PRINCIPLES OF ANTIBIOTIC USE

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Duke Center for Antimicrobial Stewardship and Infection Prevention

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Objectives

Understand why antibiotics are "special" medications
The 4 Moments of Antibiotic Decision-Making
Antimicrobial Stewardship Programs
"Action" strategies in different clinical settings

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We Love Antibiotics

Inpatient

At any given time, 65% of inpatients at DUMC are receiving at least one antibiotic

There are >31,000 antibiotic orders (new starts) placed at DUMC annually

DUMC spends >$10 million on antimicrobial agents each year

Long-term Care

Up to 70% of residents in a nursing home receive one or more courses of systemic antibiotics when followed over a year

40-75% of antibiotic prescriptions are inappropriate

Outpatient

423-553 antibiotic prescriptions per 1000 people in the US per year

30% are unnecessary, (representing 47 million prescriptions/year)

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Why We Love Antibiotics

Wonder Drug

Active intervention

Experiences

Tangible

Insurance



Antibiotics are time-tested placebos

Antibiotic Rx is easy:
- Avoids doing a structured exam or long DDx
- Avoids time-consuming discussions
- i.e. Easier to treat than diagnose or educate

Identifying Infected vs. Not Infected is hard

"Just in case" perceived to be lower risk than "watchful waiting"

Why we HAVE TO improve Antibiotic Use

Antibiotics are unlike any other drug, in that the use of the agent in one patient can compromise its efficacy in another.

A lot of antibiotic prescriptions are unnecessary or sub-optimal.

We are running out of antibiotics.

Antibiotic misuse harms patients.

Improving antibiotic use has many benefits for patients and society.



Slide adapted from Arjun Srinivasan, MD (CDC)

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Antimicrobial Use Impacts: Infection Prevention, HAIs, AND Patient Outcomes



Drug-resistance (MRSA, VRE, CRE, MDR-GNs)

C. difficile infection

Infection treatment success/failure
- Complications
- Readmissions
- Mortality
- Length of Stay

Adverse Safety Events
- Allergic reactions
- Drug toxicity events
- Acute Kidney Injury

Healthcare Resources and Cost
- (all of the above)
- Pharmacy budget; ICU days

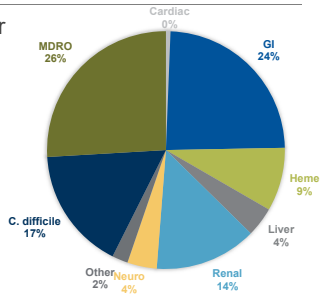
One in Five Inpatients get an Antibiotic Adverse Drug Event

1488 patients followed for 30 days after antibiotic initiation

Followed 90 days for CDI and MDRO acquisition

General medical inpatients who had at least 24h of antibiotics during admission

20% of patients experienced at least one antibiotic-associated ADE



Tamma et al. JAMA Int Med. 2017 177(9):1308-15.

Antibiotic use assoc. with *CDI* risk – even in patients who don't get Abx!

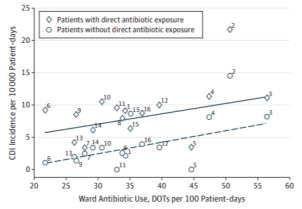
46-month, single center retrospective study

255 of 34,298 patients developed CDI (Incidence rate, 5.95 per 10,000 ptd)

Each 10% increase in ward-level antibiotic exposure was associated with a 2.1 per 10,000 increase in CDI

After adjustment for patient-level RFs, effect persisted: Relative risk, 1.34 (1.16-1.57) per 10% increase in days of therapy

Figure 2. Ward *Clostridium difficile* Infection (CDI) Incidence and Antibiotic Use Across Hospital Wards and Among Patients With and Without Direct Antibiotic Exposure



Each pair of numbered symbols represents the incidence of *C difficile* infection among the subset of patients who received antibiotics (diamonds) and those who did not (circles) within a given ward. For correspondence of ward identifiers, see Table 2. DOTs indicates days of therapy.

JAMA Intern Med. 2015;175(4):626-633

A case

86F with history of dementia, diabetes, and poor functional status presents from SNF with confusion, fever.

ED: Hypotense, non-verbal. Fluid resuscitated, cultures drawn, started on vancomycin + zosyn and admitted to the floor with diagnosis of sepsis.

Day 3: Remains on vancomycin and zosyn, progress note still says "sepsis." BCx negative. Awake/interactive.

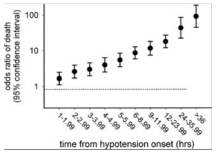
Urine culture: E. coli susceptible to multiple oral and intravenous agents.

Making the Right Decision Is Important

Getting the correct antibiotic to our sickest patients in a timely manner is critical.

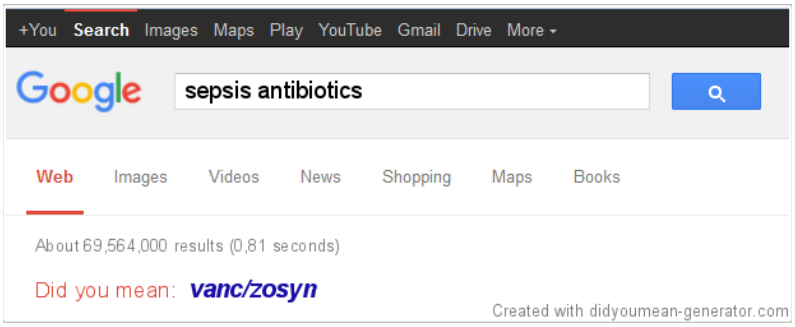
Inappropriate empiric antibiotics associated with increased mortality and longer length of stay.
- In febrile inpatients, in ICU patients

In Septic Shock, each hour delay in administration of appropriate antimicrobials is associated with increased mortality.
- Average decrease in survival of 7.6%/hour over the first 6h after shock onset



Surviving Sepsis Campaign

Fraser A, *et al.* Am J Med 2006;119:970-6
Kollef, M, *et al.* Chest 1999. 115: 462-474
Kumar et al. Crit Care Med. 2006 Jun;34(6):1589-96.



But, not for ALL infected patients

"Sepsis" without shock – a very heterogeneous population that does NOT show the same time-related associations with antibiotic/mortality

Sepsis can be hard to diagnose. Many patients with hypotension have non-infectious diagnoses.

- pulmonary emboli, fluid under/overload, toxin exposures, drug adverse effects, malignancies, bleeding, mechanical complications of surgery, obstructed organs, etc….

Overly tight limits on timing of antibiotics for suspected sepsis may cause clinicians to err on the side of over-treatment, skip diagnostic steps, and subject patients to the harms of antibiotic overuse.

