Supplementary Data

Supplementary Table 1. Categorization of oral antibiotics into broad- and narrow-spectrum of antimicrobial activity, adapted from the 2017 European Centre for Disease Prevention and Control, European Food Safety Authority Panel on Biological Hazards, European Medicines Agency Joint Scientific Opinion on a list of outcome indicators as regards surveillance of antimicrobial resistance and antimicrobial consumption in humans and food-producing animals [1]

Supplementary Table 2. Prevalence rate ratios comparing annual outpatient oral antibiotic prescription rates to reference year 2011, 2012-2016

Supplementary Table 3. US outpatient oral antibiotic prescriptions by provider specialty stratified by age group, 2011-2016

Supplementary Figure 1. US outpatient oral antibiotic prescriptions per 1,000 persons by state in 2011-2016 for children (<20 years; A) and adults (≥20 years; B)

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Antibiotic Category	Broad/narrow categorization	Generic names of antibiotics included
Narrower-spectrum penicillins	narrow	amoxicillin, ampicillin, penicillin
First-generation cephalosporins	narrow	cefadroxil, cephalexin, cephradine
Erythromycin[A]	narrow	erythromycin
Beta-lactams, increased activity	broad	amoxicillin-clavulanate
Second-and third-generation cephalosporins	broad	cefaclor, cefprozil, cefuroxime, loracarbef, cefdinir, cefditoren, cefixime, cefpodoxime, ceftibuten
Fluoroquinolones	broad	ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin, trovafloxacin
Macrolides[A]	broad	azithromycin, clarithromycin
Lincosamides	broad	clindamycin
Other	broad	telithromycin
Tetracyclines	exclude	demeclocycline, minocycline, tetracycline, doxycycline
Trimethoprim-sulfamethoxazole	exclude	erythromycin-sulfisoxazole, sulfadiazine, trimethoprim-sulfamethoxazole, sulfisoxazole, sulfisoxazole acetyl, trimethoprim
Broader-spectrum penicillins	exclude	cloxacillin, dicloxacillin, oxacillin
Other	exclude	bacitracin, chloramphenicol, linezolid, neomycin, polymyxin b sulfate, vancomycin, fidaxomicin
Urinary anti-infectives[B]	exclude	Nitrofurantoin, phenazopyridine and combinations, methenamine and combinations, fosfomycin, phosphoric acid, potassium sodium, methylene blue and combinations, nalidixic acid

A Erythromycin is categorized separately from other macrolides due to spectrum of activity.

B Not all drugs classified by IQVIA in the urinary anti-infectives category have anti-infective

activity. We have included them to be consistent with previous estimates [2].

Supplementary Table 2. Prevalence rate ratios comparing annual outpatient oral antibiotic prescription rates to reference year 2011, 2012-2016

Characteristic	Prevalence Rate Ratio (95% Confidence Interval)[A]				
	2012	**2013**	**2014**	**2015**	**2016**
Total	0.99 (0.99-0.99)	0.97 (0.97-0.97)	0.95 (0.95- 0.95)	0.96 (0.96-0.96)	0.95 (0.95-0.95)
Sex					
Male	0.99 (0.99-0.99)	0.97 (0.97-0.97)	0.95 (0.95-0.95)	0.96 (0.96-0.96)	0.95 (0.95-0.95)
Female	1.00 (1.00-1.00)	0.98 (0.98-0.98)	0.96 (0.96-0.96)	0.97 (0.97-0.97)	0.97 (0.97-0.97)
Age group, years					
0-2	0.93 (0.93-0.93)	0.87 (0.87-0.87)	0.82 (0.82-0.82)	0.83 (0.83-0.83)	0.83 (0.82-0.83)
3-9	0.93 (0.93-0.93)	0.88 (0.87-0.88)	0.83 (0.83-0.83)	0.84 (0.84-0.84)	0.85 (0.85-0.85)
10-19	0.97 (0.97-0.97)	0.93 (0.92-0.93)	0.90 (0.90-0.90)	0.91 (0.91-0.91)	0.91 (0.91-0.91)
20-39	1.00 (1.00-1.00)	0.98 (0.98-0.98)	0.97 (0.97- 0.97)	0.98 (0.98-0.98)	0.97 (0.97-0.97)
40-64	1.01 (1.01-1.01)	1.01 (1.01-1.01)	1.01 (1.01-1.01)	1.03 (1.03-1.03)	1.03 (1.03-1.03)
≥65	1.03 (1.03-1.03)	1.03 (1.03-1.03)	1.00 (1.00-1.00)	1.01 (1.01-1.01)	1.02 (1.02-1.02)
US Census Region					
Midwest	0.96 (0.96-0.96)	0.96 (0.96-0.96)	0.95 (0.95-0.95)	0.95 (0.95-0.95)	0.94 (0.94-0.94)
Northeast	0.99 (0.99-0.99)	0.98 (0.98-0.98)	0.97 (0.97-0.97)	0.97 (0.97-0.97)	0.97 (0.97-0.97)
South	1.02 (1.02-1.02)	0.98 (0.98-0.98)	0.96 (0.96-0.96)	0.96 (0.96-0.96)	0.98 (0.98-0.98)
West	0.95 (0.95-0.95)	0.94 (0.94-0.94)	0.92 (0.92- 0.92)	0.94 (0.94-0.95)	0.90 (0.90-0.90)

