Keeping West Virginia Wild, Wonderful, and Well!

A New Initiative in Outpatient Antimicrobial Stewardship

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The West Virginia Antibiotic Awareness Team

Disclosures

- This work is grant-supported by the West Virginia Department of Health & Human Resources (WV DHHR)

- This webinar is not financially supported by the West Virginia Immunizations Network (WIN), but we are sincerely thankful for continued partnership

Objectives

- Introduction to antimicrobial stewardship
- Describe national, regional, and local data related to antimicrobial use in WV
- Summarize treatment recommendations for common infections managed in the outpatient setting (e.g. respiratory, urinary and skin/soft tissue infections)
- Introduce the stewardship team & current initiatives
- Connect with networks of providers across the state to identify key factors influencing antimicrobial stewardship barriers & successes

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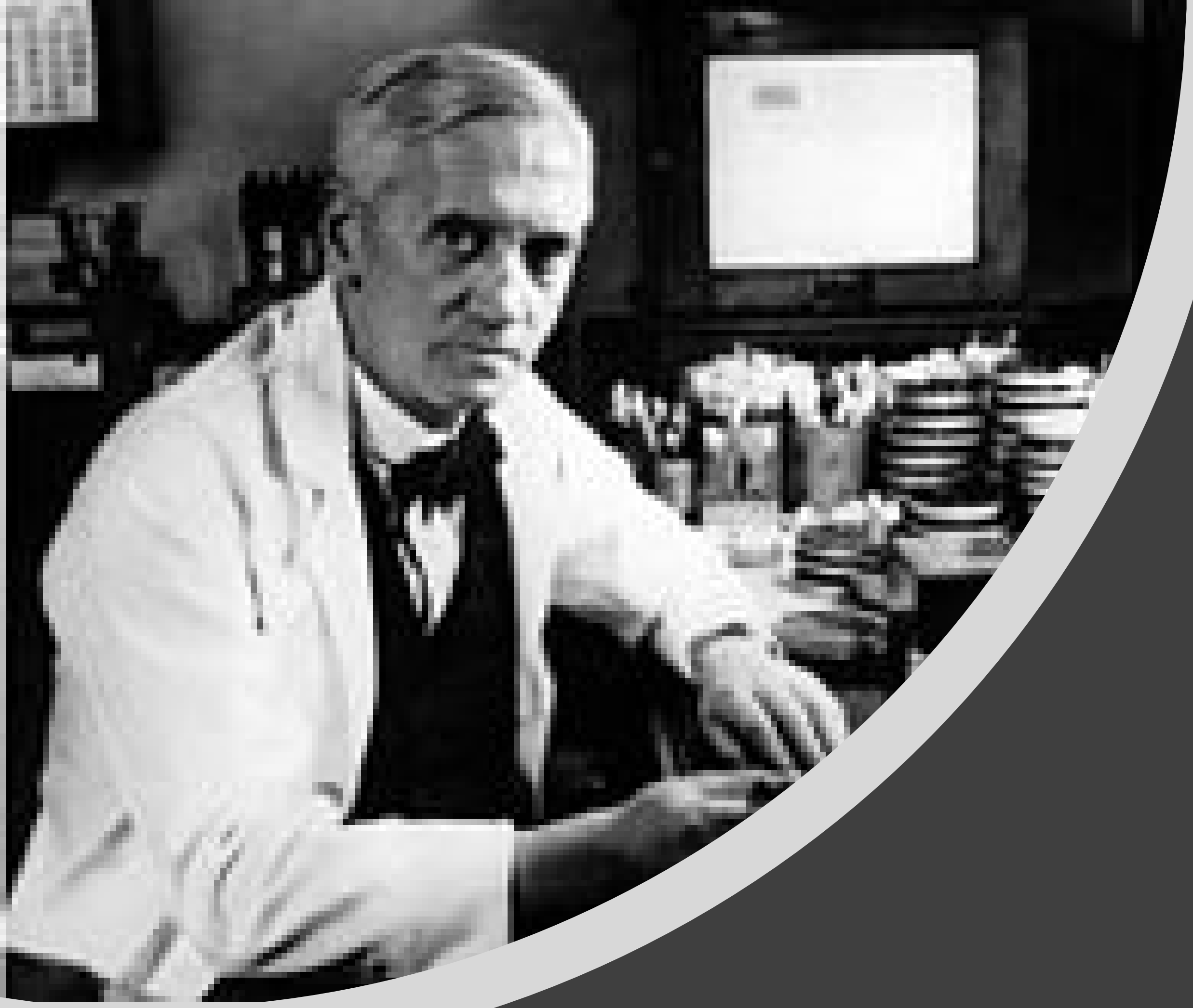
“For most of the infectious diseases on the wards of Boston City Hospital in 1937, there was nothing that could be done beyond bed rest and good nursing care. Then came the explosive news of sulfanilamide, and the start of the real revolution in medicine.”

- Lewis Thomas

Notes of a Medicine Watcher

1983 Viking Press

Source: twitter



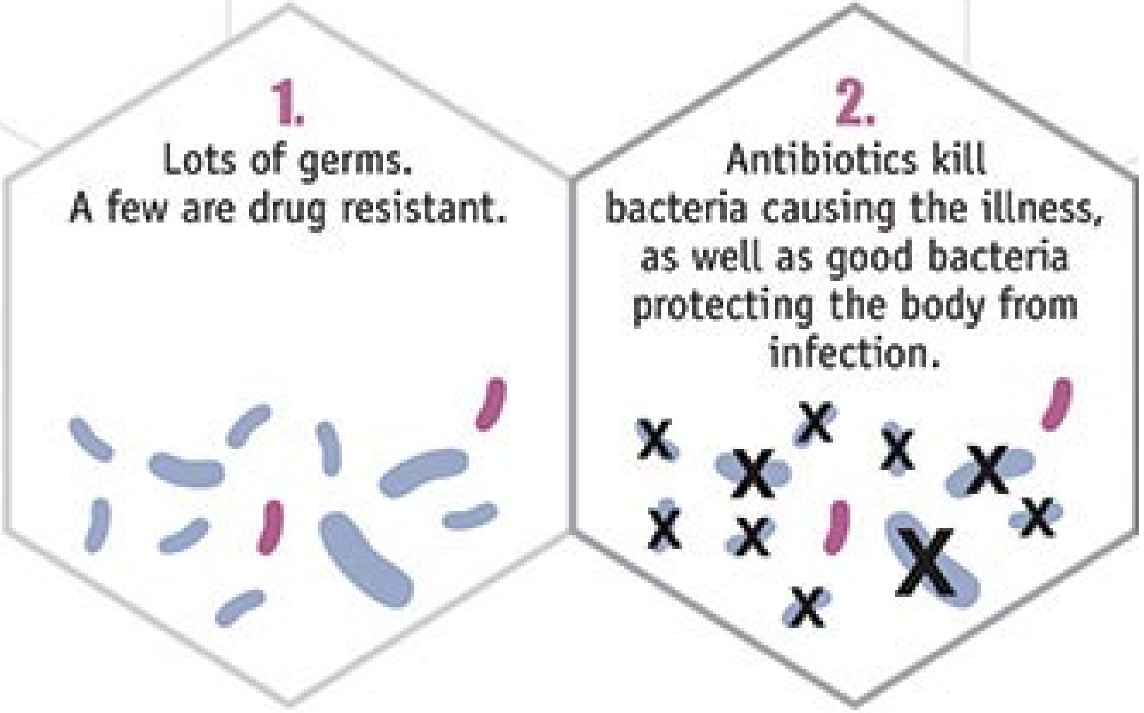
"The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who succumbs to infection with the penicillin-resistant organisms."

- Alexander Fleming

How Antibiotic Resistance Happens

West Virginia Antibiotic Awareness

How Antibiotic Resistance Happens



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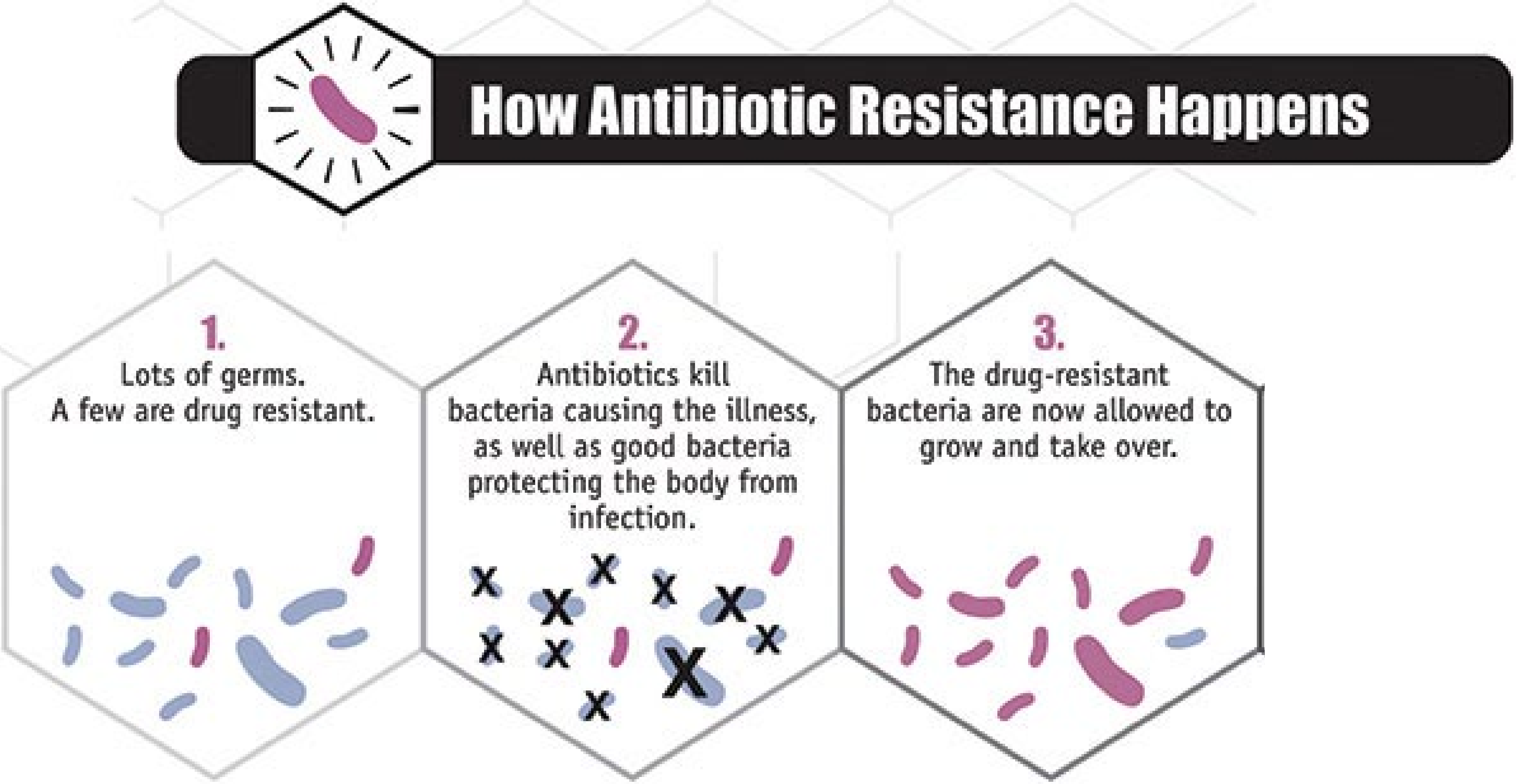