Weinberger et al. J Infect Dis. 2020 Jul 21;222(Suppl 2):S110-S118
Liu VX. Am J Respir Crit Care Med 2017; 196:856–863
Seymour CW, et al. N Engl J Med 2017; 376:2235–2244

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Sometimes, You Don't Need An Antibiotic

Don't routinely prescribe antibiotics for acute mild-to-moderate sinusitis unless symptoms last for seven or more days, or symptoms worsen after initial clinical improvement

Don't order antibiotics for adenoviral conjunctivitis

Don't routinely provide antibiotics before or after intravitreal injections

Don't prescribe oral antibiotics for uncomplicated acute tympanostomy tube otorrhea

www.choosingwisely.org

Antibiotics should not be used for apparent viral respiratory illnesses (sinusitis, pharyngitis, bronchitis)

Don't prescribe oral antibiotics for uncomplicated acute external otitis

Avoid antibiotics and wound cultures in emergency department patients with uncomplicated skin and soft tissue abscesses after successful incision and drainage and with adequate medical follow-up

Don't use antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present

AU represents a modifiable risk

AU in Nursing Homes is highly variable and correlated with AEs

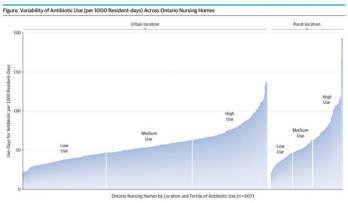


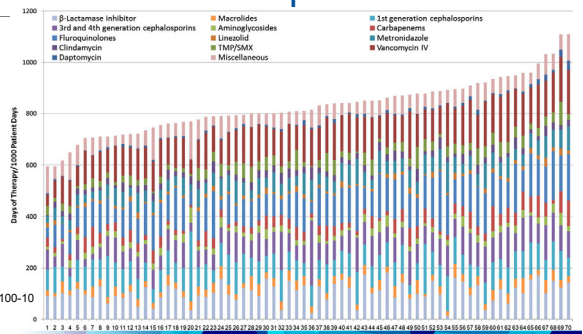
Table 3. Antibiotic-Related Adverse Outcomes Among Residents Living in Nursing Homes With Low, Medium, and High Antibiotic Use[a]

Characteristic	Antibiotic Use, No. (%)		
	Low (n = 33 822)	Medium (n = 31 425)	High (n = 24 943)
Clostridium difficile	274 (0.8)	268 (0.9)	221 (0.9)
Diarrhea or gastroenteritis	3347 (9.9)	3388 (10.8)	2889 (11.6)
Infection with antibiotic-resistant organism	412 (1.2)	431 (1.4)	319 (1.3)
Antibiotic allergy	13 (0.0)	25 (0.1)	22 (0.1)
General adverse event from medication	96 (0.3)	124 (0.4)	88 (0.4)
Any antibiotic complication with or without potential for indirect harms to nonrecipients (primary composite outcome[b])	3869 (11.4)	3890 (12.4)	3311 (13.3)
Only antibiotic complications with potential for indirect harms to nonrecipients (secondary composite outcome[b])	3797 (11.2)	3801 (12.1)	3237 (13.0)

Daneman et al. JAMA IM 2015;175 (8): 1331-1339

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Acute Care Academic Hospitals



Polk et al. CID; 2011 Dec;53(11):1100-10

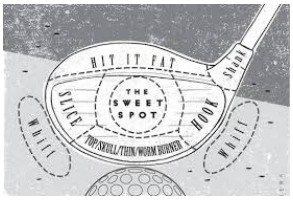
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Good use of antibiotics requires balance. It's nuanced and complex.

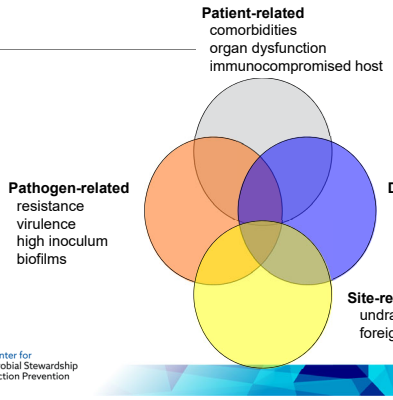
Right Diagnosis
Right Drug
Right Dose
Right Timing
Right Duration

Improve therapeutic choices (underuse)

Reduce unnecessary use (overuse)



Why "Good" Antibiotics Fail



(modified) from Moise PA et al. Lancet Infect Dis. 2009;9:617-24.

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The “4 Moments” of Antibiotic Decision-Making

1	2	3	4
Does the patient have an infection that requires antibiotics?	Have I ordered appropriate cultures before starting antibiotics? What empirical antibiotic therapy should I initiate?	A day or more has passed. Can I stop antibiotics? Can I narrow therapy? Can I change from IV to oral therapy?	What duration of antibiotic therapy is needed for this patient’s diagnosis?

Tamma PD et al. *JAMA*. 2019;321(2):139-140.

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5 or 6 “Ds” of Antimicrobial Stewardship

Goebel et al. Clin Micro Rev 2021. https://doi.org/10.1128/CMR.00003-20

Morency-Potvin, Schwartz, Weinstein. Clin Micro Rev 30: 381-407	
Diagnosis	Make and document the right diagnosis.
Debridement/ Drainage	Drainage of abscesses and removal of necrotic tissue or foreign material when required.
Drug	Use the right drug empirically according to suspected or confirmed diagnosis, risk factors for resistant pathogens, allergy, or major side effects.
Dose	Use right dose according to diagnosis, site of infection, or renal/hepatic dysfunction.
Duration	Use drugs for an appropriate duration.
De-escalation	Re-evaluate diagnosis and therapy routinely and de-escalate therapy to narrow-spectrum and/or oral agents when appropriate.

Diagnosis	Make and document the right diagnosis
Drug	Use the right empiric antibiotic
Dose	Use the right dose of antibiotic based on site of infection and renal or hepatic dysfunction
Duration	Use antibiotics for the recommended duration
De-escalation	De-escalate therapy based on susceptibilities and when urine cultures are negative

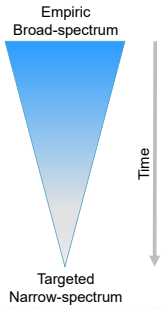
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General Indications for Antibiotics

Prophylaxis: prevent infection
- EASY! Guidelines and ordersets

Empiric: when you suspect infection but don’t exactly know with what pathogen
- Not easy. Local guidelines help (based on local micro data).

Directed: pathogen known
- Moderately easy. Follow and interpret patient-specific micro data.



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Choice of Empiric Antimicrobials

What class of pathogen am I likely to be treating?
- (Bacterial? Viral? Fungal? Other?)

