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School of Medicine

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Antimicrobial Resistance: Global Problem, Local Action

Lisa E Davidson, MD, FIDSA

Disclosures

- No financial disclosures or conflicts of interest

Objective

Describe causes of antimicrobial resistance and at least one way it can be slowed.

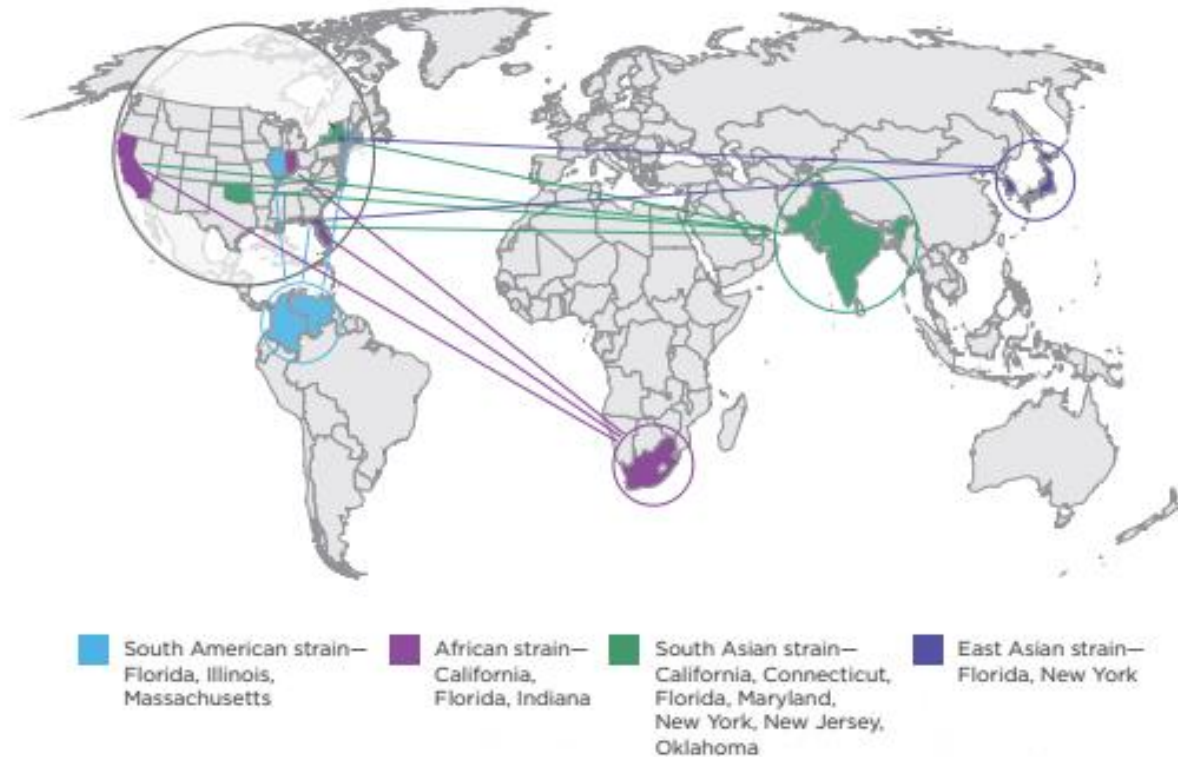
A call for help...

- 65-year-old woman, hospitalized for COVID
- Quickly intubated and admitted to ICU with severe respiratory complications
- After several weeks in isolation in the hospital, transferred to acute rehab
- Daughter gets a call – “Your mom has a resistant infection called *Candida auris*... you can’t see her.”
- What can be done?

- *C. auris*, first identified in 2009 in Asia, has quickly become a cause of severe infections around the world.
- *C. auris* is a concerning drug-resistant fungus:
 - Often multidrug-resistant, with some strains (types) resistant to all three available classes of antifungals
 - Can cause outbreaks in healthcare facilities
 - Some common healthcare disinfectants are less effective at eliminating it
 - Can be carried on patients' skin without causing infection, allowing spread to others

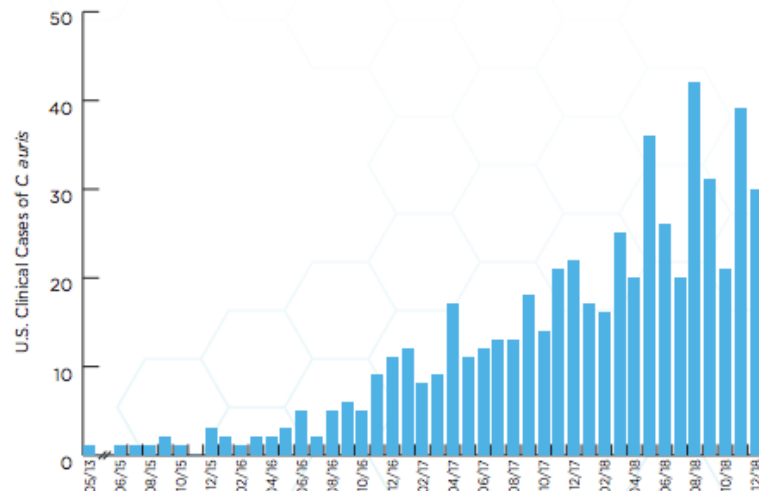
A GLOBAL THREAT

Investigators still do not know why four different strains of *C. auris* emerged around the same time across the globe. All four strains have been found in the United States, likely introduced through international travel and subsequent spread in U.S. healthcare facilities.