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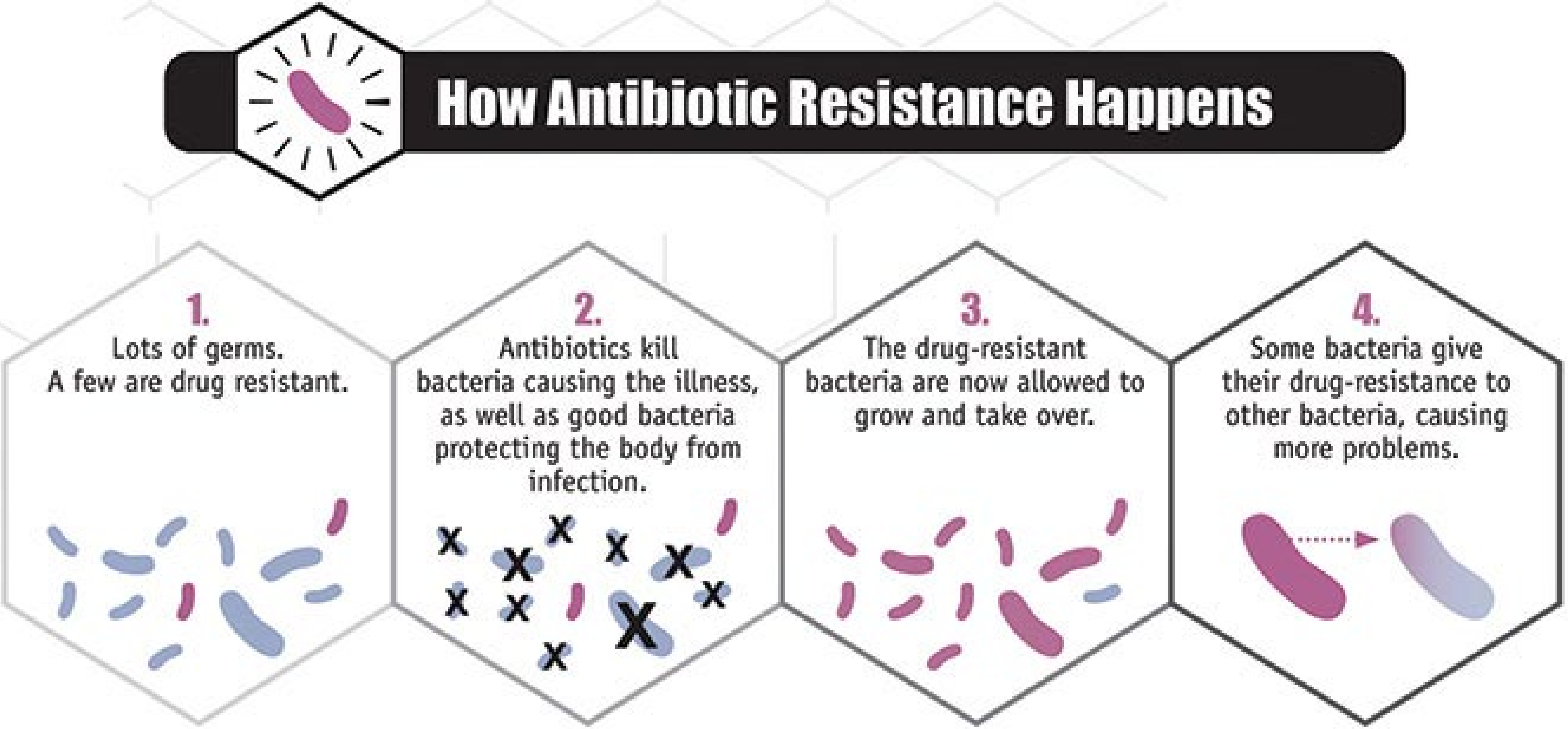
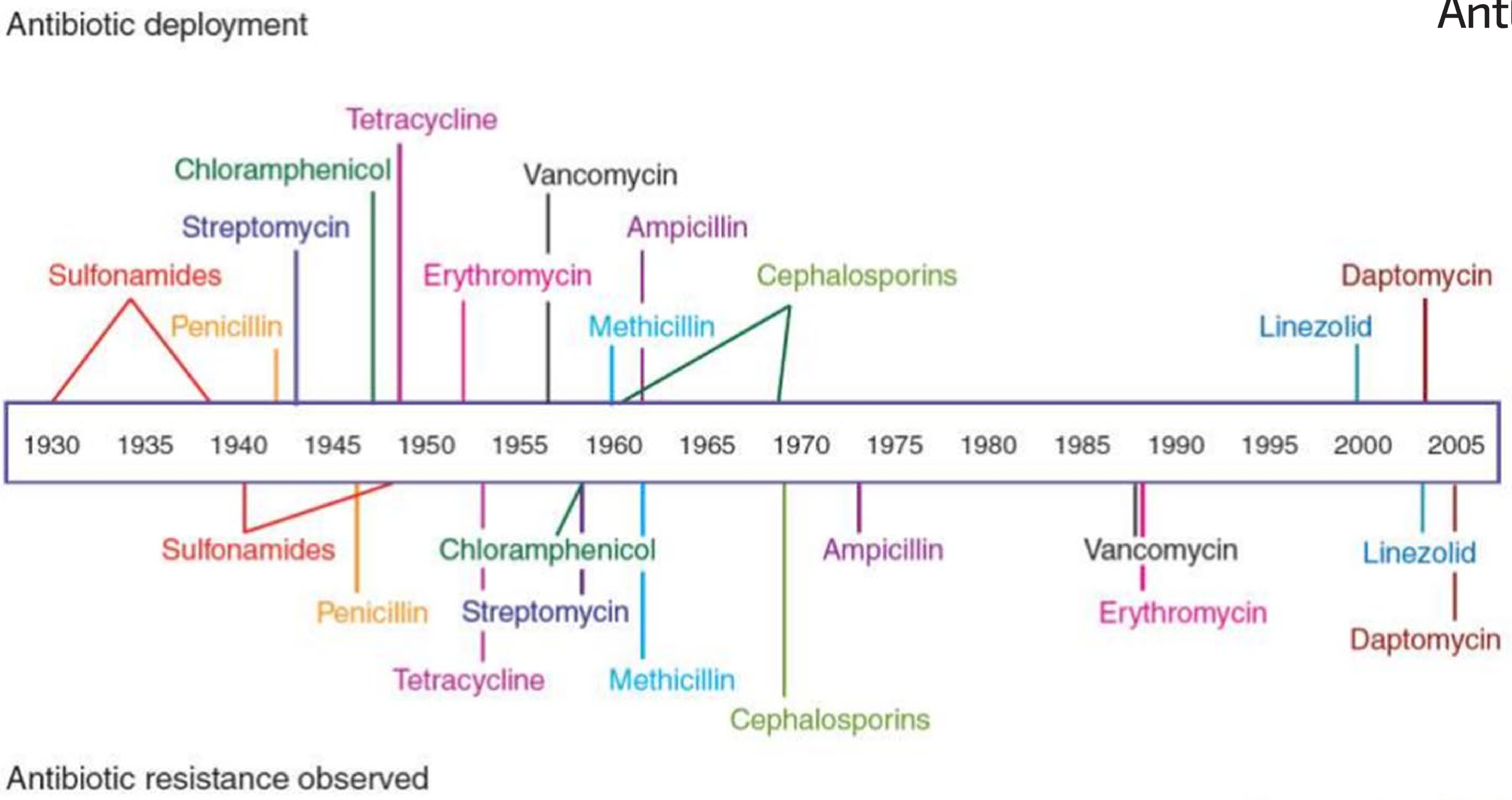


How Antibiotic Resistance Happens

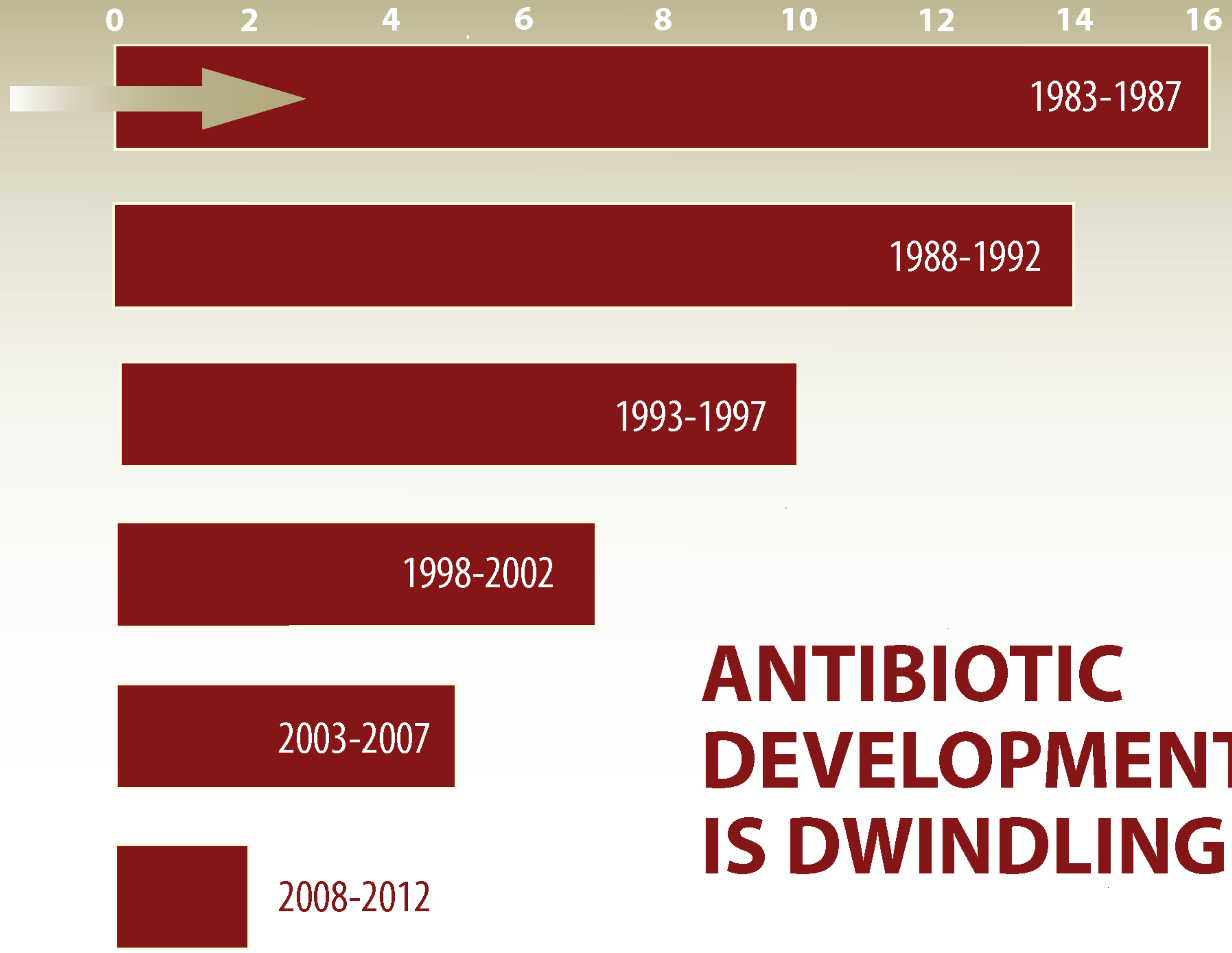
EVERY DOSE , EVERY DAY OF ANTIMICROBIAL EXPOSURE COUNTS!



Clatworthy 2007

Penicillin	Vancomycin	Imipenem	Daptomycin
• Discovered 1943	• Discovered 1972	• Discovered 1985	• Discovered 2003
• Resistance 1945	• Resistance 1988	• Resistance 1998	• Resistance 2004
(2 years)	(16 years)	(13 years)	(1 year)

Total Number of New Antibacterial Agents



ANTIBIOTIC DEVELOPMENT IS DWINDLING

Source: *The Epidemic of Antibiotic-Resistant Infections*, CID 2008:46 (15 January)
Clin Infect Dis. (2011) May 52 (suppl 5): S397-S428. doi: 10.1093/cid/cir153

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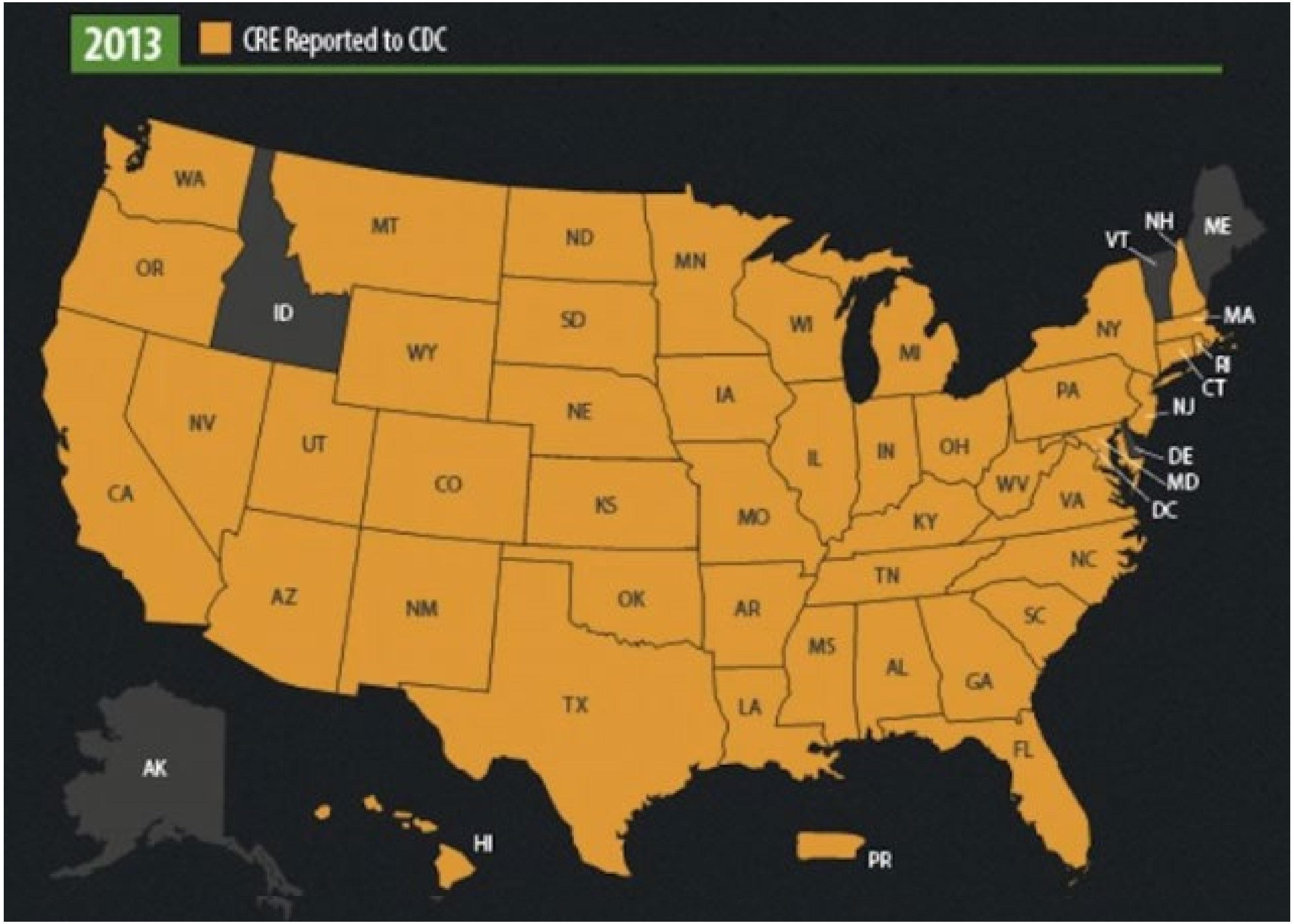
2013
CRE Reported to CDC
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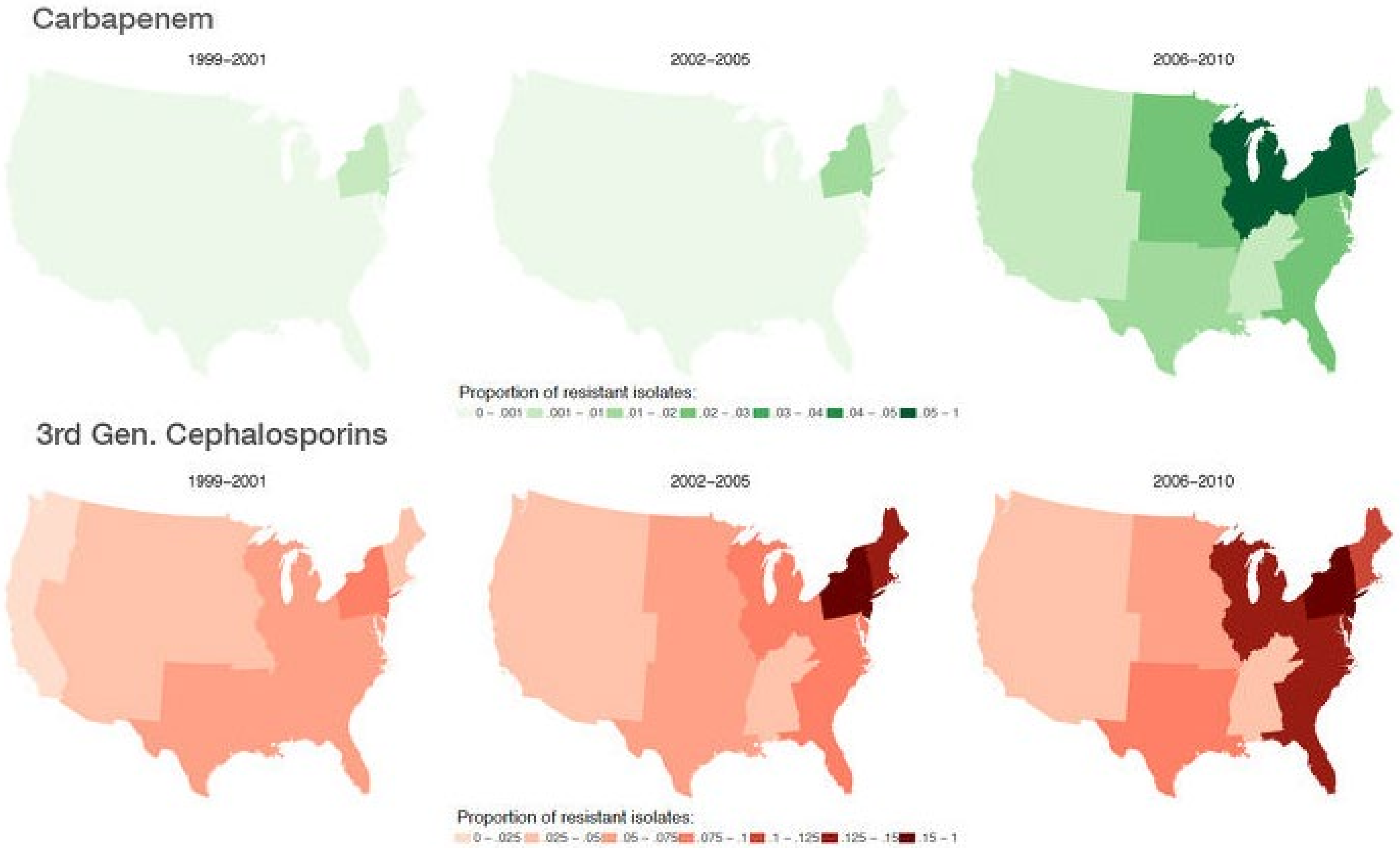
Carbapenem and 3rd. gen. cephalosporin resistance among *K. pneumoniae* highest along the East Coast, but present in all regions of the country