If bacterial, what organisms are most likely?
- (Gram positive? Gram negative? Anaerobe?)

What information can I get to guide treatment?
- Microbiology data?

Do I need to order any other diagnostic tests?

How sick is my patient? How risky would it be if I miss?

Is my patient “special”? – allergy, ADEs, immune status

2

Have I ordered appropriate cultures before starting antibiotics?

What empirical antibiotic therapy should I initiate?

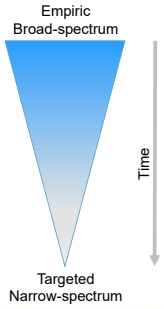
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De-escalation

De-escalation is a core principle of Antimicrobial Stewardship.

Target/narrow antibiotic therapies after more clinical data returns

Stop therapy when infection has been ruled out



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Clinical information: Small pieces over time.

Clinical information trickles in over time.

This means clinicians have to reassess regularly.

This also means they get interrupted with ‘real-time’ notifications and need to respond.

This a complex process: unpredictable, unknowns, uncertainty.

Putting the puzzle together completely takes attention, follow up on details, ability to make decisions in the setting of unknowns, AND an eye on the long-term goals.



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DIAGNOSIS

Microbiologic Culture
- "Gold standard"
- Requires sampling of site of infection *prior to* therapy
- Allows determination of antimicrobial susceptibility

Growth?
- Stain (Prelim ID)
- Definitive ID
- Susceptibility testing





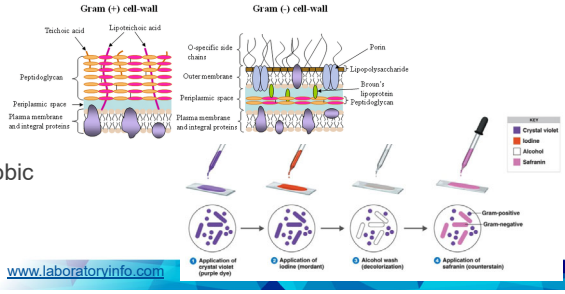
DIAGNOSIS: Stain

Direct Visualization

Gram stain
- Often provide clues to etiology (may allow presumptive diagnosis in some cases)
- Gram Positive
- Gram Negative
- Non-staining

Shape
- Cocci
- Rods

Aerobic/Anaerobic



www.laboratoryinfo.com

Quick and Dirty Anti-bacterial Classification

Gram positive – skin, lung, guts, devices

Gram negative – guts, urine, some lung, chronic wounds

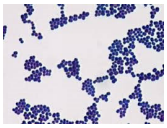
Atypicals – lung, STIs

Anaerobes –gas- and abscess-forming, bad odors

Antifungals – guts, devices, immunosuppressed + abx-exposed hosts

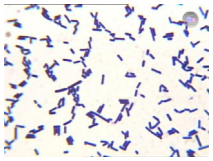
GRAM POSITIVE ORGANISMS

Gram positive cocci
- *Staphylococcus aureus*
- Coagulase negative staphylococcus
- *Streptococcus pneumoniae*
- *Streptococcus* sp.
- *Enterococcus* sp.



Gram positive – skin, lung, guts, devices

Gram positive rods
- *Bacillus* sp. (aerobes)
- *Clostridium* sp. (anaerobes)



MSSA:
Cefazolin
Nafcillin/Oxacillin

MRSA:
Vancomycin
Daptomycin
TMP/SMX

Strep:
Penicillin
Ampicillin/Amoxicillin

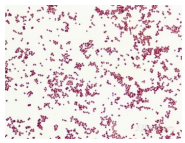
Ceftriaxone

Enterococci: Ampicillin, Vancomycin

VRE: Daptomycin, Linezolid

GRAM NEGATIVE ORGANISMS

Gram negative cocci
- *Neisseria meningitidis*
- *Neisseria gonorrhoeae*

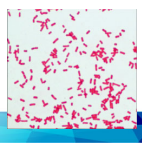


Gram negative rods (enteric)
- *E. coli*
- *Klebsiella* sp.
- *Enterobacter* sp.
- *Proteus* sp.
- *Serratia* sp.

CA-Enterics:
Ceftriaxone
Quinolones
TMP/SMX

Gram- negative: guts, urine, some lung

Gram negative rods (non-enteric, non-lactose fermenters)
- *Pseudomonas aeruginosa*
- *Stenotrophomonas maltophilia*
- *Acinetobacter* sp.



Anti-pseudomonal or HA-Resistant Enterics:
Pip/tazo
Cefepime
Ceftazidime
(Carbapenem)

Antibiotics with Anti-anaerobic Activity

Class	Agents (Route)	*B. fragilis* susceptibility[4-7]
Beta-lactam beta-lactamase inhibitor combinations	amoxicillin/clav (PO) ampicillin/sulb (IV) piperacillin/tazo (IV)	90-97% 97% > 99%
Cephalosporin	cefotetan (IV) cefoxitin (IV)	N/A 83-90%
Carbapenem	doripenem (IV) ertapenem (IV/IM) meropenem (IV) imipenem (IV)	> 99%
Fluoroquinolone	moxifloxacin (IV/PO)	66-70%
Other	clindamycin (IV/PO) metronidazole (IV/PO) tigecycline (IV)	66-70% > 99% 81-96%



B. fragilis is the most common group of gut anaerobes.
Then GPCs (*Clostridium* spp.)

Also consider: mouth, vaginal sources

Gas- and abscess-forming, bad odors

C. difficile is a special case (oral vancomycin).

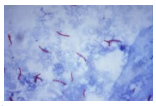
NON-STAINING PATHOGENS

- "Atypicals" -- Not stained by Gram's method (Intracellular)
  - *Legionella* sp. (Antigen test of the urine)
  - *Chlamydia (PCR)*
  - *Rickettsia (Serology)*
- Mycobacteria
  - *M. tuberculosis*
  - Non-tuberculous mycobacteria

Macrolides:
Azithromycin
Clarithromycin

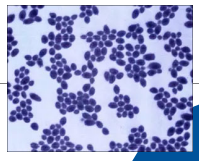
Tetracyclines:
Doxycycline
Minocycline

Community-acquired pneumonia	Pathogens	CXR pattern
Typical pneumonia	Bacterial: *S. Pneumoniae* *H. Influenzae*	Lobar, dense
Atypical pneumonia	Viral: influenza, RSV Bacterial: *Legionella* *Mycoplasma* *Chlamydia*	Diffuse, patchy



Ziehl-Neelsen Stain of TB

Antifungals



Candida/Yeast
- Fluconazole
- Echinocandins (micafungin, caspofungin)

