Convergence in Antimicrobial Use and Factors Influencing Resistance

Ramanan Laxminarayan

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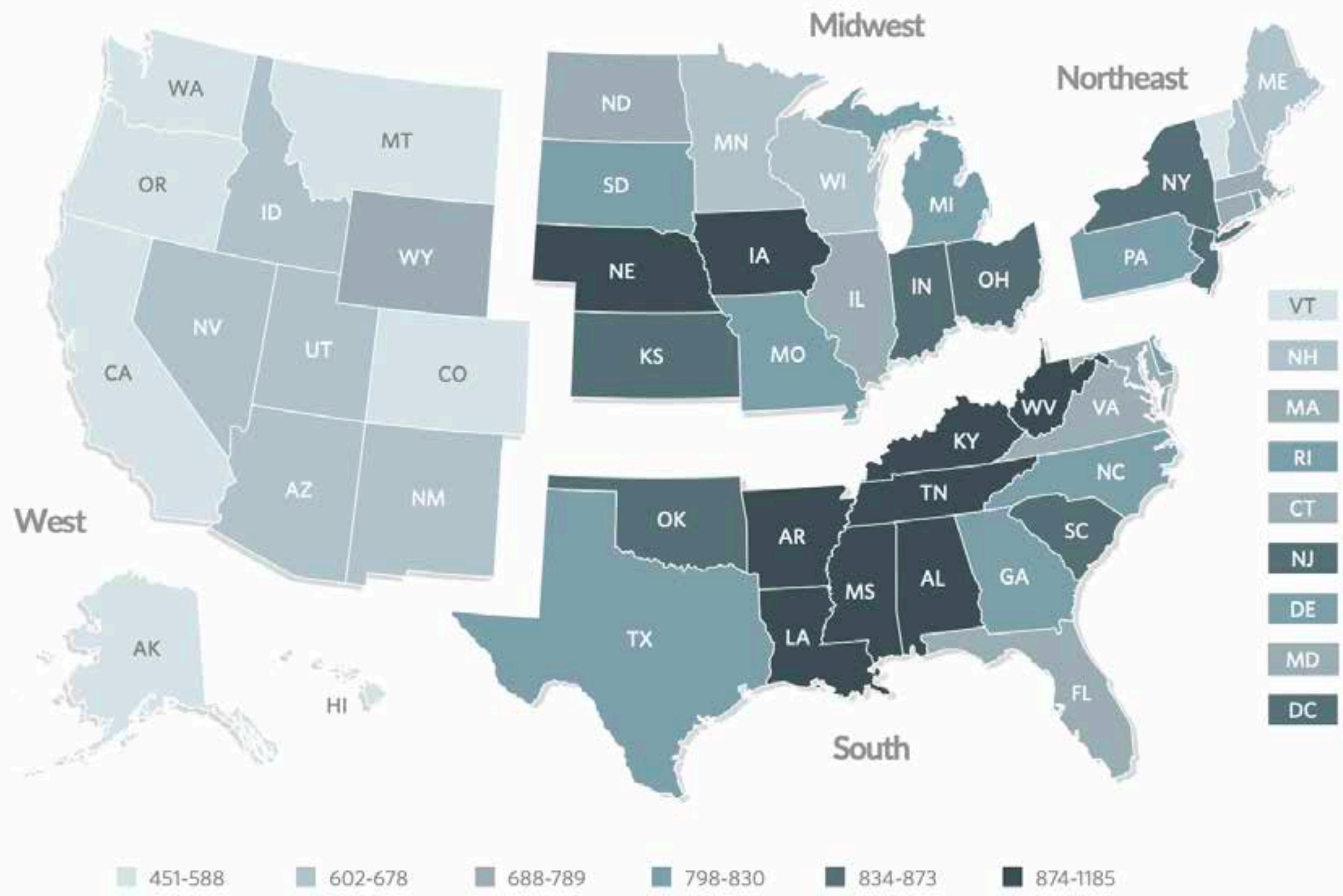
Outpatient Antibiotic Prescriptions by State, 2018

Antibiotic prescriptions per 1,000 persons



J Antimicrob Chemother
doi:10.1093/jac/dku563

Journal of Antimicrobial Chemotherapy

Influence of provider and urgent care density across different socioeconomic strata on outpatient antibiotic prescribing in the USA

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Received 14 September 2014; returned 3 October 2014; revised 5 December 2014; accepted 13 December 2014

Objectives: Despite a strong link between antibiotic use and resistance, and highly variable antibiotic consumption rates across the USA, drivers of differences in consumption rates are not fully understood. The objective of this study was to examine how provider density affects antibiotic prescribing rates across socioeconomic groups in the USA.

Methods: We aggregated data on all outpatient antibiotic prescriptions filled in retail pharmacies in the USA in 2000 and 2010 from IMS Health into 3436 geographically distinct hospital service areas and combined this with socioeconomic and structural factors that affect antibiotic prescribing from the US Census. We then used fixed-effect models to estimate the interaction between poverty and the number of physician offices per capita (i.e. physician density) and the presence of urgent care and retail clinics on antibiotic prescribing rates.

Results: We found large geographical variation in prescribing, driven in part by the number of physician offices per capita. For an increase of one standard deviation in the number of physician offices per capita there was a 25.9% increase in prescriptions per capita. However, the determinants of the prescription rate were dependent on socioeconomic conditions. In poorer areas, clinics substitute for traditional physician offices, reducing the impact of physician density. In wealthier areas, clinics increase the effect of physician density on the prescribing rate.

Conclusions: In areas with higher poverty rates, access to providers drives the prescribing rate. However, in wealthier areas, where access is less of a problem, a higher density of providers and clinics increases the prescribing rate, potentially due to competition.

Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data

Thomas P Van Boeckel, Sumanth Gandra, Ashvin Ashok, Quentin Caudron, Bryan T Grenfell, Simon A Levin, Ramanan Laxminarayan

Summary

Background Antibiotic drug consumption is a major driver of antibiotic resistance. Variations in antibiotic resistance across countries are attributable, in part, to different volumes and patterns for antibiotic consumption. We aimed to assess variations in consumption to assist monitoring of the rise of resistance and development of rational-use policies and to provide a baseline for future assessment.

Lancet Infect Dis 2014

Published Online
July 10, 2014
http://dx.doi.org/10.1016/S1473-3099(14)70780-7

PNAS

Global increase and geographic convergence in antibiotic consumption between 2000 and 2015

Eili Y. Klein[a,b,c,1], Thomas P. Van Boeckel[d], Elena M. Martinez[a], Suraj Pant[a], Sumanth Gandra[a], Simon A. Levin[e,f,g,1], Herman Goossens[h], and Ramanan Laxminarayan[a,f,i]

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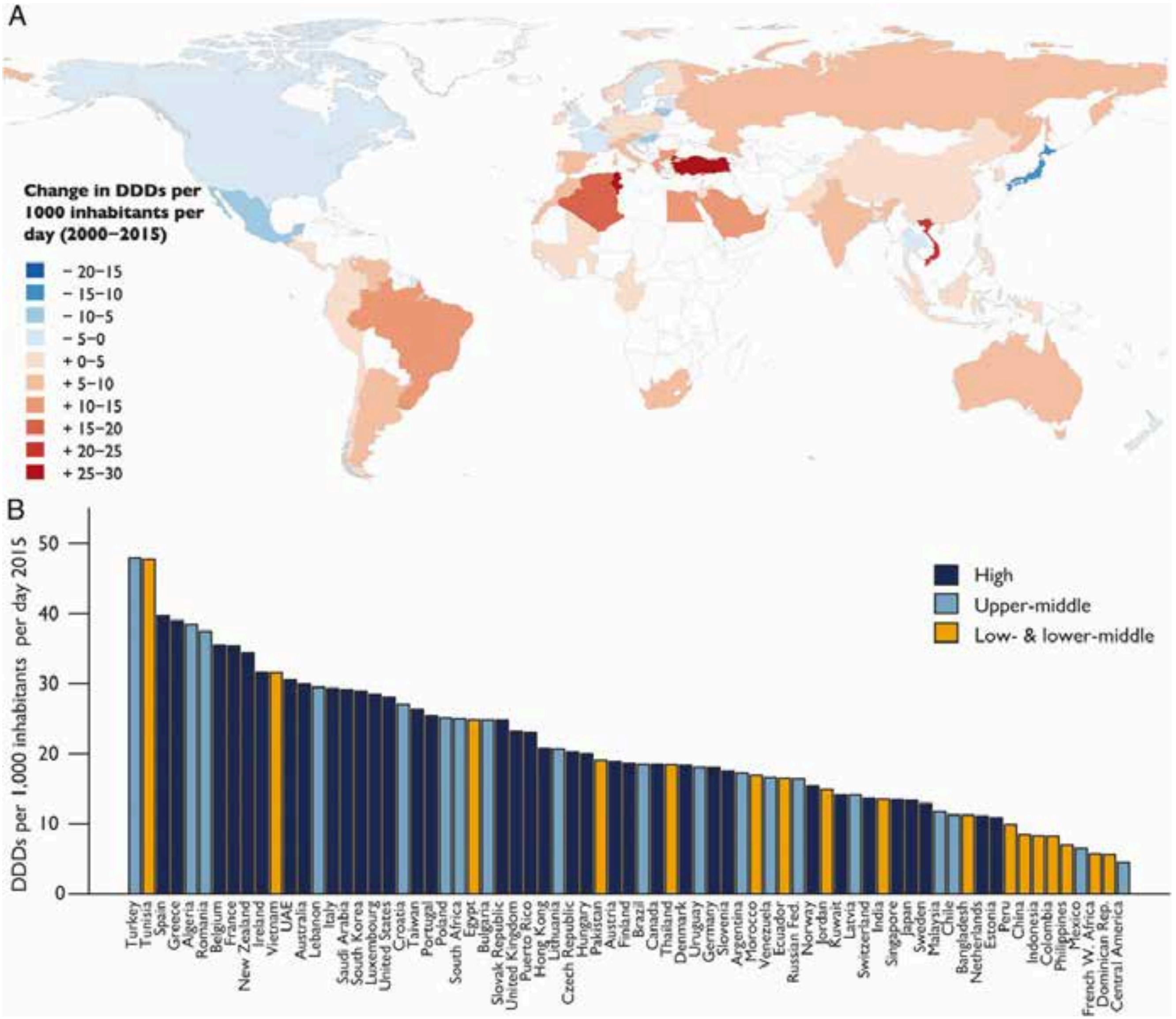
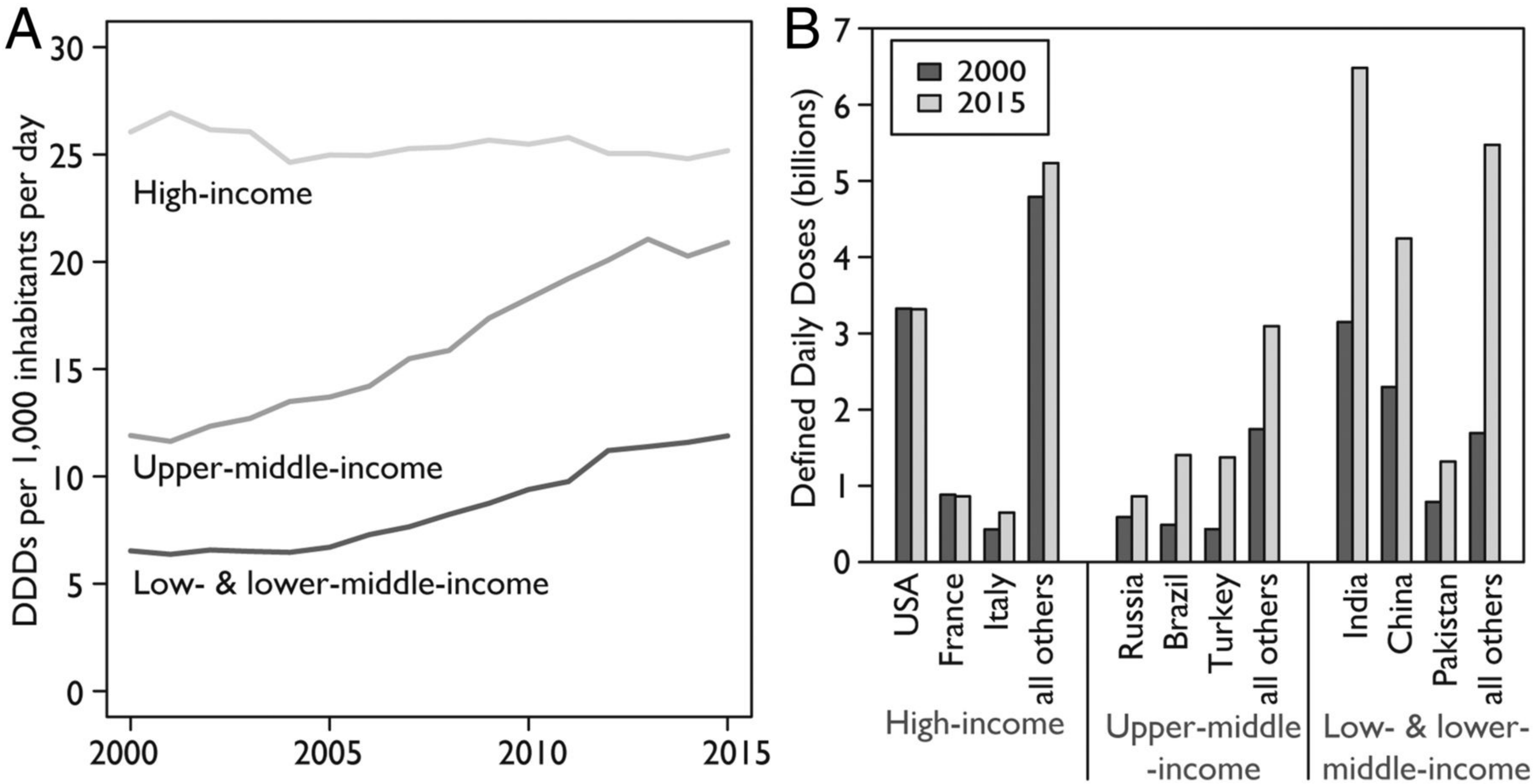
Global antibiotic consumption by country: 2000–2015.



