How Can Antimicrobial Use Data Inform Antimicrobial Stewardship Strategies

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UNMC Nebraska Medicine

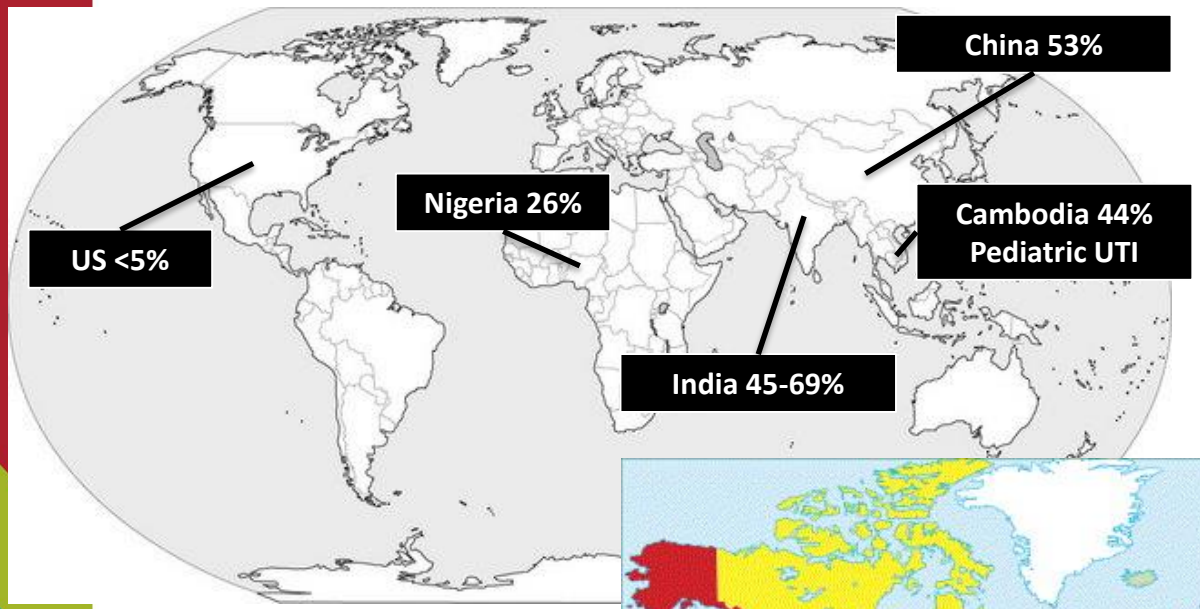
Objectives

- Understand the rationale for developing an antimicrobial stewardship program
- Review antimicrobial use metrics useful for informing antimicrobial stewardship strategies
- Provide practical examples on employing antimicrobial use data to inform antimicrobial stewardship strategies