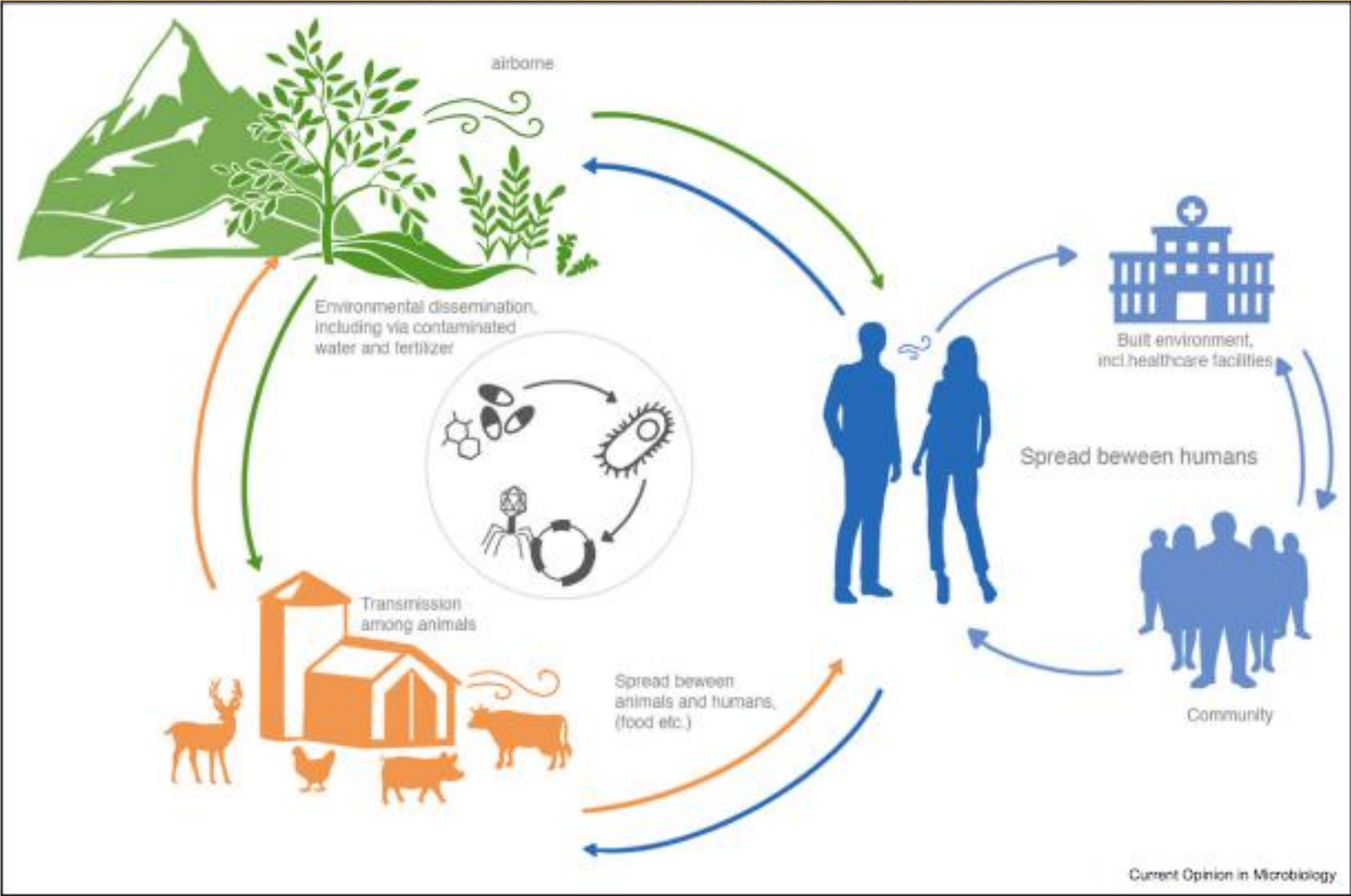


CASES OVER TIME

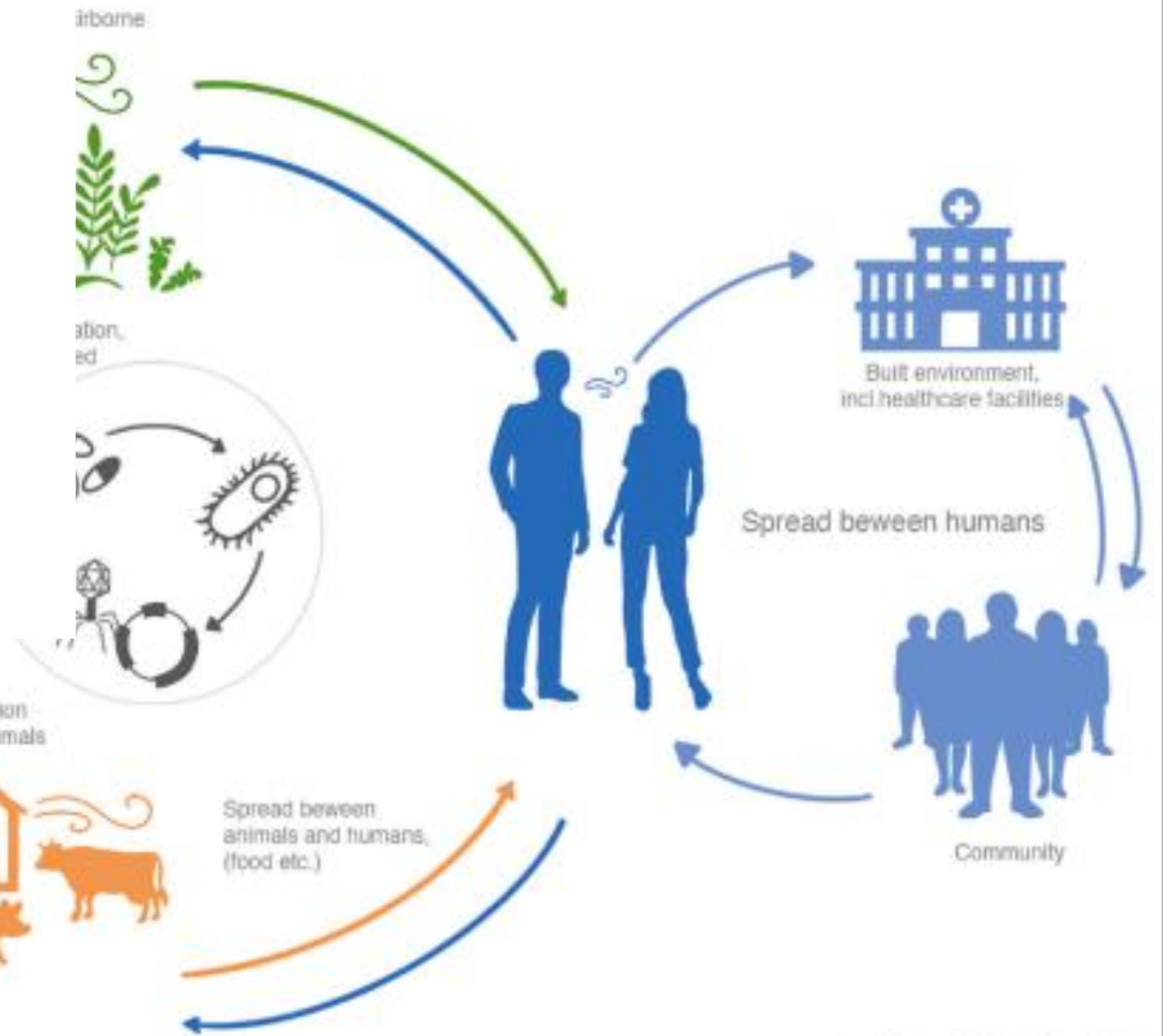
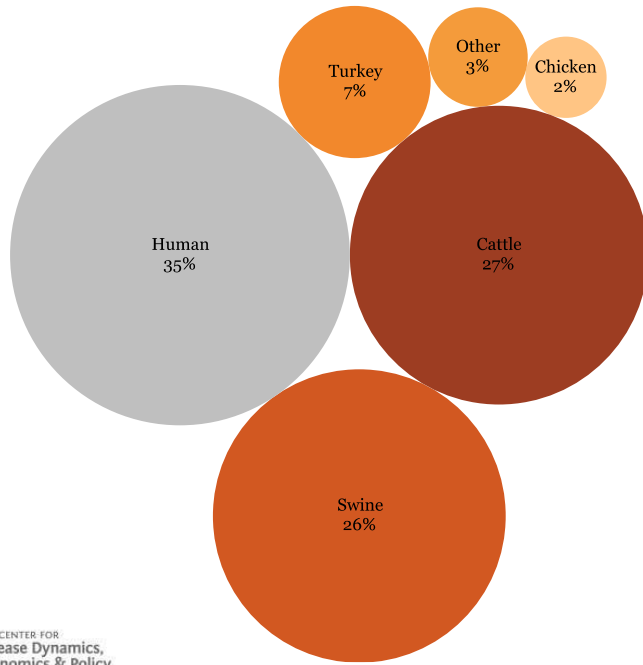
C. auris began spreading in the United States in 2015. Reported cases increased 318% in 2018 when compared to the average number of cases reported in 2015 to 2017.

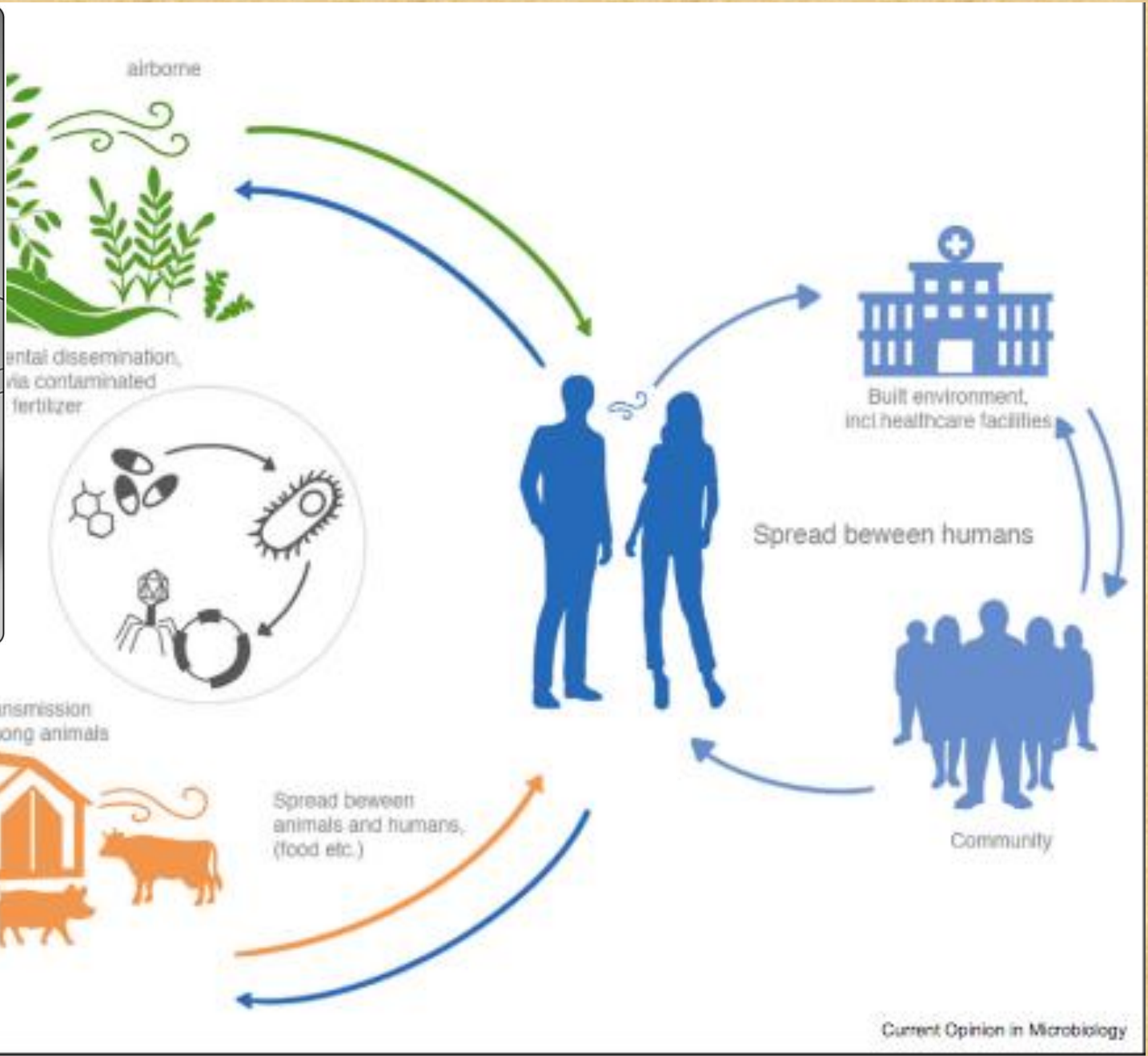
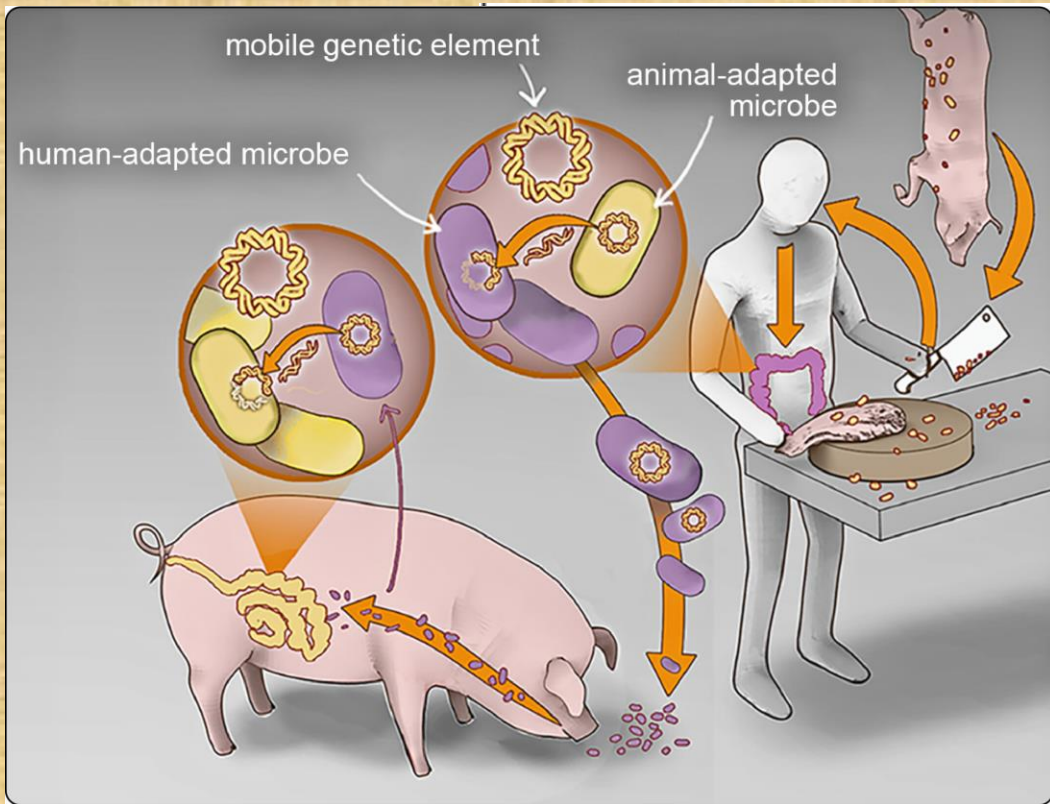


