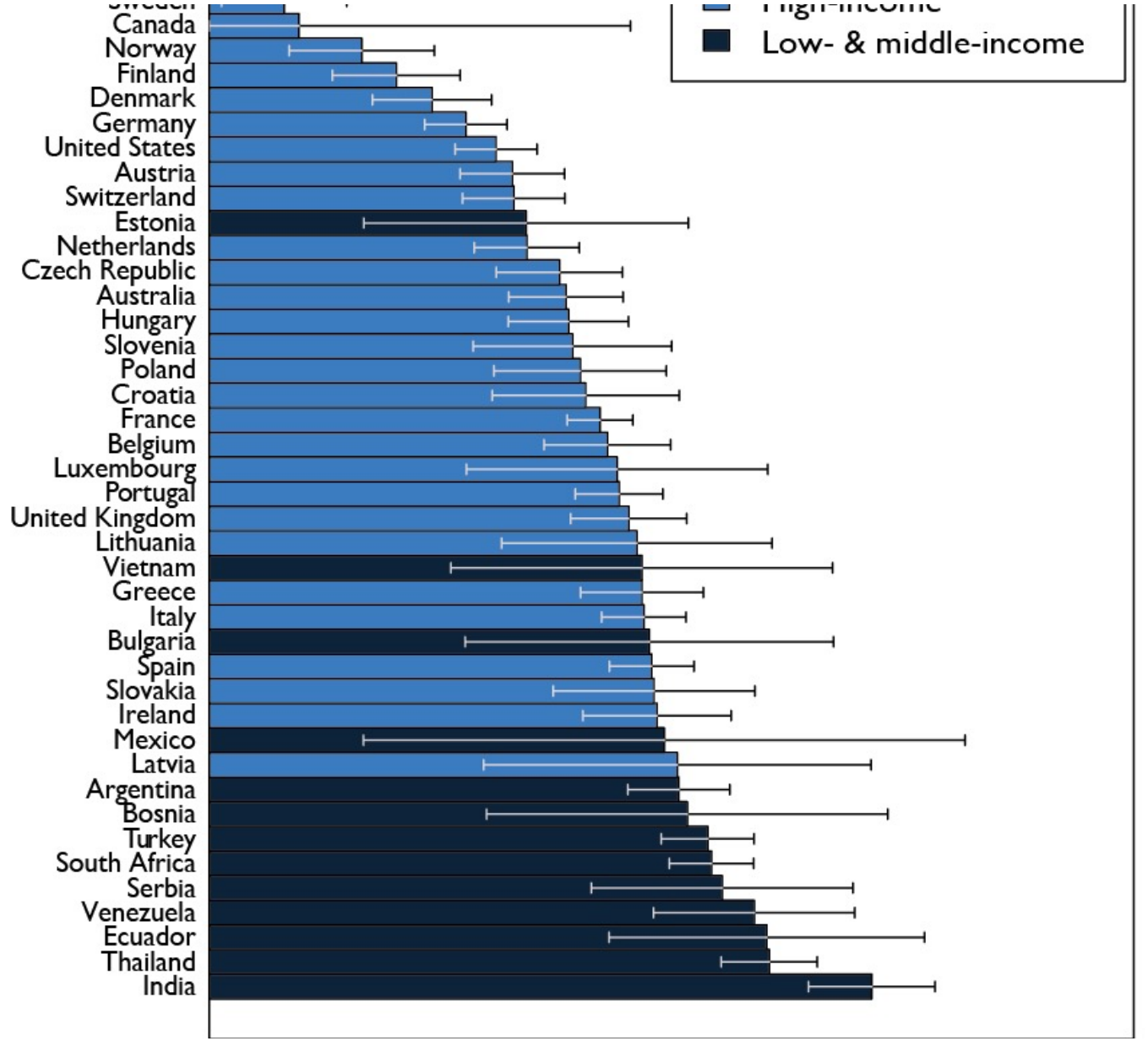
Global antibiotic use and resistance, by income class [1]

- Variability in per capita antibiotic use measured in defined daily doses for high-income countries (A) and LMICs (B). Weighted average global resistance rate for the specified antibiotic-pathogen combination in high-income countries (C) and LMICs (D), using the most recent data available for 2012–15 and based on pooled worldwide resistance rates for the disease-causing organisms considered by the WHO as priority pathogens. DDD=defined daily doses. Penicillins (B)=broad spectrum. Penicillins (N)=narrow spectrum



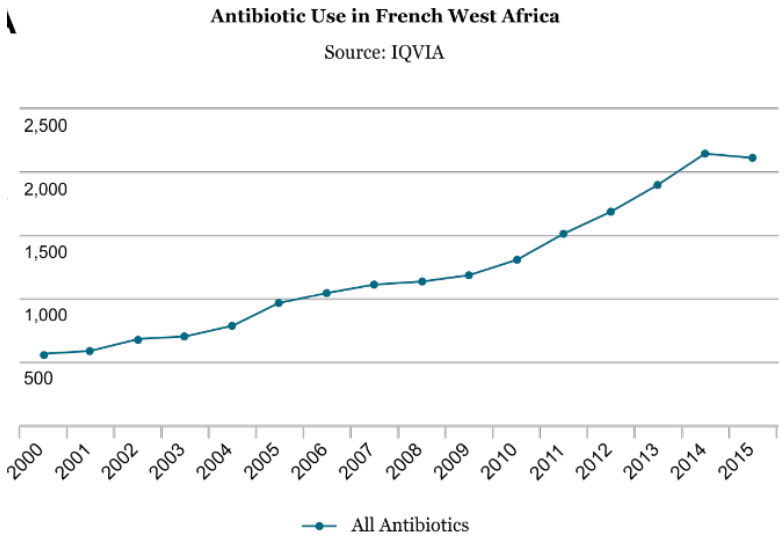
Drug Resistance Index across countries [2]

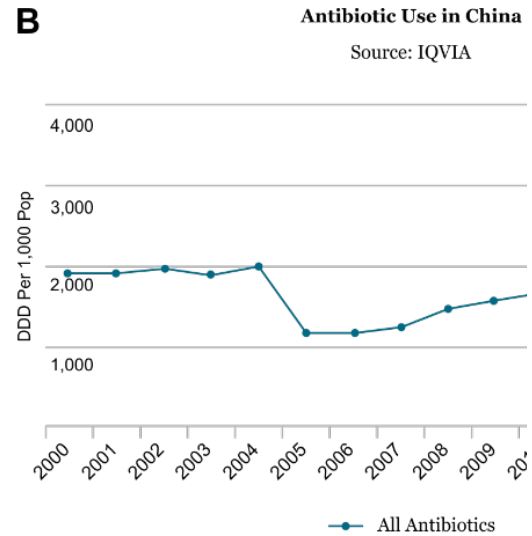
- Each bar represents the DRI for countries reporting antibiotic resistance for five or more pathogens and 15 or more pathogen-antibiotic combinations for at least one year between 2012 and 2015. Data for the most recent year are shown. Country income classifications were based on World Bank analytical classifications for fiscal year 2015.