[A] Rate ratio and 95% confidence interval derived using a Poisson model with a log link with year as a categorical variable and the year 2011 as the reference.

Supplementary Table 3. US outpatient oral antibiotic prescriptions by provider specialty stratified by age group, 2011-2016

Provider Specialty	Children (<20 years) Prescriptions, No. in Millions (%)						P, Test for trend [A]	Adults (≥20 years) Prescriptions, No. in Millions (%)						P, Test for trend [A]
	2011	2012	2013	2014	2015	2016		2011	2012	2013	2014	2015	2016	
Family Practice	13.1 (17.4)	11.8 (16.7)	10.3 (15.4)	9.3 (14.6)	8.7 (13.5)	7.9 (12.3)	<0.01	52.3 (27.3)	52.1 (26.4)	50.1 (25.4)	47.9 (24.2)	47.2 (23.2)	45.4 (22.1)	<0.01
Internal Medicine	2.2 (2.9)	2.0 (2.8)	1.7 (2.6)	1.6 (2.5)	1.4 (2.2)	1.3 (1.9)	<0.01	30.7 (16.0)	30.3 (15.4)	29.3 (14.9)	28.0 (14.1)	27.0 (13.3)	25.9 (12.6)	<0.01
Pediatrics	30.7 (40.8)	28.1 (39.6)	25.8 (38.6)	23.7 (37.1)	23.4 (36.1)	23.3 (35.9)	<0.01	1.7 (0.9)	1.5 (0.8)	1.3 (0.7)	1.4 (0.7)	1.3 (0.6)	1.2 (0.6)	<0.01
Dentistry	2.0 (2.7)	1.9 (2.7)	1.9 (2.8)	1.9 (2.9)	1.9 (2.9)	1.9 (2.9)	<0.01	20.4 (10.6)	21.1 (10.7)	22.2 (11.2)	22.6 (11.4)	23.1 (11.4)	23.8 (11.6)	<0.01
Nurse Practitioner	6.5 (8.6)	6.9 (9.8)	7.6 (11.3)	8.5 (13.3)	10.2 (15.7)	11.4 (17.6)	<0.01	13.3 (6.9)	15.5 (7.9)	17.7 (9.0)	20.6 (10.4)	24.7 (12.2)	28.0 (13.6)	<0.01
Physician Assistants	5.2 (6.9)	5.5 (7.7)	5.9 (8.9)	6.3 (9.8)	7.0 (10.8)	7.2 (11.1)	<0.01	12.6 (6.5)	14.4 (7.3)	16.4 (8.3)	18.1 (9.1)	20.6 (10.2)	21.9 (10.6)	<0.01
Emergency Medicine	3.9 (5.1)	3.6 (5.1)	3.2 (4.8)	3.0 (4.7)	3.1 (4.9)	3.1 (4.7)	0.06	10.5 (5.5)	11.1 (5.7)	10.9 (5.5)	11.0 (5.6)	11.6 (5.7)	11.6 (5.7)	0.21
Surgery	1.4 (1.9)	1.3 (1.9)	1.3 (1.9)	1.3 (2.0)	1.2 (1.9)	1.2 (1.9)	0.80	8.3 (4.3)	8.4 (4.3)	8.5 (4.3)	8.5 (4.3)	8.4 (4.2)	8.5 (4.1)	0.04
Dermatology	2.5 (3.4)	2.3 (3.3)	2.2 (3.3)	2.1 (3.3)	1.9 (2.9)	1.8 (2.8)	0.02	5.7 (3.0)	5.6 (2.9)	5.5 (2.8)	5.4 (2.7)	5.2 (2.5)	5.0 (2.5)	<0.01
Medical Subspecialty	0.4 (0.5)	0.3 (0.5)	0.3 (0.4)	0.3 (0.4)	0.2 (0.4)	0.2 (0.3)	<0.01	7.0 (3.6)	6.9 (3.5)	6.5 (3.3)	6.3 (3.2)	6.2 (3.0)	6.2 (3.0)	<0.01
Obstetrics/ Gynecology	0.6 (0.8)	0.5 (0.7)	0.5 (0.7)	0.4 (0.7)	0.4 (0.6)	0.3 (0.5)	<0.01	6.5 (3.4)	6.4 (3.3)	6.3 (3.2)	6.1 (3.1)	5.9 (2.9)	5.7 (2.8)	<0.01
Urology	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.3 (0.4)	0.2 (0.4)	1.00	6.2 (3.2)	6.2 (3.2)	6.1 (3.1)	6.0 (3.0)	6.0 (2.9)	5.9 (2.9)	<0.01