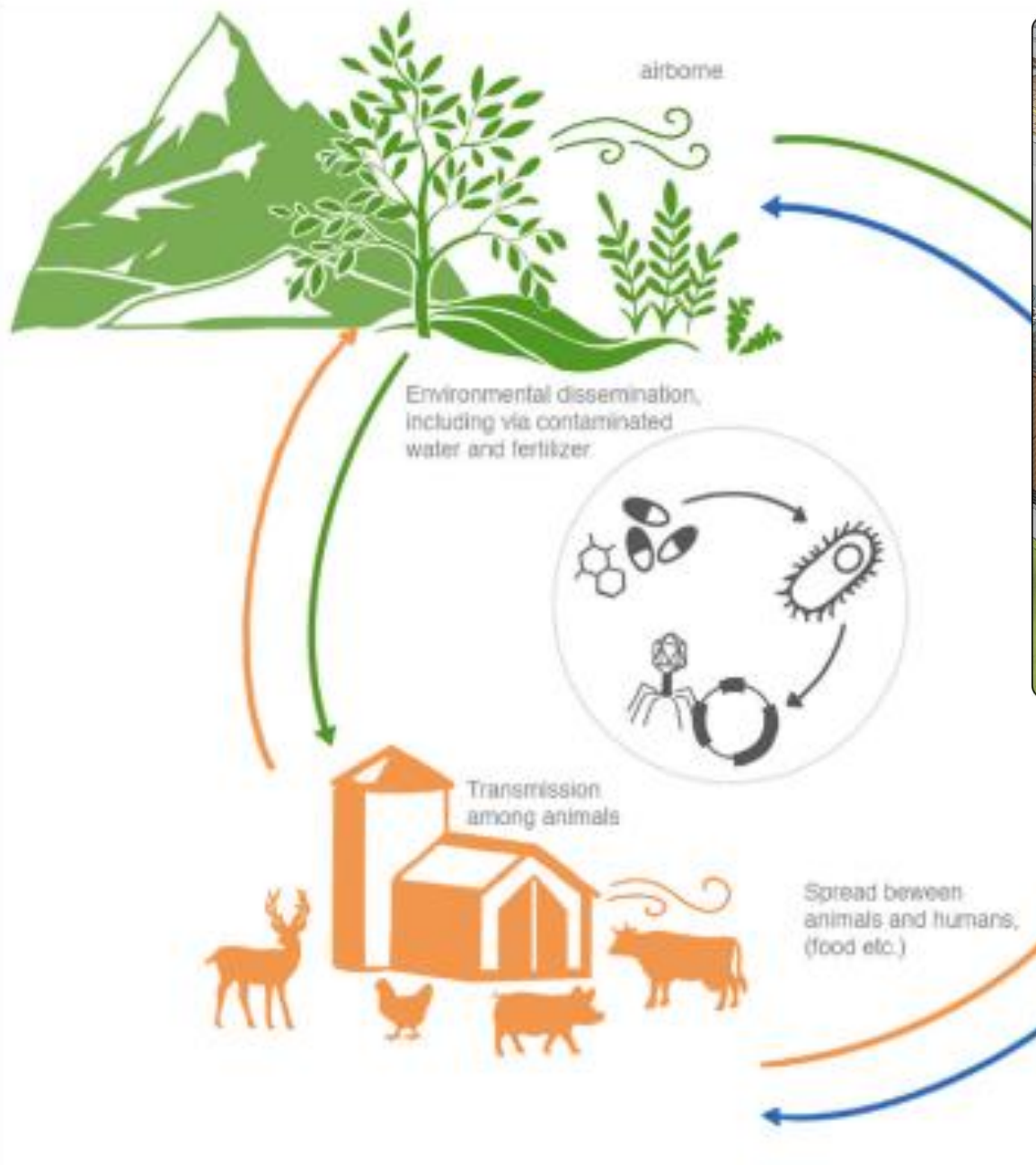
U.S. Department of Health and Human Services
Centers for Disease Control and Prevention



US Sales of Medically Important Antibiotics for Use in Human Medicine and Food-Producing Species

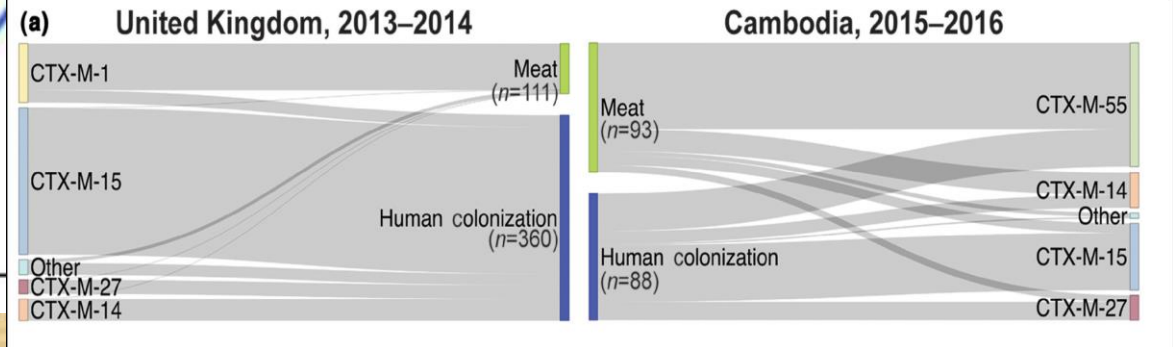
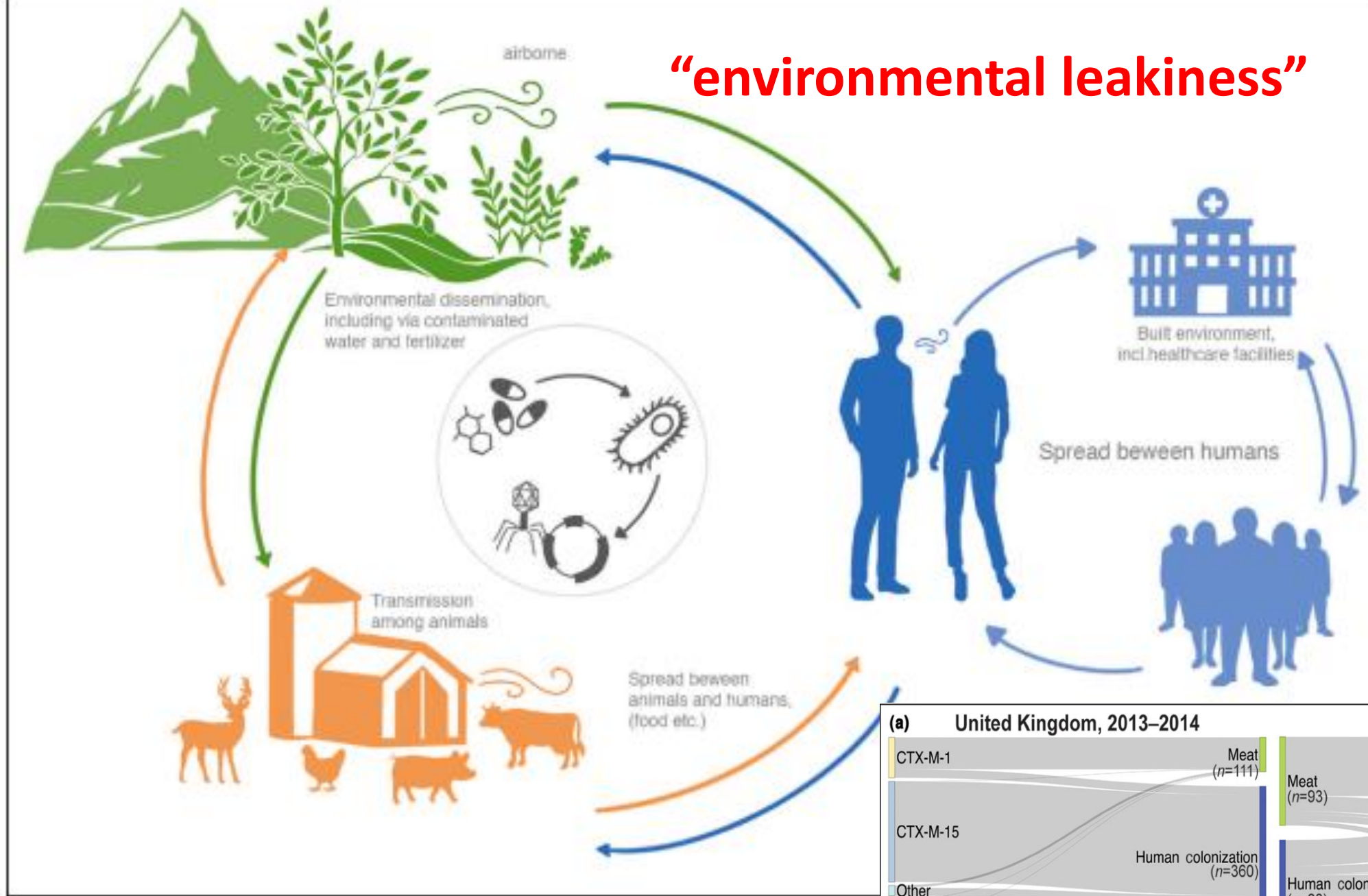






Current Opinion in Microbiology

“environmental leakiness”