Disclosure

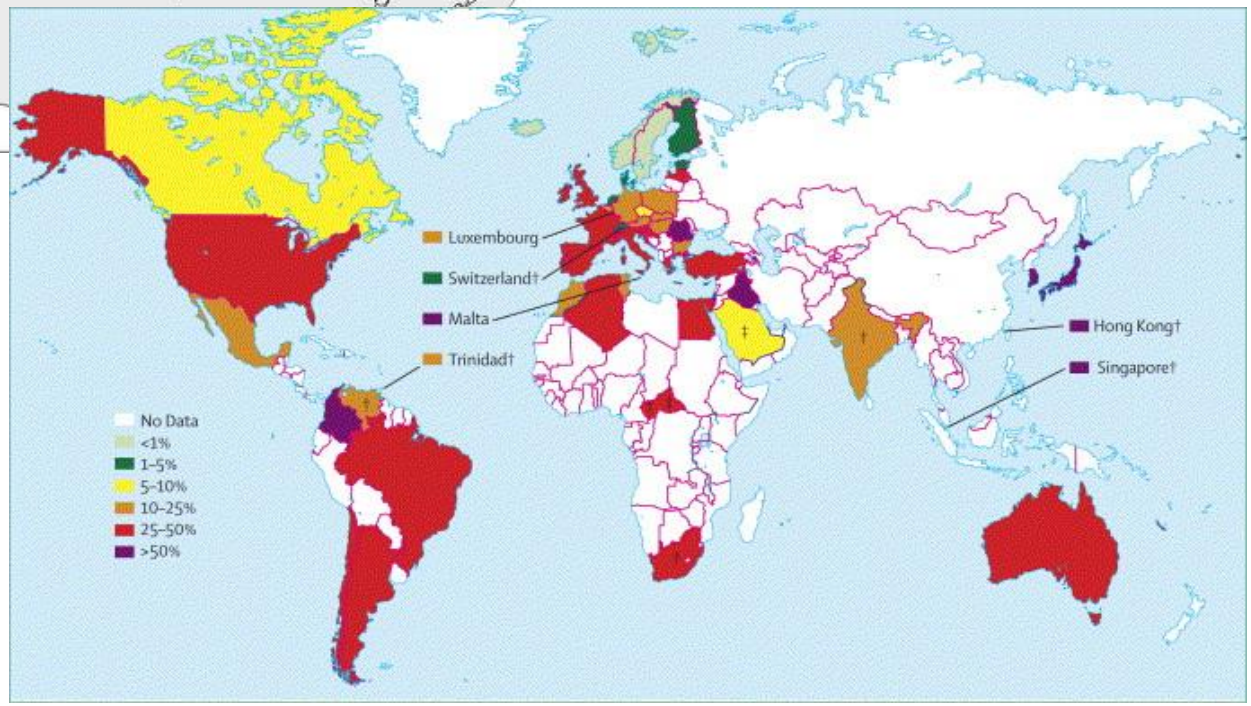
None

Worldwide Prevalence of Antibiotic Resistance



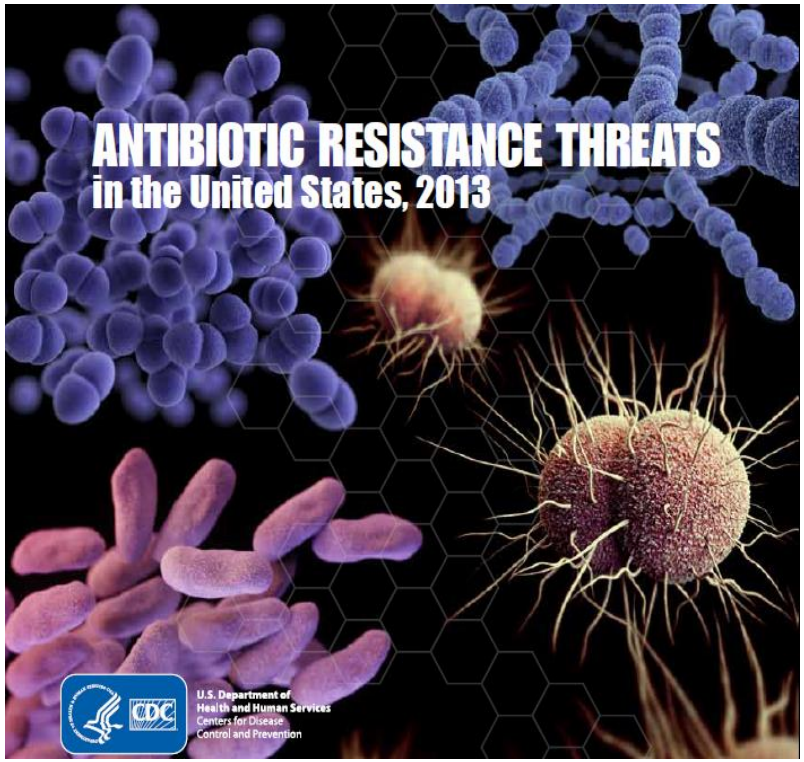
Prevalence of *E. coli* Resistant to 3rd Generation Cephalosporins (ESBL)

MRSA Prevalence



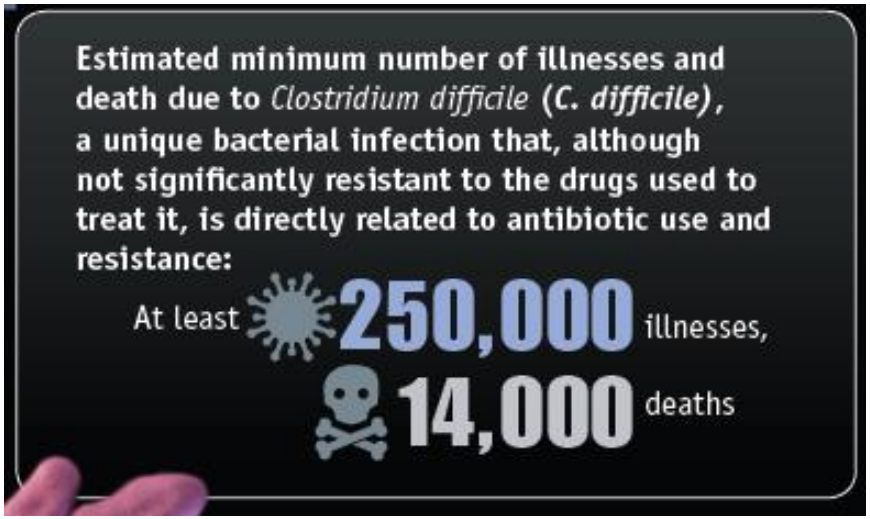
Doi Y, et al. *Clin Infect Dis*. 2013;56:641-8.
Qiao LD, et al. *BMJ Open*. 2013;3:e004152.
Sanchez GV, et al. *Emerg Infect Dis*. 2013;19:133-6.
Ogbolu DO, et al. *Int J Antimicrob Agents*. 2011;37:62-6.
Moore CE, et al. Paediatr Int Child Health. 2016;36:113-6.
Pathak A, et al. *Infect Drug Resist*. 2012;5:65-73.
Kaur N, et al. *J Clin Diagn Res*. 2014;8:DC01-3.
Grundmann H, et al. *Lancet* 2006;368:874-85.