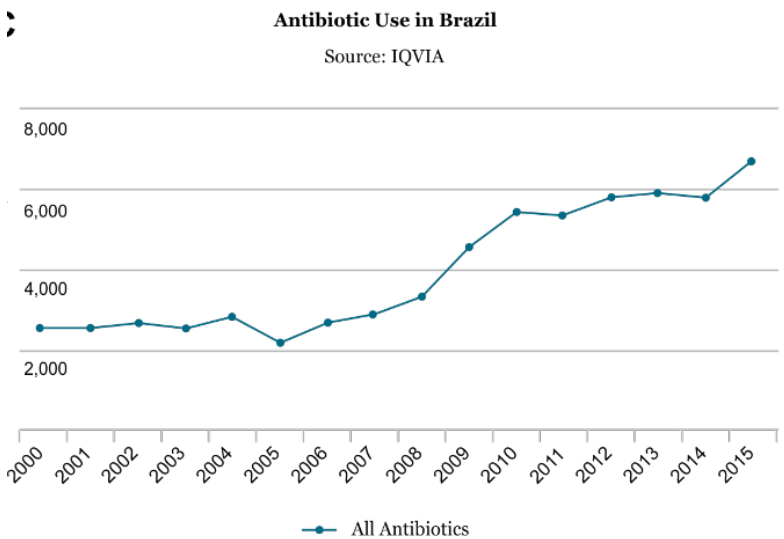


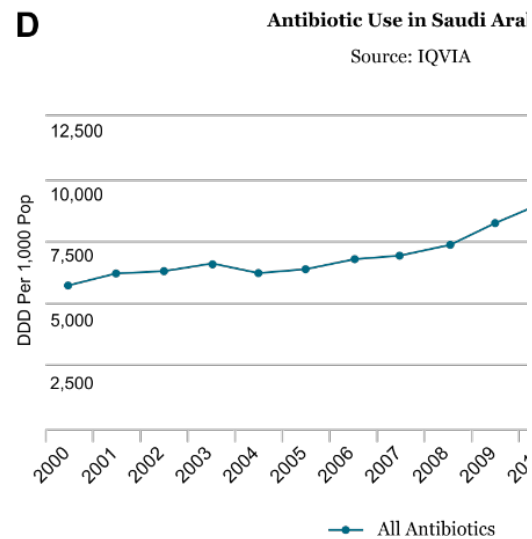
Increases in total antibiotic use, 2000–2015 [3]

- Total antibiotic use in DDDs per 1,000 people in (A) West Africa, (B) Brazil, (C) China, and (D) Saudi Arabia