Eili Y. Klein et al. PNAS doi:10.1073/pnas.1717295115

Global antibiotic consumption by country income classification: 2000–2015.

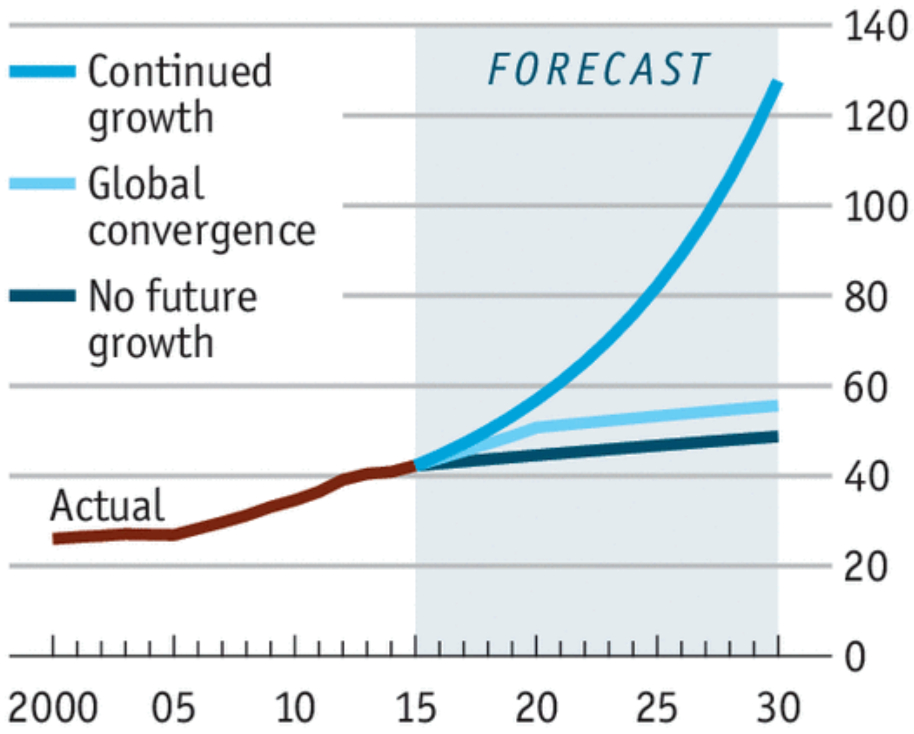


Eili Y. Klein et al. PNAS doi:10.1073/pnas.1717295115

Global consumption of antibiotics

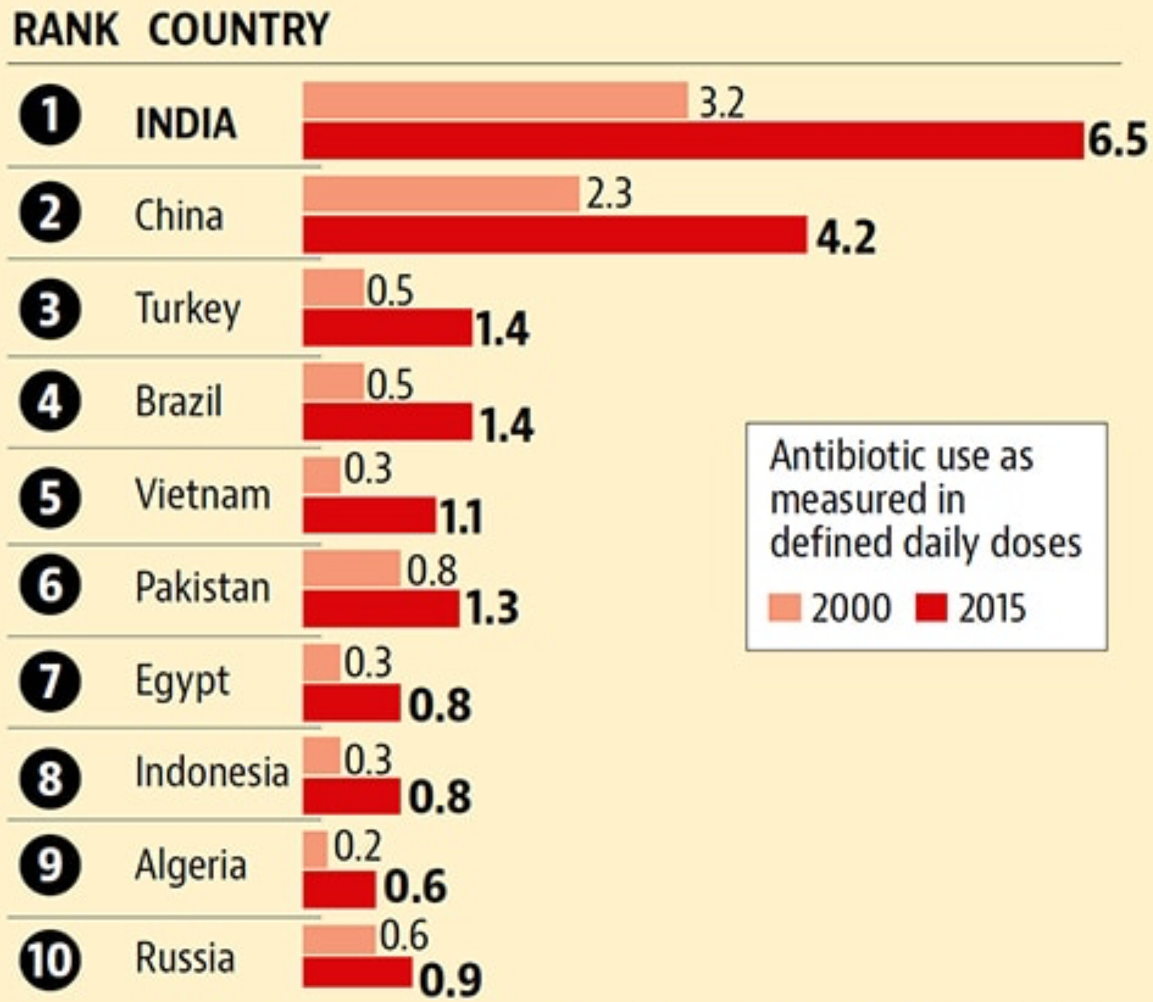
2015-30 scenario-based forecasts

Daily dosage, bn

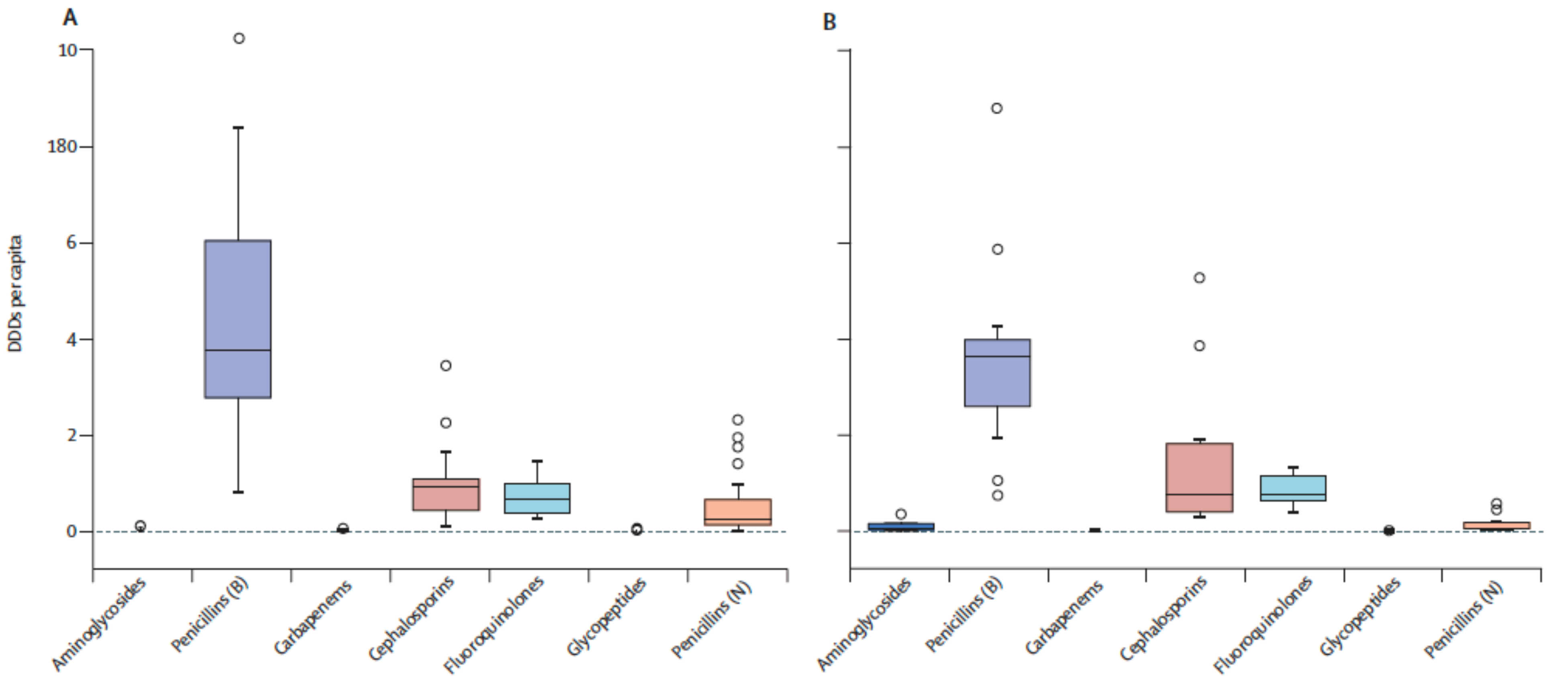


Source: "Global increase and geographic convergence in antibiotic consumption between 2000 and 2015", by Eili Klein et al., Proceedings of the National Academy of Sciences, March 2016

Countries with highest increase in consumption

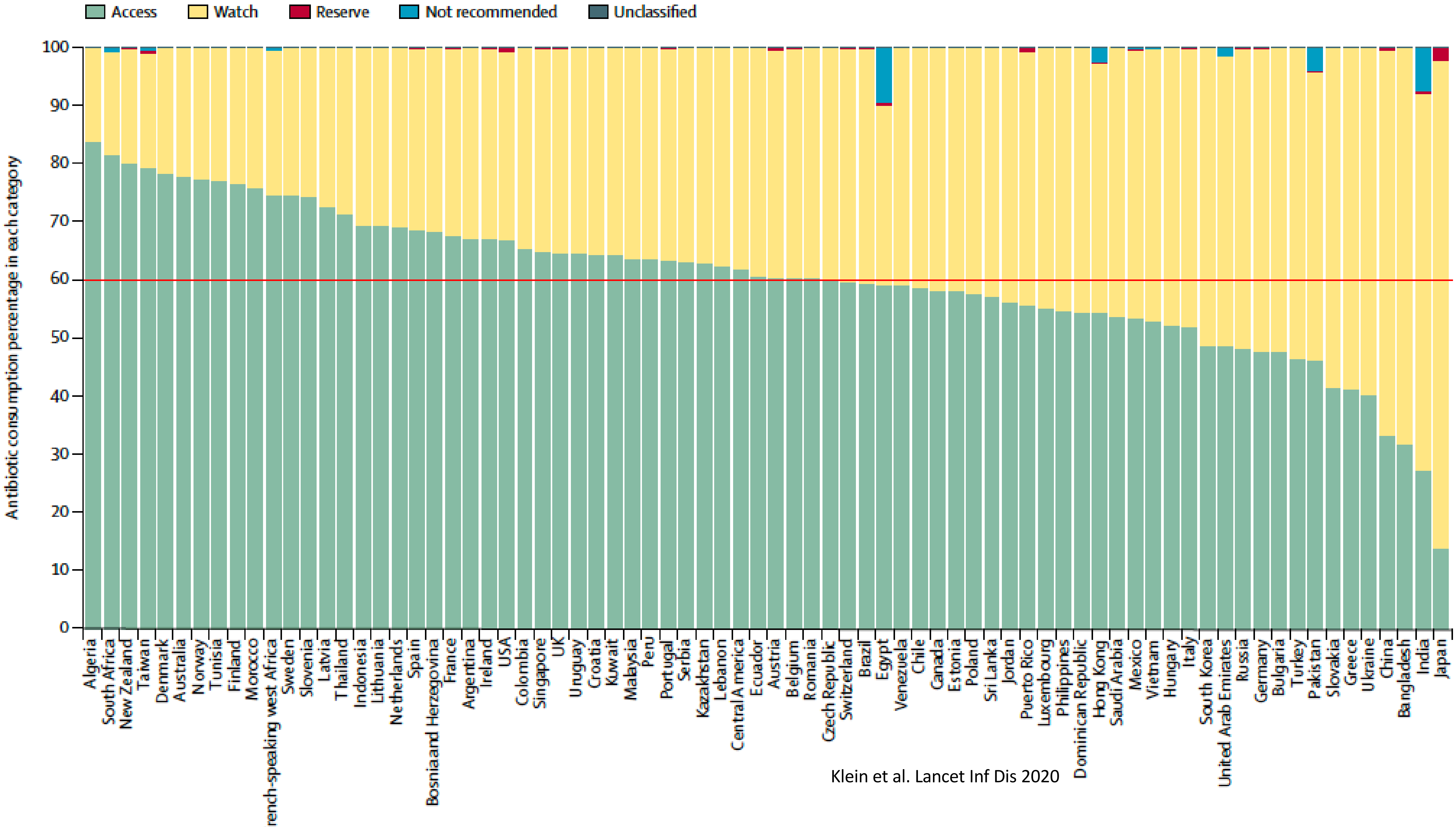


Rank according to volume increase; Source: Proceedings of the National Academy of Sciences



The upper bar plots show the variability in per capita antibiotic use measured in defined daily doses for high-income countries (A) and low-income and middle-income countries (B). The black line is the median, the colored bars are the quartiles, the whiskers are the extremes, and outliers are plotted as circles.

Klein et al. Lancet Inf Dis 2020