Antibiotic Resistance Spreads Easily Across the Globe

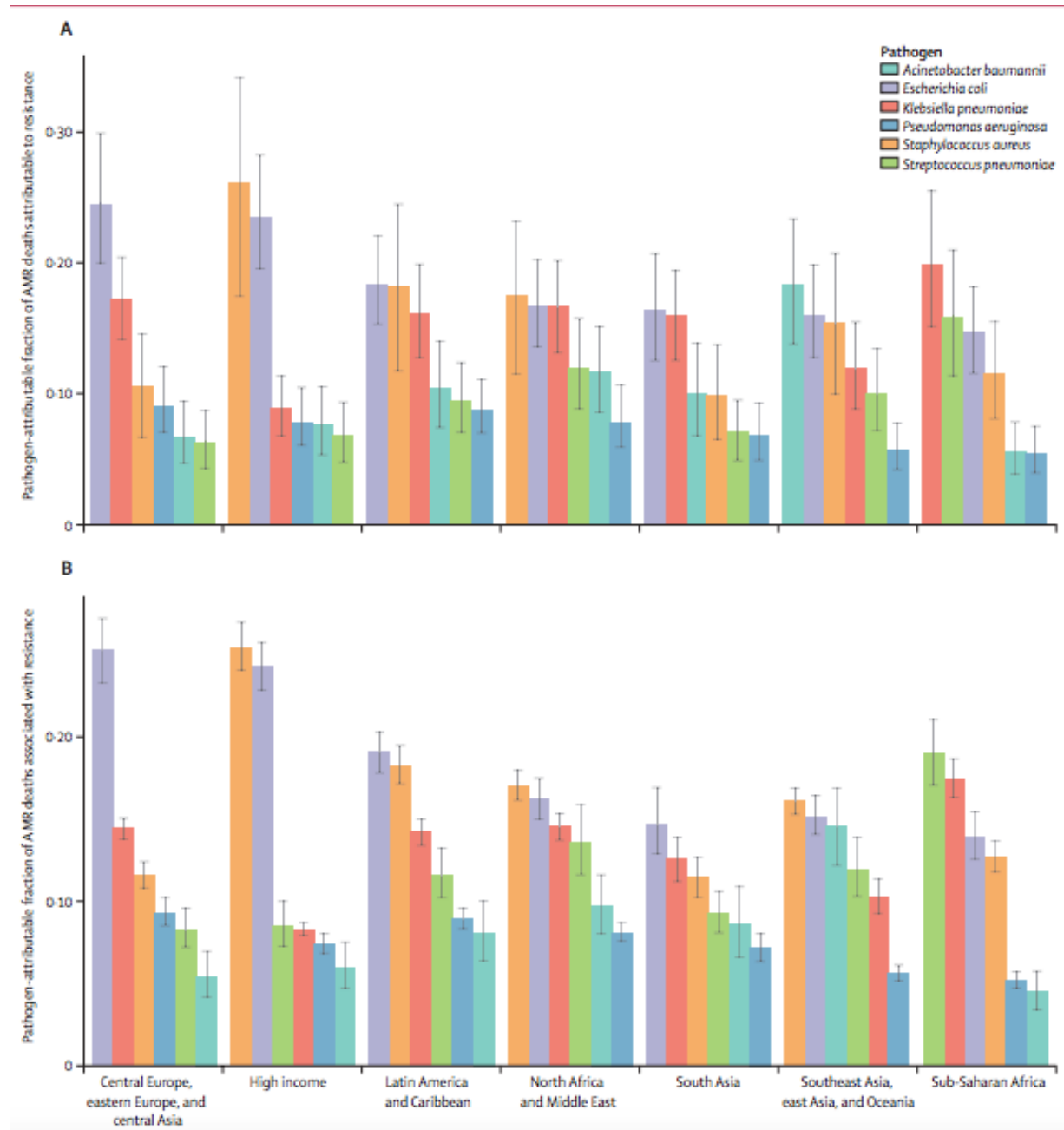
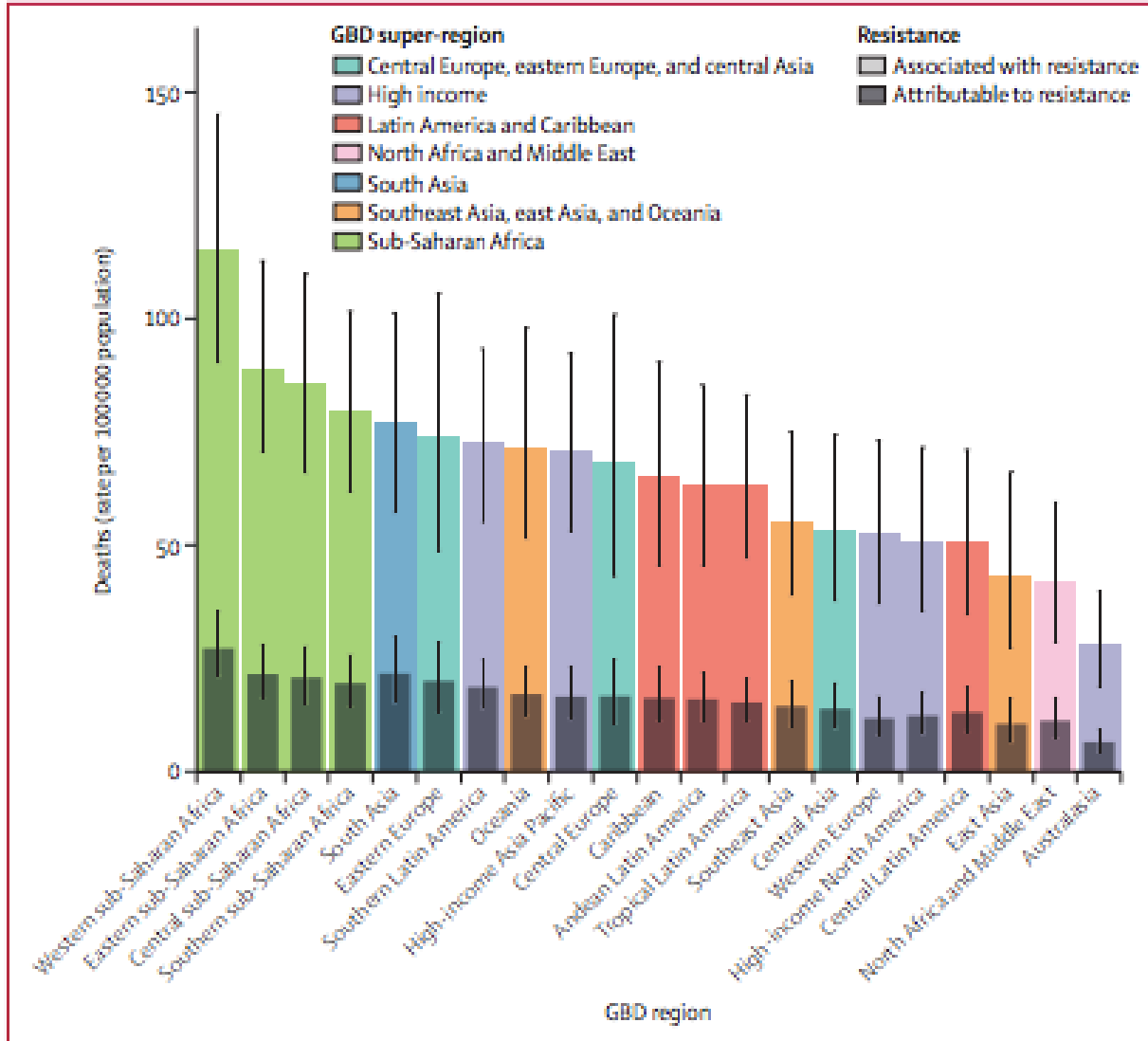
Resistant bacteria and fungi can spread across countries and continents through people, animals, and goods.



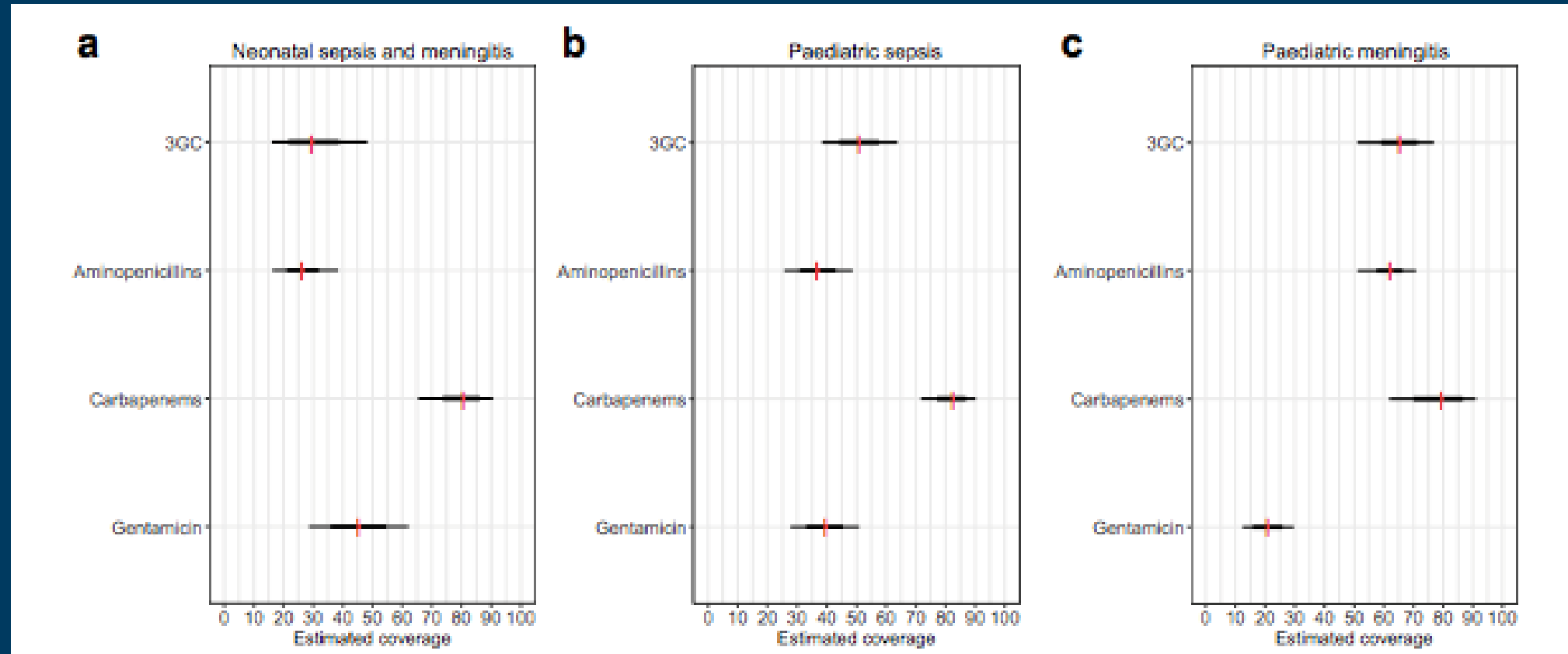
One billion people cross through international borders each year. This includes 350 million travelers arriving in the United States through more than 300 points of entry.