Cryptococcus
- Amphoterocin + flucytosine
- Fluconazole

Molds (Rhizopus/Mucor, Aspergillus)
- Voriconazole
- Posaconazole, Isavuconazole
- Itraconazole

http://drfungus.org

Guts, devices, immunosuppressed + abx-exposed hosts

MSG ERC doctor fungus
Your online reference to all things mycological

DIAGNOSIS

Antigen tests
- Very useful for following (and sometimes diagnosing) viral infections: HIV, HBV, COVID-19
- Occasionally useful for other pathogens (e.g., Cryptococcus)
- Quick/rapid tests are often based on antigen testing
- Urine is sometimes used for antigen tests (e.g. Legionella urine antigen)





DIAGNOSIS

Serology
- For bacterial infections, generally not useful in early diagnosis (usually requires acute and convalescent tests)
- For viral infections, IgM may allow early diagnosis (e.g., HepA)
- Works ok for difficult to access/culture pathogens

DIAGNOSIS

PCR and other "molecular" tests
- Increasingly used, highly sensitive
- Allows diagnosis of non-culturable pathogens (e.g., norovirus) and faster identification(e.g., pertussis, MRSA in blood);
- Subject to false positives due to sensitivity (e.g. *C. difficile*)





Patients are individuals.



Drug interactions
Age
Allergies
Pregnancy, breast feeding
Toxicity (idiosyncratic reactions)
Dose adjustment for renal and/or hepatic dysfunction
Ability to absorb an oral antibiotic
Immune status

Adherence:
- Cost
- Taste
- Frequency of administration
- Pill size
- Duration of therapy
- Multiple drug therapy
- Adverse effects
- Current symptoms

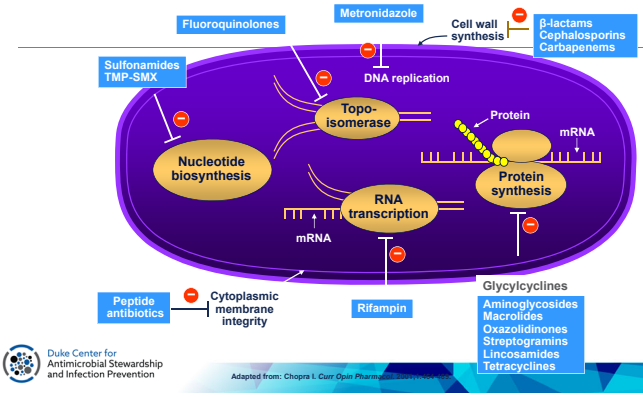
Pathogens are tricky.

Antibiotic = A drug that kills or inhibits the growth of bacterial pathogens

Resistant = Somewhat arbitrary designation that implies that an antimicrobial will not inhibit bacterial growth at clinically achievable concentrations

Susceptible = Somewhat arbitrary designation that implies that an antimicrobial will inhibit bacterial growth at clinically achievable concentrations

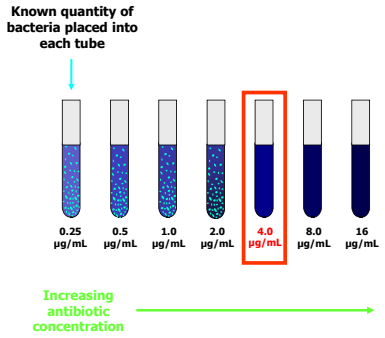
Mechanisms of Action of Antibiotics



Adapted from: Chopra I. *Curr Opin Pharmacol*. [illegible]

MIC = Minimal inhibitory concentration. Lowest concentration of antimicrobial that inhibits growth of bacteria. Commonly used in clinical lab

Breakpoint = The MIC that is used to designate between susceptible and resistant.



Durations (old approach)

- Most guideline-recommended antibiotic durations are based on…
- Qualified with "it depends…"
- Duration questions are ~70% of ID consults.

The answer, Dr. Gilbert, is that this is highly-specialized knowledge, rarefied information that only 100% Board-Certified, USDA-inspected Infectious Diseases Doctors know. And since I'm concerned that your article might give readers the wrong impression about our scientific credibility, I'll now divulge what we've learned, and how to apply it.

To figure out how long antibiotics need to be given, use the following rules:

1. Choose a multiple of 5 (fingers of the hand) or 7 (days of the week).
2. Is it an outpatient problem that is relatively mild? If so, choose something less than 10 days. After application of our multiples rule, this should be 5 or 7 days.
3. Is it *really* mild, so much so that antibiotics probably aren't needed at all but clinician or patient are insistent? Break the 5/7 rule and go with 3 days. Ditto uncomplicated cystitis in young women.
4. Is it a serious problem that occurs in the hospital or could end up leading to hospitalization? With the exception of community-acquired pneumonia (5 or 7 days), 10 days is the minimum.
5. Patient not doing better at the end of some course of therapy? Extend treatment, again using a multiple of 5 or 7 days.
6. Does the infection involve a bone or a heart valve? Four weeks (28 days) at least, often 6 weeks (42 days). Note that 5 weeks (35 days) is not an option — here the 5's and 7's cancel each other out, and chaos ensues.
7. The following lengths of therapy are inherently weird, and should generally be avoided: 2, 4, 6, 8, 9, 11, 12, 13 days. Also, 3.14159265 days.

In this highly data-driven exercise, it is imporant also to note the *number* of rules — ***seven***, as in days of the week.

https://blogs.jwatch.org/hiv-id-observations/index.php/how-to-figure-out-the-length-of-antibiotic-therapy/2010/10/22/



Paul E. Sax, MD
Contributing Editor
NEJM JOURNAL WATCH INFECTIOUS DISEASES

Trials comparing short- vs. longer-course antibiotics have shown short-course is just as effective

	Antibiotic Duration	
Disease	**Short**	**Long**
Community-acquired pneumonia	3-5 days	7-10 days
Nosocomial pneumonia (HAP/VAP)	≤ 8 days	10-15 days
Pyelonephritis	5-7 days	10-14 days
Intraabdominal infection	4 days	10 days
Acute exacerbation of chronic bronchitis (AECB) and COPD	≤ 5 days	≥ 7 days
Acute bacterial sinusitis	5 days	10 days
Cellulitis	5-6 days	10 days
Chronic osteomyelitis	42 days	84 days

5 is the new 7

Spellberg B. JAMA Intern Med 2016;176(9):1254-1255.

WHAT IS ANTIMICROBIAL STEWARDSHIP?

Duke University School of Medicine

dcasip.medicine.duke.edu

IDSA/SHEA/PIDS definition

"coordinated interventions designed to improve and measure the appropriate use of [antibiotic] agents by promoting the

selection of the optimal [antibiotic] drug regimen including

dosing,

duration of therapy, and

route of administration."