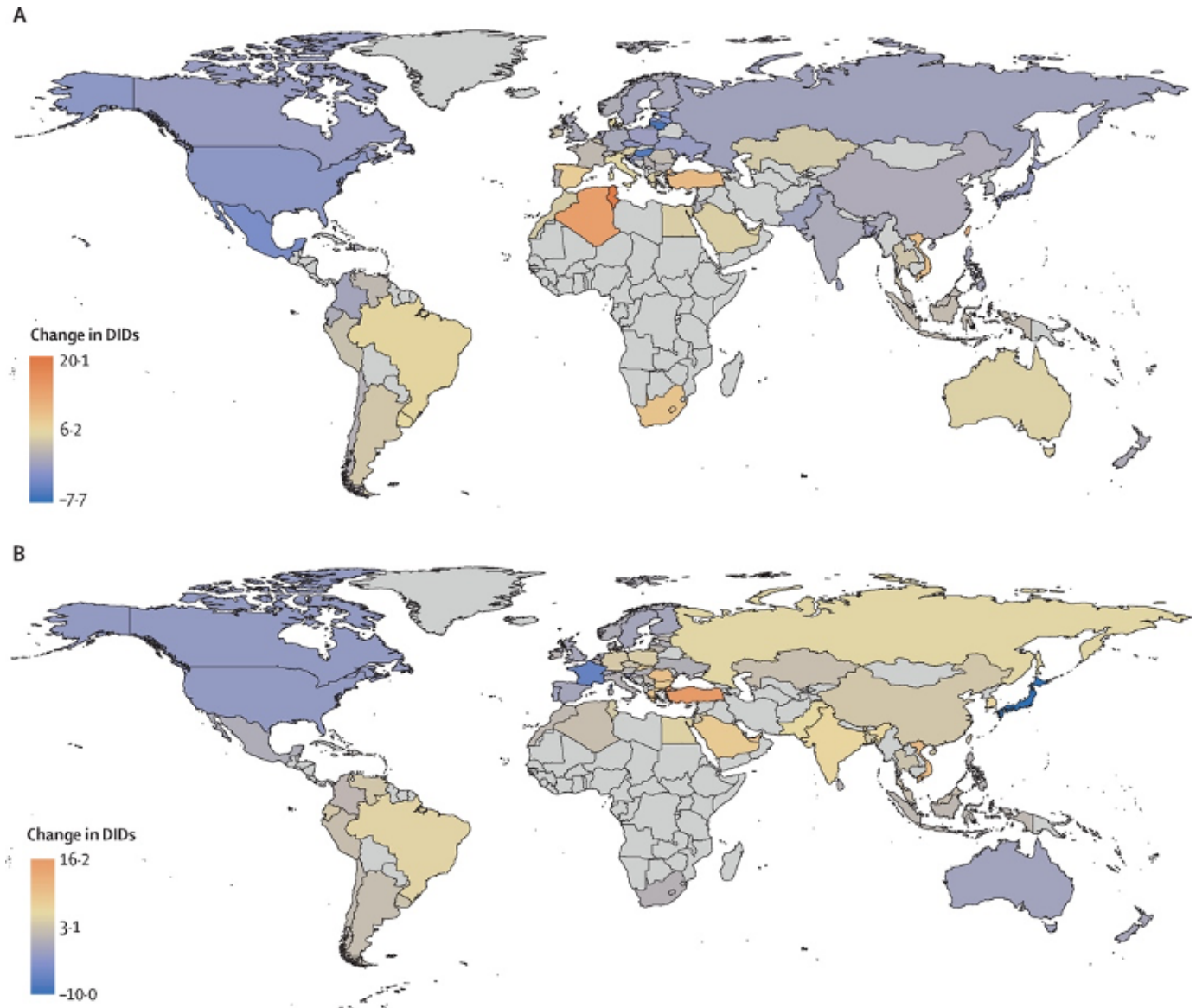








DDDs per 1000 inhabitants (DIDs)
2000–2015

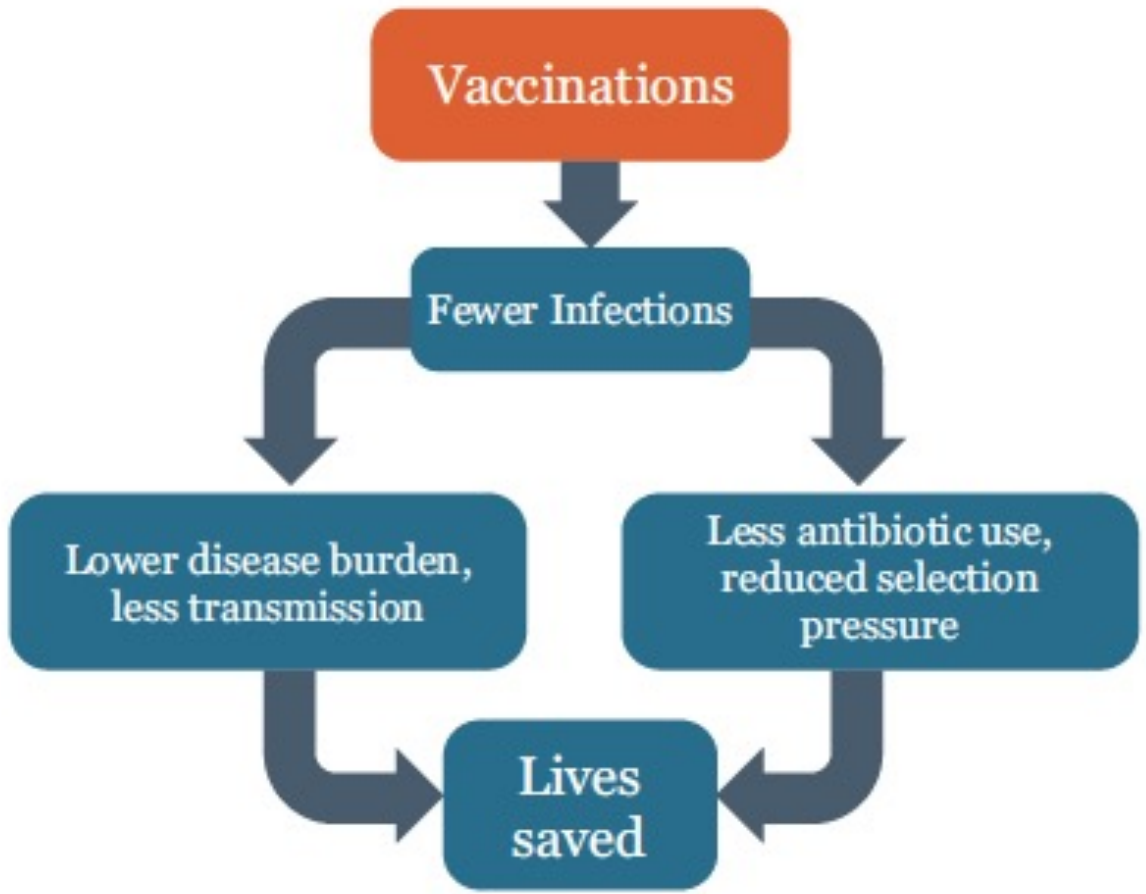


CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

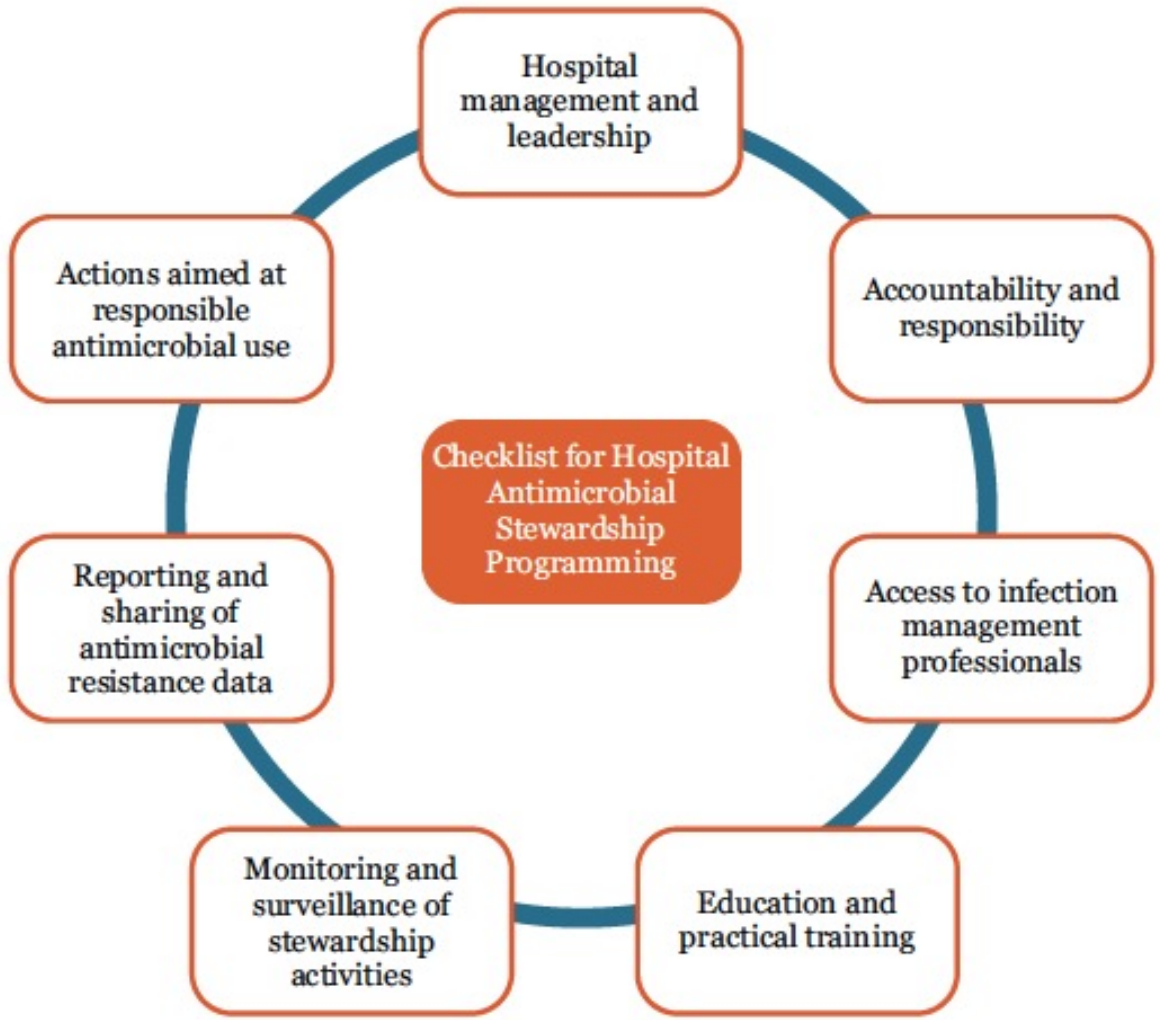
nics, Policy DELHI

UNIVERSITY

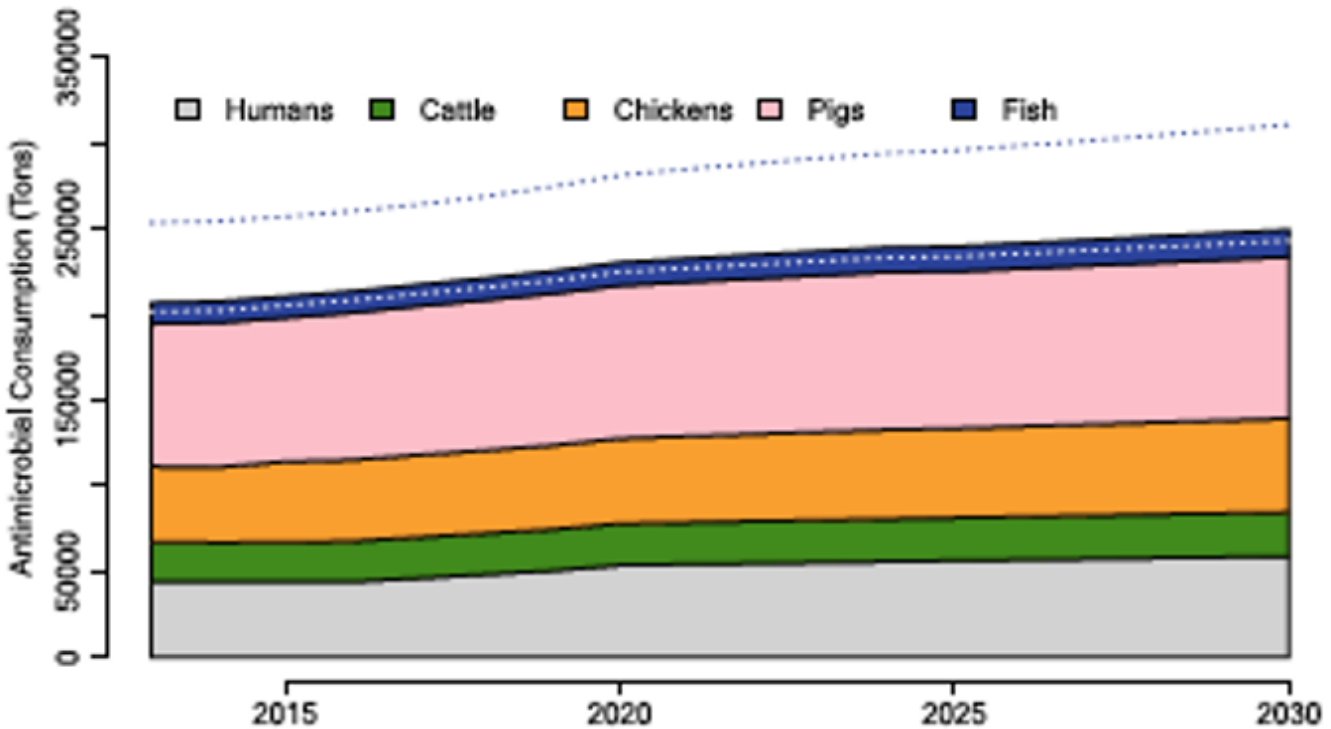