Klein et al. Lancet Inf Dis 2020

***Figure 2:* Relative and absolute consumption of Access antibiotics and Watch antibiotics, 2000–15**
Median consumption in countries at each income level, expressed as DIDs, for Access antibiotics (A) and Watch antibiotics (B). (C) Median access-to-watch index in countries at each income level. DIDs=defined daily doses per 1000 inhabitants per day. HIC=high-income countries. LMIC-UM=upper-middle income countries. LMIC-LM=lower-middle income countries.

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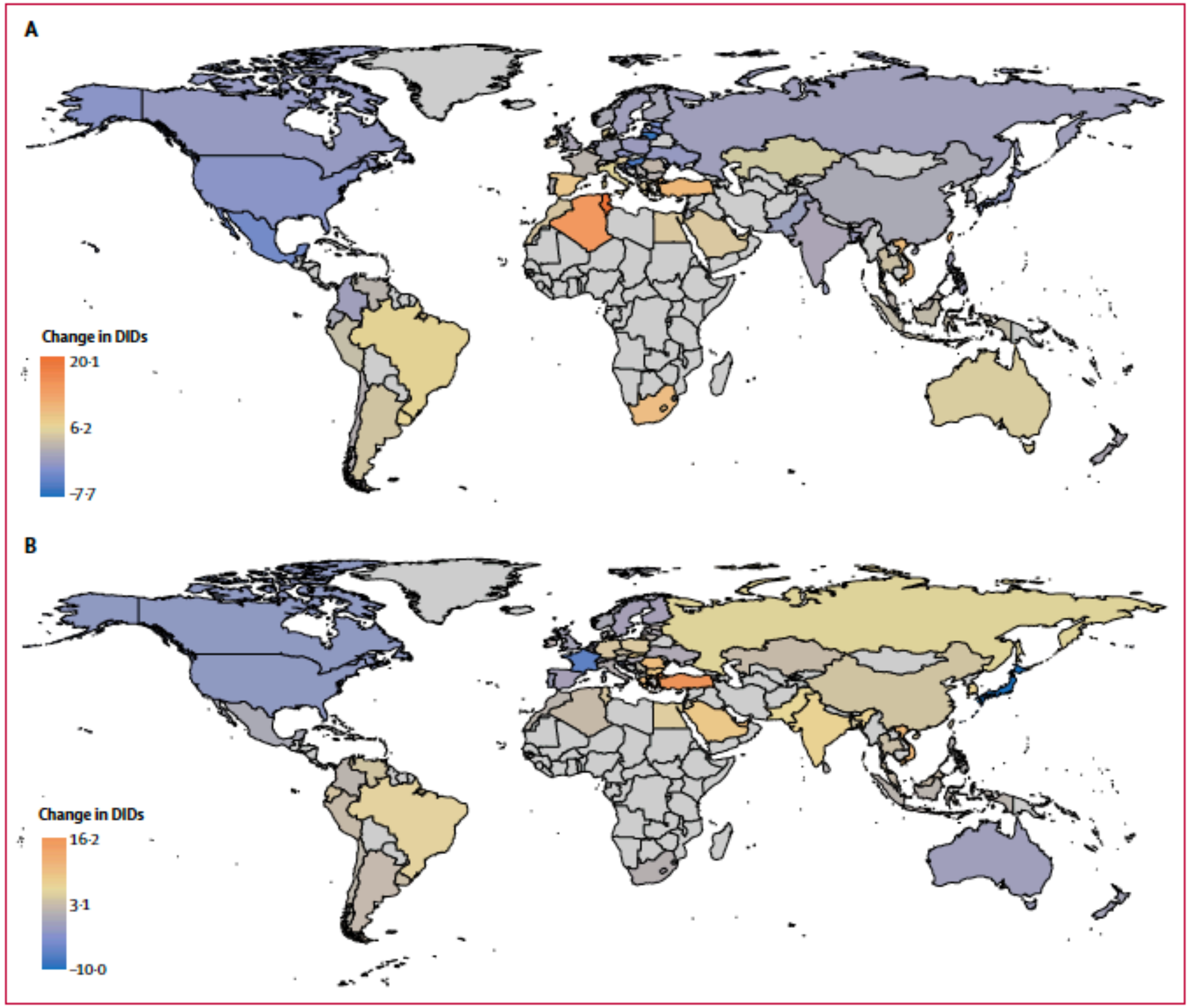

***Figure 3:* Change in the national consumption of Access antibiotics and Watch antibiotics, 2000–15**
Change in consumption of Access antibiotics (A) and Watch antibiotics (B) expressed in DIDs. Due to availability of data, change in consumption was calculated from 2002 for Algeria; from 2005 for Bangladesh, Croatia, Kazakhstan, Netherlands, and Vietnam; from 2007 for Sri Lanka; from 2010 for Ukraine; and from 2011 for Bosnia and Herzegovina, and Serbia. DIDs=defined daily doses per 1000 inhabitants per day.