-- Infectious Diseases Society of America (IDSA), the Society for Healthcare Epidemiology of America (SHEA), and the Pediatric Infectious Diseases Society (PIDS)

Barlam et al. *CID* 2016; 62(10): e51-77.
Fishman et al. *ICHE* 2012; 33:322-7.

Antimicrobial Stewardship Program

Decision support for prescribers of antimicrobials.

Coordinated program

Multidisciplinary teams
- MD, PharmD, RN, micro, IP, IT

Multi-level interventions:
- Educational
- Systems-based vs. 1:1
- Technology
- Active vs. Passive



Dellit et al. Clin Inf Dis. 2007;44(2):159-177.

Goals of Antimicrobial Stewardship

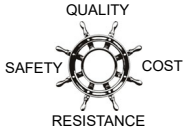
Primary:
- Improve quality and increase safety through appropriate use of antimicrobials
  - Improve therapeutic choices (underuse)
  - Reduce unnecessary use (overuse)

Secondary:
- Decrease emergence of resistance

Desirable "side effects" from an ASP:
- Decrease costs for health system
- Satisfy regulatory requirements (2017)

The goal is NOT to decrease antibiotic use…

It's to IMPROVE antibiotic use!



Moehring and Anderson. Curr Infect Dis Rep 2012

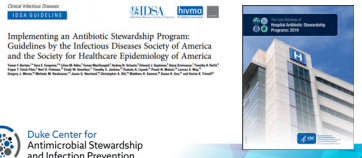
Resources for Inpatient Stewardship

IDSA/SHEA guidelines on Implementing an ASP (2009, 2016): *CID* 2016;62(10):e51–e77

CDC Core Elements Document(s) (2014, 2019): https://www.cdc.gov/antibiotic-use/healthcare/pdfs/hospital-core-elements-H.pdf

The Joint Commission Standard (2017): https://www.jointcommission.org/assets/1/6/New_Antimicrobial_Stewardship_Standard.pdf

CMS Condition of Participation (2020): Federal Register 9/30/2019



Strength of Rec	Strategies
Strong	Preauthorization/restriction Prospective audit & feedback CDI-focused intervention PK monitoring (AG) IV/PO switch Duration-focused intervention
Weak	Facility-specific guidelines Syndrome-specific intervention Time-out/Auto Stop Computerized Decision Support PK monitoring (Vanco) Alternate dosing for Beta Lactams Penicillin allergy assessments Stratified antibiograms Cascaded reporting of susceptibilities Rapid diagnostics: virus, blood culture Serial procalcitonin in ICU sepsis Fungal markers in Hem malignancy Febrile Neutropenia guidelines Antifungals in immunocompromised DOT>DDD AU data
Good Clinical Practice	Cost > purchasing data Choose clinical outcome metrics wisely Promote AS in SNFs, NICUs, terminally ill
Rec Against	Antibiotic Cycling Didactic education alone

"Action" for inpatient ASPs

LOTS of potential AS strategies suggested in Guidelines

Must be tailored to institutional need and priorities

AVOID: overtaxed ASP personnel

CID 2016;62(10):e51–e77

"Actions" for Inpatient Stewardship

Preauthorization/restriction (before prescribing)
- Can be time/personnel intensive
- Must think through unintended consequences and process snafus
- Not for all hospitals – local culture plays a role
- Best if for targeted agents (not every antibiotic order…)

Post-prescription audit and feedback (after prescribing)
- Front-line stewardship "experts" actively review patients on antibiotics and give feedback to prescribers 1:1
- Time intensive, but effective
- Better for personal relationships
- Need ID "back up" for tough cases

"Handshake" Stewardship
or
Stewardship Rounds

Face to face is better than phone/pager/zoom.

CID 2016;62(10):e51–e77
Hurst A et al. PIDJ 2016;35(10):1104-10

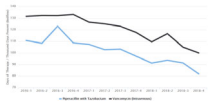
https://www.cdc.gov/nhsn/PDFs/pscManual/11pscAURcurrent.pdf

"Tracking" Antibiotic Use

NHSN AU Option is optional/voluntary for acute care hospitals
- ONLY uses electronic data from EHRs (no manual surveillance and no subjective components)

Rate: Days of therapy (DOT) per 1,000 days present
- DOT = calendar days of treatment regardless of number of doses
- Separate drugs counted separately
- Denominator is DIFFERENT than patient days

Data is stratified by Agent, Route, Unit location



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Benchmarking AU between Hospitals

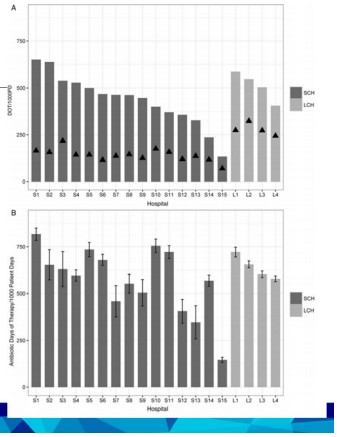
Ongoing area of research, more data emerging

What you want to measure:
- Prescribing practices and decision-making

What you get:
- Tonnage or measure of abx exposure – not "appropriate" abx

Problems:
- Case mix
- Hospital size
- Clinical service lines (e.g. surgical specialties, types of ICUs, moms/babies)
- Assume more = bad (not always true clinically)

<u>Should be viewed as a starting point for further investigation and explanation.</u>



Ibrahim, Polk. Expert Rev Anti Infect Ther 10 (4):445-57.
Stenehjem. CID 2016;63(10):1273–80

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NHSN Standardized Antibiotic Administration Ratio (SAAR)

Standardized Antibiotic Administration Ratio: Observed/Expected based on NHSN baseline + limited risk adjustment with information from annual survey
- Heavily stratified: Pediatric (8), NICU (7), and Adult (7) agent groups; Pediatric (5), NICU (3), and Adult (8) NHSN unit types. No benchmarks for highly specialized units.