Consequences of Antibiotic Resistance



Deaths Due to Resistant Pathogens

Deaths Due *C. difficile* Infections



Clinical and Financial Impact of Antibiotic Resistance

- Patients with MRSA bacteremia with likelihood of mortality compared to MSSA bacteremia (OR 1.93)[1]

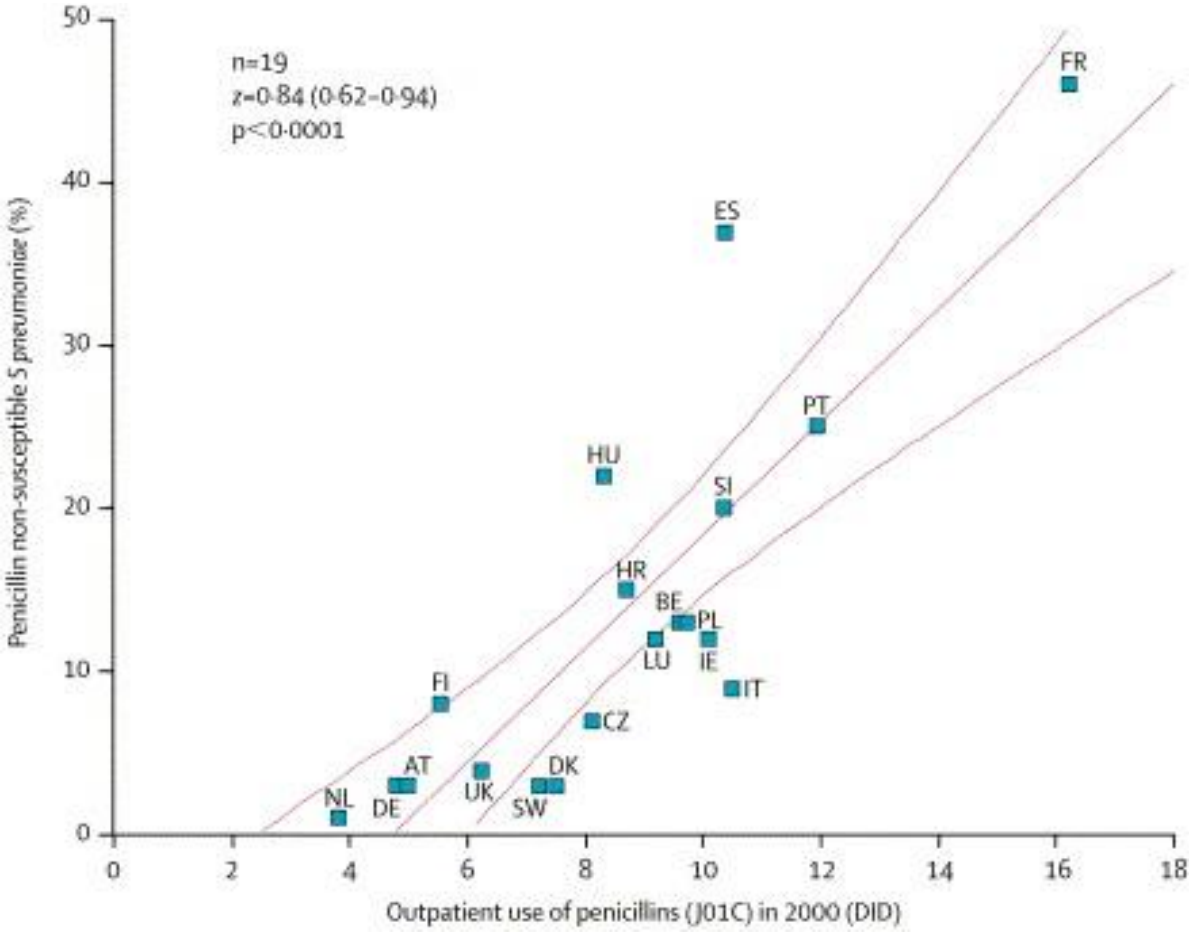
- MRSA vs. MSSA surgical site infection[2]
  - 90-day mortality: 20.7% vs. 6.7%
  - Median length of stay: 23 days vs. 14 days
  - Median charges: $92,363 vs. $52,791

- Costs associated antimicrobial resistance infection[3]
  - Excess medical costs: $18,588 to $29,069 per patient
  - Excess length of stay: 6.4 to 12.7 days
  - Attributable mortality: 6.5%
  - Societal costs: $10.7 to $15.0 million
  - Overall increased costs: $13.5 million per year

1. Cosgrove SE, et al. Clin Infect Dis 2003;36:53-9.
2. Engemann JJ, et al. Clin Infect Dis 2003;36:592-8.
3. Roberts RR, et al. Clin Infect Dis 2009;49:1175-84.

Where Does All This Resistance Come From?

Correlation between Penicillin Use and Prevalence of Penicillin Non-Susceptible *S. pneumoniae*



Goossens H, et al. *Lancet*. 2005;365:579-87.