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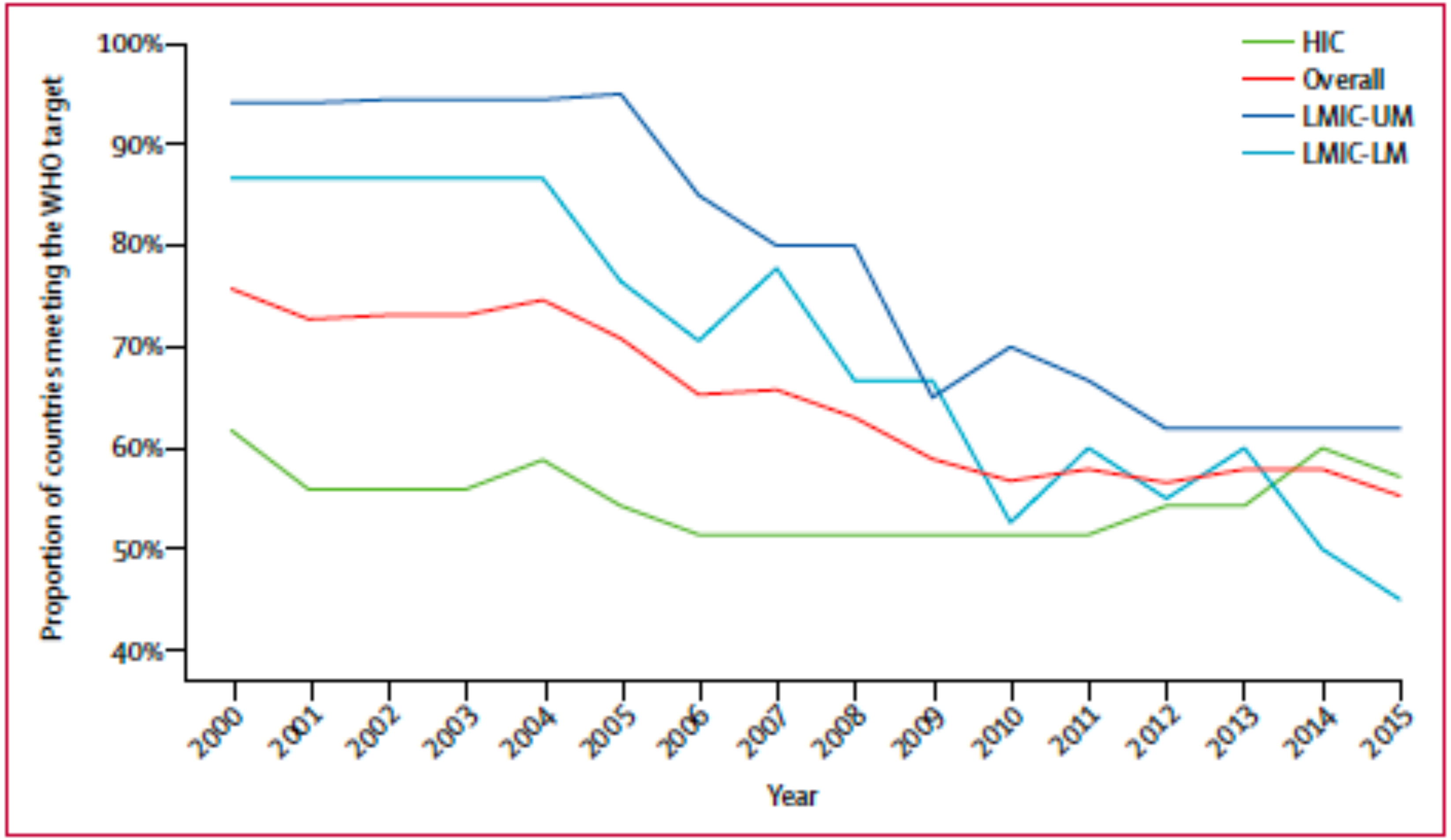


Figure 4: Proportion of countries that met the WHO target of at least 60% Access antibiotics in total antibiotic consumption, stratified by income level, 2000–15

HIC=high-income countries. LMIC-UM=upper-middle income countries. LMIC-LM=lower-middle income countries.

Klein et al. Lancet Inf Dis 2020

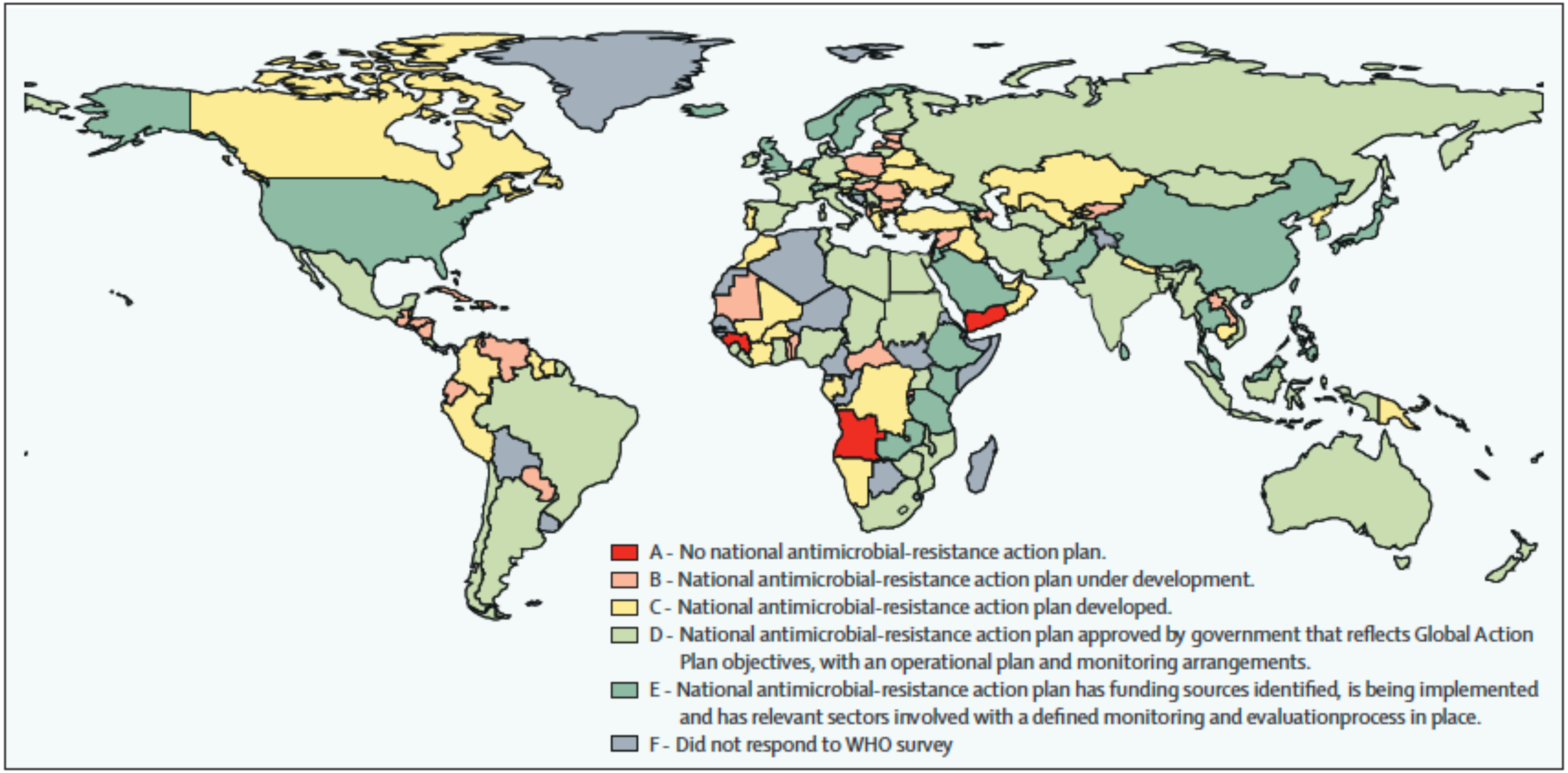
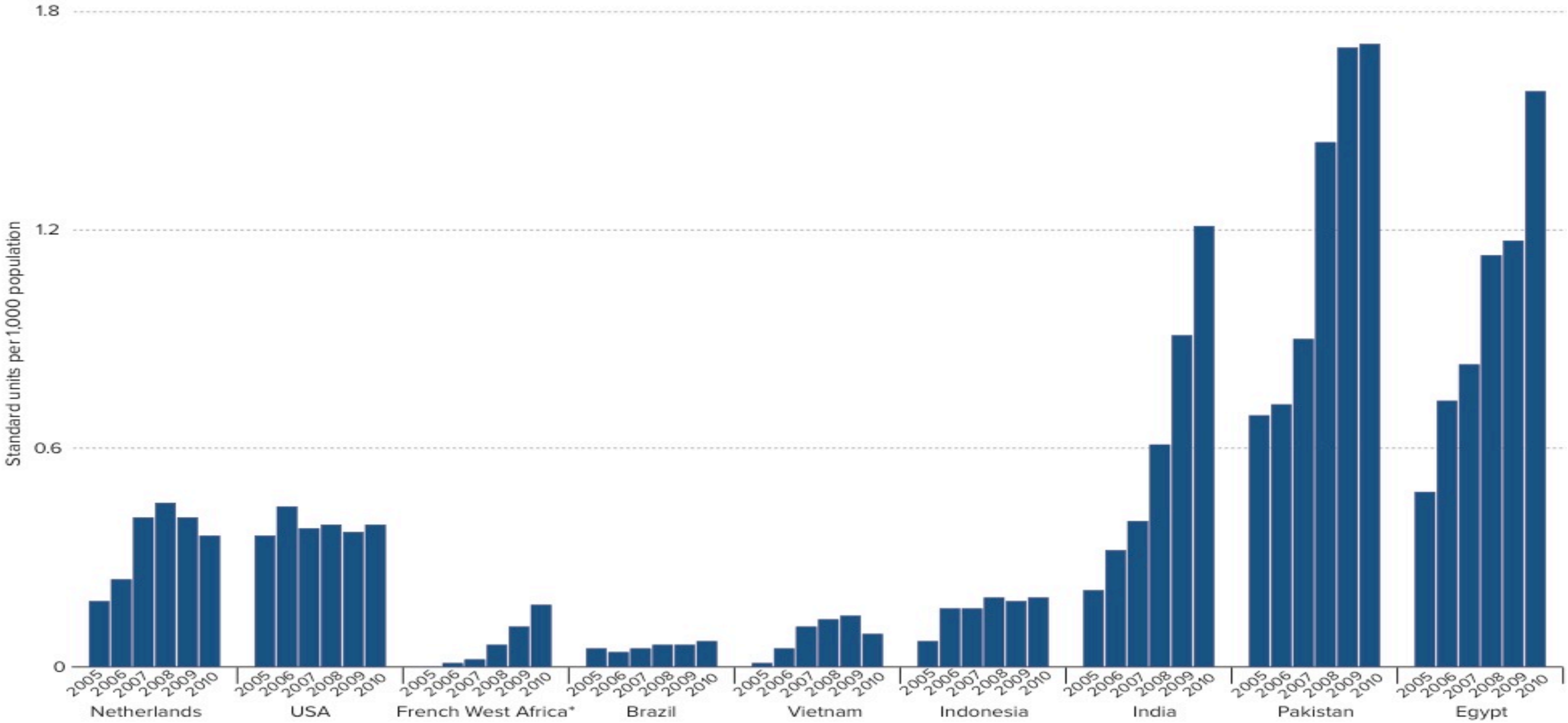


***Figure 2*: Countries' progress with development of a national action plan on antimicrobial resistance**
Reproduced with permission from WHO.