Latest baseline: 2017 or 2018
- Current SAAR targets should generally be <1

https://www.cdc.gov/nhsn/pdfs/datastat/2019-au-report-508.pdf
https://www.cdc.gov/nhsn/pdfs/ps-analysis-resources/aur/au-saar-guide-508.pdf

National Healthcare Safety Network
SAARs Table - All Adult and Pediatric Standardized Antimicrobial Administration Ratios (SAARs) High-Level Indicators and High-Value Targets by Location (2017 Baseline)
As of: September 24, 2020 at 4:13 PM
Data Range: All AU_SAAR_2017
If (((location = "MICU")))
Broad spectrum antibacterial agents predominantly used for hospital-onset infections used in adult SAAR ICUs

Facility Org ID	SAAR Type 2017 Baseline	Location	Summary Yr/Qtr	CDC Location	Antimicrobial Days	Predicted Antimicrobial Days	Days Present	SAAR	SAAR p-value	95% Confidence Interval
13860	Adult_BSHO_ICU_2017	MICU	2018Q4	IN:ACUTE:CC:M	245	326.444	1035	0.751	0.0000	0.661, 0.849
13860	Adult_BSHO_ICU_2017	MICU	2019Q3	IN:ACUTE:CC:M	262	218.444	621	1.199	0.0046	1.061, 1.351

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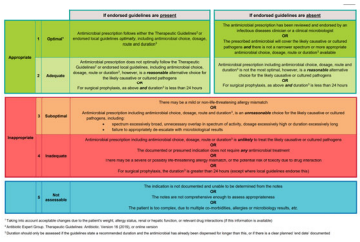
Measuring "Appropriate" or "Optimal" antimicrobial use in the Inpatient Setting

Will generally introduce subjectivity and require individual case review by a trained individual

More focused to syndrome and/or drug
- "MUE" + adherence with local guidelines

Typically sampled prevalence or retrospective study, but can be prospective and integrated into intervention delivery

Big time personnel effort

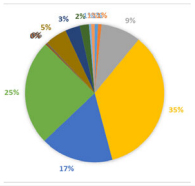


https://www.ncas-australia.org/ncas-publications

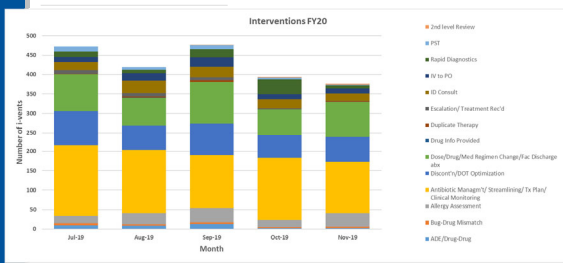
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iVENTs

"The Grind"



1. Antibiotic streamlining/de-escalation (35%)
2. Dose/Drug (25%)
3. Duration/Discontinuation (17%)
4. Allergy assessment (9%)
5. ID consult rec (5%)
6. IV/PO switch (3%)



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CMS: ASP required in Long-term Care

CMS Requirement for Long-term Care ASPs

<u>Barriers to Implementation of AS in LTC</u>:

Knowledge/Evidence

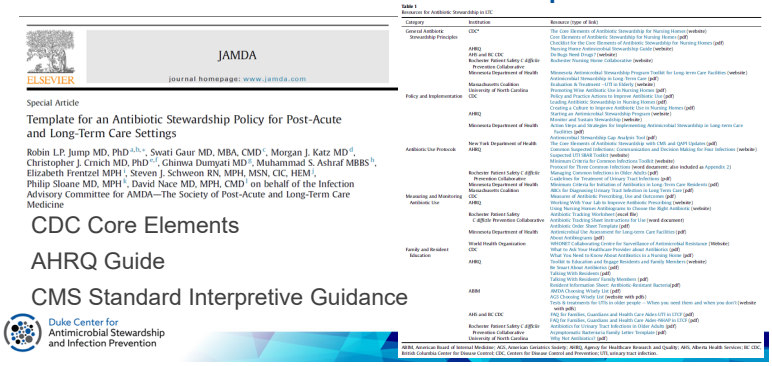
Expertise

Different stakeholders + processes of care than acute care

Personnel and turnover

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Resources for LTC Stewardship



JAMDA

journal homepage: www.jamda.com

Special Article

Template for an Antibiotic Stewardship Policy for Post-Acute and Long-Term Care Settings

Robin LP. Jump MD, PhD[a,b,*], Swati Gaur MD, MBA, CMD[c], Morgan J. Katz MD[d], Christopher J. Crnich MD, PhD[e,f], Ghinwa Dumyati MD[g], Muhammad S. Ashraf MBBS[h], Elizabeth Frentzel MPH[i], Steven J. Schweon RN, MPH, MSN, CIC, HEM[j], Philip Sloane MD, MPH[k], David Nace MD, MPH, CMD[l] on behalf of the Infection Advisory Committee for AMDA—The Society of Post-Acute and Long-Term Care Medicine

CDC Core Elements

AHRQ Guide

CMS Standard Interpretive Guidance

Table 1
Resources for Antibiotic Stewardship in LTC

Category	Institution	Resource (type of link)
General Antibiotic Stewardship Principles	CDC*	The Core Elements of Antibiotic Stewardship for Nursing Homes (website) Core Elements of Antibiotic Stewardship for Nursing Homes (pdf) Checklist for the Core Elements of Antibiotic Stewardship for Nursing Homes (pdf) Implementing an Antibiotic Stewardship Guide (website) Do Bugs Need Drugs? (website)
	AHRQ AHA and HC CDC Rochester Patient Safety C.diff-lcle Prevention Collaborative Minnesota Department of Health	Rochester Nursing Home Collaborative (website) Minnesota Antimicrobial Stewardship Program Toolkit for Long-term Care Facilities (website)
	Massachusetts Coalition University of North Carolina	Antimicrobial Stewardship in Long Term Care (pdf) Evaluation & Treatment <UTI in Elderly (website)
Policy and Implementation	CDC	Implementing an Antibiotic Stewardship Program (pdf) Policy and Practice Actions to Improve Antibiotic Use (pdf)
	AHRQ	Leading Antibiotic Stewardship in Nursing Homes (pdf) Creating a Culture to Improve Antibiotic Use in Nursing Homes (pdf) Starting an Antimicrobial Stewardship Program (website)
	Minnesota Department of Health	Core Elements of Antibiotic Stewardship (pdf) Action Steps and Strategies for Implementing Antimicrobial Stewardship in Long-term Care Facilities (pdf)
	New York Department of Health	Antimicrobial Stewardship Gap Analysis Tool (pdf) The Core Elements of Antibiotic Stewardship with CMS and QAPI Updates (pdf)
Antibiotic Use Protocols	AHRQ	Common Suspected Infections: Communication and Decision Making for Four Infections (website) Suspected UTI SBAR Toolkit (website)
	Rochester Patient Safety C.diff-lcle Prevention Collaborative Minnesota Department of Health Massachusetts Coalition	Suspected Urinary Tract Infection Toolkit (website) Protocol for Three Common Infections (word document; also included as Appendix 2) Managing Common Infections in Older Adults (pdf) Guidelines for Treatment of Urinary Tract Infections (pdf) Minimum Criteria for Initiation of Antibiotics in Long-Term Care Residents (pdf) ABCs for Diagnosing Urinary Tract Infections in Long-Term Care (pdf)
Measuring and Monitoring Antibiotic Use	CDC AHRQ	Measures of Antibiotic Prescribing, Use and Outcomes (pdf) Using Nursing Homes Antibiograms to Choose the Right Antibiotic (website)
	Rochester Patient Safety C.diff-lcle Prevention Collaborative	Antibiotic Tracking Worksheet (excel file) Antibiotic Tracking Sheet Instructions for Use (word document) Antibiotic Order Sheet Template (pdf)
	Minnesota Department of Health	Antibiotic Time-out Checklist for Long-Term Care Facilities (pdf)
Family and Resident Education	World Health Organization CDC	About Antibiotics (pdf) NHSN/HAI Collaborating Centre for Surveillance of Antimicrobial Resistance (Website) What to Ask Your Healthcare Provider about Antibiotics (pdf)
	AHRQ	What You Need to Know About Antibiotics in a Nursing Home (pdf) Toolkit to Education and Engage Residents and Family Members (website) Be Smart About Antibiotics (pdf) Get Smart About Antibiotics Talking With Resident Family Members (pdf) Resident Information Sheet: Antibiotic-Resistant Bacteria (pdf)
	ABIM	AMDA Choosing Wisely List (pdf) ACG Choosing Wisely List (website with pdf) Tests & treatments for UTIs in older people — When you need them and when you don't (website with pdf)
	AHA and HC CDC	FAQ for Families, Guardians and Health Care Aides-UTI in LTCF (pdf) FAQ for Families, Guardians and Health Care Aides-HAAP in LTCF (pdf)
	Rochester Patient Safety C.diff-lcle Prevention Collaborative University of North Carolina	Antibiotics for Urinary Tract Infections in Older Adults (pdf) Asymptomatic Bacteria in Family Letter Template (pdf) Why Not Antibiotics? (pdf)