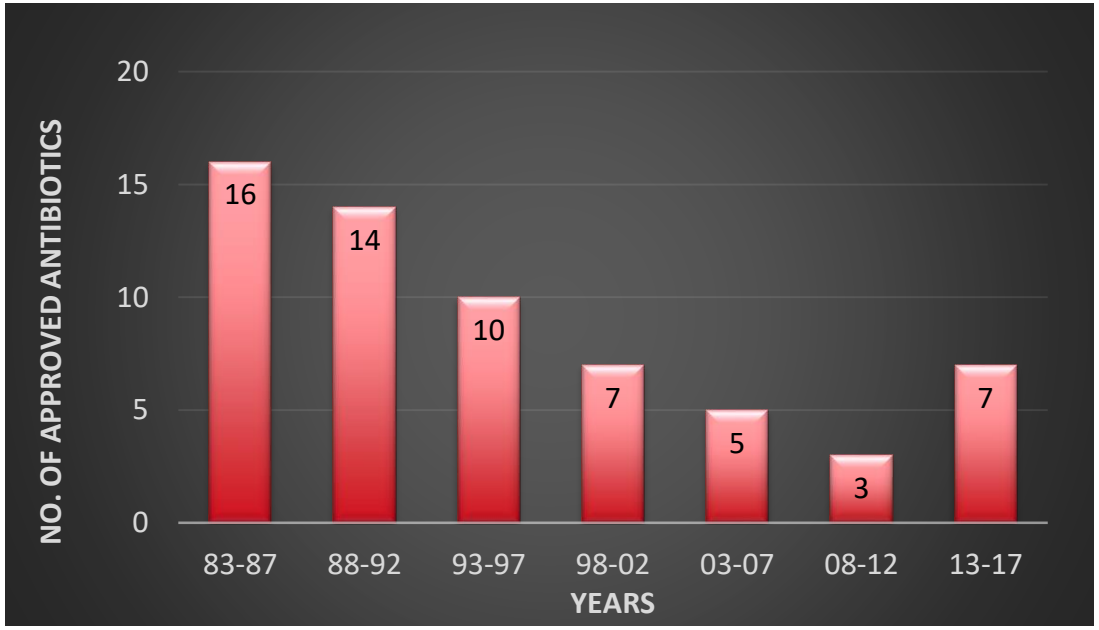
Evidence of Antibiotic Overuse in Acute Care Facilities

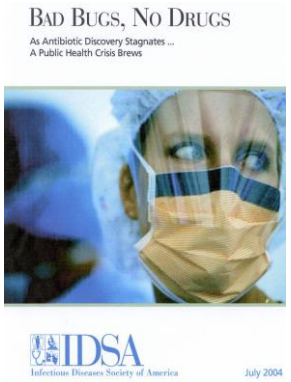
- ~20-50% of inappropriate prescribing in acute care settings[1]
- Prospective review of new antibiotic start over 2 weeks in 650-bed tertiary hospital[2]
- Total of 1941 days of therapy (DOT) for 129 patients captured
- 30% (>500 DOT) considered unnecessary

Reason for Unnecessary DOT	No. Pt (%)
Non-infectious or non-bacterial	187 (32)
Colonization or contamination	94 (16)
Longer duration than needed	192 (33)
Timely adjustment not made	20 (3)
Redundant coverage	60 (10)
Spectrum of activity not indicated	23 (4)

1. CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Atlanta, GA: US DHHS, CDC; 2014.
2. Hecker MT, *et al*. Arch Intern Med 2003:163:972-8.

Limited New Antibiotic Options





Bad Bugs Need Drugs

10x'20

Ten new ANTIBIOTICS by 2020

Target = ESKAPE

E*nterococcus faecium*
S*taphylococcus aureus*
K*lebsiella pneumoniae*
A*cinetobacter baumannii*
P*seudomonas aeruginosa*
E*nterobacter* species

Infectious Diseases Society of America. Clin Infect Dis 2011;52(suppl 5):S397-S428.

Theuretzbacher U. Recent FDA Antibiotic Approvals: Good news and Bad News. Available at: http://cddep.org/blog/posts/recent_fda_antibiotic_approvals_good_news_and_bad_news#sthash.adecdYpE.dpbs.

Drug@FDA: FDA Approved Drug Products. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.

Antibiotic-Associated Adverse Drug Events (ADE)

- Review of national database for ED visits due to ADE over 2 yrs
- >140,000 ED visit annually due to ADE from antibiotics
  - Translate to 1 in 5 ED visits
- Allergic reactions most common reason (>100,000 annual visits)
- Penicillins (37%) and fluoroquinolones (14%) were most commonly implicated
- Conclusions: small reduction in unnecessary use can significantly decrease ADE risks

- 10-month review of patients who received >24 hrs of antibiotics
- ~1500 patients (27% of admissions) met criteria
  - 20% developed ADE
- 287 regimens without clear indications
  - 56 (20%) were associated with ADE
  - Include 7 cases of *Clostridium difficile* infection
- ADE risks increase by 3% for every 10 days of therapy (DOT)

Shehab N, *et al*. Clin Infect Dis 2008;47:735-43.
Tamma PD, *et al*. JAMA Intern Med 2017;177:1308-15.

What Do We Do?

Options

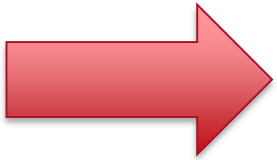
1. ~~Create new drugs~~
2. Learn to use what we have more wisely

Antimicrobial Stewardship

3. Infection prevention will also help

What is Antimicrobial Stewardship?