| Provider Specialty | Children (<20 years) | | | | | | | Adults (≥20 years) | | | | | | |
| | Prescriptions, No. in Millions (%) | | | | | | P, Test for trend [A] | Prescriptions, No. in Millions (%) | | | | | | P, Test for trend [A] |
	2011	2012	2013	2014	2015	2016		2011	2012	2013	2014	2015	2016	
Otolaryn-gology	1.1 (1.5)	1.0 (1.4)	0.9 (1.3)	0.7 (1.2)	0.7 (1.1)	0.7 (1.1)	<0.01	3.0 (1.6)	2.9 (1.5)	2.9 (1.5)	2.8 (1.4)	2.8 (1.4)	2.7 (1.3)	<0.01
Infectious Diseases	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)	1.00	1.2 (0.6)	1.2 (0.6)	1.2 (0.6)	1.2 (0.6)	1.3 (0.7)	1.4 (0.7)	0.04
Internal Medicine/ Pediatrics	0.5 (0.7)	0.5 (0.7)	0.4 (0.7)	0.4 (0.6)	0.4 (0.6)	0.4 (0.6)	0.02	0.8 (0.4)	0.8 (0.4)	0.8 (0.4)	0.8 (0.4)	0.8 (0.4)	0.8 (0.4)	1.00
Pediatric Subspecialty	0.7 (0.9)	0.6 (0.9)	0.6 (0.9)	0.6 (0.9)	0.6 (0.9)	0.6 (0.9)	1.00	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	0.1 (0.0)	1.00
Unspecified Specialty	2.3 (3.1)	2.3 (3.2)	2.0 (3)	1.8 (2.8)	1.4 (2.1)	1.4 (2.1)	0.01	5.1 (2.7)	5.6 (2.8)	5.0 (2.5)	4.7 (2.4)	3.8 (1.9)	3.6 (1.8)	<0.01
Other	1.8 (2.3)	1.8 (2.5)	1.9 (2.8)	1.8 (2.8)	1.8 (2.7)	1.8 (2.8)	0.06	6.6 (3.5)	6.8 (3.4)	6.7 (3.4)	6.7 (3.4)	7.3 (3.6)	7.5 (3.7)	0.14

Abbreviations: No., Number.

[A] P-value of T-test for slope of linear model of year (continuous) as a predictor of proportion of antibiotic prescriptions (continuous).