Laxminarayan et al. Lancet Inf Dis 2020

Carbapenem retail sales in selected countries, 2005–2010 (per 1,000 population)



Source: Laxminarayan et al. 2013 (based on IMS MIDAS)

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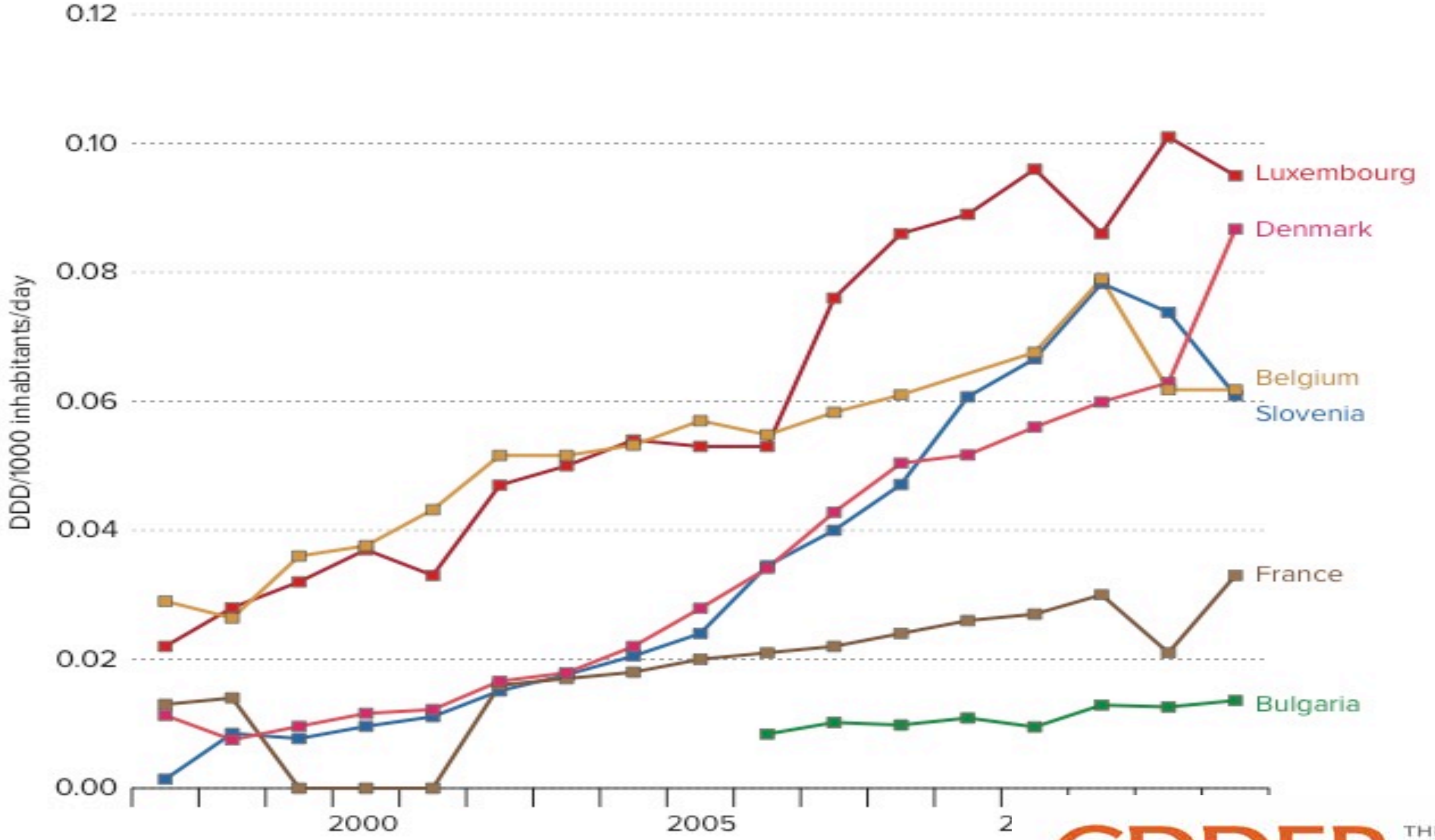
*An IMS grouping of Benin, Burkina Faso, Cameroon, Côte d'Ivoire, Gabon, Guinea, Mali, Republic of the Congo, Senegal, and Togo

Carbapenem consumption in the hospital sector in selected European countries, 1997–2013



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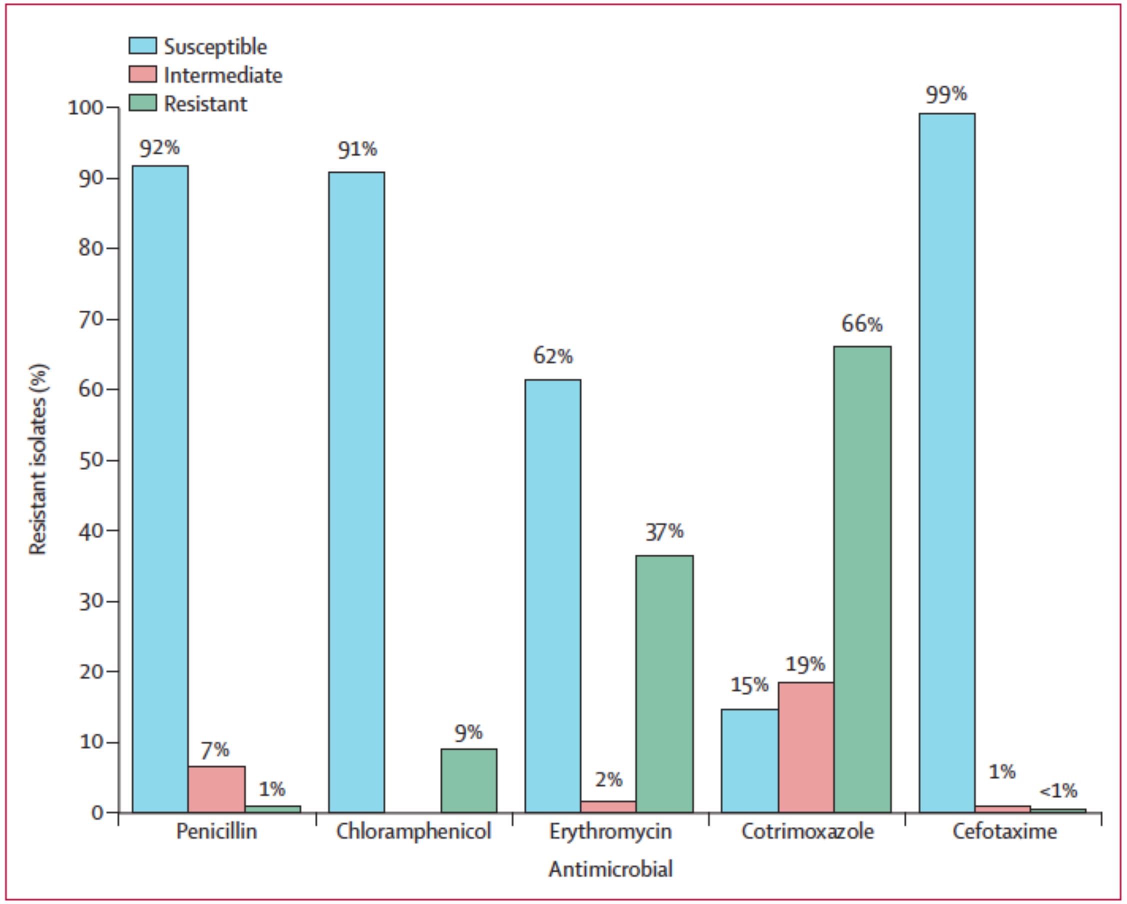
ESAC-Net 2015

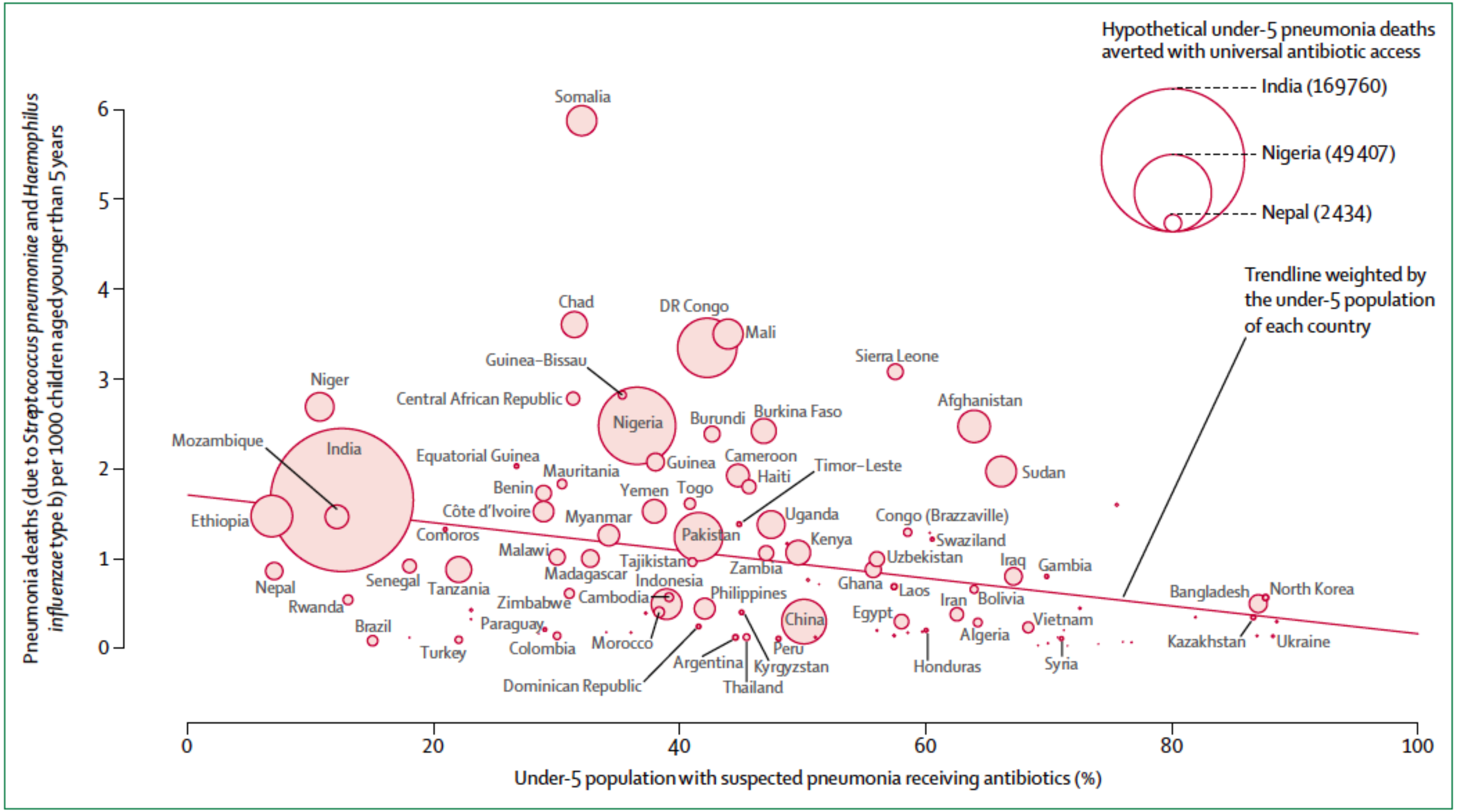
Having antibiotics is not sufficient – they must be used
Penicillin is effective but not widely available