West Virginia Antibiotic Awareness



Note: Data for 2010 available through July.

Data source: Braykov NB, Eber MR, Klein EY, Morgan DJ, Laxminarayan R. Trends in Resistance to Carbapenems and Third- Generation Cephalosporins among Clinical Isolates of Klebsiella pneumoniae in the United States, 1999-2010. Infect Control and Hospital Epidemiology. 2013; 34(3)

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

Why Care?


ANTIBIOTIC RESISTANCE THREATS IN THE UNITED STATES
2019

New National Estimate*

Each year, antibiotic-resistant bacteria and fungi cause at least an estimated:

2,868,700 infections

35,900 deaths

+

*Clostridioides difficile*** is related to antibiotic use and antibiotic resistance:

223,900 cases

12,800 deaths

Reference: https://www.cdc.gov/drugresistance/biggest-threats.html

Urgent Threats

- Carbapenem-resistant Acinetobacter
- Candida auris
- Clostridioides difficile
- Carbapenem-resistant Enterobacteriaceae
- Drug-resistant Neisseria gonorrhoeae

Serious Threats

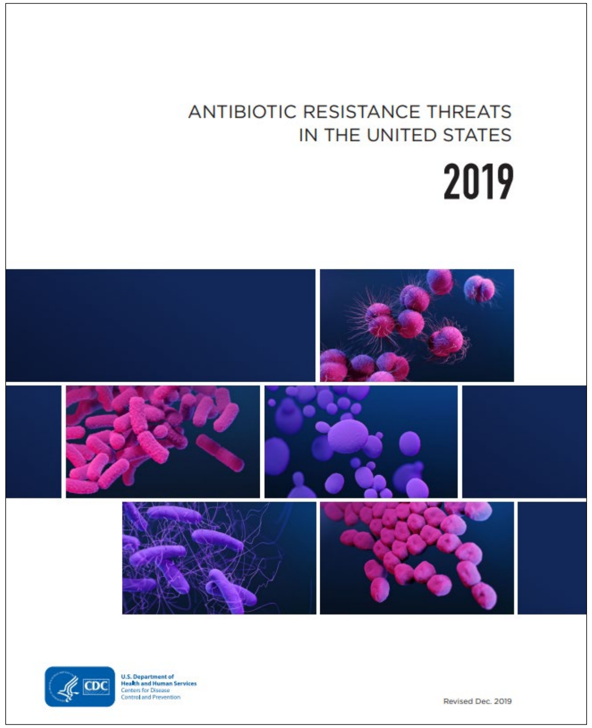
- Drug-resistant Campylobacter
- Drug-resistant Candida
- ESBL-producing Enterobacteriaceae
- Vancomycin-resistant Enterococci
- Multidrug-resistant Pseudomonas aeruginosa
- Drug-resistant nontyphoidal Salmonella
- Drug-resistant Salmonella serotype Typhi
- Drug-resistant Shigella
- Methicillin-resistant Staphylococcus aureus
- Drug-resistant Streptococcus pneumoniae
- Drug-resistant Tuberculosis

Concerning Threats

- Erythromycin-resistant group A Streptococcus
- Clindamycin-resistant group B Streptococcus

Watch List

- Azole-resistant Aspergillus fumigatus
- Drug-resistant Mycoplasma genitalium
- Drug-resistant Bordetella pertussis



Reference: https://www.cdc.gov/drugresistance/biggest-threats.html

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

*Antimicrobial Resistance Collaborators**

Summary

Background Antimicrobial resistance (AMR) poses a major threat to human health around the world. Previous publications have estimated the effect of AMR on incidence, deaths, hospital length of stay, and health-care costs for specific pathogen–drug combinations in select locations. To our knowledge, this study presents the most comprehensive estimates of AMR burden to date.

Lancet 2022; 399: 629–55

Published Online January 20, 2022 https://doi.org/10.1016/S0140-6736(21)02724-0

- **4·95 million** (3·62-6·57) deaths associated with bacterial AMR
- **1·27 million** (95% UI 0·911-1·71) deaths attributable to bacterial AMR

Antibiotic resistance and patient outcomes

- Increase in mortality, morbidity, length of hospitalization and cost of care
  - *S. aureus*
  - *Enterococcus* species
  - Gram-negative bacilli

- Delays in therapy or severity of illness likely contribute to worse outcomes.

Cosgrove S, CID 2006


DON'T PANIC
VALTERIO

Potential harms associated with antimicrobial treatment

- Antimicrobial resistance
- *Clostridium difficile* infections
- Idiosyncratic reactions
- Changes to the pediatric microbiome
- Side effects /safety profile of each antibiotic

Clostridium difficile infections

- Almost half a million infections are reported among patients in USA within a single year.
- 30,000 died within 30 days of diagnosis
- 76% of CDI in children had preceding antibiotic use.
- CDI in children is attributed to 7-12 admissions per 10,000 (KIDS database)
- Pediatric CDI is associated with increase mortality, longer length of hospitalization and higher costs among hospitalized children.

Lessa et. Al, N Engl J Med 2015
Sandora, PIDJ 2011
Zilberg, EID 2010
Sammons, CID 2013

Idiosyncratic reactions

- Steven Johnson Syndrome
- DRESS Syndrome
- Interstitial nephritis
- Drug Fever
- Serum Sickness
- Nicolau Syndrome

Changes in the microbiome

- Linked to obesity
- Linked to auto-immune illness
- Linked to asthma/allergies
- Significant alteration in microbiome of exposed neonates

1. Lassiter C. J Dairy Sci. 1955; Cho, Nature 2012; Trehan, NEJM 2013, 2016, Gough EK BMJ, Saari et al, Pediatrics, 2015, Bailey JAMA peds 2014, Gerber 2016
2. Horton, Pediatrics, 2015, *Pediatrics 2012;130:e794-e803*
3. Hirsch, AG Clin Exp Allergy, 2016, Metsala, Clinical and Experimental Immunology, 2014

U.S. ED visits for adverse drug events form antibiotics in children 2011-2015

- NEISS-CADES project (CDC, US consumer product safety commission and FDA)
- About 70,000 national visits for adverse events due to drugs
- Assuming that 29-41% of outpatient prescribing is inappropriate, that amounts to **20,000-28,000 ED visits simply due to unnecessary antibiotics**.

Lovegrove, JPIDS 2018

U.S. ED visits for adverse drug events form antibiotics in children 2011-2015

- 69,464 ED visits for antibiotic AEs each year
- 46.2% of all ED visits for adverse drug events
- 40.7% involved children less than 2 years old
- 86.1% involved an allergic reaction
- Amoxicillin was the most frequent

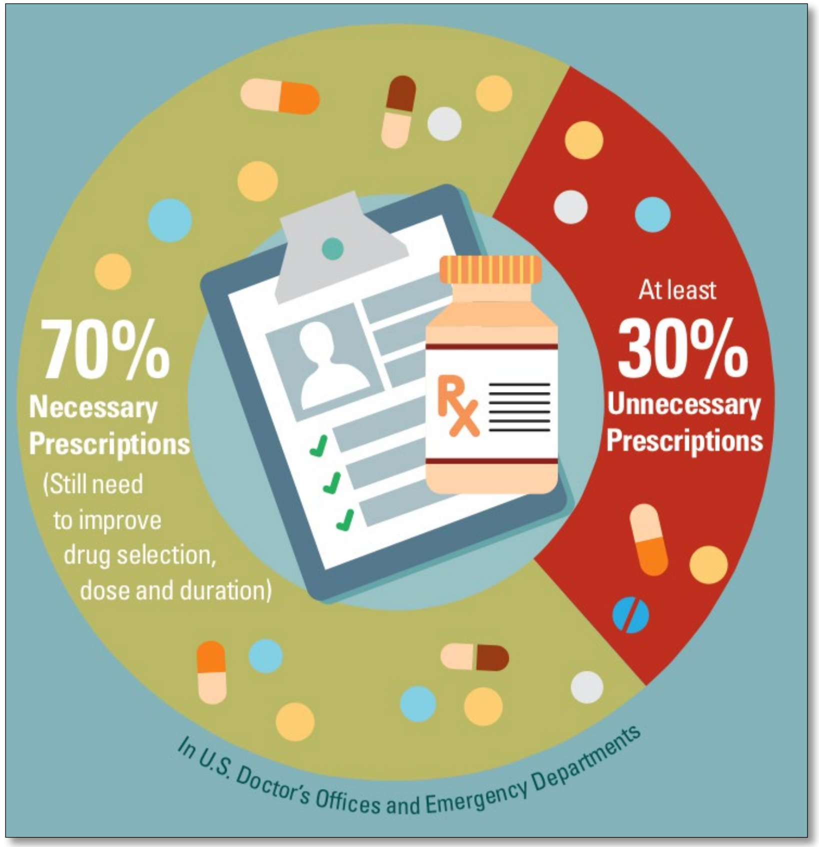
Lovegrove, JPIDS 2018

Importance of Outpatient Stewardship

- An estimated **80-90%** of antibiotic use occurs in the *outpatient setting*

- At least **30%** of antibiotics prescribed in the outpatient setting are <u>unnecessary</u>