- Rational, systematic approach to antibiotic use
- Using or implementing processes that are designed to optimize antibiotic use
- Include interventions to guide clinicians:
  - When are antibiotics needed?
  - Which antibiotics should be used?
  - What is the optimal dose, route, duration of therapy?
- Focus is on **patient and public health** with goals to:
  - Cure / prevent infection
  - Minimize toxicity
  - Minimize resistance



Reduce Costs of Care

Regulatory Requirements

Joint Commission

Requirement

New Antimicrobial Stewardship Standard

APPLICABLE TO HOSPITALS AND CRITICAL ACCESS HOSPITALS

Effective January 1, 2017

Medication Management (MM)

Note: *An example of an educational tool that can be used for patients and families includes the Centers for Disease Control and Prevention's Get Smart document, "Viruses or Bacteria—What's got you sick? at http://www.cdc.gov/getsmart/community/downloads/getsmart-chart.pdf.*

Joint Commission Requirements

New standards for hospitals, CAH, LTCF (MM.09.01.01), effective 1/1/2017

1. Establish ASP as a priority
2. Educate practitioners on resistance and ASP activities
3. Educate patients/families on appropriate antibiotic use
4. Create ASP that is multidisciplinary
5. Include 7 CDC ASP core elements
6. Use approved multidisciplinary management protocol
7. Collect, analyze, report data on ASP
8. Act on improvement opportunities identified by ASP

Joint Commission Online

Oct. 4, 2017

EP deletion: MM.09.01.01, EP3 going away

Effective Oct. 1, The Joint Commission is deleting element of performance (EP) 3 for Medication Management (MM) 09.01.01 for hospitals and critical access hospitals. This EP will **still be in effect for nursing care centers**.

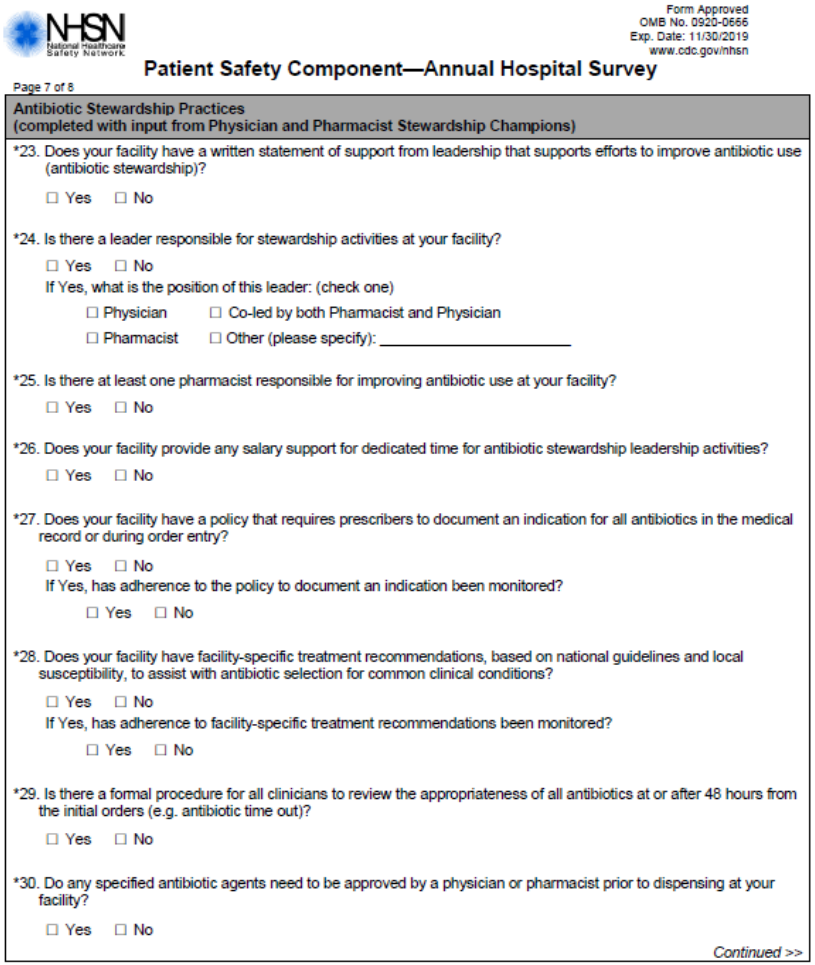
https://www.jointcommission.org/assets/1/6/New_Antimicrobial_Stewardship_Standard.pdf
https://www.jointcommission.org/assets/1/23/JC_Online_Oct._4.pdf

CMS Requirement for Conditions of Participation

- Rules proposed on 6/16/2016; yet to be finalized
- 42 CFR 482.42
  - …require a hospital to develop and maintain an antibiotic stewardship program
  - …to improve hospital antibiotic prescribing practices
  - …curb patient risk for possibly deadly CDIs
- Goals and responsibilities
  - Document evidence-based antibiotic use
  - Demonstrate sustained improvements in proper antibiotic use
  - Use nationally recognized guidelines to monitor and improve antibiotic use
  - Competency-based training on ASP guidelines, policy, and procedure

FY2018-21: Medicare Beneficiary Quality Improvement Project (MBQIP) Measures

	Patient Safety/Inpatient
Core/Required Improvement Initiatives	**OP-27:** Influenza Vaccination Coverage Among Healthcare Personnel (HCP) *(Facilities report a single rate for inpatient and outpatient settings)* **IMM-2:** Influenza Immunization for inpatients **Antibiotic Stewardship:** Measured via Center for Disease Control National Healthcare Safety Network (CDC NHSN) Annual Facility Survey **Inpatient ED Measures:** • **ED-1:** Median Time from ED Arrival to ED Departure for *Admitted* ED Patients • **ED-2:** Admit Decision Time to ED Departure Time for *Admitted* Patients



NHSN National Healthcare Safety Network

Form Approved
OMB No. 0920-0666
Exp. Date: 11/30/2019
www.cdc.gov/nhsn

Patient Safety Component—Annual Hospital Survey

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Antibiotic Stewardship Practices
(completed with input from Physician and Pharmacist Stewardship Champions)

*23. Does your facility have a written statement of support from leadership that supports efforts to improve antibiotic use (antibiotic stewardship)?