A resistant threat anywhere can quickly become a threat at home.
Global capacity is needed to slow development and prevent spread of antibiotic resistance.

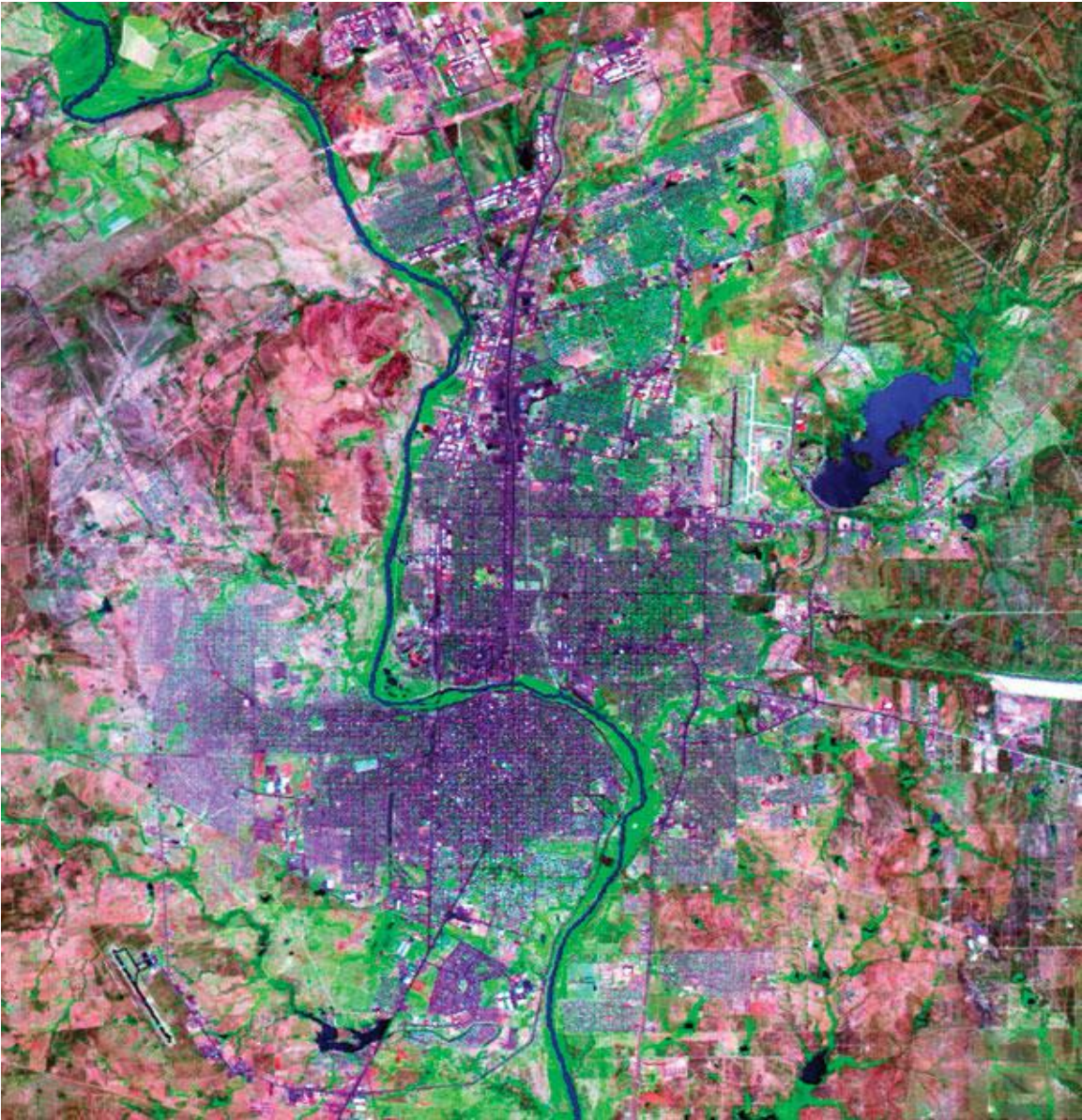
1.27 million deaths a year are associated with bacterial antimicrobial resistance



Coverage gaps in empiric antibiotic regimens used to treat serious bacterial infections in neonates and children in Southeast Asia and the Pacific



The Lancet Regional Health - Southeast Asia 2023;▪: 100291 Published Online <https://doi.org/10.1016/j.lansea.2023.100291>



- Urban dengue is common in most countries of the Americas, but rare in the United States
- Outbreak in Nuevo Laredo, Tamaulipas, Mexico, and Laredo, Texas, United States — contiguous cities that straddle the international border
- Incidence of recent cases, indicated by immunoglobulin M antibody serosurvey, was higher in Nuevo Laredo
- But the vector, *Aedes aegypti*, was more abundant in Laredo
- Environmental factors that affect contact with mosquitoes, such as air-conditioning and human behavior, appear to account for this paradox
 - **Prevalence of dengue in the United States is primarily due to economic, rather than climatic, factors**



**HOW DO WE TAKE A
GLOBAL PROBLEM AND
MAKE LOCAL CHANGE?**



System challenges

- Limited health worker education on AMR
- Poor water, sanitation and safe waste management
- Poor IPC programmes and practices
- Weak immunization programmes

- Limited health service coverage and lack of financial protection for the entire population
- Lack or insufficient health-care services, diagnostics and antimicrobials and trained health workers
- Use of substandard or falsified diagnostics and antimicrobials
- Weak referral systems

- Limited laboratory capacity
- Limited health worker education in appropriate diagnostics and in interpreting or using results
- Poor diagnostic services

- Weak regulation of over-the-counter (OTC) medicines
- No quality-assured treatment, standardized treatment guidelines or stewardship
- Inappropriate prescribing of antimicrobials



People's challenges

- Poor health education
- No access to clean water or sanitation
- Poor adherence to practices to prevent transmission of infection
- Poor access or missed vaccinations and vaccine hesitancy

- Catastrophic out of pocket spending on health services, diagnostics or medicines
- Poor access to and lack of awareness of available local health services
- Loss to follow-up

- Incorrect or delayed diagnosis
- Poor access to local diagnostic services
- Limited awareness of the importance of timely, accurate diagnosis

- Inappropriate self-medication (eg. use of OTC or leftover antimicrobials, incomplete treatment cycle)
- Increased risk of suboptimal treatment, leading to complications or longer recovery
- Higher risk of morbidity or mortality due to infections that are difficult to treat or untreatable



Prevention of infection



Access to health services



Diagnosis



Treatment

People-centered approach to addressing antimicrobial resistance in human health: WHO core package of interventions to support national action plans. Geneva: World Health Organization; 2023. Licence: CC BY-NC-SA 3.0 IGO



Clearly defined standards and quality incentives from Health System Leaders



Engagement of local site champions



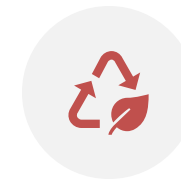
Develop tools and education for BOTH clinicians and patients



Leverage the EMR and electronic resources

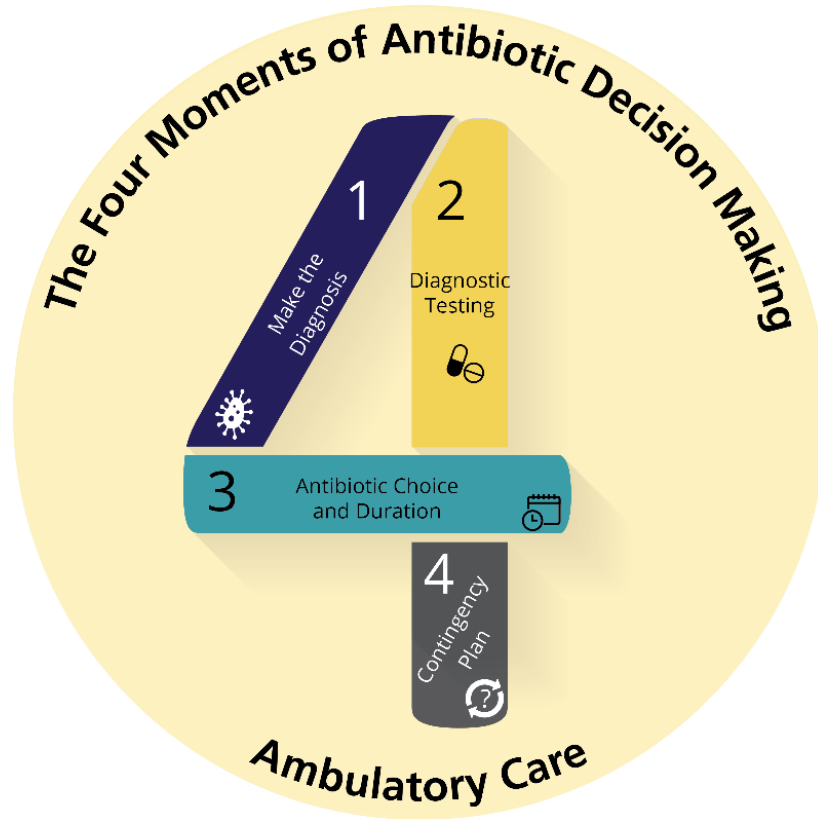


Provider data — easily accessible, transparent, focused feedback



Sustainability

The Four Moments of Antibiotic Decision Making



1. Does my patient have an infection that requires antibiotics?
2. Do I need to order any diagnostic tests?
3. If antibiotics are indicated, what is the narrowest, safest, and shortest regimen I can prescribe?
4. Does my patient understand what to expect and the follow-up plan?



What's the harm in treating a viral infection with antibiotics?

Adverse drug events

- Antibiotic-associated diarrhea

- Yeast infections

- Rash/allergic reaction

Disruption of normal bacteria that colonize the intestinal and upper respiratory tract

- Selection for antibiotic-resistant bacteria

Clostridioides difficile infection

Increased Health Care Costs and Adverse Drug Events Associated With Inappropriate Antibiotic Selection in Privately Insured Adult Patients

	Excess cost per patient	Excess national costs (2017)	Adverse events
Pharyngitis	\$67	\$49.6 million	Nausea/vomiting/abdominal pain, <i>C. difficile</i> infection, non- <i>C. difficile</i> diarrhea
Sinus infections	\$18	\$19.1 million	Nausea/vomiting/abdominal pain

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Adverse patient outcomes

Inappropriate antibiotics were associated with an increased risk of adverse drug events:

Clostridioides difficile infection (*C. diff*), formerly known as *Clostridium difficile*, is a **potentially life-threatening infection** that can be caused by antibiotic exposure.