- A recent study by the CDC found only **50%** of outpatient antibiotic prescribing was for the recommended first-line antibiotic[1]



https://www.cdc.gov/antibiotic-use/stewardship-report/outpatient.html

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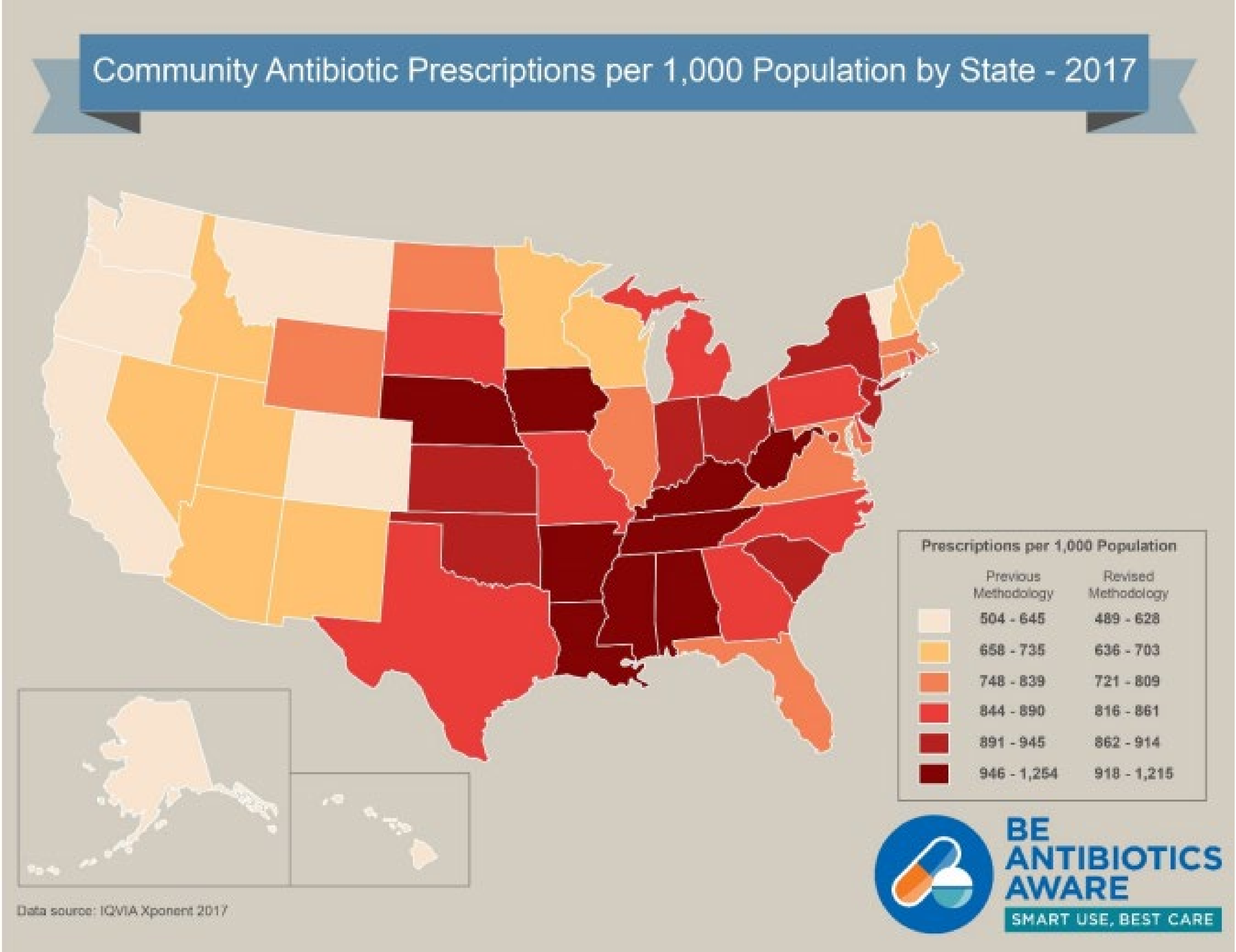
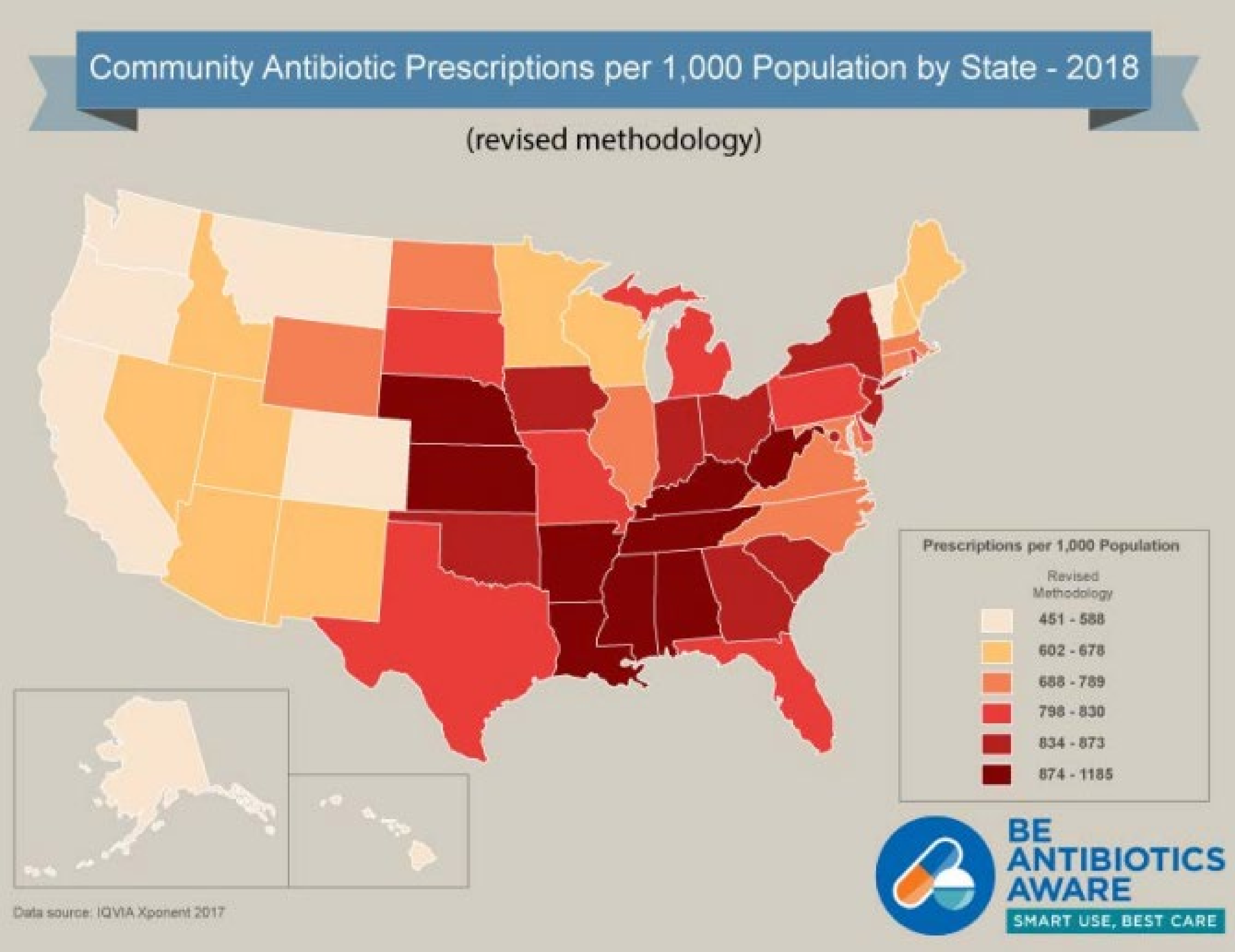
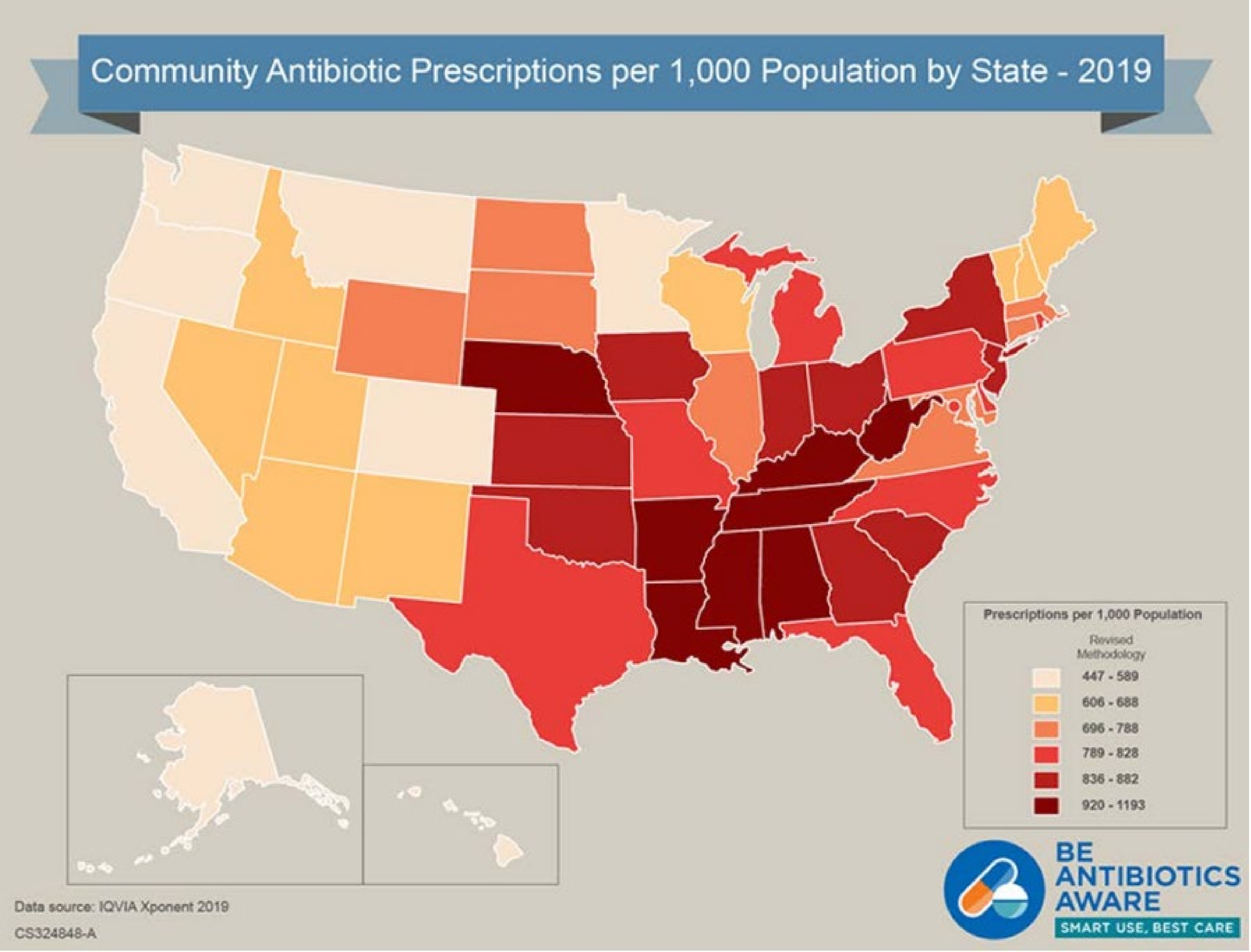


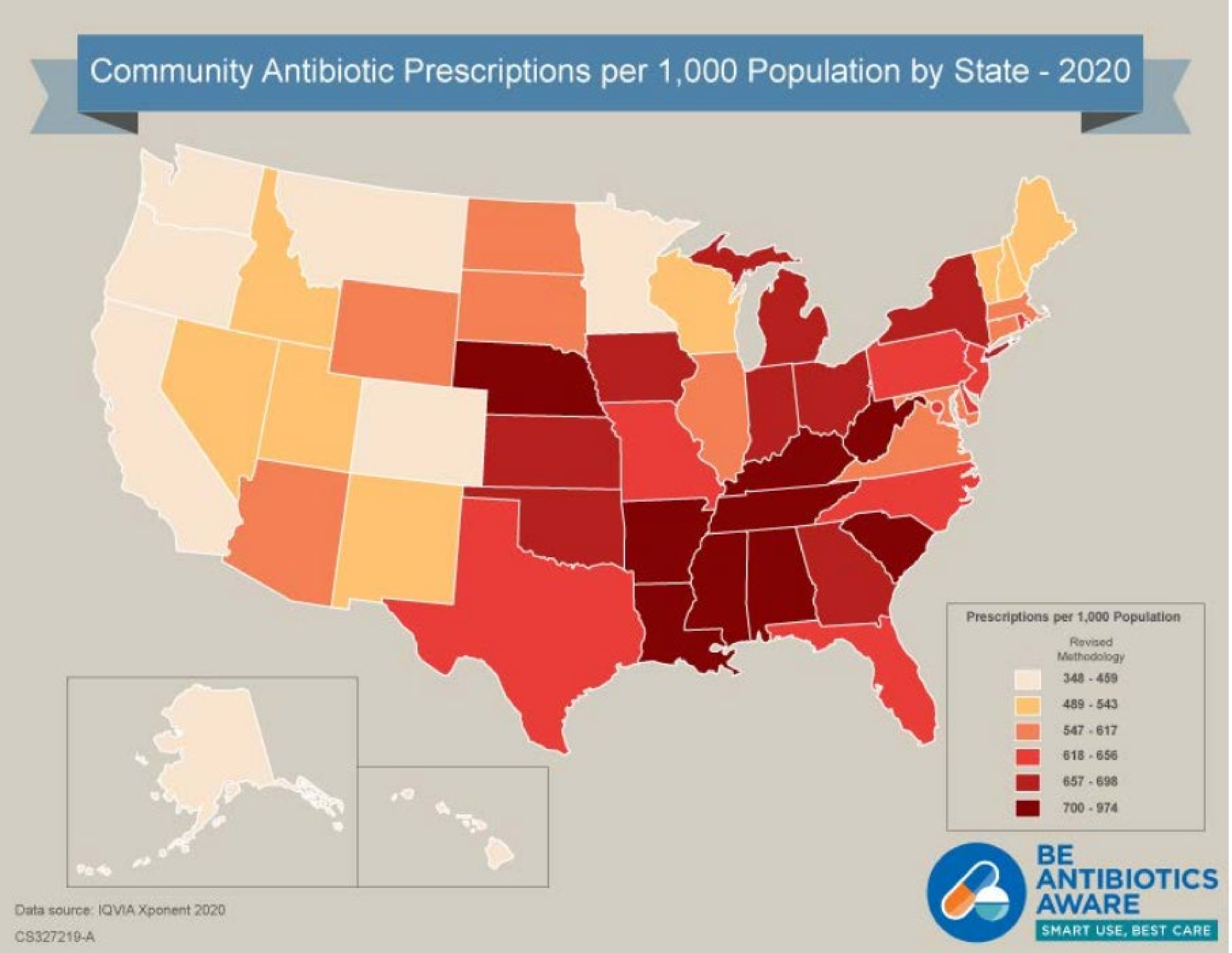
West Virginia 1st
1,215 prescriptions
per 1,000 population



West Virginia 1st
1,185 prescriptions
per 1,000 population



West Virginia 1st
1,193 prescriptions
per 1,000 population



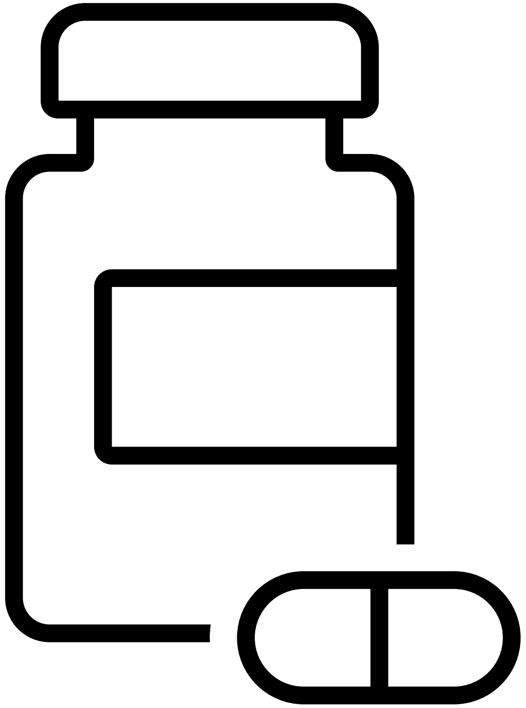
West Virginia 1st
974 prescriptions per 1,000 population

CDC Data - 2020

Rank	Location	Rate (per 1,000 population)
1	West Virginia	974
2	Mississippi	956
3	Alabama	922
4	Louisiana	920
5	Kentucky	887
6	Arkansas	844
7	Tennessee	842
8	Nebraska	718
9	South Carolina	700
10	Ohio	698

Why outpatient ASP in West Virginia?