☐ Yes ☐ No

*24. Is there a leader responsible for stewardship activities at your facility?

☐ Yes ☐ No

If Yes, what is the position of this leader: (check one)

☐ Physician ☐ Co-led by both Pharmacist and Physician

☐ Pharmacist ☐ Other (please specify): _____

*25. Is there at least one pharmacist responsible for improving antibiotic use at your facility?

☐ Yes ☐ No

*26. Does your facility provide any salary support for dedicated time for antibiotic stewardship leadership activities?

☐ Yes ☐ No

*27. Does your facility have a policy that requires prescribers to document an indication for all antibiotics in the medical record or during order entry?

☐ Yes ☐ No

If Yes, has adherence to the policy to document an indication been monitored?

☐ Yes ☐ No

*28. Does your facility have facility-specific treatment recommendations, based on national guidelines and local susceptibility, to assist with antibiotic selection for common clinical conditions?

☐ Yes ☐ No

If Yes, has adherence to facility-specific treatment recommendations been monitored?

☐ Yes ☐ No

*29. Is there a formal procedure for all clinicians to review the appropriateness of all antibiotics at or after 48 hours from the initial orders (e.g. antibiotic time out)?

☐ Yes ☐ No

*30. Do any specified antibiotic agents need to be approved by a physician or pharmacist prior to dispensing at your facility?

☐ Yes ☐ No

Continued >>

https://www.ruralcenter.org/sites/default/files/FY18_21%20MBQIP%20Measures%20%28July%202017%29.pdf
https://www.cdc.gov/nhsn/forms/57.103_pshospsurv_blank.pdf

ASP Core Elements for Hospitals, Small and Critical Access Hospitals

- Leadership Commitment
- Accountability
  - Single MD Leader
- Drug Expertise
  - Pharmacist Leader
- Action
- Tracking
- Reporting
- Education

https://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html
https://www.cdc.gov/getsmart/healthcare/implementation/core-elements-small-critical.html

Comparison of ASP Core Element Documents

Core Element	Hospital ASP	Small & Critical Access Hospital ASP
Leadership Commitment	Formal statement, job descriptions, training support	Formal statement, approve ASP policy, integrate with QI, training support
Accountability	Single physician leader	C-suite physician accountable for outcomes
Drug Expertise	Pharmacist leader + other key support (e.g., micro, IP, IT, QI, RN)	Pharmacist leader, offer access to training, remote consultation
Action	Broad: time-out, audit-feedback Pharmacy: IV→PO, dose adjustment Infection: treatment guidelines (e.g., UTI)	Infection: UTI, CAP, SSTIs Drug: carbapenems, pip/tazo, IV vanco Pharmacist: IV→PO, dose adjustment RN: culture technique, monitor response
Tracking	Process: compliance to guidelines, policies Use: DOT, DDD per 1000 patient-days Outcome: antibiotic resistance, CDI rates	Submit AU/AR data to NHSN Monitor UTI, CAP, SSTI guideline compliance Medication use evaluations for selected drugs
Reporting	Process, use, outcome measures to frontline staff +/- NHSN	Regular report, provider-specific report, newsletters/emails
Education	Regularly to prescribers and staff	Incorporate in orientation and re-credentialing process; focus on UTI, CAP, SSTI interventions

https://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html
https://www.cdc.gov/getsmart/healthcare/implementation/core-elements-small-critical.html

The Stewardship Team

- Ideally anyone who prescribes, dispenses, administers, or receives antibiotics
- Should be multidisciplinary
- Core members
  - Infectious diseases physician / physician with ASP training
  - Pharmacist with ID / ASP certificate training
- Additional members
  - Infection preventionists
  - Clinical microbiologists
  - Information system specialists
  - Members of Quality Improvement
  - Nurses
  - Hospital epidemiologists

Dellit TH, et al. Clin Infect Dis 2007;44:159-77.
Fishman N. Infect Control Hosp Epidemiol 2012;33:322-7.
CDC. Core Elements of Hospital Antibiotic Stewardship Programs. Available at: http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html.

Nurses in Antimicrobial Stewardship Activities


WHITE PAPER

ANA AMERICAN NURSES ASSOCIATION | CDC

Redefining the Antibiotic Stewardship Team:

Recommendations from the American Nurses Association/Centers for Disease Control and Prevention Workgroup on the Role of Registered Nurses in Hospital Antibiotic Stewardship Practices

Effective Date: 2017

Executive Summary

The purpose of this American Nurses
White Paper is to inform registered
and facilitate their embracing an exp
programs (ASPs) and activities. The
series of online meetings, culminatin
conference with a selection of nurse
as having expertise and/or interest i
purpose of the workgroup is to explo
more engaged and take a leadership
antibiotic stewardship efforts. The fi
reviews ASPs and the current state o
second section is a summary of the
ASPs; gaps in nurses' knowledge and
the 21st century. The third part explo
ongoing stewardship efforts and offe

The mark 'CDC' is owned by the US Department of
permission. Use of this logo is not an endorsement
or enterprise.