AHRQ, American Board of Internal Medicine; ACG, American Geriatrics Society; AHRQ, Agency for Healthcare Research and Quality; AHS, Alberta Health Services; BC CDC, British Columbia Center for Disease Control; CDC, Centers for Disease Control and Prevention; UTI, urinary tract infection.

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Examples of Stewardship "Action" in LTC

Antibiotic use protocols – "Minimum Criteria" for Abx starts

Test/diagnostic stewardship
- UA/culture
- *C. difficile*

Durations/length of therapy and guides for common infection
- UTI
- Pneumonia
- Cellulitis

"Active monitoring" as an alternative to empiric antibiotics in patients who have a clinically undifferentiated problem (e.g. "not at baseline")

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Example: Antibiotic Use Protocol

Target: nursing assessment

Identifies "red flag" symptoms

Includes "notes" that identify key areas for baseline knowledge

Provides next steps alternative (other than an antibiotic)

AHRQ Toolkit: "Minimum Criteria for Common Infections"

Minimum Criteria for Initiating Antibiotics for a Skin and Soft Tissue Infection

Initiate antibiotics if the following criteria are met:

○ New or increasing purulent drainage at a wound, skin, or soft-tissue site

OR

○ At least **two** of the following:
- Fever (temperature > 100°F [37.9°C] or two repeated temperatures of 99°F [37°C]), or
- Redness, or
- Tenderness, or
- Warmth, or
- Swelling that is new or increasing at the affected site

Notes:

1. For residents that regularly run a lower temperature, use a temperature of 2°F (1°C) above the baseline as a definition of a fever.
2. Herpes zoster is a virus and therefore does not require antibiotics but appropriate antivirals.
3. Odor is not a standalone criterion for treatment with antibiotics
4. Deeper infections such as bursitis may present with similar signs/symptoms.
5. Underlying osteomyelitis should be considered when managing a resident with an infected diabetic or decubitus ulcer.
6. Thromboembolic disease should be considered when a resident presents with an erythematous or swollen leg.
7. These criteria do not apply to residents with burns.
8. Gout can at times be mistaken for cellulitis or vice versa.

If none of the minimum criteria are met, consider initiating the following:

- Assess vital signs, including temp, every _____ hours for _____ hours; and/or
- Notify Physician/NP/PA if symptoms worsen or if unresolved in _____ hours.

Regardless of whether the minimum criteria are met or not, consider initiating the following:

- For discomfort or prior to cleaning/dressing changes, consider using acetaminophen or other pain relievers as needed.

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Active Monitoring

This is an active process

More frequent vital signs

Oral hydration

Assess for pain, changes in medicine, other reasons like a bad night's sleep

(or disagreement with a loved one)

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Order Set

□ Obtain vital signs (BP, Pulse, Resp Rate, Temp, Pulse Ox) every ____ hours for ____ days.

□ Record fluid intake each shift for _____ days.

□ Notify physician if fluid intake is less than _____ cc daily.

□ Offer resident _____ ounces of water / juice every _____ hours.

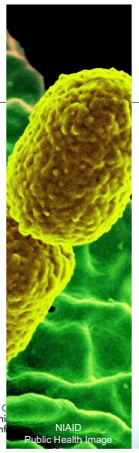
□ Notify physician, NP, or PA if condition worsens, or if no improvement in _____ hours.

□ Obtain the following blood work _____ .

□ Consult pharmacist to review medication regimen.

□ Contact the physician, NP, PA with an update on the resident's condition on _____.

Nace *et al.*, JAMDA 2014;15:133-139

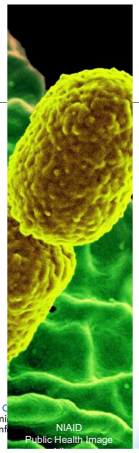


NIAID Public Health Image

Potential Policies & Procedures: UTI

- Concerns about stinky or cloudy urine should lead to increased hydration and perhaps, watchful waiting/careful observation.
- Automatic review of all medication changes by outside providers.
- Send residents to the Emergency Room with a note clearly stating what you are (and are not) worried about.

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NIAID Public Health Image

Potential Policies & Procedures: UTI

- Clear criteria for collecting a urine sample
- Documented protocol for proper sample collection and handling
- Communication tools when nurses call a covering provider
- Proactively talk to residents and their family members—on admission and during change of status

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Resources for Outpatient Stewardship

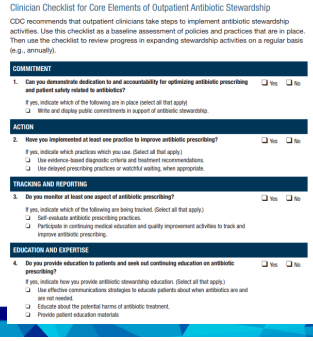
Outpatient Standard for TJC (Jan 2020)

4 “Core Elements”

Type of outpatient practice setting is highly varied

- Adult/pediatric
- Specialty clinics
- Retail clinics
- Urgent Care

https://www.cdc.gov/antibiotic-use/community/pdfs/16_268900-A_CoreElementsOutpatient_508.pdf



Clinician Checklist for Core Elements of Outpatient Antibiotic Stewardship

CDC recommends that outpatient clinicians take steps to implement antibiotic stewardship activities. Use this checklist as a baseline assessment of policies and practices that are in place. Then use the checklist to review progress in expanding stewardship activities on a regular basis (e.g., annually).