- Identified a clear need
- Limited resources & unique obstacles
- Opportunity to serve & make a sustainable difference
- Long-term commitment & ongoing research opportunities including state & privately-funded partnerships



WV Pediatric Medicaid Project

- **Model study:** Smith MJ, et al. Kentucky Medicaid Outpatient Prescribing
- **Data use agreement (DUA):** Marshall, WV Medicaid, Duke
- **IRB:** Marshall IRB exemption
- **Data source:** Medicaid pharmacy and medical claims data
- **Study type:** cross-sectional analysis
- **Target population:** patients aged 0 months to 19 years who received an oral antibiotic prescription between January 1, 2018 & December 31, 2019

Primary Study Aims

- **Aim 1a:** Exploratory analysis reviewing WV medical and pharmacy pediatric Medicaid claims data to establish baseline demographic and clinical descriptive statistics to guide ASP interventions.
- **Aim1b:** Hypothesis generation for future analysis including models assessing diagnosis-specific prescribing, choice and duration of antibiotic therapy, potential modification across the population, etc.
- **Hypothesis:** pediatric Medicaid patients received broad-spectrum, outpatient antibiotics at higher rates than national average

Study Results

*This work has been published in the *Journal of Pediatric Infectious Diseases Society* (*JPIDS*) under the following reference:

Kilgore JT, Lanata MM, Willis JM, McCarthy MJ, Becker JB, Evans JE, Smith MJ. Utilization of West Virginia Pediatric Medicaid Claims Data to Guide Outpatient Antimicrobial Stewardship Interventions. *JPIDS*, 2021;piab125, PMID: 34939655. DOI: 10.1093/jpids/piab125.

Table 1. WV pediatric (<20 years) Medicaid patient population demographic summary by CY.

	CY 2018				CY 2019			
	Patients	Rxs	%	Rate per 1,000	Patients	Rxs	%	Rate per 1,000
Total (all WV Medicaid Claims)	204,606	234,482		1,146	201,925	224,847		1,114
Provider type / Specialty								
Physician / Pediatrics		39,983	17.1%			38,349	17.1%	
Physician / Other Specialty[a]		59,501	25.4%			51,759	23.0%	
Other Provider[a] / Pediatrics		5,278	2.3%			4,912	2.2%	
Other Provider / Other Specialty		129,720	55.3%			129,827	57.7%	
Spectrum of antibiotic coverage								
Broad-spectrum		107,551	45.9%			100,847	44.9%	
Narrow-spectrum		126,931	54.1%			124,000	55.2%	
Race/ethnicity								
African American / Non-Hispanic	25,039	25,570	10.9%	1,021	25,607	26,333	11.7%	1,028
Caucasian / Non-Hispanic	151,606	180,770	77.1%	1,192	148,341	172,010	76.5%	1,160
Other[c]	27,961	28,142	12.0%	1,006	27,977	26,504	11.8%	947
Sex								
Female	101,040	125,941	53.7%	1,246	99,664	120,274	53.5%	1,207
Male	103,564	108,541	46.3%	1,048	102,261	104,573	46.5%	1,023
Age Groupings (years)[c]								
0-2	34,732	48,719	20.8%	1,403	33,964	45,642	20.3%	1,344
3-9	75,220	91,328	39.0%	1,214	73,223	87,828	39.1%	1,199
10-19	94,654	94,435	40.3%	998	94,738	91,377	40.6%	965
Geographic location (WVMR)								
WVMR 1	47,304	48,842	20.8%	1,033	46,838	48,056	21.4%	1,026
WVMR 2	54,472	61,819	26.4%	1,135	54,701	60,100	26.7%	1,099
WVMR 3	49,469	52,425	22.4%	1,060	49,461	49,554	22.0%	1,002
WVMR 4	46,291	65,027	27.7%	1,405	46,048	63,314	28.2%	1,375
Geographic location (population density)								
Rural	28,457	36,373	1,278	28,114	34,674		1,233	28,457
Suburban	55,289	71,784	1,298	54,487	68,402		1,255	55,289
Urban	120,230	125,398	1,043	118,827	121,205		1,020	120,230

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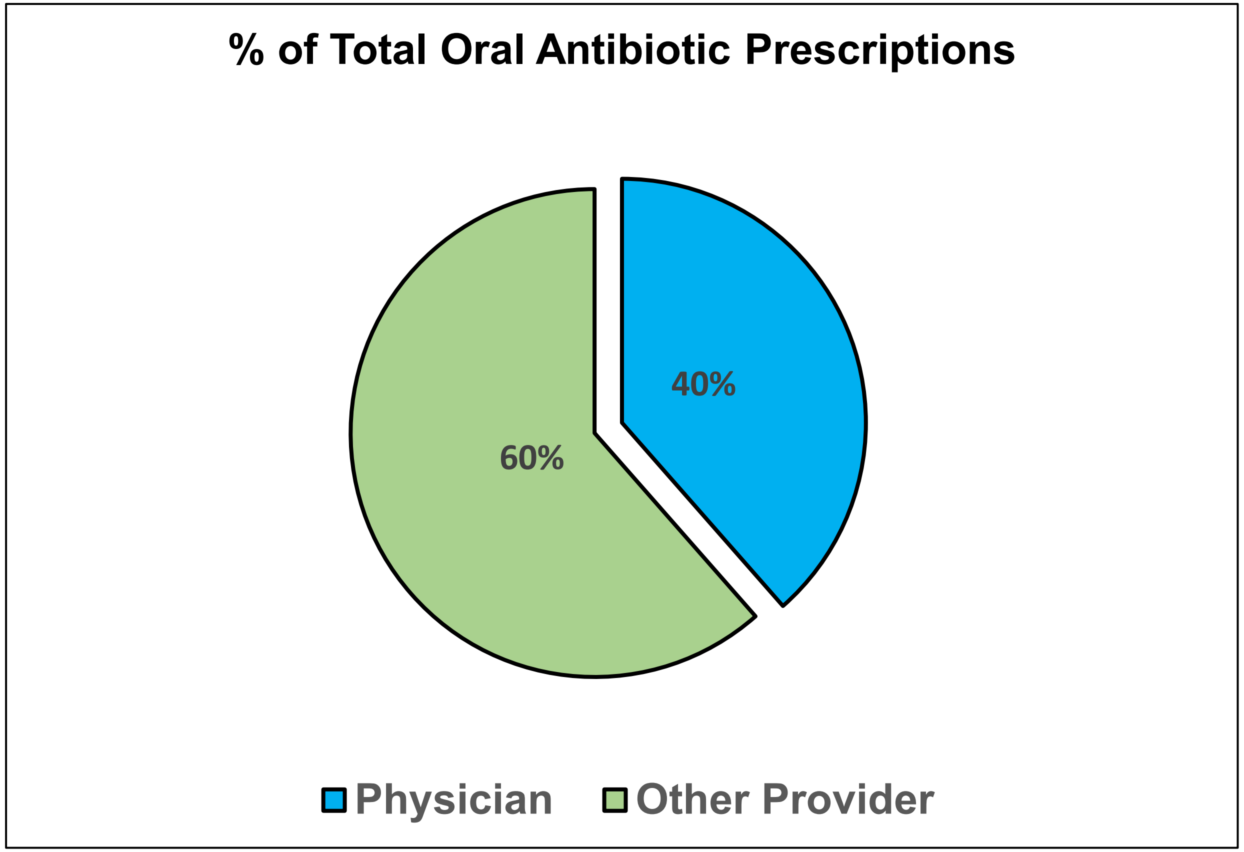
Figure 1. Antibiotic prescribing in WV children, 2019.



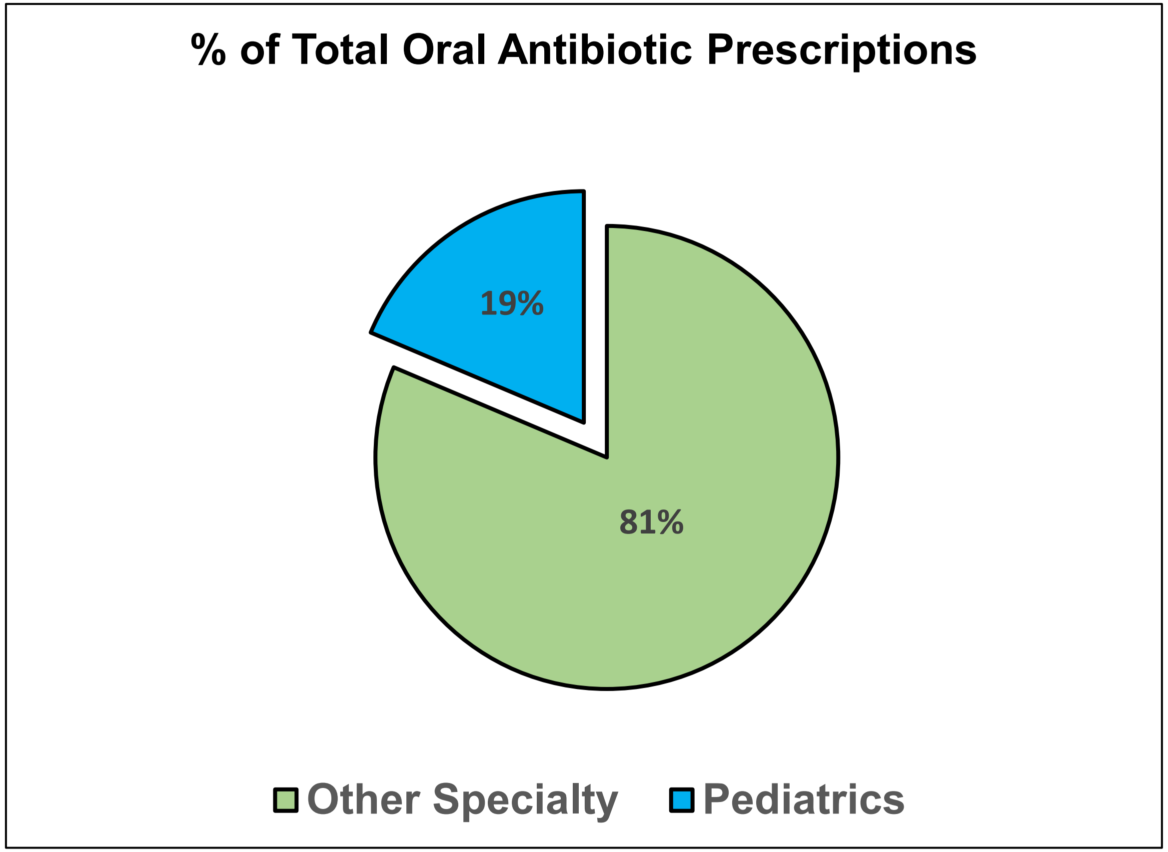


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Figure 2. Antibiotic prescribing in WV children, 2019.