ASP Task	Core Elements	Example of Nurse's Role
Triage/Isolation	Accountability Drug Expertise Education	Initially assess source of infection Identifies appropriate precaution
Early / appropriate culture	Accountability Drug Expertise Tracking	Obtain cultures before antibiotics Monitor/report culture results
Adverse events monitoring	Action Tracking Education	Monitor/report adverse events
Antibiotic dosing	Drug expertise Action Tracking Education	Obtain appropriate drug levels
Transition of care to different acuity level	Action Tracking Education	Communicate clinical information (diagnosis, management) to LTCF/VNA

Available at: http://www.nursingworld.org/ANA-CDC-AntibioticStewardship-WhitePaper. Accessed 9/26/17.

IDSA/SHEA Stewardship Strategies

General interventions

- Prospective audit and feedback
- Restriction / pre-authorization
- Practice guidelines
- Improvement of outcomes and antibiotic use based on syndrome
- Reduce use of *C difficile*-associated antibiotics
- Clinical decision support system
- Education / Encourage prescribers to review antibiotic regimens

Pharmacy-Based Strategies

- Pharmacokinetic monitoring service
- IV to PO conversion
- Use of pharmacokinetic / pharmacodynamic-optimized alternate dosing regimen
- Allergy assessment
- Shortest effective duration of therapy

Dellit TH, et al. Clin Infect Dis 2007;44:159-77.
Barlam TF, et al. Clin Infect Dis 2016;62:e51-77.

IDSA/SHEA Stewardship Strategies

Laboratory-Based Strategies

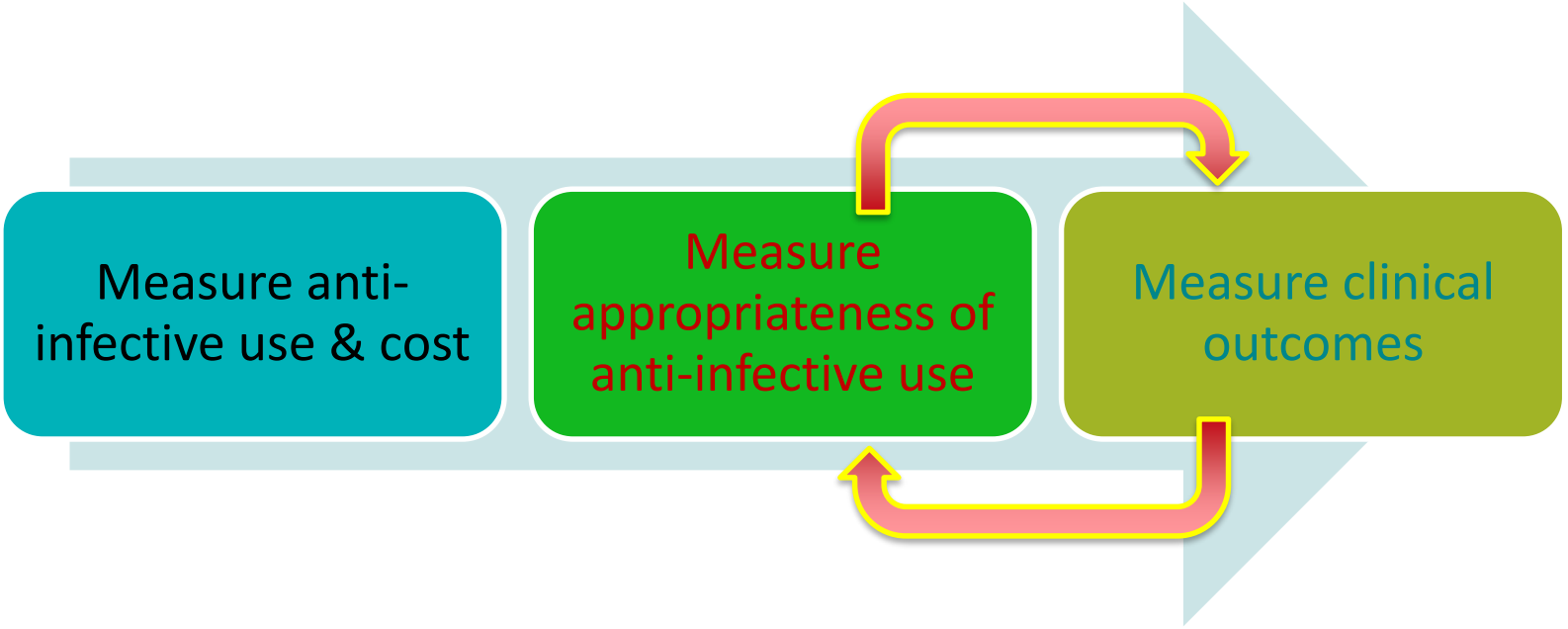
- Antibiograms based on sample source, location, age
- Selective susceptibility reporting
- Rapid testing for viral respiratory pathogens
- Rapid diagnostic for blood cultures
- Procalcitonin to reduce antibiotic use
- Fungal biomarkers to reduce antifungal use

Population-Based Strategies

- Guidelines for febrile neutropenia
- Antifungals in immunocompromised
- LTCF interventions
- Neonatal ICU
- Terminally ill patients

Dellit TH, et al. Clin Infect Dis 2007;44:159-77.
Barlam TF, et al. Clin Infect Dis 2016;62:e51-77.