COMMITMENT

1. **Can you demonstrate dedication to and accountability for optimizing antibiotic prescribing and patient safety related to antibiotics?** ❑ Yes ❑ No
   If yes, indicate which of the following are in place (select all that apply)
   - ❑ Write and display public commitments in support of antibiotic stewardship.

ACTION

2. **Have you implemented at least one practice to improve antibiotic prescribing?** ❑ Yes ❑ No
   If yes, indicate which practices which you use. (Select all that apply.)
   - ❑ Use evidence-based diagnostic criteria and treatment recommendations.
   - ❑ Use delayed prescribing practices or watchful waiting, when appropriate.

TRACKING AND REPORTING

3. **Do you monitor at least one aspect of antibiotic prescribing?** ❑ Yes ❑ No
   If yes, indicate which of the following are being tracked. (Select all that apply.)
   - ❑ Self-evaluate antibiotic prescribing practices.
   - ❑ Participate in continuing medical education and quality improvement activities to track and improve antibiotic prescribing.

EDUCATION AND EXPERTISE

4. **Do you provide education to patients and seek out continuing education on antibiotic prescribing?** ❑ Yes ❑ No
   If yes, indicate how you provide antibiotic stewardship education. (Select all that apply.)
   - ❑ Use effective communications strategies to educate patients about when antibiotics are and are not needed.
   - ❑ Educate about the potential harms of antibiotic treatment.
   - ❑ Provide patient education materials

“Action” in Outpatient Stewardship

Most literature in Primary or Urgent Care

Peer comparison + data feedback

- Most commonly done for upper respiratory infection
- Identify diagnoses (e.g. viral URI) for which antibiotics should not be given. Benchmark % given abx with peers
  - HEDIS measures (primary care and pediatrics)

Suggested alternatives

Accountable justification

“Nudge” letter/poster

Education combined with the above

Gerber. JAMA 2013;309(22):2345-2352
Meeker. JAMA 2016; 315(6)562-570
Meeker. JAMA Intern Med. 2014;174(3):425-431.

We want to give you some important information about antibiotics.

Antibiotics, like penicillin, fight infections due to bacteria that can cause some serious illnesses. But these medicines can cause side effects like skin rashes, diarrhea, or yeast infections. If your symptoms are from a virus and not from bacteria, you won't get better with an antibiotic, and you could still get these bad side effects.

Antibiotics also make bacteria more resistant to them. This can make future infections harder to treat. This means that antibiotics might not work when you really need them. Because of this, it is important that you only use an antibiotic when it is necessary to treat your illness.

How can you help? Carefully follow your doctor's instructions. He or she will tell you if you should or should not take antibiotics.

When you have a cough, sore throat, or other illness, your doctor will help you select the best possible treatments. If an antibiotic would do more harm than good, your doctor will explain this to you, and may offer other treatments that are better for you.

Your health is very important to us. As your doctors, we promise to treat your illness in the best way possible. We are also dedicated to avoid prescribing antibiotics when they are likely to do more harm than good.

If you have any questions, please feel free to ask your doctor, nurse, or pharmacist.

A case, continued.

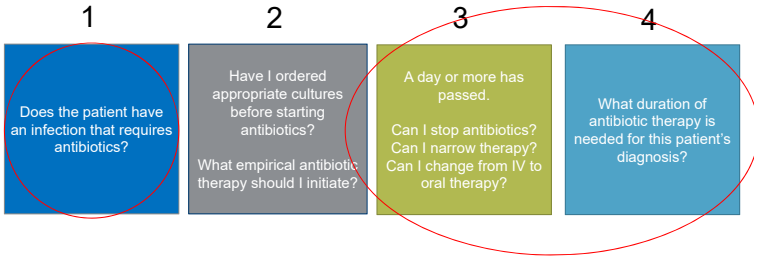
86F with history of dementia, diabetes, and poor functional status presents from SNF with confusion, fever.

Day 3: Remains on vancomycin and zosyn. Progress note still says “sepsis.” BCx negative. Awake/interactive.

Clinical pharmacist reviews the patient for vancomycin dosing, sees urine +E. coli susceptible to multiple oral and intravenous agents.

Contacts the provider.

Clinical Discussion



Tamma PD et al. *JAMA*. 2019;321(2):139-140.

Summary

Antibiotics are life-saving medicines that are often misused.

Antimicrobial decision-making is complex.

Optimized antimicrobial use through antimicrobial stewardship protects patients from unintended consequences.

Antimicrobial use affects individuals AND populations. Healthcare exposed populations are the most at risk.

Antimicrobial Stewardship Programs are required in US healthcare facilities and a key component of infection prevention.

THANK YOU!

Rebekah.Moehring@duke.edu

Antibiotics with Gram Positive (+) Activity

S. aureus	MRSA	VRE	*E. faecalis*
Nafcillin/Oxacillin			Ampicillin
Ampicillin/Sulbactam, Piperacillin/Tazobactam			Ampicillin/Sulbactam, Piperacillin/Tazobactam
Cephalosporins	Ceftaroline (only)		
Carbapenems			
(Fluoroquinolones)			
Vancomycin	Vancomycin		Vancomycin
Clindamycin	Clindamycin +/-		
Linezolid	Linezolid	Linezolid	Linezolid
Daptomycin	Daptomycin	Daptomycin	Daptomycin
Telavancin	Telavancin		
TMP-SMX	TMP-SMX		
Dalvabancin, Oritavancin	Dalvabancin, Oritavancin		

Antibiotics with Gram Negative (-) Activity

E. coli	*K. pneumoniae*	*Enterobacter*	*P. aeruginosa*
(Ampicillin)			
(Amp/sulb)	(Amp/sulb)		
Pip/Tazo	Pip/Tazo	Pip/Tazo	Pip/Tazo
Cephalosporins	Cephalosporins	3rd, 4th, 5th gen.	Ceftaz/Cefepime
Carbapenems	Carbapenems	Carbapenems	Imip, Mero, Dori
Aztreonam	Aztreonam	Aztreonam	Aztreonam
Aminoglycosides	Aminoglycosides	Aminoglycosides	Amino-glycosides
Fluoroquinolone	Fluoroquinolone	Fluoroquinolone	Cipro and Levo
Trimeth/Sulf	Trimeth/Sulf	Trimeth/Sulf	