Two routes by which vaccination can reduce incidence of AMR [5]



Core components of the Checklist for Hospital Antimicrobial Stewardship Programming [6]



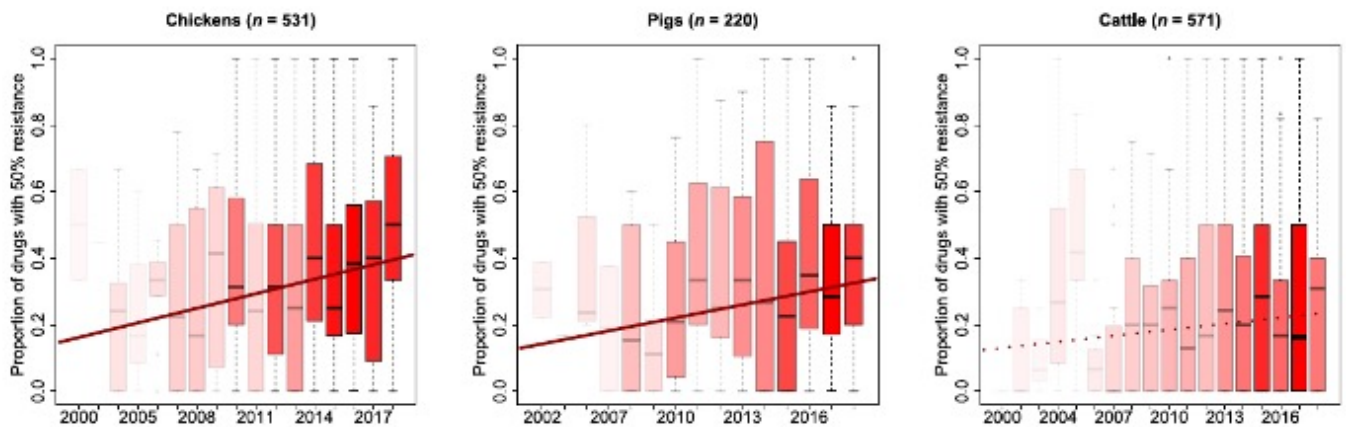
Global antimicrobial consumption, 2013–2030 [7]



Note: Dotted lines represent the 95% uncertainty interval for fish.