The Centers for Disease Control and Prevention classifies *C. diff* as one of the **top five most urgent pathogens**.

Patients who received inappropriate antibiotics for pharyngitis (sore throat) were significantly more likely to get a *C. diff* infection:

8x higher risk
(children)



3x higher risk
(adults)



When is a diagnostic test indicated?



When it changes management

Is the patient high risk for hospitalization or have significant comorbidities?

Is there an immunocompromised patient in the home?

If the patient requests a test, is it covered by insurance?



Communication is key!

Use effective communication strategies to address patients' beliefs and concerns

- Wanting to feel that their symptoms are being taken seriously
- Understanding conflicting practices among clinicians regarding provision of antibiotic prescriptions
- Worries about becoming sicker or not being able to reach a clinician



OTC Checklists for Adults, Teens, Peds

Treating your symptoms- for Adults only

- Here are some medicines and other ways to treat your symptoms. **Do not use if the box is not checked**
- Tell your doctor if you have problems with high blood pressure, diabetes, or other health problems
- Try to use medicine that **only** takes care of your symptom. Medicines such as Tylenol Cold&Flu®, that treat many symptoms can cause side effects
- Acetaminophen is the drug in Tylenol®. It is also used in other medicines for fever or pain. Too much acetaminophen can harm your liver. Do not take more than ordered. Check the medicine label to see if it has acetaminophen in it
- Look on the medicine label to find the active ingredient listed in the "Use" boxes below



Drug Facts	
Active ingredient (in each tablet)	Purpose
Chlorpheniramine maleate 2 mg	Antihistamine

- Show this sheet to your pharmacist if you need help finding the right medicine

If you have	Use	Such as	Comments
Aches,Pain,Fever 	<input type="checkbox"/> Acetaminophen	Tylenol®	
	<input type="checkbox"/> Ibuprofen	Advil®, Motrin®	
	<input type="checkbox"/> Naproxen	Aleve®	
Sore Throat 	<input type="checkbox"/> Throat Lozenges	Cepacol Throat Lozenges®	
	<input type="checkbox"/> Throat Sprays	Chloraseptic Spray®	
	<input type="checkbox"/> Herbal tea with honey	Throat Coat®	
	<input type="checkbox"/> Gargles	Warm Salt Water Gargle	
Cough 	<input type="checkbox"/> Guaifenesin and Dextromethorphan	Mucinex DM®, Tussin DM®, Robitussin DM®	
	<input type="checkbox"/> Guaifenesin	Mucinex®	Helps thin mucus
	<input type="checkbox"/> Dextromethorphan	Delsym®, Robitussin®, Vicks Formula 44®	Use for dry cough
	<input type="checkbox"/> Menthol	Vicks Vapor Rub®, Cough Drops	
Stuffy Nose 	<input type="checkbox"/> Pseudoephedrine	Sudafed® Decongestant-12 hour	Must buy at the pharmacy with photo ID
	<input type="checkbox"/> Chlorpheniramine	Coricidin®, Chlor-Tab®, Chlor-Trimeton®	
	<input type="checkbox"/> Decongestant nose spray with xylometazoline, oxymetazoline or phenylephrine	Afrin®, Allerest® or Otrivin® Nasal Spray Neo-Synephrine®	Use up to 5 days
	<input type="checkbox"/> Nasal Irrigation	Saline Irrigation or Nose Spray	

More info on the back of this sheet

Treating your symptoms- for Adults only

If you have	Use	Such as	Comments
Itchy, Irritated, Dry Eyes 	<input type="checkbox"/> Ketotifen Eye Drops	Alaway®, Claritin Eye®, Zaditor®, Zyrtec Itchy Eye®	Helps with itchy eyes
	<input type="checkbox"/> Eye drops with naphazoline or tetrahydrozoline	Naphcon-A®, Opcon-A®, Visine®, Clear Eyes®	Helps with red eyes
	<input type="checkbox"/> Ocular Lubricant	Artificial Tears	Helps with dry eyes
	<input type="checkbox"/> Cool or Warm Compress		5 to 10 minutes each hour, as needed
Allergy Symptoms such as sneezing, runny nose, itching, post-nasal drip 	<input type="checkbox"/> Fexofenadine	Allegra®, Aller-Ease®	
	<input type="checkbox"/> Loratadine	Claritin®, Alavert®	
	<input type="checkbox"/> Cetirizine	Zyrtec®	
	<input type="checkbox"/> Levocetirizine	Xyzal®	
	<input type="checkbox"/> Chlorpheniramine	Chlor-Tab®, Chlor-Trimeton®	Found in many OTC allergy meds
Allergy Symptoms with stuffy nose	<input type="checkbox"/> Steroid nose spray with triamcinolone, budesonide or fluticasone	Flonase®, Nasocort®, Rhinocort®	
	<input type="checkbox"/> Antihistamine+ Decongestant	Allegra-D®, Claritin-D®, Zyrtec-D®	

Other tips:

How long will my symptoms last?

Fever: Up to 5 days (most often 2 to 3 days)
 Sore throat: Up to 9 days (most often 5 to 6 days)
 Cough: Up to 2 weeks (most often 7 to 14 days)
 Runny nose: Up to 2 weeks (most often 5 to 7 days)

Call your doctor if you have any of these

- Short of breath
- Chest pain
- Shaking chills
- Fever of 102 or more with other symptoms
- Coughing up blood (more than a streak)
- Getting better and then get worse

Carolinas HealthCare System complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex.

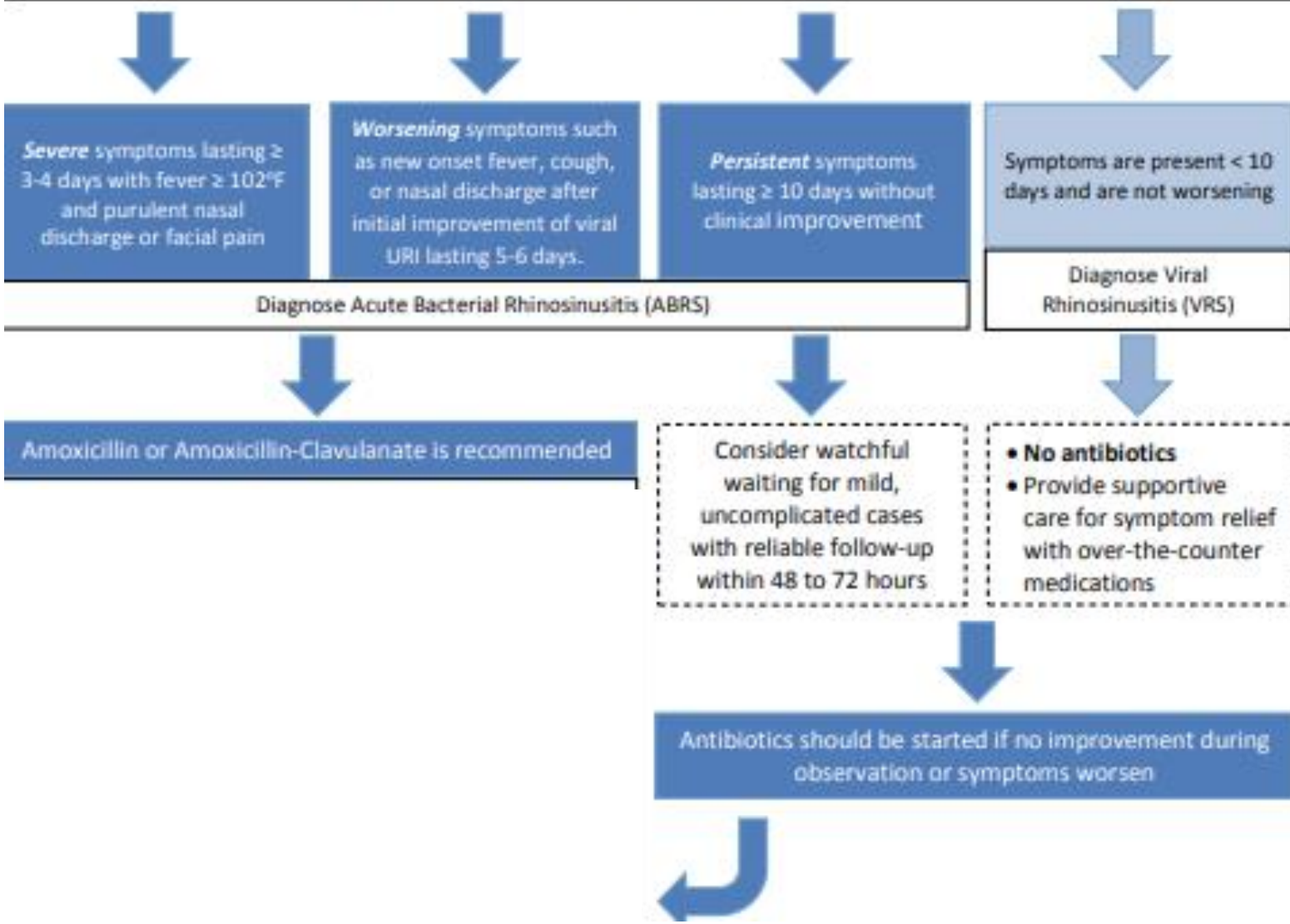
ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1-800-821-1535.
 CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1-800-821-1535.



Recommended Management of Acute Uncomplicated Rhinosinusitis in Pediatrics and Adults

Patient presents with signs/symptoms of acute rhinosinusitis of duration < 4 weeks

Purulent nasal drainage (cloudy or colored) accompanied by nasal obstruction (congestion, blockage, stuffiness), facial pain-pressure-fullness (involving anterior face, periorbital or manifest with headache), or both.