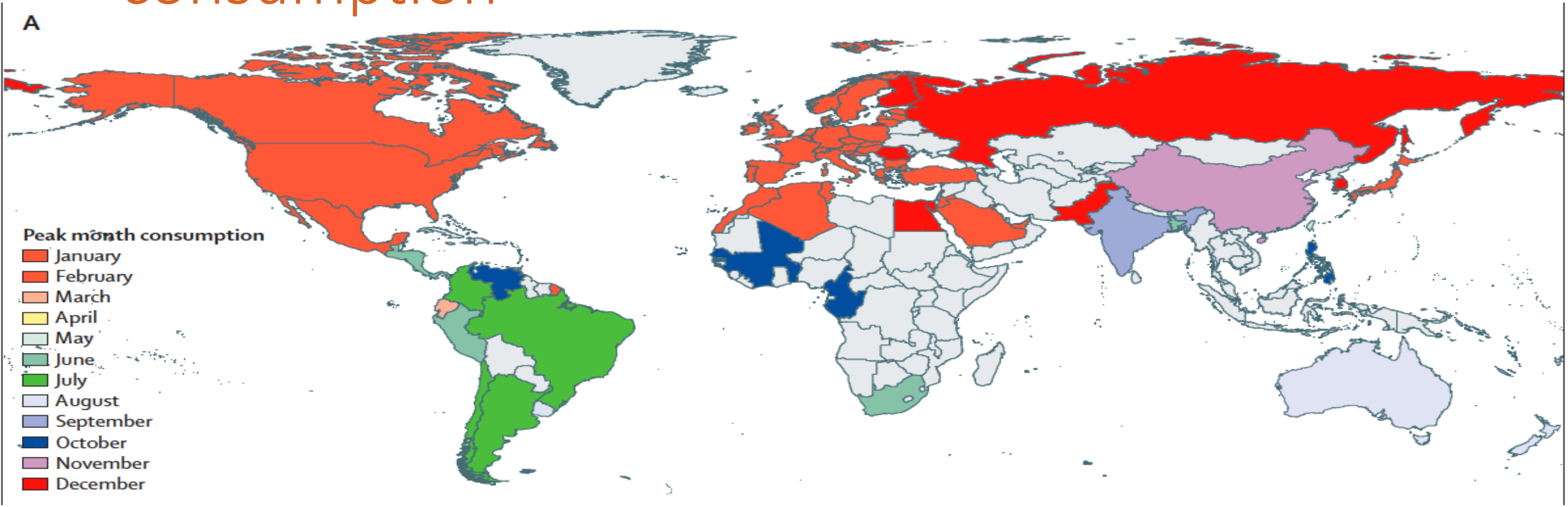
Antimicrobial susceptibility pattern of 361 *Streptococcus pneumoniae* isolates

Manoharan Lancet Inf Dis, 2017

Avertable pneumonia deaths avertable with improved antibiotic access



The flu season is a key driver of antibiotic consumption



Van Boeckel et al, Lancet Inf Dis, 2014

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

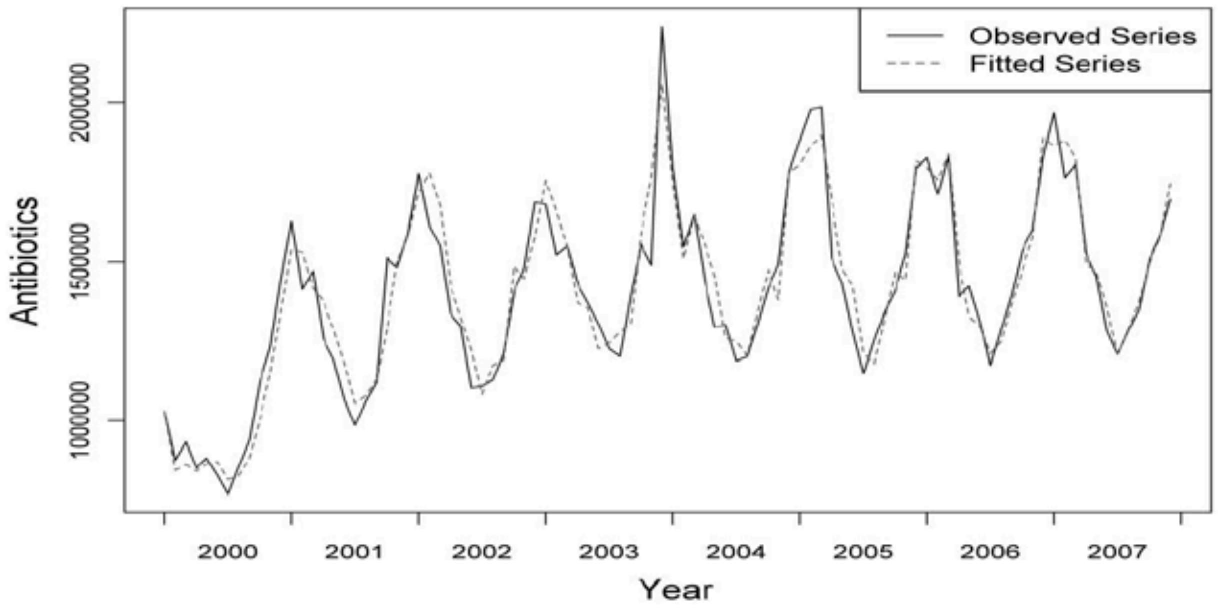


FIGURE 1. Observed and fitted antibiotics series from 2000 to 2007. The solid line represents the actually observed antibiotics series; the dashed line represents the fitted antibiotics series from the time series regression model that uses influenza-like illness as an explanatory series.

Polgreen et al Inf Cont Hosp Epi, 2011

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]

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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.