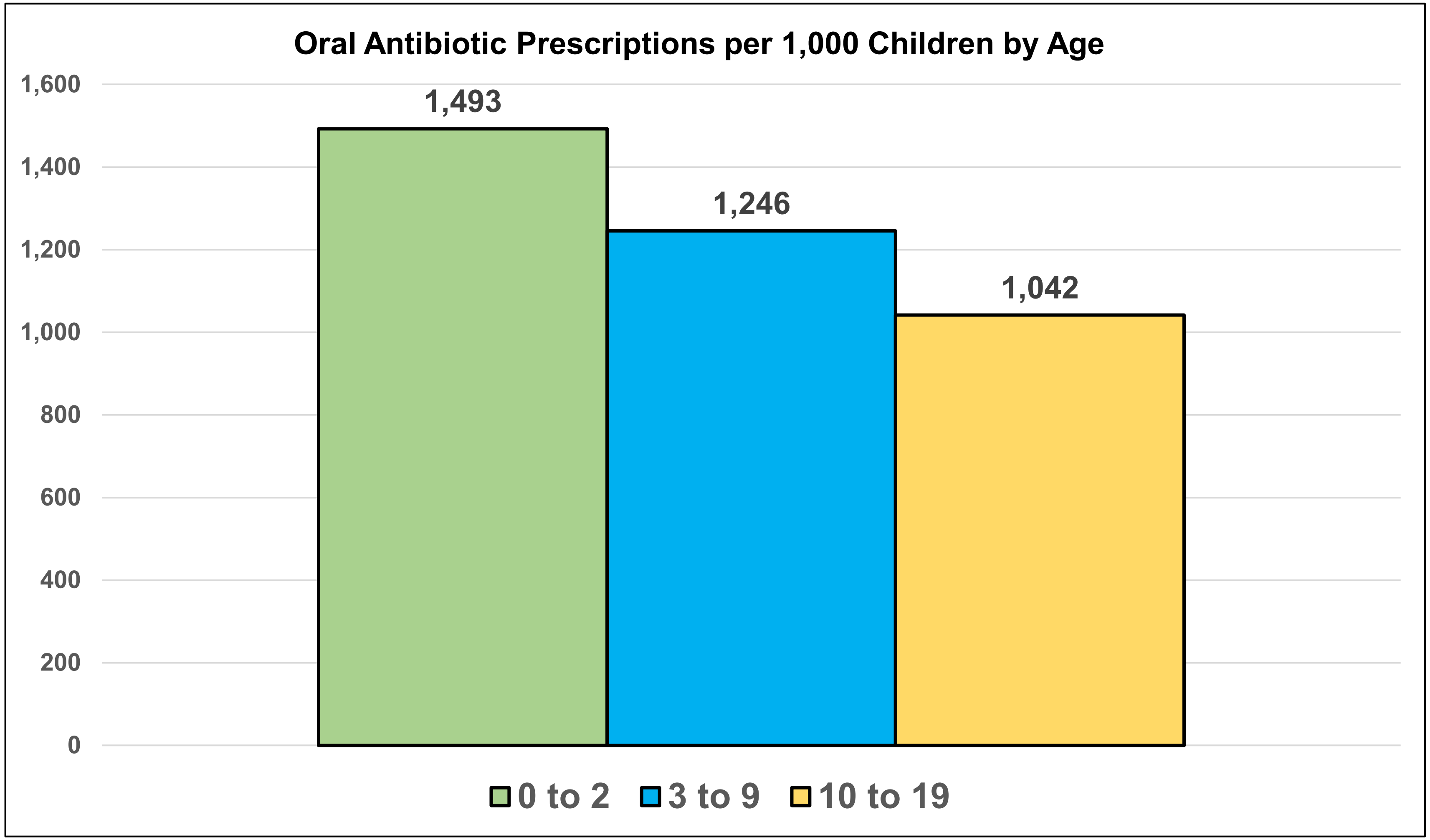

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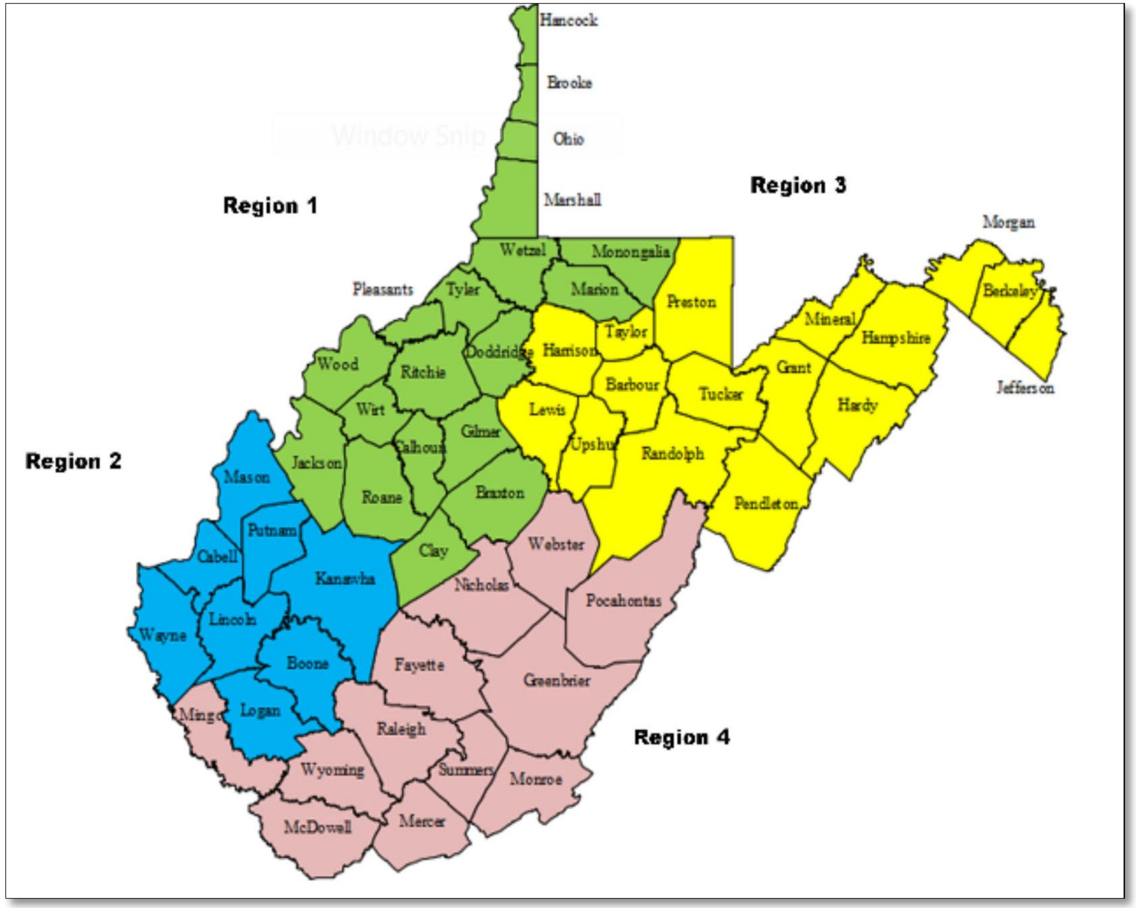
Figure 3. Antibiotic prescribing in WV children, 2019.



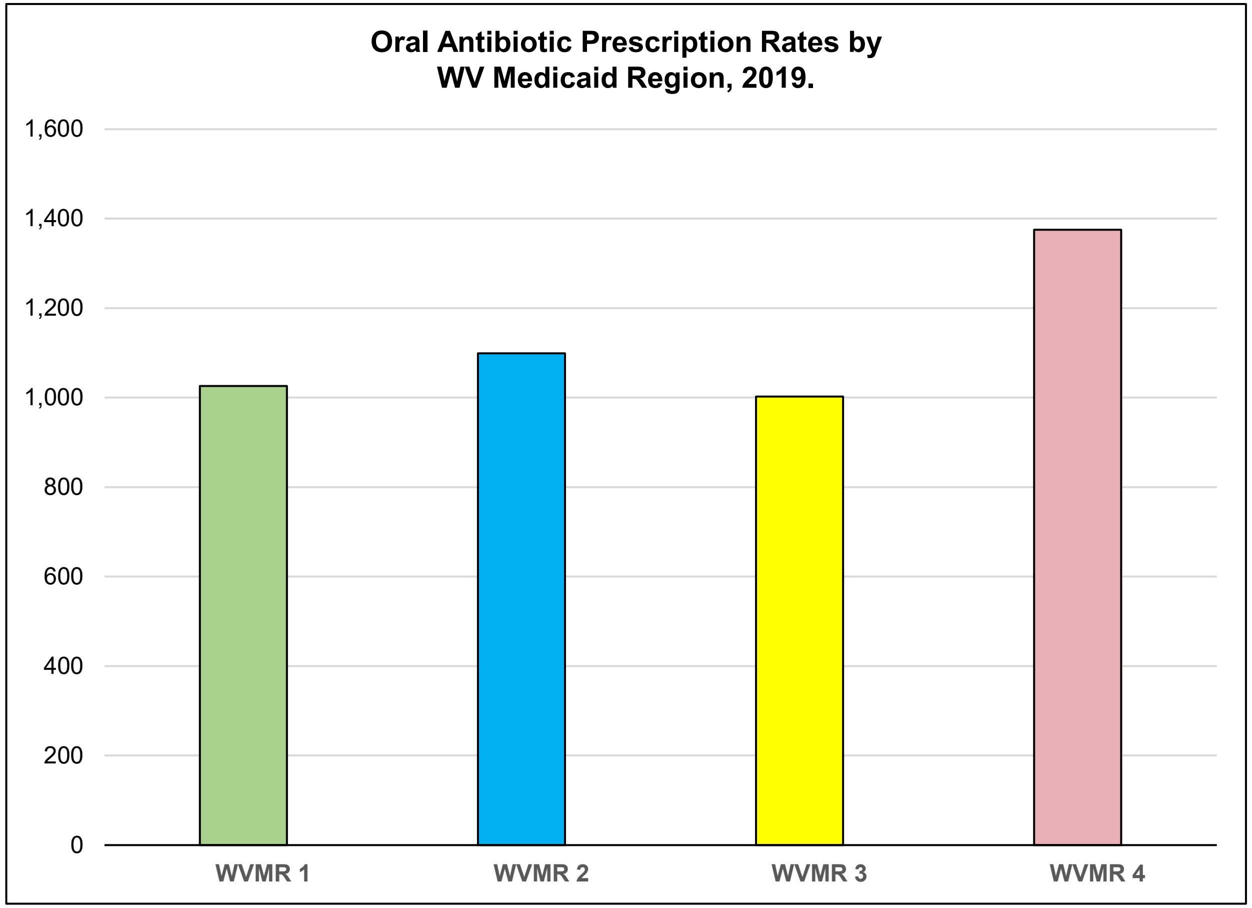


Figure 4. GIS mapping of prescriptions per 1,000 WV children by county, WVMR with total cost & CY, 2018 *(4a,c)* & 2019 *(4b,d)*.

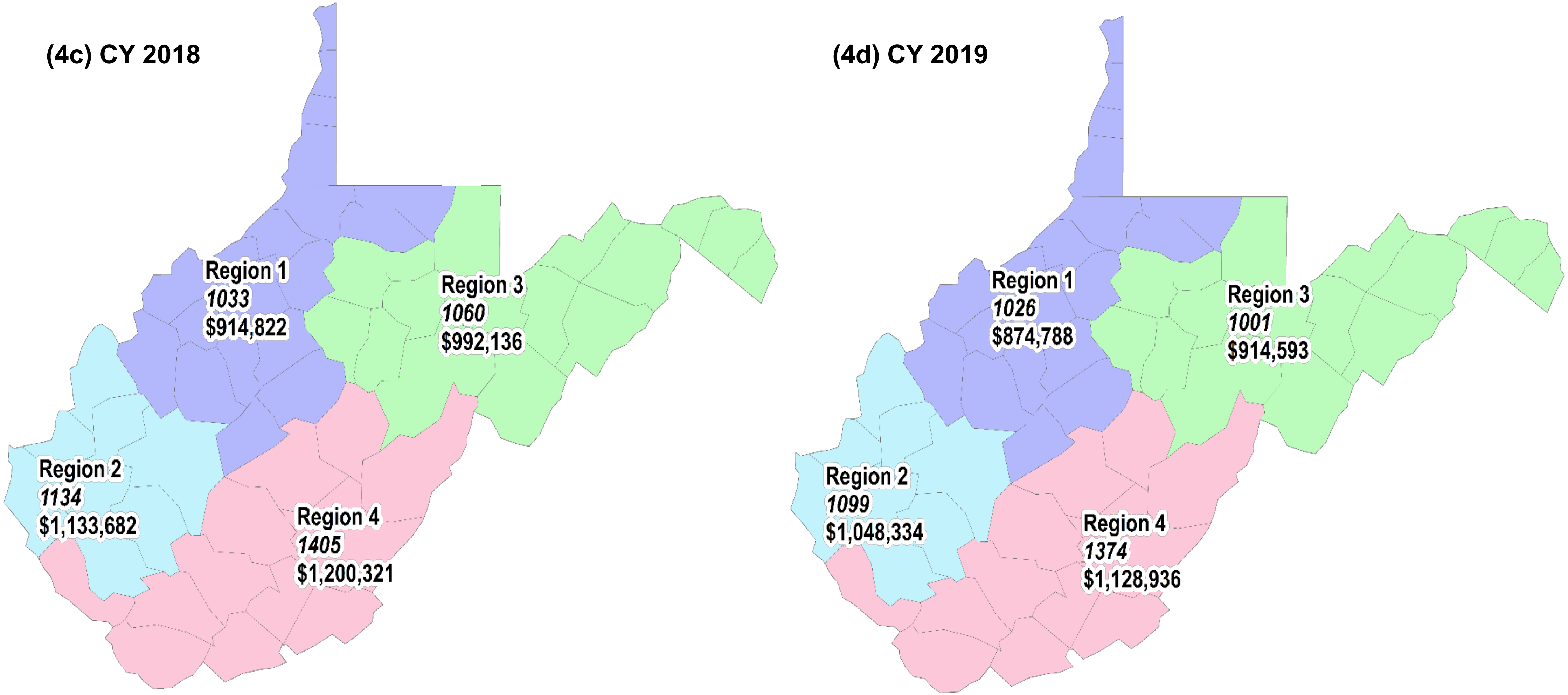


Table 2. Total WV Medicaid spending (USD $) by CY.

Oral Antibiotic Prescriptions, Age 0-19 (*n* = 204,606 children, 2018; n = 201,925 children, 2019)					
CY	Total Prescriptions	Prescriptions per 1,000 children	Total Spending, oral (USD $)	Total Spending, all (USD $)	Average spending per prescription, oral (USD $)
2018	234,482	1,146	$4,366,091	$7,796,701	$18.62
2019	224,847	1,114	$4,041,687	$7,731,375	$17.98

Table 3. Review of top 10 most prescribed oral antibiotics, CYs 2018 & 2019.