Supplementary Figure 1. US outpatient oral antibiotic prescriptions per 1,000 persons by state in 2011-2016 for children (<20 years; A) and adults (≥20 years; B)

A

B

Outpatient antibiotic
prescriptions per 1,000 persons

320-653	654-748	749-860
861-927	928-1033	1038-1538
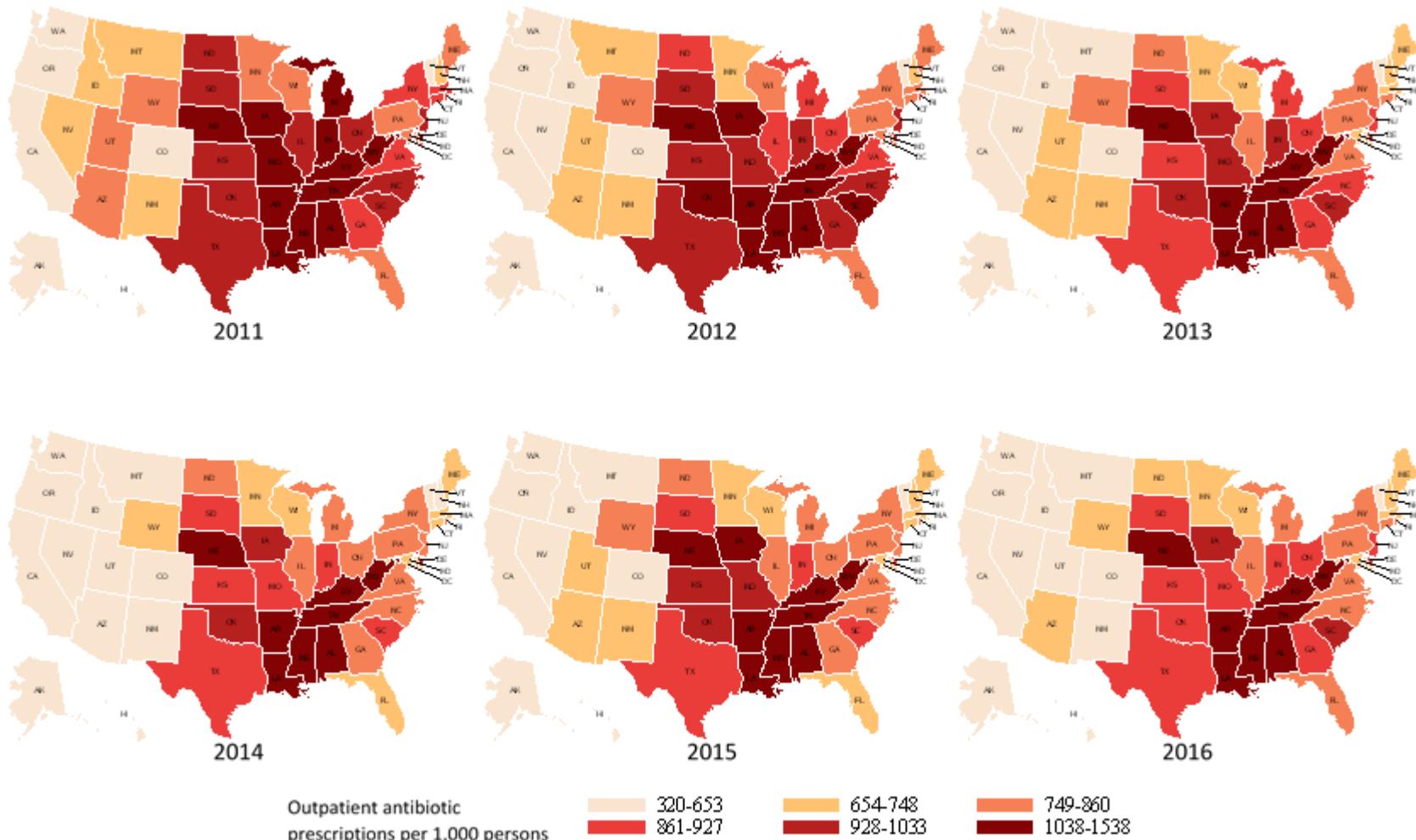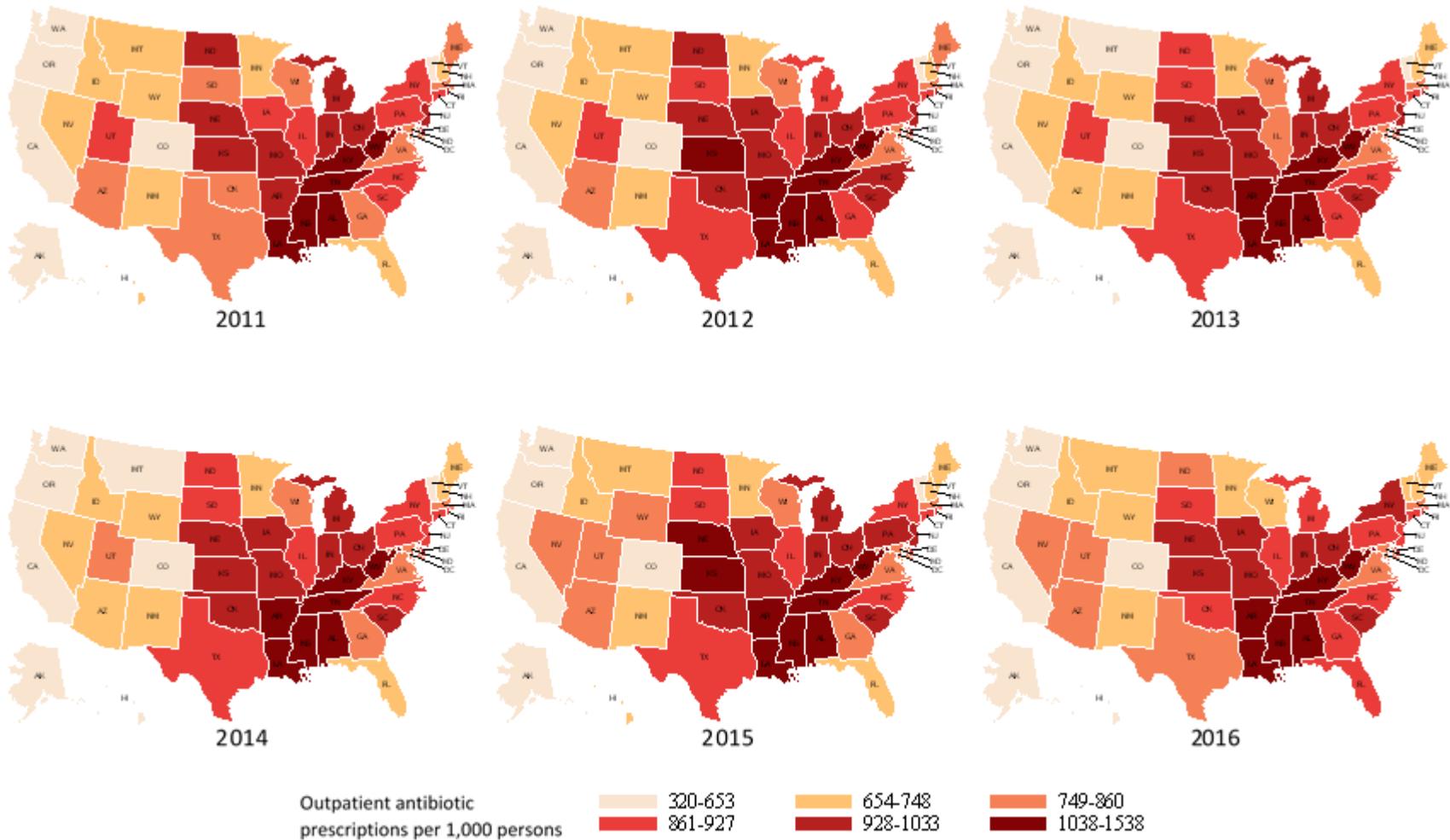
Supplementary Data References

1.   ECDC (European Centre for Disease Prevention and Control), EFSA BIOHAZPanel

        (European Food Safety Authority Panel on Biological Hazards), CVMP (EMA

        Committee for Medicinal Products for Veterinary Use). ECDC, EFSA and EMA Joint

        Scientific Opinion on a list of outcome indicators as regards surveillance of antimicrobial

        resistance and antimicrobial consumption in humans and food-producing animals. EFSA

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2.   Hicks LA, Bartoces MG, Roberts RM, et al. US outpatient antibiotic prescribing variation

        according to geography, patient population, and provider specialty in 2011. Clin Infect

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