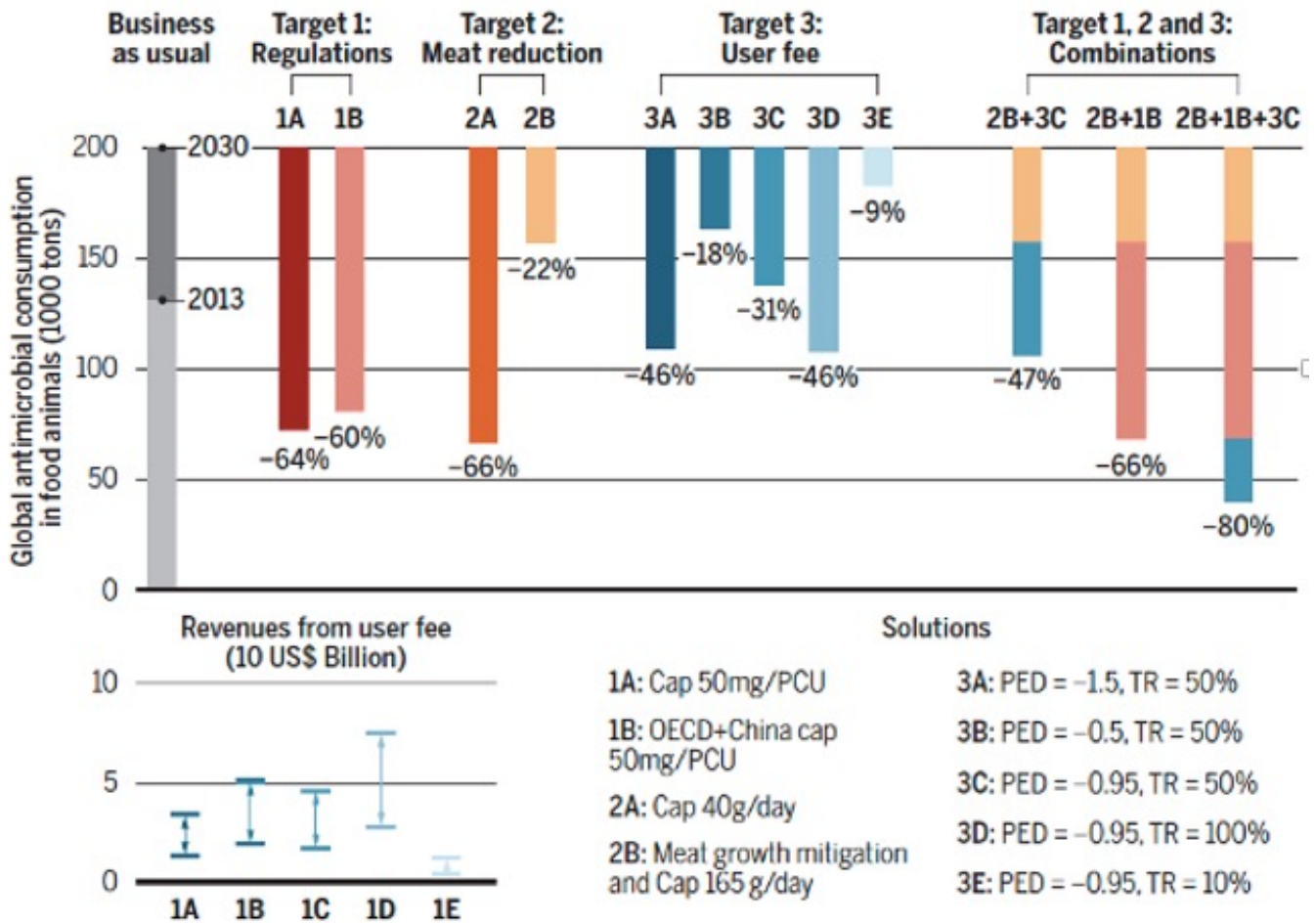
PRINCETON UNIVERSITY

Increase in antimicrobial resistance in LMICs [8]

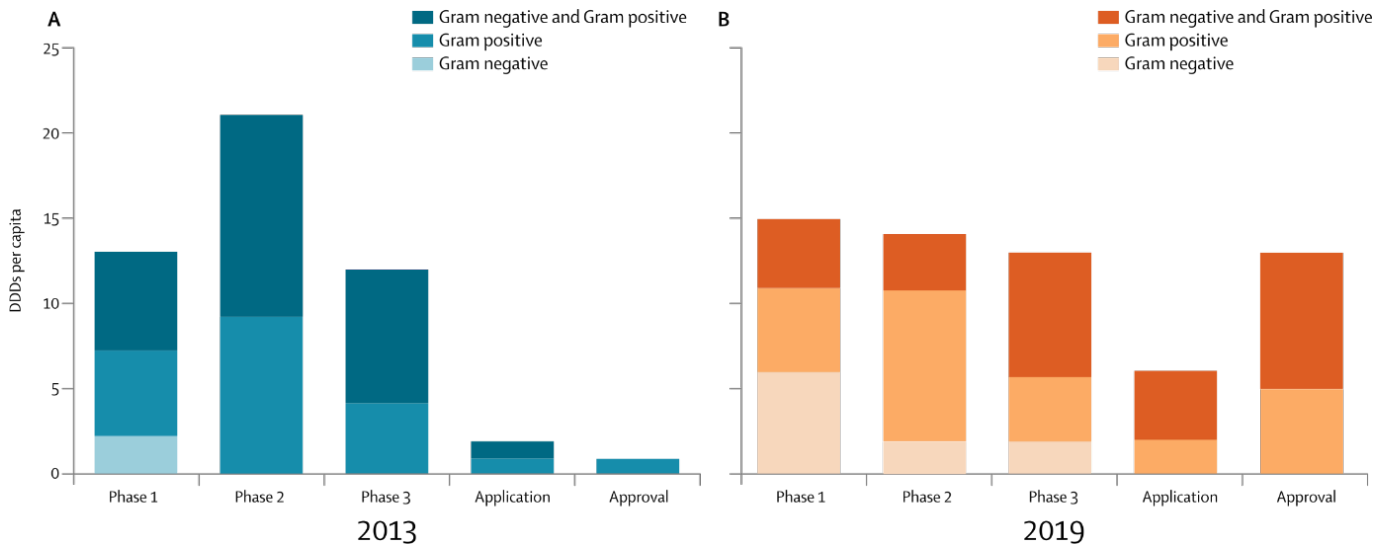


Antimicrobial consumption in food animals by 2030 [9]

Business as usual and intervention policies are shown. Revenue ranges are estimated for different fee rates (TR) and price elasticities of demand (PED). For 3C, 3D, and 3E, PEDs are derived from time series of imports of veterinary antimicrobials in each country (Protocol S4); the global average PED was -0.95. See supplementary materials for discussions of uncertainty in all estimates shown in figures. PCU, population correction unit.