Amoxicillin or Amoxicillin-Clavulanate is recommended

- Adults:**
- Mild to moderate:
 - Amoxicillin-clavulanate 875-125 mg oral BID x 5-7 days
 - Severe with fever $\geq 102^{\circ}\text{F}$ and threat of suppurative complications, > 65 years of age, recent hospitalization, antibiotic use in the past month or in those immunocompromised:
 - High-dose amoxicillin-clavulanate 2000-125 mg oral BID x 5-7 days for adequate coverage of penicillin non-susceptible *S. pneumoniae*.
 - Alternate Therapy (reserved for patients who fail first-line therapy or for penicillin allergy):
 - Doxycycline 100 mg oral BID x 5-7 days **or**
 - Levofloxacin 500 mg oral daily x 5-7 days

- Pediatrics:**
- Uncomplicated, mild to moderate in children ≥ 2 years who do not attend daycare and have not been treated with antimicrobials within the last 4 weeks:
 - High-dose amoxicillin (90 mg/kg/day oral divided BID – max 2 grams per dose) x 10 days
 - Moderate to severe symptoms or children < 2 years, attend daycare, recent hospitalization, those treated with antimicrobials within the last 4 weeks, or those failing first-line treatment:
 - High-dose amoxicillin-clavulanate 90 mg/kg/day (amoxicillin component) oral divided BID x 10 days
 - Alternate Therapy (reserved for penicillin allergy or those failing first-line treatment):
 - Third-generation cephalosporin +/- clindamycin 30-40 mg/kg/day oral divided TID x 10 days
 - Levofloxacin 10 mg/kg/dose oral once daily (≥ 5 years) and 10 mg/kg/dose oral BID (< 5 years) x 10 days

Why should the C-suite care?

1) Inappropriate inpatient antibiotics = increased resistant infections = increased hospitalization

= VBP penalty

2) Inappropriate outpatient antibiotics

= increased adverse events

= increased visits/ED visits/pharmacy expenditures

= increased HAI and hospitalizations

- 30-day health expenditures higher among inappropriate antibiotic prescribing (\$18-67 per patient for bacterial infection, ~\$40million)

3) PATIENT EXPERIENCE

1) ASHE 2022 Jan 12;2(1):e5

2) Butler et al CID 2023;76(6):986-95



From: **Association of Inappropriate Outpatient Pediatric Antibiotic Prescriptions With Adverse Drug Events and Health Care Expenditures**

JAMA Netw Open. 2022;5(5):e2214153. doi:10.1001/jamanetworkopen.2022.14153

Table 3. Annual National Attributable 30-Day Expenditures of Inappropriate Antibiotic Prescriptions Among the US Commercially Insured Population, Aged 6 Months to 17 Years^a

Index diagnoses	Attributable expenditures, 2018 US \$				
	Inpatient medical	Emergency department	Outpatient medical	Outpatient pharmacy	Total
Bacterial infections (primary analysis)					
Suppurative OM	1 235 313	777 904	7 846 200	15 441 487	25 300 317
Pharyngitis	-750 188	2 564 653	6 706 388	12 752 577	21 271 338
Sinusitis	-503 873	277 773	407 416	6 899 358	7 078 513
Viral infections (secondary analysis)					
Influenza	-98 806	-53 888	1 132 300	615 754	1 594 541
Viral URI	5 430 897	439 555	8 243 074	5 023 360	19 132 099
Bronchiolitis	-334 451	48 984	88 877	159 028	-37 871
Bronchitis	1 059 296	-2 593 873	-4 624 124	2 988 452	-3 173 797
Non-suppurative OM	-16 270	-962 935	-17 980 659	3 569 023	-15 395 644

Abbreviations: OM, otitis media; URI, upper respiratory infection.

^a Bronchiolitis cohort was restricted to ages 6 months to 3 years; bronchitis cohort was restricted to ages 5 to 17 years. The 95% confidence intervals are presented in eTable 16 in the [Supplement](#).

Table Title:

Annual National Attributable 30-Day Expenditures of Inappropriate Antibiotic Prescriptions Among the US Commercially Insured Population, Aged 6 Months to 17 Years^aAbbreviations: OM, otitis media; URI, upper respiratory infection.

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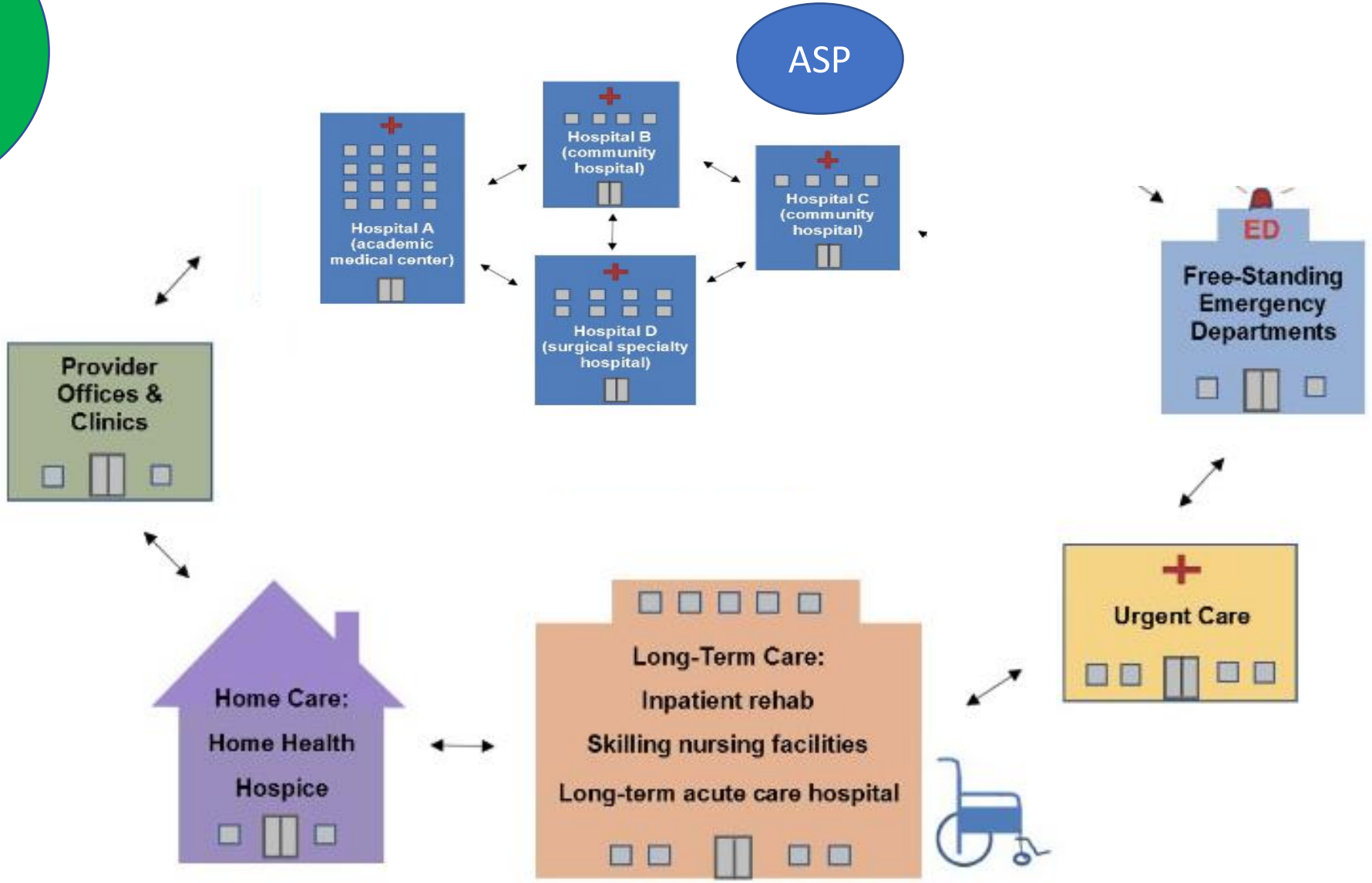
COMMUNITY HEALTH INSURERS
PRACTICES E-VISIT
PRIMARY PHARMACY MEDICAID VIRTUAL
PUBLIC HEALTH DEPARTMENTS
AMAZON LOCAL SYSTEMS
HEALTH CARE
ANTIMICROBIAL PBMS PRESCRIBING
DIRECT BASED PHARMACY TELEMEDICINE COMMERCIAL INDEPENDENT EMPLOYER SPECIALISTS
MEDICARE ADVANTAGE
EMERGENCY ROOM



Insurance companies = providers

Telemedicine E-consults

Hospital at Home



The future of healthcare is outside the hospital...

- US hospitals facing BILLIONS of dollars in losses
- Hospital inpatient growth slow, but LOS increasing
- Monumental (but very slow) shift from FFS to VBP
- Outpatient volumes predicted to grow by 15-20% over next decade
- Home care services also estimated to grow up to 20%
- Massive increase in telehealth and AI based platforms

Vizient Impact of Change Forecast 2022: https://www.sg2.com/wp-content/uploads/2022/11/2022_IoC_Forecast_Media.pdf

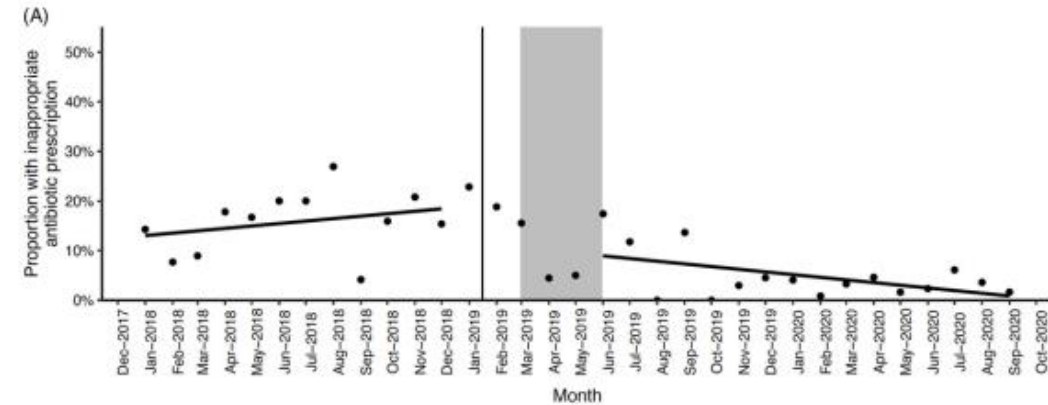
<https://www.aha.org/guidesreports/2022-09-15-current-state-hospital-finances-fall-2022-update>

The future is virtual...