Antibiotic Use ar

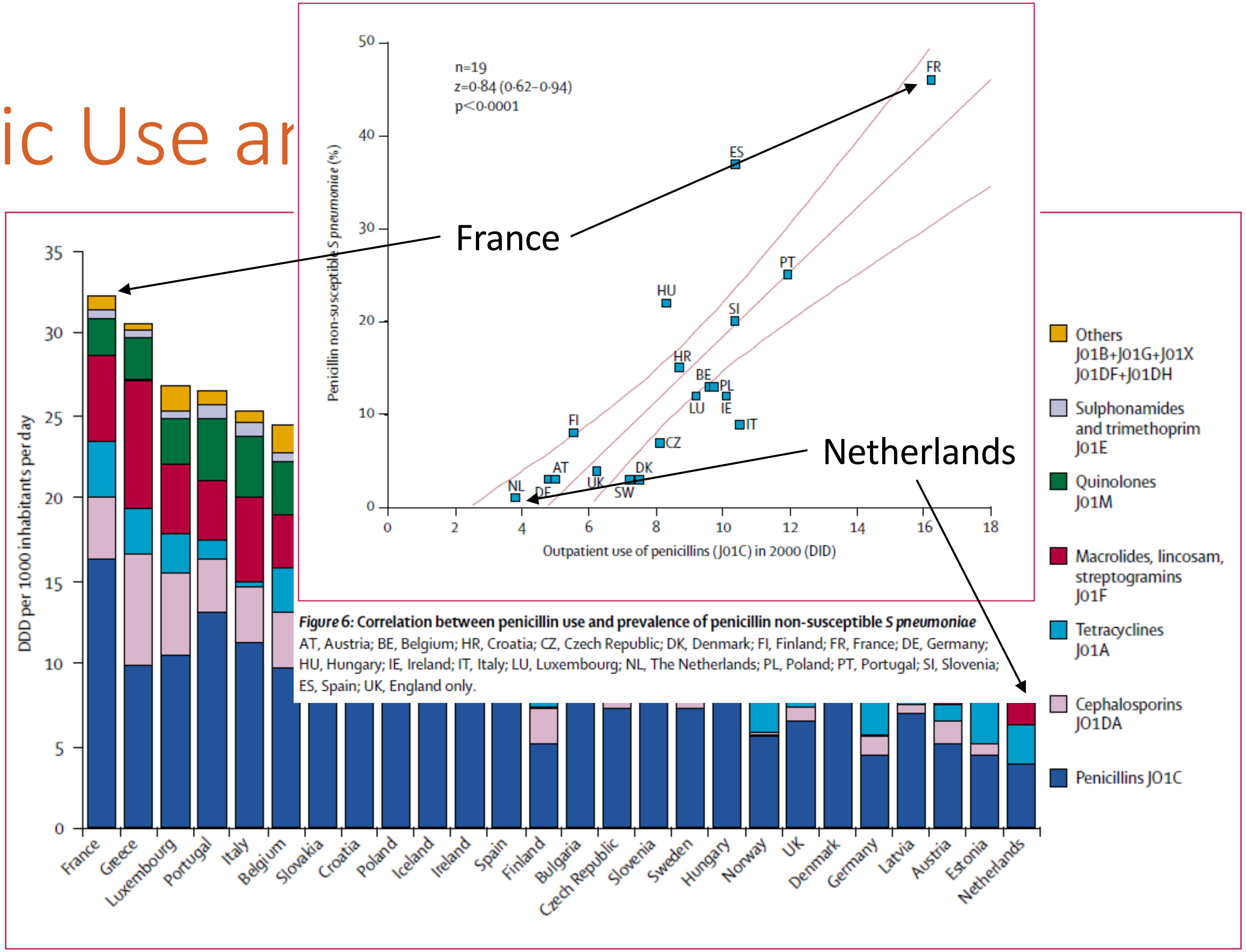
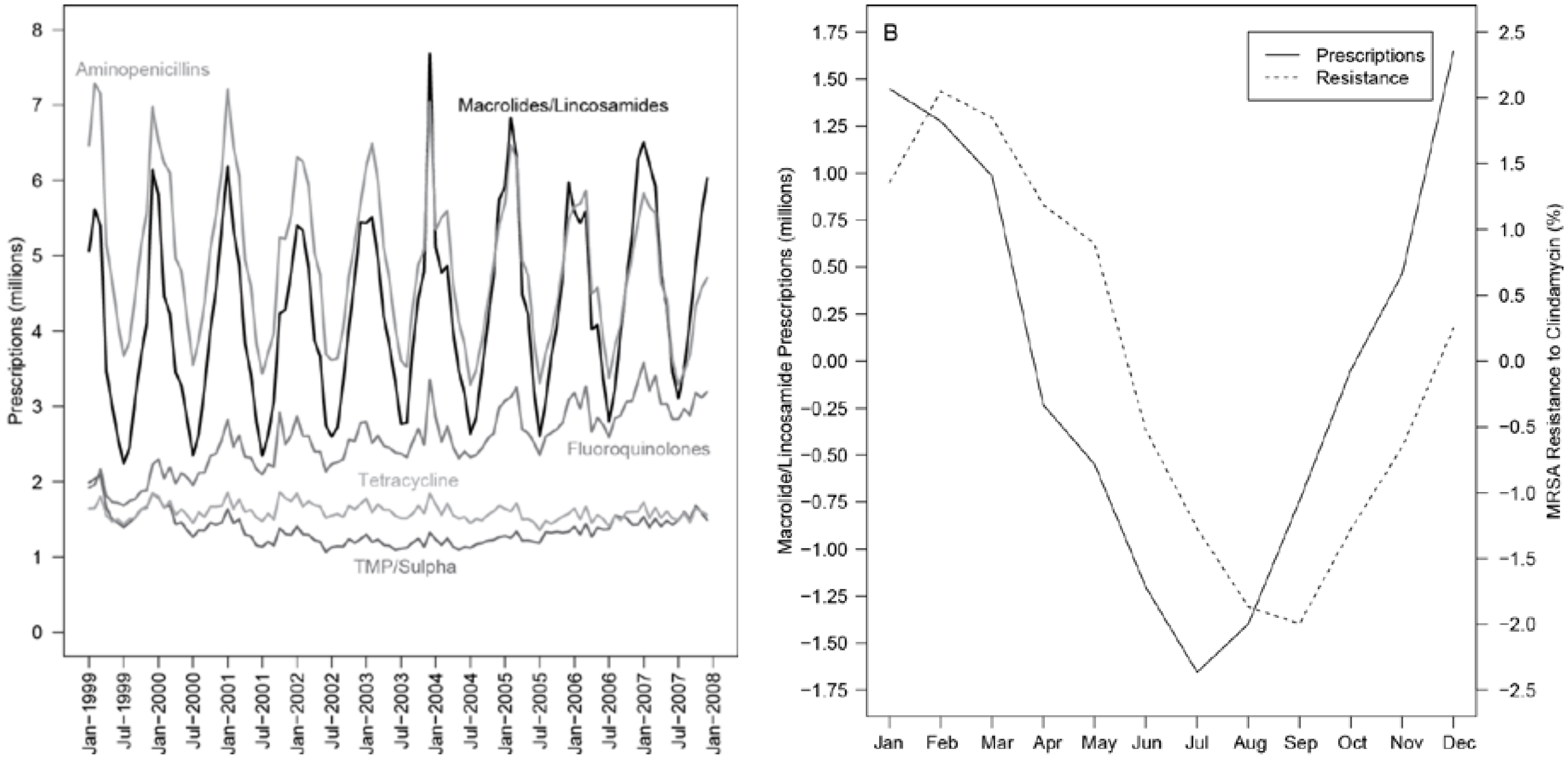


Figure 6: **Correlation between penicillin use and prevalence of penicillin non-susceptible *S pneumoniae***
AT, Austria; BE, Belgium; HR, Croatia; CZ, Czech Republic; DK, Denmark; FI, Finland; FR, France; DE, Germany; HU, Hungary; IE, Ireland; IT, Italy; LU, Luxembourg; NL, The Netherlands; PL, Poland; PT, Portugal; SI, Slovenia; ES, Spain; UK, England only.