Antibiotic development between 2013 and 2019 [1]



CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

PRINCETON UNIVERSITY

Dashboard India

India

South Asia| Low- & lower-middle income

Policy Indicators*

- Enrolment in Global Antimicrobial Resistance Surveillance System (GLASS) ✓
- National Action Plan on AMR (NAP) Published ✓
- AMU surveillance in humans ✓
- AMU surveillance in animals ✗
- AMR surveillance in humans ✓
- AMR surveillance in animals ✓

*As per information available by December 2020

Antimicrobial Resistance Indicators*

Humans

69.97% of isolates tested	72.06% of isolates tested	87.71% of isolates tested
MRSA	**CRE**	**ESBL**
Methicillin-resistant *Staphylococcus aureus*	Carbapenem-resistant *Klebsiella pneumoniae*	3G cephalosporin-resistant *Escherichia coli*

N/A	N/A
DRI	**DRI**
Drug Resistance Index for WHO Critical pathogens 2020	Drug Resistance Index for MRSA, CRE, and ESBL positive *E.coli* 2020

Note:

a) *Resistance rates include isolates categorized as either resistant or intermediate on antimicrobial susceptibility testing.*

b) *The Drug Resistance Index (DRI) is an aggregate measure that combines antibiotic use and resistance into a single metric, with value of 0 indicating 100% susceptibility and value of 100 indicating 100% resistance. DRI values for the year 2020 are projections based on DRI values for 2005- 2015.*

c) *WHO critical pathogens are ESBL positive Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae, carbapenem-resistant Acinetobacter baumannii, & carbapenem-resistant Pseudomonas aeruginosa.*

Animals

Salmonella spp.		*E.coli*	
Ampicillin	16.5%	Ampicillin	69.6%
Ciprofoxacin	0	Ciprofoxacin	7%
Colistin	n/a	Colistin	0
Tetracycline	16.50%	Tetracycline	38.66%

*As per information available by December 2020

Note: N/A stands for Not Applicable

Antimicrobial Use Indicators

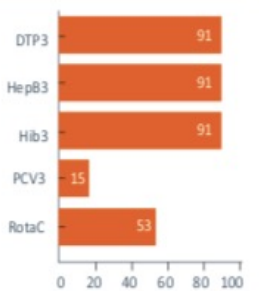
Humans

Total Use, 2010 (DDDs in Mill)	5411	Per Capita Use, 2010 (DDD)	4.40
Total Use, 2020 (DDDs in Mill)	7976	Per Capita Use, 2020 (DDD)	5.74
Change in total use, 2010-20 (DDDs in Mill)	2564.77	Change in per capita use, 2010-20 (DDD)	1.35
% Change in total use, 2010-20	47.40%	% Change in per capita use, 2010-2020	30.64%
Global average of % change in total use, 2010-20	74.49%	Global average of % change in per capita use, 2010-20	35.12%
Regional average of % change in total use, 2010-20	38.34%	Regional average of % change in per capita use, 2010-20	20.44%

Animals

Estimated Total Antimicrobial Use, 2020 (Tonnes)	2160.02
Estimated Total Antimicrobial Use, 2030 (Tonnes)	2236.74

Public Health Indicators



% of children vaccinated (2019)

28.3	Infant Mortality Rate per 1,000 live births (2019)	143.37	Under-five pneumococcal death rate per 100,000 children (2017)
102677.89	Under-five deaths from diarrheal diseases (2017)	193	Incidence of tuberculosis per 100,000 people (2019)
93.44	Access to improved drinking water source (%) (2017)	72.05	Access to improved sanitation facilities (%) (2017)
59.54	Access to basic handwashing facilities including soap and water (%) (2017)		
0.9	Physicians per 1,000 people (2018)	1.7	Nurses and midwives per 1,000 people (2018)
3.54%	Current health expenditure % of GDP (2018)	3.39%	Domestic general government health expenditure % of general government expenditure (2018)
62.67%	Out-of-pocket expenditure % of current health expenditure (2018)	$ 72.83	Current health expenditure per capita (2018)

Note: N/A stands for Not Applicable

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

Dashboard Italy

Italy

Europe & Central Asia| High income

Policy Indicators*

- Enrolment in Global Antimicrobial Resistance Surveillance System (GLASS) ✓
- National Action Plan on AMR (NAP) Published ✓
- AMU surveillance in humans ✓
- AMU surveillance in animals ✓
- AMR surveillance in humans ✓
- AMR surveillance in animals ✓

*As per information available by December 2020

Antimicrobial Resistance Indicators*

Humans

- 33.98% of isolates tested — MRSA (Methicillin-resistant *Staphylococcus aureus*)
- 29.84% of isolates tested — CRE (Carbapenem-resistant *Klebsiella pneumoniae*)
- 29.69% of isolates tested — ESBL (3G cephalosporin-resistant *Escherichia coli*)
- 59.65 — DRI (Drug Resistance Index for WHO Critical pathogens 2020)
- 68.49 — DRI (Drug Resistance Index for MRSA, CRE, and ESBL positive *E.coli* 2020)

Note:
a) Resistance rates include isolates categorized as either resistant or intermediate on antimicrobial susceptibility testing.
b) The Drug Resistance Index (DRI) is an aggregate measure that combines antibiotic use and resistance into a single metric, with value of 0 indicating 100% susceptibility and value of 100 indicating 100% resistance. DRI values for the year 2020 are projections based on DRI values for 2005- 2015.
c) WHO critical pathogens are ESBL positive Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae, carbapenem-resistant Acinetobacter baumannii, & carbapenem-resistant Pseudomonas aeruginosa.