Top 10 most prescribed oral antibiotics	Prescription frequency (% annual total)		Total spending (USD $), (% annual total)	
	CY 2018	CY 2019	CY 2018	CY 2019
Amoxicillin	83,286 (35.5)	81,632 (36.3)	$1,017,390 (23.3)	$1,025,222 (25.4)
Cefdinir	39,167 (16.7)	39,096 (17.4)	$906,407 (20.8)	$758,034 (18.8)
Azithromycin	33,821 (14.4)	29,950 (13.3)	$528,174 (12.1)	$450,242 (11.1)
Amoxicillin clavulanate	28,789 (12.3)	27,579 (12.3)	$680,053 (15.6)	$599,090 (14.8)
Trimethoprim-sulfamethoxazole (TMP-SMX)	14,689 (6.3)	13,170 (5.9)	$327,323 (7.5)	$267,202 (6.6)
Cephalexin	12,798 (5.5)	12,849 (5.7)	$250,034 (5.7)	$245,155 (6.1)
Doxycycline	4,812 (2.1)	5,212 (2.3)	$96,117 (2.2)	$82,583 (2.0)
Minocycline	3,774 (1.6)	3,465 (1.5)	$77,592 (1.8)	$69,744 (1.7)
Nitrofurantoin	3,393 (1.4)	3,054 (1.4)	$166,435 (3.8)	$315,968 (7.8)
Clindamycin	3,188 (1.4)	2,963 (1.3)	$110,366 (2.5)	$102,666 (2.5)
	CY 2018	CY 2019	CY 2018	CY 2019
Total 10 most prescribed oral antibiotics, total (%)	227,717 (97.1)	218,970 (97.4)	$4,159,891 (95.3)	$3,915,906 (96.9)
All oral antibiotics, total (100%)	234,465	224,828	$4,365,719	$4,041,143

Figure 5. Antibiotic prescribing in WV children, 2019.

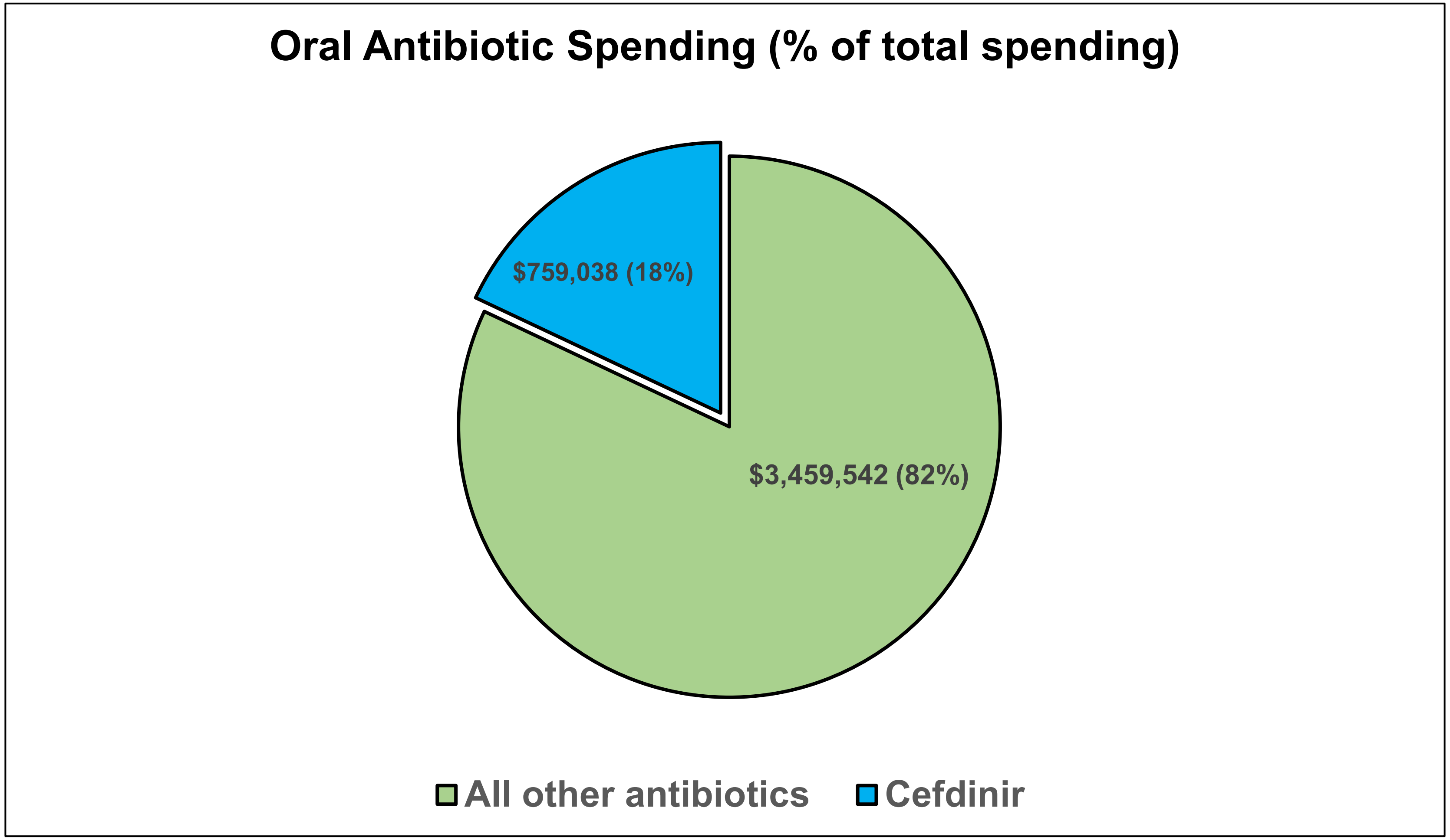


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Figure 6a. Top 5 antibiotic prescription frequencies for common outpatient infectious diagnoses, CY 2018 & 2019.

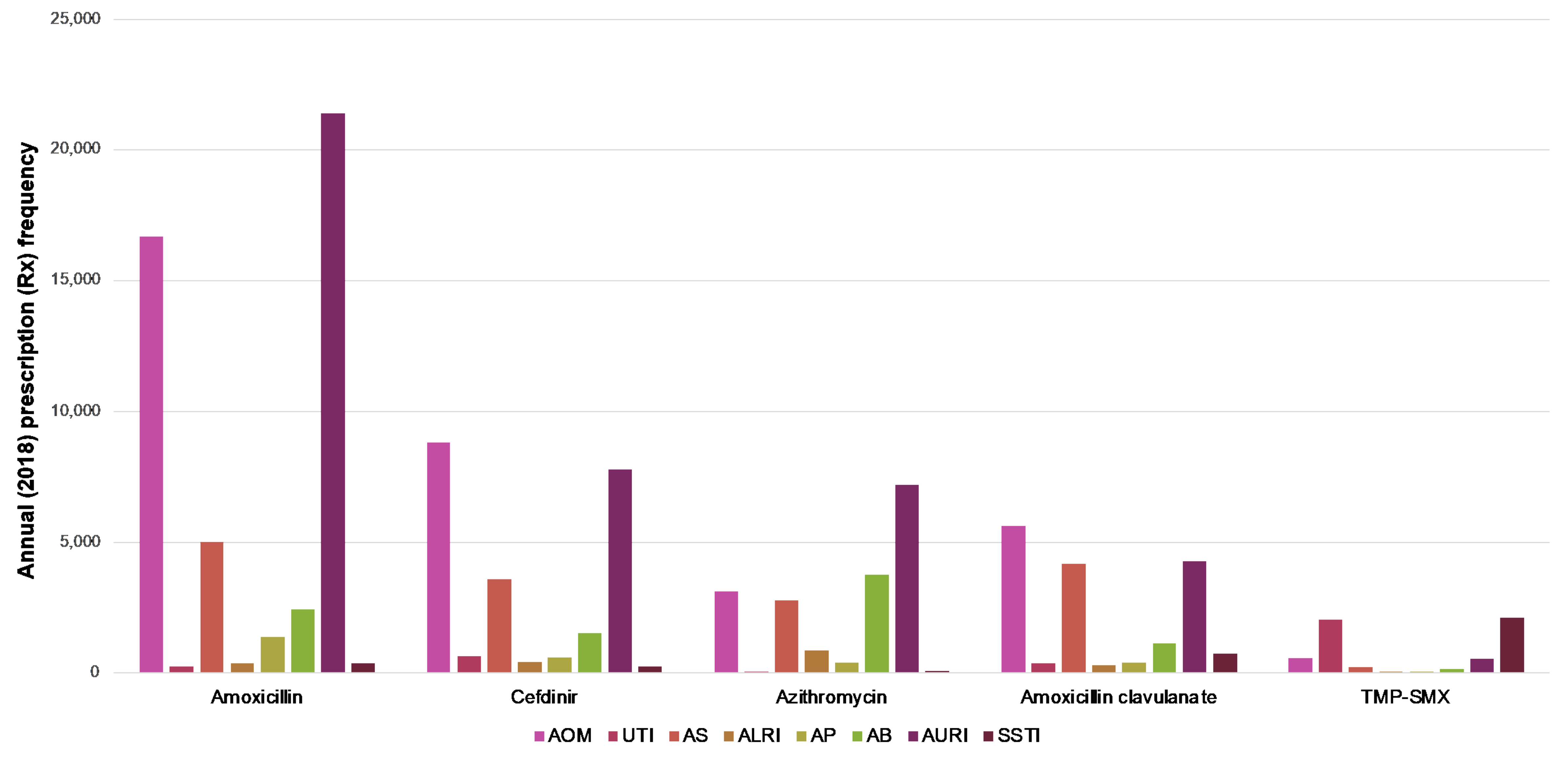
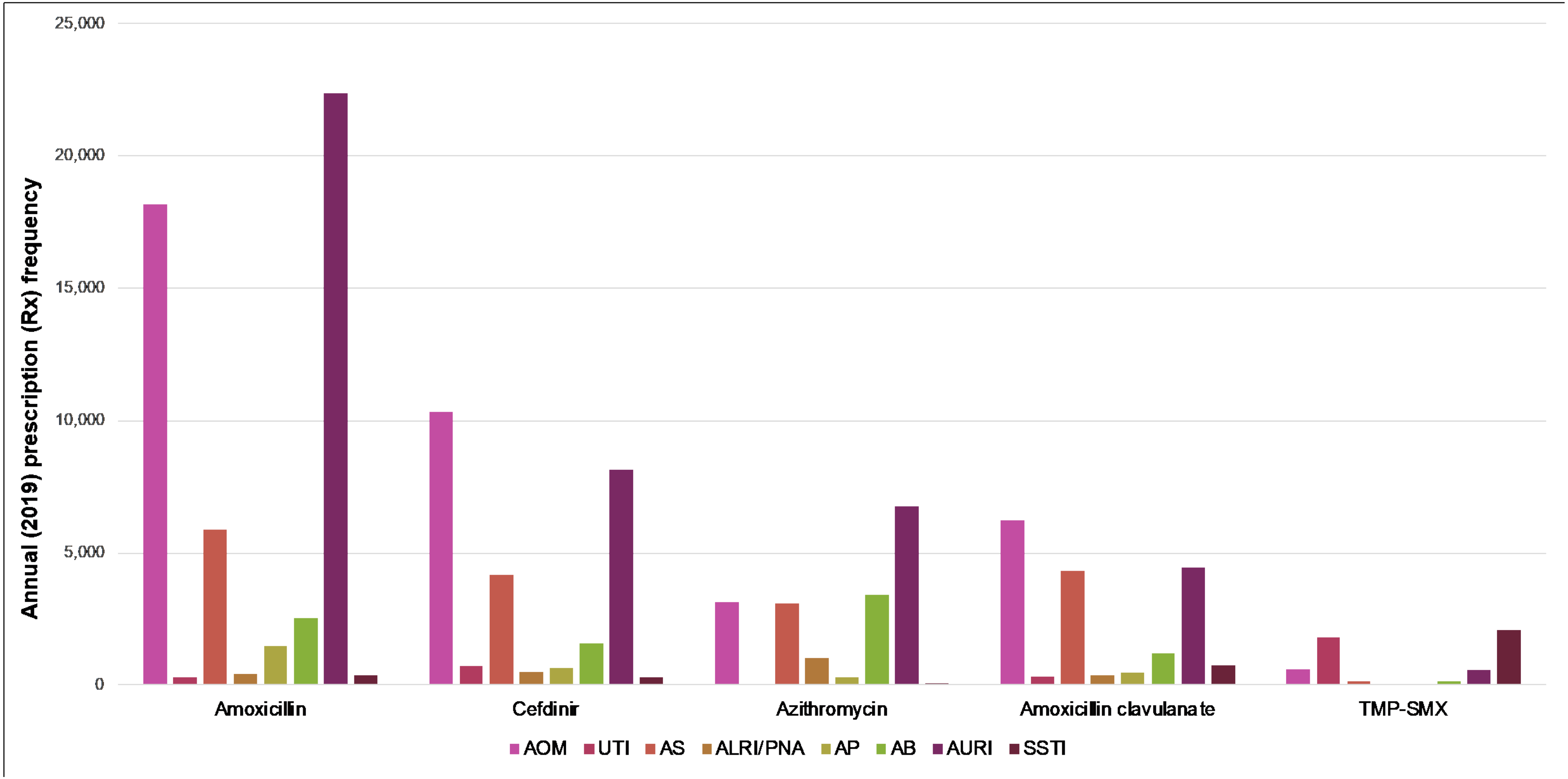


Figure 6b. Top 5 antibiotic prescription frequencies for common outpatient infectious diagnoses, CY 2018 & 2019.



How can we make this better?