Figure 1: **Total outpatient antibiotic use in 26 European countries in 2002**

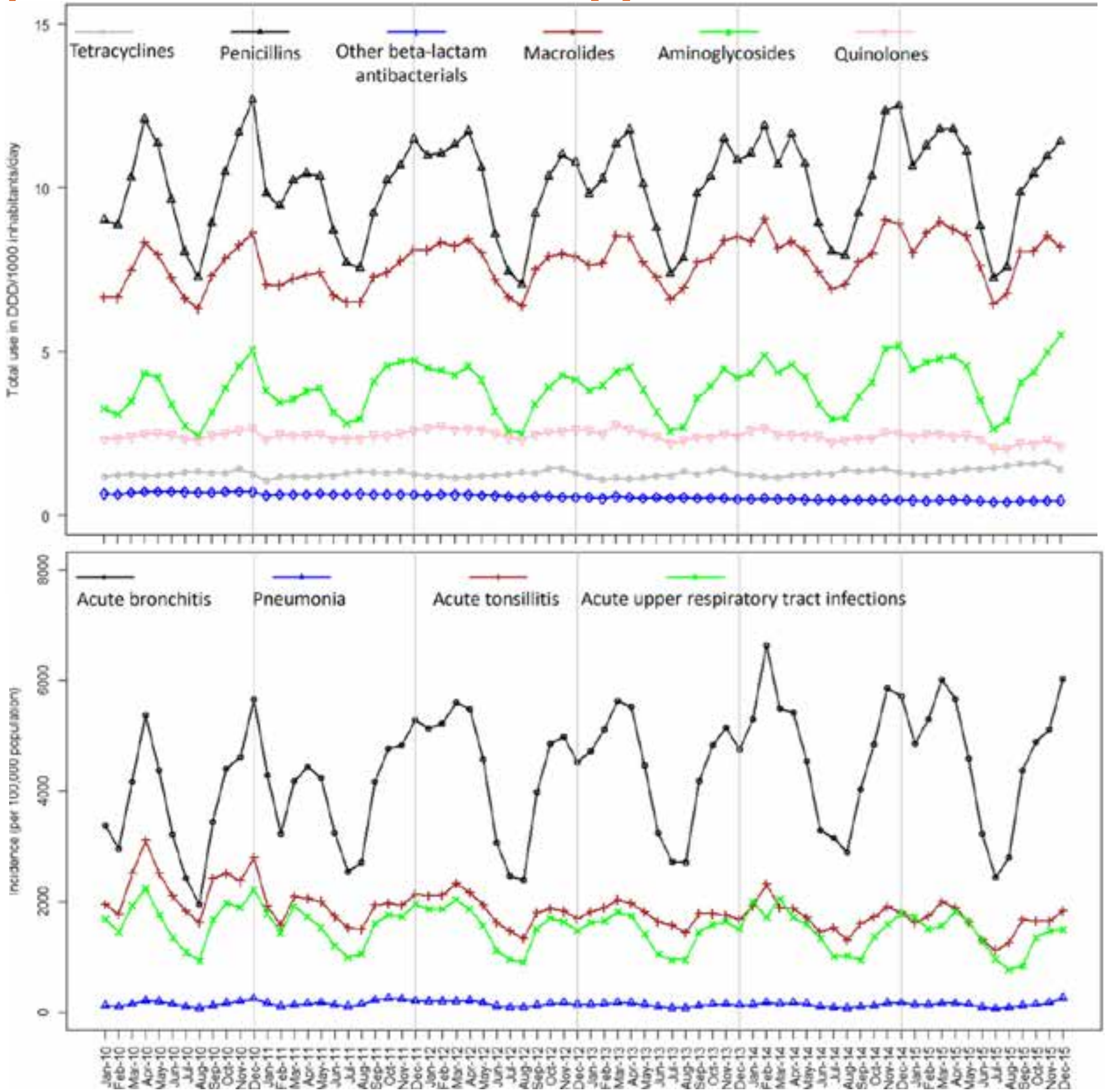
Goossens et al 2005

Antibiotic Use and Resistance



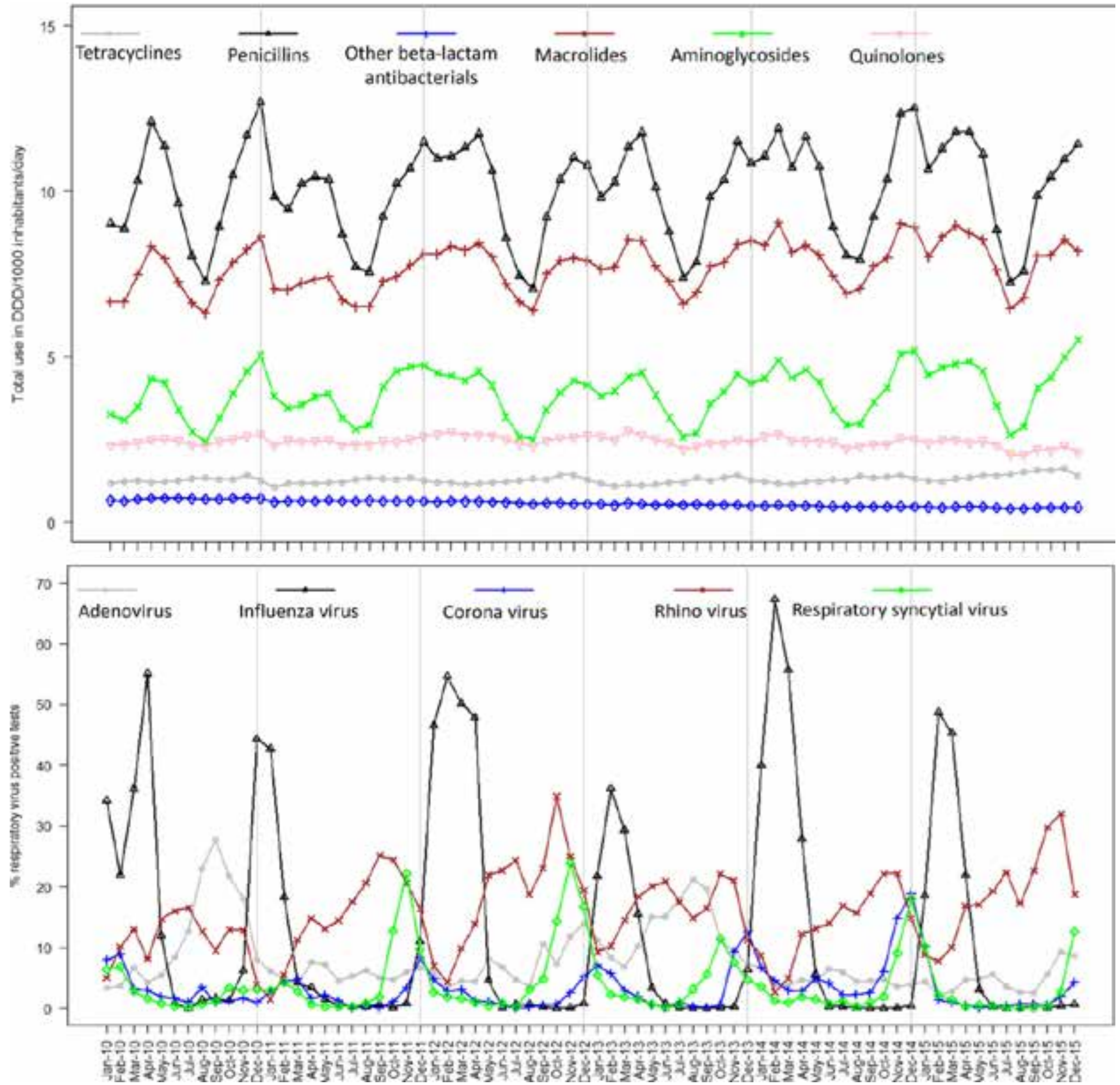
Sun et al, Clin Inf Dis. 2012

Seasonality of Prescribing Affects Resistance Rates



Ryu et al. (2018) Temporal relationship between antibiotic use and respiratory virus activities in the Republic of Korea: a time-series analysis *Antimicrobial Resistance and Infection Control* 7:56

Seasonality of Prescribing Not Associated with Viruses



Ryu et al. (2018) Temporal relationship between antibiotic use and respiratory virus activities in the Republic of Korea: a time-series analysis *Antimicrobial Resistance and Infection Control* 7:56

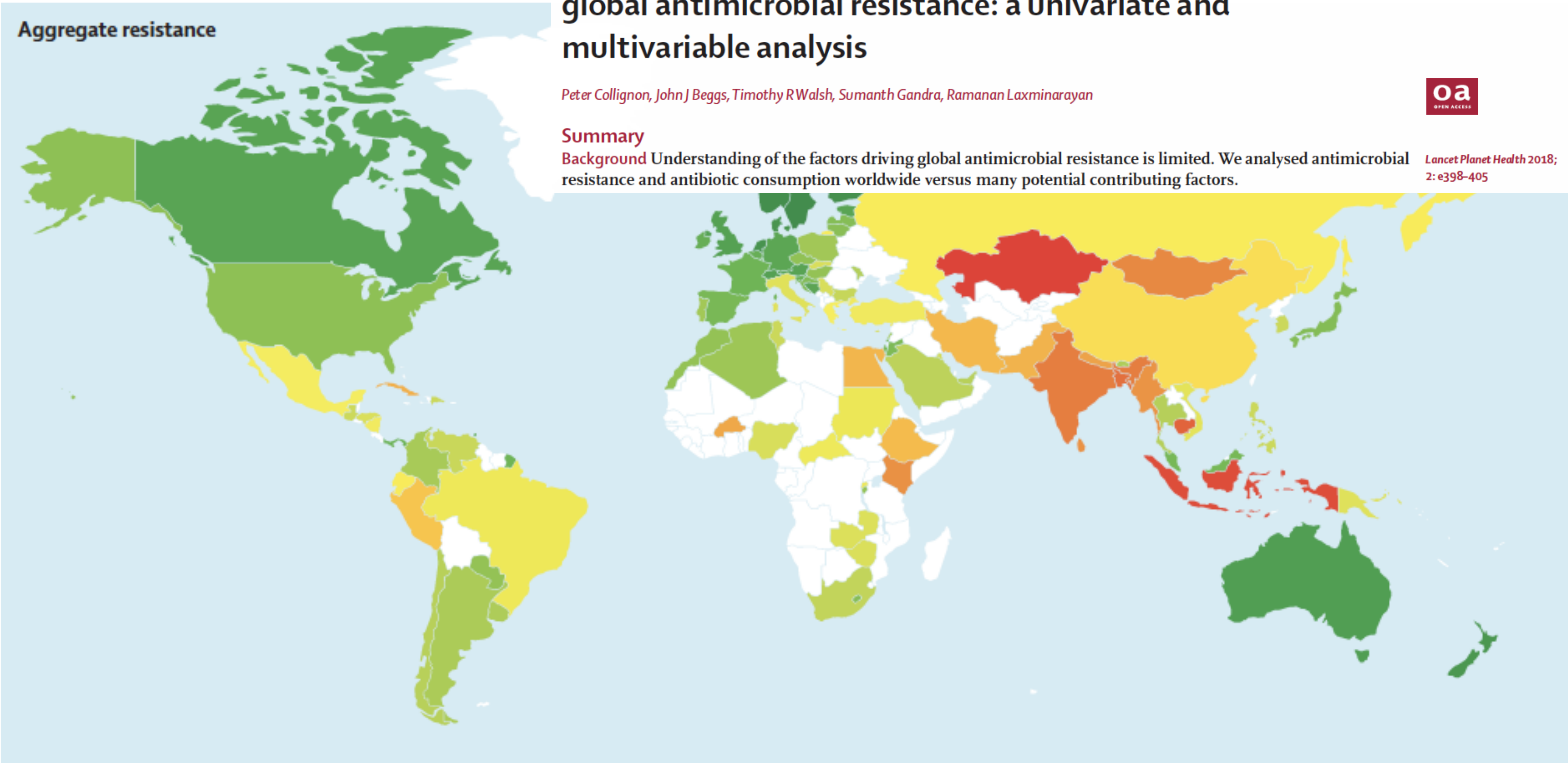
Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis

Peter Collignon, John J Beggs, Timothy R Walsh, Sumanth Gandra, Ramanan Laxminarayan

Summary

Background Understanding of the factors driving global antimicrobial resistance is limited. We analysed antimicrobial resistance and antibiotic consumption worldwide versus many potential contributing factors.

Lancet Planet Health 2018; 2: e398–405



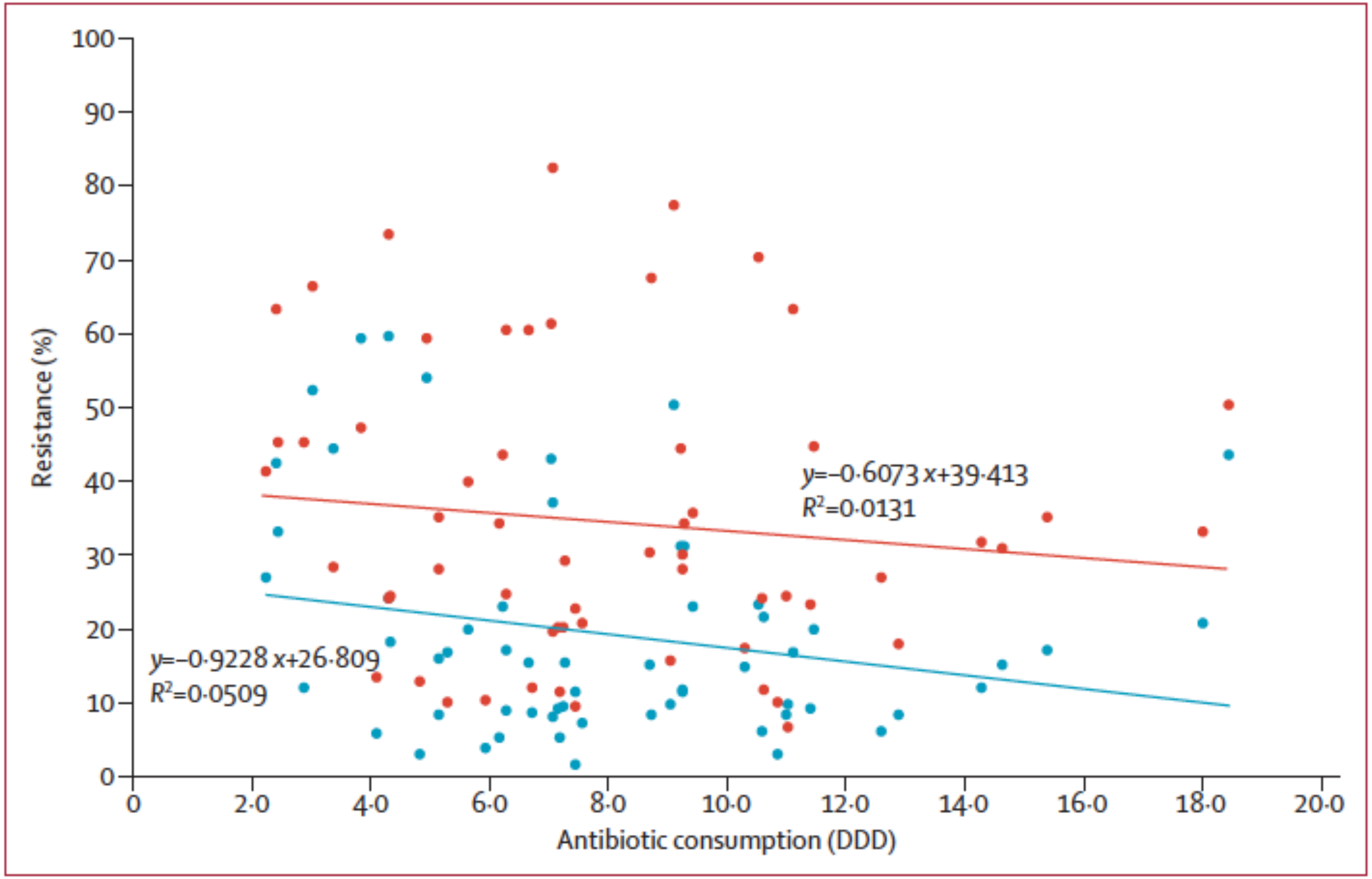


Figure 2: Escherichia coli **resistance levels for fluoroquinolones and third-generation cephalosporins compared with antibiotic consumption**

Collignon et al. Lancet Plan Health 2018

	Effect on resistance rate of 1 SD increase in each explanatory variable (logit)	p value
Usage (standardised)	–0·88	0·64
Governance index	–7·89	0·025
Health expenditure index	–5·54	0·093
GDP per capita (standardised)	6·62	0·030
Education index	7·93	0·058
Infrastructure index	–16·84	0·014
Climate index	2·01	0·33
R^2	0·54	..

GDP=gross domestic product. R^2=coefficient of determination.

Table 2: **Effect of changes in indices on the resistance of *Escherichia coli* to third-generation cephalosporins and fluoroquinolones**

Collignon et al. Lancet Plan Health 2018

Resistancemap.org