Animals

Salmonella spp.		*E.coli*	
Ampicillin	35.73%	Ampicillin	70.05%
Ciprofoxacin	58.26%	Ciprofoxacin	60
Colistin	2.96%	Colistin	0.6%
Tetracycline	46.86%	Tetracycline	63.25%

*As per information available by December 2020

Note: N/A stands for Not Applicable

Antimicrobial Use Indicators

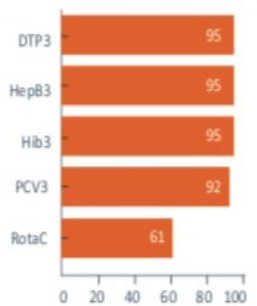
Humans

Total Use, 2010 (DDDs in Mill)	694	Per Capita Use, 2010 (DDD)	11.71
Total Use, 2020 (DDDs in Mill)	640	Per Capita Use, 2020 (DDD)	10.00
Change in total use, 2010-20 (DDDs in Mill)	-53.97	Change in per capita use, 2010-20 (DDD)	-1.15
% Change in total use, 2010-20	-7.77%%	% Change in per capita use, 2010-2020	-9.78%
Global average of % change in total use, 2010-20	74.49%	Global average of % change in per capita use, 2010-20	35.12%
Regional average of % change in total use, 2010-20	81.85%	Regional average of % change in per capita use, 2010-20	22.10%

Animals

- Estimated Total Antimicrobial Use, 2020 (Tonnes): 1057.18
- Estimated Total Antimicrobial Use, 2030 (Tonnes): 1055.09

Public Health Indicators



% of children vaccinated (2019)

- 2.7 — Infant Mortality Rate per 1,000 live births (2019)
- 1.43 — Under-five pneumococcal death rate per 100,000 children (2017)
- 12.86 — Under-five deaths from diarrheal diseases (2017)
- 7.1 — Incidence of tuberculosis per 100,000 people (2019)
- 99.44 — Access to improved drinking water source (%) (2017)
- 98.87 — Access to improved sanitation facilities (%) (2017)
- N/A — Access to basic handwashing facilities including soap and water (%) (2017)
- 4.0 — Physicians per 1,000 people (2018)
- 5.7 — Nurses and midwives per 1,000 people (2018)
- 8.67% — Current health expenditure % of GDP (2018)
- 13.24% — Domestic general government health expenditure % of general government expenditure (2018)
- 23.55% — Out-of-pocket expenditure % of current health expenditure (2018)
- $ 2989.00 — Current health expenditure per capita (2018)

Note: N/A stands for Not Applicable

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

Dashboard Croatia

Croatia

Europe & Central Asia | Upper middle income

Policy Indicators*

- Enrolment in Global Antimicrobial Resistance Surveillance System (GLASS) ✓
- National Action Plan on AMR (NAP) Published ✗
- AMU surveillance in humans ✓
- AMU surveillance in animals ✓
- AMR surveillance in humans ✓
- AMR surveillance in animals ✓

*As per information available by December 2020

Antimicrobial Resistance Indicators*

Humans

- 26.42% of isolates tested — MRSA (Methicillin-resistant *Staphylococcus aureus*)
- 06.77% of isolates tested — CRE (Carbapenem-resistant *Klebsiella pneumoniae*)
- 15.67% of isolates tested — ESBL (3G cephalosporin-resistant *Escherichia coli*)
- 47.46 — DRI (Drug Resistance Index for WHO Critical pathogens 2020)
- 51.16 — DRI (Drug Resistance Index for MRSA, CRE, and ESBL positive *E.coli* 2020)

Note:
a) Resistance rates include isolates categorized as either resistant or intermediate on antimicrobial susceptibility testing.
b) The Drug Resistance Index (DRI) is an aggregate measure that combines antibiotic use and resistance into a single metric, with value of 0 indicating 100% susceptibility and value of 100 indicating 100% resistance. DRI values for the year 2020 are projections based on DRI values for 2005- 2015.
c) WHO critical pathogens are ESBL positive Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae, carbapenem-resistant Acinetobacter baumannii, & carbapenem-resistant Pseudomonas aeruginosa.

Animals

Salmonella spp.		*E.coli*	
Ampicillin	12.96%	Ampicillin	40%
Ciprofoxacin	48.33%	Ciprofoxacin	82.4%
Colistin	0	Colistin	0
Tetracycline	15.53%	Tetracycline	38.8%

*As per information available by December 2020

Note: N/A stands for Not Applicable

Croatia

Antimicrobial Use Indicators

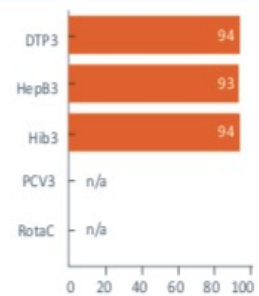
Humans

Total Use, 2010 (DDDs in Mill)	45	Per Capita Use, 2010 (DDD)	10.30
Total Use, 2020 (DDDs in Mill)	40	Per Capita Use, 2020 (DDD)	9.76
Change in total use, 2010-20 (DDDs in Mill)	-5.06	Change in per capita use, 2010-20 (DDD)	-0.54
% Change in total use, 2010-20	-11.11%	% Change in per capita use, 2010-2020	-5.21%
Global average of % change in total use, 2010-20	74.49%	Global average of % change in per capita use, 2010-20	35.12%
Regional average of % change in total use, 2010-20	81.85%	Regional average of % change in per capita use, 2010-20	22.10%

Animals

- Estimated Total Antimicrobial Use, 2020 (Tonnes): 21.45
- Estimated Total Antimicrobial Use, 2030 (Tonnes): 22.33

Public Health Indicators



% of children vaccinated (2019)

- 4.1 — Infant Mortality Rate per 1,000 live births (2019)
- 1.76 — Under-five pneumococcal death rate per 100,000 children (2017)
- 1.79 — Under-five deaths from diarrheal diseases (2017)
- 8 — Incidence of tuberculosis per 100,000 people (2019)
- 99.59 — Access to improved drinking water source (%) (2017)
- 99.02 — Access to improved sanitation facilities (%) (2017)
- N/A — Access to basic handwashing facilities including soap and water (%) (2017)
- N/A — Physicians per 1,000 people (2018)
- N/A — Nurses and midwives per 1,000 people (2018)
- 6.83% — Current health expenditure % of GDP (2018)
- 12.35% — Domestic general government health expenditure % of general government expenditure (2018)
- 10.48% — Out-of-pocket expenditure % of current health expenditure (2018)
- $ 1014.22 — Current health expenditure per capita (2018)

Note: N/A stands for Not Applicable

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

Dashboard China

China

East Asia & Pacific | Upper middle income

Policy Indicators*

- Enrolment in Global Antimicrobial Resistance Surveillance System (GLASS): ✗
- National Action Plan on AMR (NAP) Published: ✓
- AMU surveillance in humans: ✓
- AMU surveillance in animals: ✓
- AMR surveillance in humans: ✓
- AMR surveillance in animals: ✓

*As per information available by December 2020

Antimicrobial Resistance Indicators*

Humans

- **37.90%** of isolates tested — **MRSA** (Methicillin-resistant *Staphylococcus aureus*)
- **36.10%** of isolates tested — **CRE** (Carbapenem-resistant *Klebsiella pneumoniae*)
- **64.40%** of isolates tested — **ESBL** (3G cephalosporin-resistant *Escherichia coli*)