500

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- **Summarize treatment recommendations for common infections managed in the outpatient setting (e.g. respiratory, urinary and skin/soft tissue infections)**
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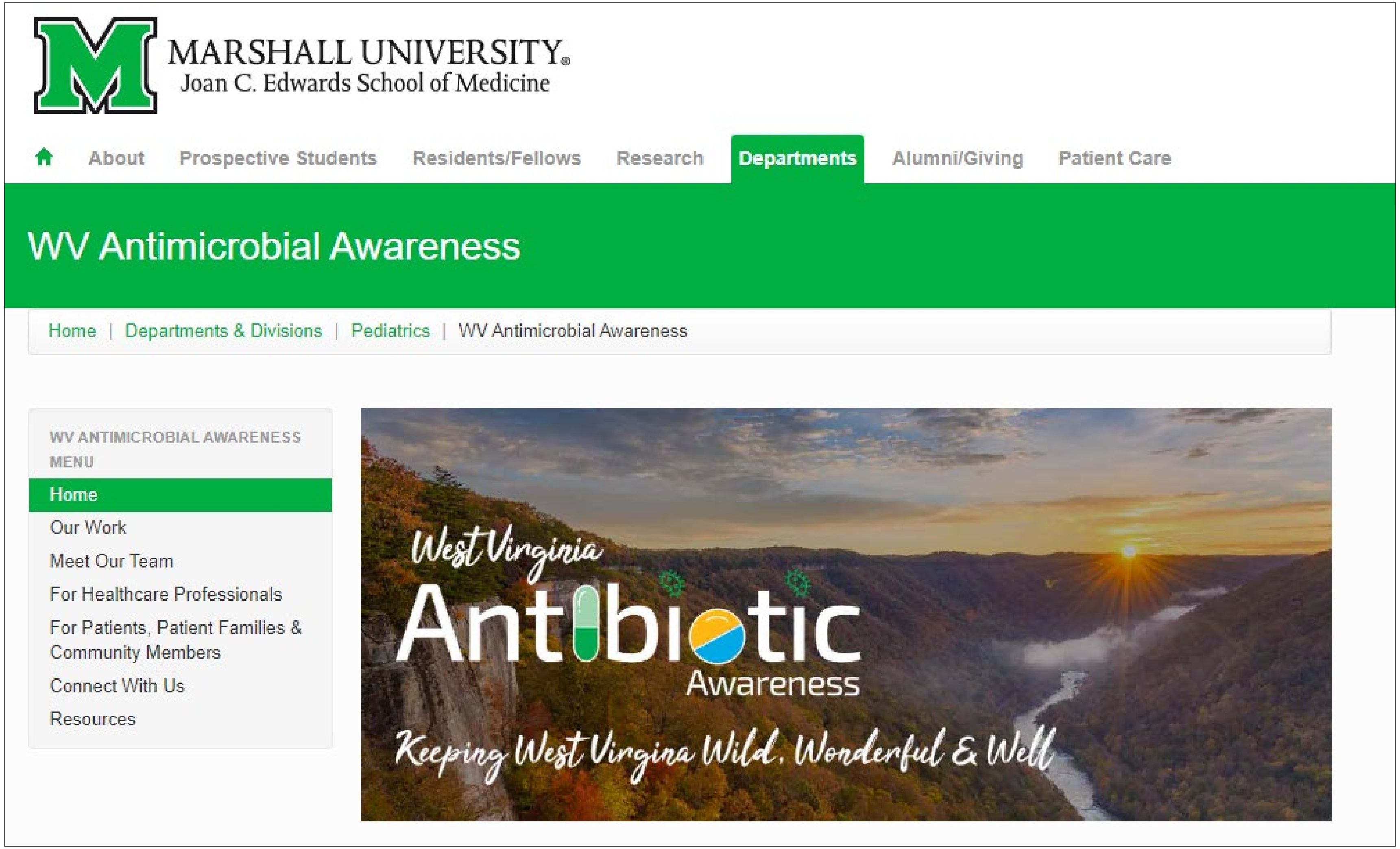
- Connect with networks of providers across the state to identify key factors influencing antimicrobial stewardship barriers & successes.

Know your guidelines!



https://jcesom.marshall.edu/departments-divisions/pediatrics/wv-antimicrobial-awareness/

WV ANTIMICROBIAL AWARENESS MENU

- Home
- Our Work
- Meet Our Team
- For Healthcare Professionals
- For Patients, Patient Families & Community Members
- Connect With Us
- Resources

Our Goal: "Right Drug, Right Dose, Right Duration."

Helpful management summaries for common outpatient antibiotic uses

Below are links from trusted sources on the management of common conditions based on age.

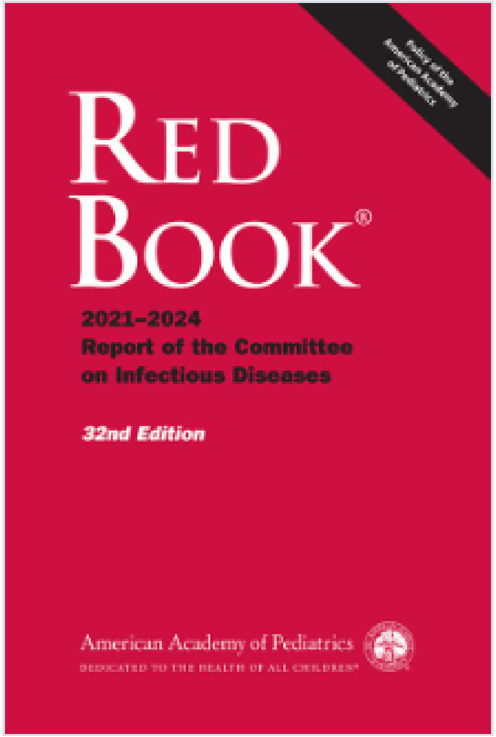
PEDIATRICS

- Urinary tract infection (UTI)
- Community-acquired pneumonia (CAP)
- Group A strep pharyngitis
- Acute otitis management (AOM)
- Bacterial rhinosinusitis
- Skin and soft tissue

ADULTS

- Community-acquired pneumonia (CAP)
- Bacterial rhinosinusitis
- Skin and soft tissue

Other guideline references



Red Book: 2021–2024 Report of the Committee on Infectious Diseases (32ND EDITION)

By Committee on Infectious Diseases, American Academy of Pediatrics;
David W. Kimberlin, MD, FAAP; Elizabeth D. Barnett, MD, FAAP; Ruth Lynfield, MD, FAAP;
Mark H. Sawyer, MD, FAAP

American Academy of Pediatrics
ISBN electronic: 978-1-61002-578-2
Publication date: January 2021

Pediatric Acute Otitis Media (AOM)

- **First-line**: amoxicillin
  - If patient has received amoxicillin within past 30 days: amoxicillin-clavulanate

- **Duration**:
  - >6 years: 5 days
  - 2-5 years: 7 days
  - <2 or severe symptoms: 10 days

Pediatric Acute Bacterial Pharyngitis

- **First-line**: penicillin or amoxicillin
- Penicillin allergy: cephalexin, clindamycin, or azithromycin

- **Duration**: 10 days

Pediatric Acute Bacterial Sinusitis

- **First-line**: amoxicillin or amoxicillin-clavulanate
- Penicillin allergy: clindamycin or levofloxacin

- **Duration**: 5-7 days

Pediatric Community Acquired Pneumonia (CAP)

- Empiric antibiotic therapy:
  - Amoxicillin, ampicillin, or penicillin for fully immunized patients in regions without high prevalence of penicillin-resistant pneumococcus
- Penicillin allergy: clindamycin or levofloxacin
- Suspected atypical pathogen: add macrolide

- **Duration**: 5 days from uncomplicated CAP improving during that time

Pediatric Urinary Tract Infection (UTI)

- **First-line**: cephalexin, sulfamethoxazole-trimethoprim, ampicillin + gentamicin, ceftriaxone, ciprofloxacin

- **Duration**:
  - 7-10 days
  - 3-5 days (simple cystitis in adolescents)

Objectives

- Introduction to antimicrobial stewardship
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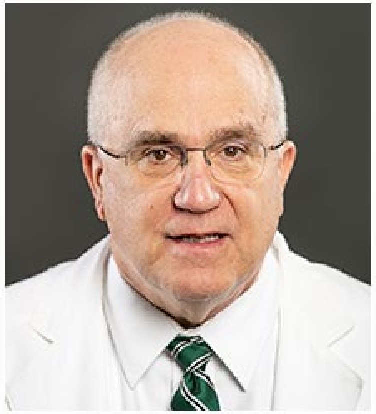
West Virginia Antibiotic Awareness

Jacob Kilgore, MD, MPH, FAAP

Mariana Lanata, MD, FAAP



Joseph E. Evans, MD, FAAP

Michael J. Smith, MD, MSCE, FAAP

Borden Samples, PharmD, BCPS

Bethany Wattles, PharmD, MHA

Jennifer Sparks, PharmD

Brandi Holthaus, MD

Jonathan Willis, MS

Top row (left to right)

Jacob T. Kilgore

Mariana Lanata

Joseph E. Evans

Middle row (left to right)

Michael J. Smith

Borden Samples

Bethany Wattles

Bottom row (left to right)

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Outpatient Antibiotic Use and the Need for Increased Antibiotic Stewardship Efforts

Rachel M. Zetts, MPH, Andrea Stoesz, MPH, Brian A. Smith, MPH, David Y. Hyun, MD

THE PEW CHARITABLE TRUSTS

Drivers for outpatient prescriptions:

- Patient satisfaction and pressure
- Time constraints
- Diagnostic uncertainty
- External responsibility

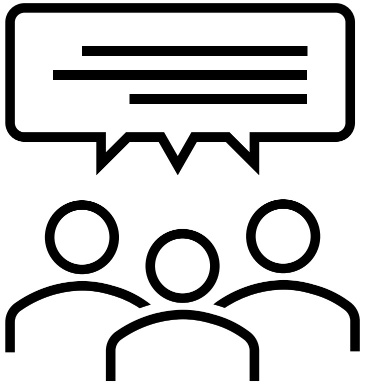
Zetts, Pediatrics 2018

Please, share your thoughts!

What are your main reasons to prescribe antibiotics?

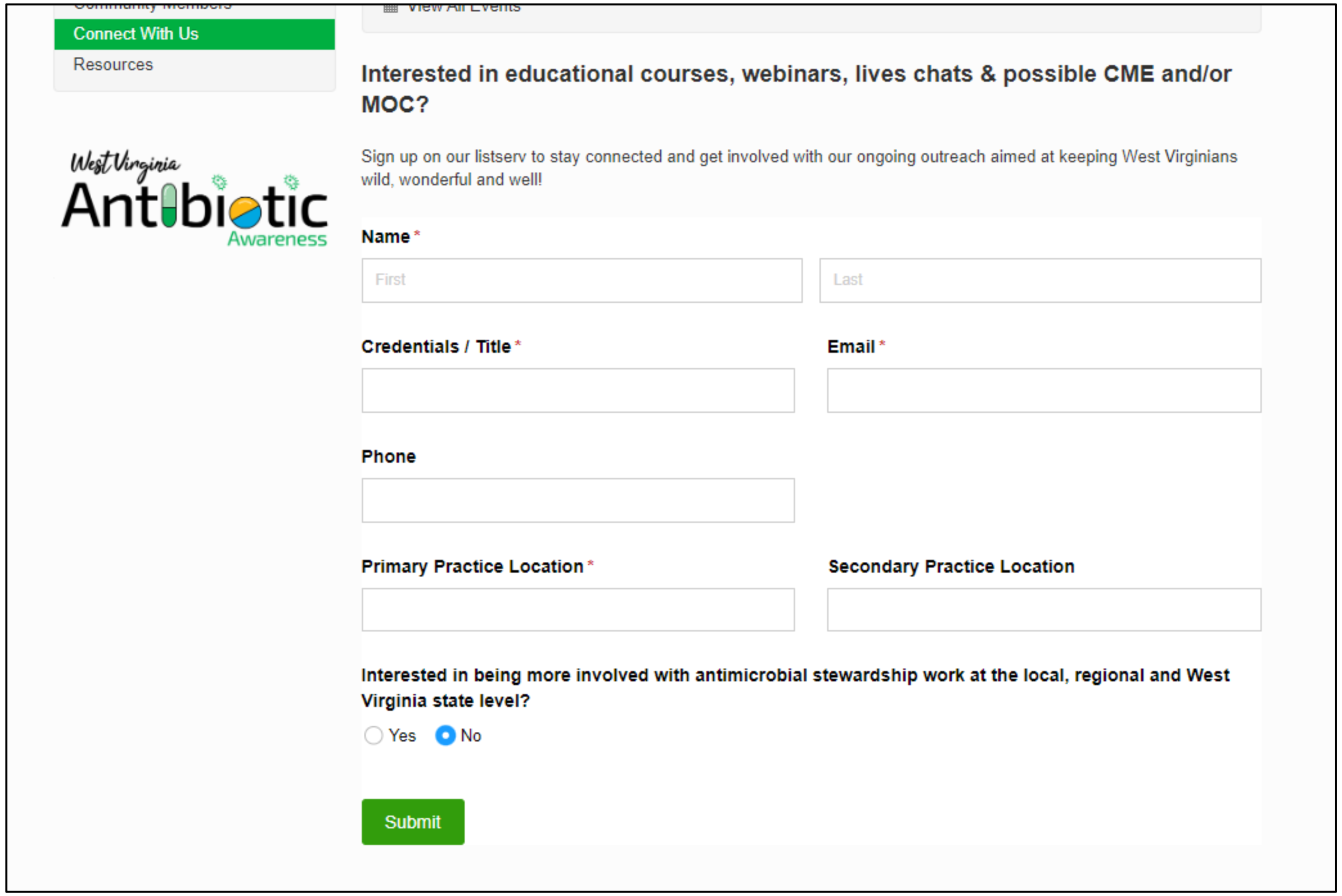
What barriers are you all facing?

How can we help?



Connect with us!

- Please join our Listserv!


Connect With Us
Resources

West Virginia Antibiotic Awareness

Interested in educational courses, webinars, lives chats & possible CME and/or MOC?

Sign up on our listserv to stay connected and get involved with our ongoing outreach aimed at keeping West Virginians wild, wonderful and well!

Name *
First
Last

Credentials / Title *

Email *

Phone

Primary Practice Location *

Secondary Practice Location

Interested in being more involved with antimicrobial stewardship work at the local, regional and West Virginia state level?

Yes No

Submit

- Reach us directly at:

wvabxawarness@gmail.com

THANK YOU

Together, we can help keep WV wild, wonderful & well!

West Virginia Antibiotic Awareness

https://jcesom.marshall.edu/departments-divisions/pediatrics/wv-antimicrobial-awareness/