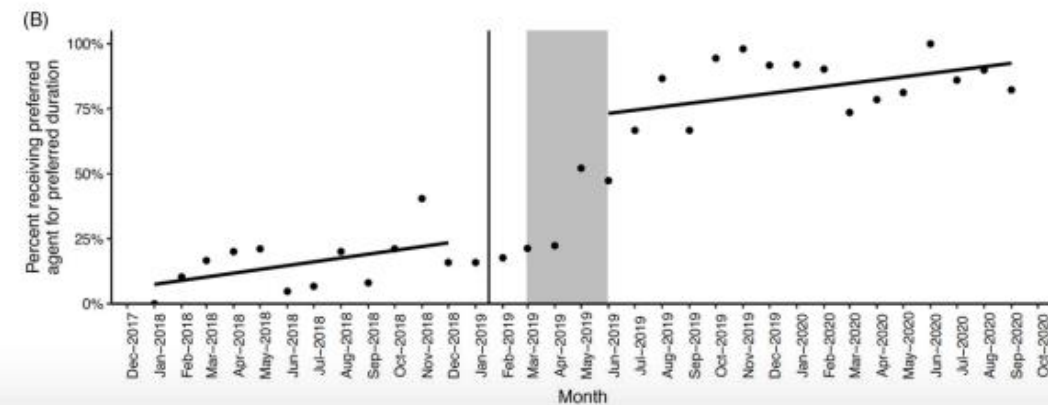
- Telemedicine/Telehealth
- E-visits/E-consults
- Virtual Visit/Virtual Care
- Hospital at Home

Improving antibiotic use for sinusitis and upper respiratory tract infections: A virtual-visit antibiotic stewardship initiative

- Bundled stewardship intervention to improve antibiotic use in E-visits for URTIs
- Adult patients who completed E-visits for “cough,” “flu,” or “sinus symptoms” at



	Coefficient	Standard error	t-statistic	P-value
<i>Level change after intervention</i>	-0.114	0.057	-2.01	0.056
<i>Slope change after intervention</i>	-0.01	0.005	-1.933	0.065



Know What Affects Health



Source: www.cdc.gov/chinav

Social Determinants of Health

Social Determinants of Health (SDH) are conditions in the environment in which people live, work, play, and worship that affect a wide range of health and quality of life outcomes.

- Healthy People 2020

Our environments cultivate our communities and our communities nurture our health.

When inequities are high and community assets are low, health outcomes are worst.



When inequities are low and community assets are high, health outcomes are best.



Social Determinants of Health

Economic Stability	Neighborhood and Physical Environment	Education	Food	Community and Social Context	Health Care System
Employment	Housing	Literacy	Hunger	Social integration	Health coverage
Income	Transportation	Language	Access to healthy options	Support systems	Provider availability
Expenses	Safety	Early childhood education		Community engagement	Provider linguistic and cultural competency
Debt	Parks	Vocational training		Discrimination	Quality of care
Medical bills	Playgrounds	Higher education		Stress	
Support	Walkability				
	Zip code / geography				

Health Outcomes

Mortality, Morbidity, Life Expectancy, Health Care Expenditures, Health Status, Functional Limitations



4 ways poverty makes people vulnerable to



AMR

Antimicrobial
Resistance

1.

Inability to pay for or find time to access healthcare can delay treatment of infections.

2.

Lack of access to clean water and sanitation increases the risk of AMR spread.

3.

Unaffordable treatment can lead to self-medication, incomplete treatment, or seeking alternative inappropriate treatment.

4.

Limited diagnostics can prevent people from getting the treatment they need.



**Global economic
inequity drives AMR.**

Disparities in vaccination coverage among children persist and are widening for some groups



CDC.gov

Clinicians can help reduce disparities by:

- Emphasizing strong clinical recommendations
- Identifying additional venues for vaccine administration
- Enhancing reminder and recall interventions

bit.ly/mm7244e3

NOVEMBER 3, 2023

MMWR

Vaccination Coverage by Age 24 Months Among Children Born in 2019 and 2020

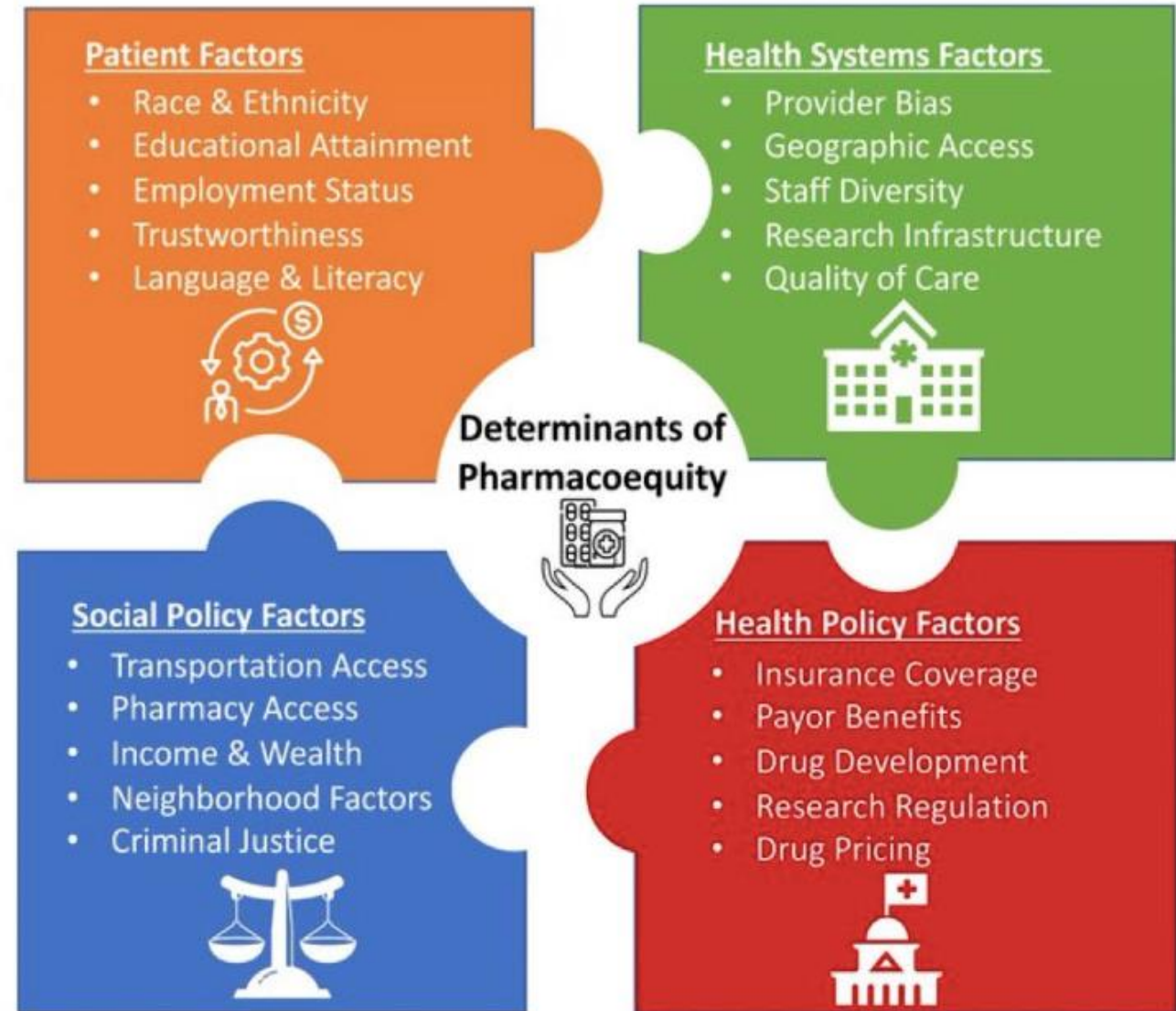
Vaccination coverage among children remains high, but disparities persist and are widening for some groups. Lower vaccination coverage was seen among children living below poverty level, children insured by Medicaid, other insurance, or with no insurance, children in rural areas, and Black, Hispanic, and American Indian/Alaska Native children.

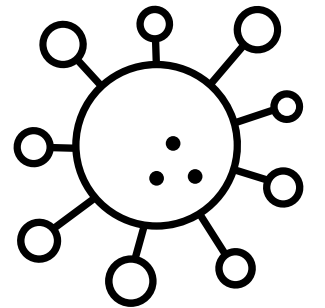
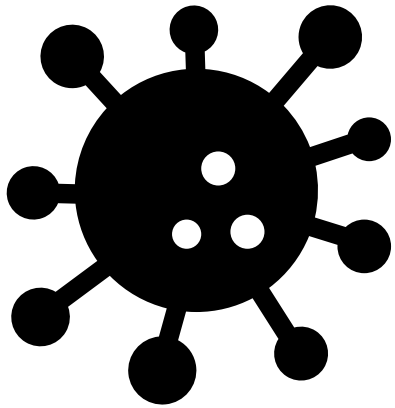
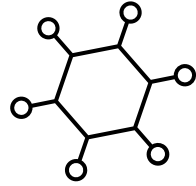
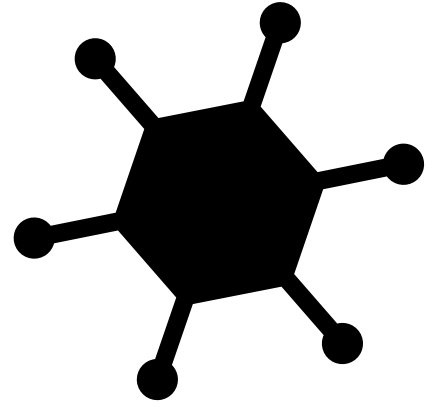
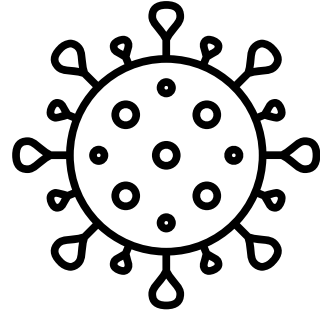
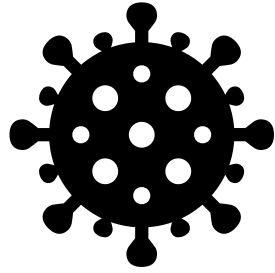
Do we have pharmacoequity in antibiotic prescribing?

- White outpatient patients more likely to be prescribed antibiotics when not indicated
- Prescribing may be affected by provider characteristics and provider training
- Differences in prescribing by SES, insurance, and where you live

What is Pharmacoequity?

“Ensuring all individuals, regardless of race and ethnicity, socioeconomic status, or availability of resources, have access to the highest-quality medications required to manage their health needs.”





THANK YOU!!!!

LISA.DAVIDSON@ATRIUMHEALTH.ORG