DRI	DRI
N/A	N/A
Drug Resistance Index for WHO Critical pathogens 2020	Drug Resistance Index for MRSA, CRE, and ESBL positive *E.coli* 2020

Note:

a) *Resistance rates include isolates categorized as either resistant or intermediate on antimicrobial susceptibility testing.*

b) *The Drug Resistance Index (DRI) is an aggregate measure that combines antibiotic use and resistance into a single metric, with value of 0 indicating 100% susceptibility and value of 100 indicating 100% resistance. DRI values for the year 2020 are projections based on DRI values for 2005- 2015.*

c) *WHO critical pathogens are ESBL positive Enterobacteriaceae, carbapenem-resistant Enterobacteriaceae, carbapenem-resistant Acinetobacter baumannii, & carbapenem-resistant Pseudomonas aeruginosa.*

Animals

Salmonella spp.		*E.coli*	
Ampicillin	43.6%	Ampicillin	84%
Ciprofoxacin	21.60%	Ciprofoxacin	50%
Colistin	89.00%	Colistin	48%
Tetracycline	71.25%	Tetracycline	80%

*As per information available by December 2020

Note: N/A stands for Not Applicable

China

Antimicrobial Use Indicators

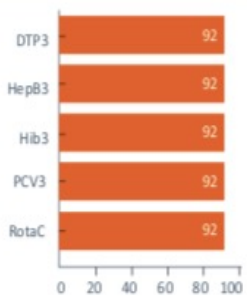
Humans

Total Use, 2010 (DDDs in Mill)	2262	Per Capita Use, 2010 (DDD)	1.69
Total Use, 2020 (DDDs in Mill)	8990	Per Capita Use, 2020 (DDD)	6.43
Change in total use, 2010-20 (DDDs in Mill)	6727.46	Change in per capita use, 2010-20 (DDD)	4.74
% Change in total use, 2010-20	297.32%	% Change in per capita use, 2010-2020	280.40%
Global average of % change in total use, 2010-20	74.49%	Global average of % change in per capita use, 2010-20	35.12%
Regional average of % change in total use, 2010-20	158.87%	Regional average of % change in per capita use, 2010-20	139.61%

Animals

Estimated Total Antimicrobial Use, 2020 (Tonnes)	43024.24
Estimated Total Antimicrobial Use, 2030 (Tonnes)	45038.85

Public Health Indicators



% of children vaccinated (2019)

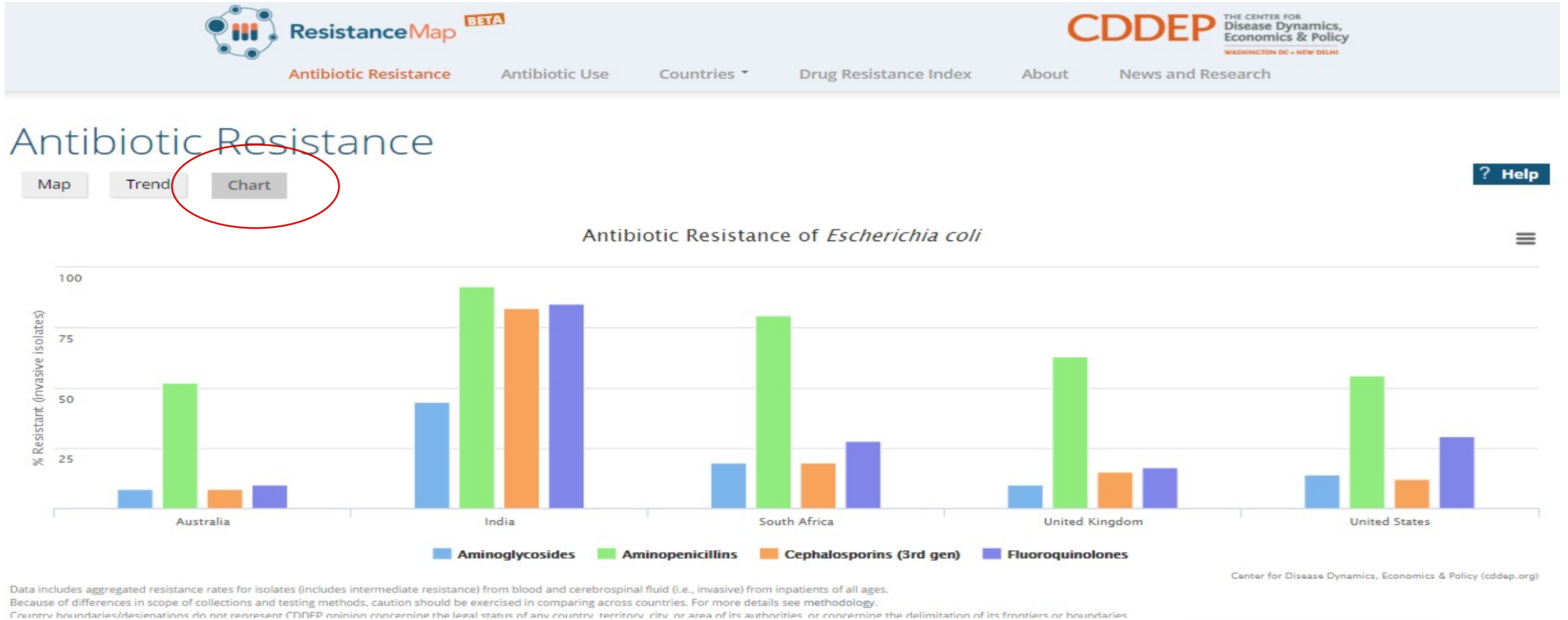
31.9 Infant Mortality Rate per 1,000 live births (2019)		146.5 Under-five pneumococcal death rate per 100,000 children (2017)	
9551.78 Under-five deaths from diarrheal diseases (2017)		58 Incidence of tuberculosis per 100,000 people (2019)	
67.98 Access to improved drinking water source (%) (2017)	51.18 Access to improved sanitation facilities (%) (2017)	24.65 Access to basic handwashing facilities including soap and water (%) (2017)	
2.5 Physicians per 1,000 people (2018)		N/A Nurses and midwives per 1,000 people (2018)	

5.35% Current health expenditure % of GDP (2018)	8.85% Domestic general government health expenditure % of general government expenditure (2018)	35.75% Out-of-pocket expenditure % of current health expenditure (2018)	$ 501.06 Current health expenditure per capita (2018)

Note: N/A stands for Not Applicable

CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy
WASHINGTON DC • NEW DELHI

Resistancemap.org



CDDEP THE CENTER FOR Disease Dynamics, Economics & Policy WASHINGTON DC • NEW DELHI

PRINCETON UNIVERSITY