Antibiotic Stewardship Outcome Metrics



- Drug purchases
- Anti-infective tonnage
- Anti-infective cost/pt day
- Anti-infective RX rate
- DDD/1000 pt days
- DOT/1000 pt days
- LOT/1000 pt days

- Empiric & definitive therapy
- Local guideline adherence
- Susceptibility mismatch
- Redundant anaerobic
- Most active therapy
- De-escalation
- Time to active therapy

Be careful!!

- Mortality
- Length of stay
- Readmission
- Resolution of infection
- Adverse events
- Antibiogram changes
- *C. difficile* infections

DDD = defined daily dose; DOT = days of therapy; LOT = length of therapy

Courtesy of Dr. Trevor Van Schooneveld, Medical Director of Nebraska Medicine Antimicrobial Stewardship Program.

Antibiotic Use Data for Driving ASP Interventions

- Antibiotic use data do not imply appropriateness
  - Can be used as is for ASP interventions
  - Most commonly intervene on agents with the highest use (e.g., highest days of therapy / 1000 patient-day)
- Performing medication use evaluation (MUE) in conjunction to determine more targeted approach
- Medication use evaluation reviews
  - Indications for therapy
  - Duration of therapy based on indication
  - Prescribing services / individual prescribers
  - Appropriateness of therapy

Using Data to Drive ASP Interventions

- High days of therapy for a specific agent
  - ❑ Review duration of therapy for all new orders
  - ❑ Review facility resistance pattern
  - ❑ Use treatment guidelines
  - ❑ General prescriber education

- High days of therapy for a specific infection
  - ❑ Use treatment guidelines for specific indication
  - ❑ Prescriber education on treatment of specific infection
  - ❑ Prevention strategies for infection available?

Using Data to Drive ASP Interventions

- High days of therapy by a specific service / prescriber
  - ❑ Determine reason for use
  - ❑ Enlist department ASP champion to assist
  - ❑ Service education (e.g., at grandrounds)
  - ❑ One-on-one prescriber education (e.g., verbal discussion, prescriber report card)
  - ❑ Use facility treatment guidelines

- High days of therapy due to inappropriateness
  - ❑ General prescriber education on reasons to prescribe appropriately (e.g., minimize resistance / toxicity)
  - ❑ Treatment guidelines for multiple infection syndromes
  - ❑ Increase use of tools / lab tests to guide appropriateness

Tracking Antimicrobial Use
Days of Therapy (DOT)

Parameter to Track	Data Organization	Data Output	Logistics
• Antibiotic days of therapy	• Overall • Categorize by antibiotic class • Categorize by individual agent • Categorize by prescribers • Categorize by indications	• Days of therapy per 1000 patient-days	• Request pharmacy and information technology assistance • Info from medication administration records

Other Antibiotic Use Metrics

Metric	Advantage	Disadvantage
Defined Daily Dose *(developed by WHO to convert antibiotic use to a unit of presumed average daily dose)*	• Provide method for intra- and inter-facility benchmarking; • Can be calculated without computerized pharmacy records	• Daily doses defined by WHO may not be commonly used daily doses; • Inaccurate in certain populations (e.g, renal insufficiency, pediatrics); • Require standardization using patient-days
Length of Therapy *(total duration of therapy regardless of how many agents used per day)*	• More accurate measure of treatment duration for a specific infectious syndrome than DOT; • Allow inter- and intra-facility benchmarking; • Not affected by combination therapy	• Cannot be used to compare use of different drugs; • Cannot determine percentage of patients on combination therapy
Antimicrobial Expenditure	• Easily understood and relevant to administrators; • Easy to determine based on purchasing data; • Can be used to justify FTE for ASP activities	• Costs can fluctuate; • Purchase volume may be influenced by shortage or drug hoarding; • May not represent actual use (e.g., wastage, expired drugs)
Total Antimicrobial Tonnage	• Easy to obtain from drug purchasing record; • Not affected by price change	• Very rough approximation of antimicrobial use; • Purchasing data may not reflect actual use (e.g., expired drugs)

Benchmarking Antibiotic Use

- CDC document on how to submit antibiotic use data to NHSN AUR module
- Objectives
  - Provide risk-adjusted inter- and intra-facility benchmarking
  - Evaluate trends of usage over time at the facility and nationally
- Data for submission must follows the High Level (HL7) Clinical Data Architecture (CDA)

Antimicrobial Use and Resistance (AUR) Module

Table of Contents

From: https://www.cdc.gov/nhsn/pdfs/pscmanual/11pscaurcurrent.pdf. Accessed 9/16/2017.

Benchmarking Antibiotic Use

- Standardized Antimicrobial Administration Ratio (SAAR)
  - Benchmarking measure developed by CDC
- Express observed antibiotic use (*days of therapy*) to predicted use based on:
  - Facility (size, teaching)
  - Location (ICU, medicine ward, pediatric)
- Analogous to Standardized Infection Ratio (SIR)
- All antimicrobial agents PLUS 4 categories
  - Broad-spectrum agents for nosocomial bacteria (meropenem)
  - Broad-spectrum agents for community bacteria (ceftriaxone)
  - Anti-MRSA agents (vancomycin IV)
  - Agents for surgical site infection prophylaxis (cefazolin)

Examples of Antimicrobials for Tracking

Class	Specific Agents	Class	Specific Agents
Penicillins	*Ampicillin* *Oxacillin* *Nafcillin*	Fluoroquinolones	*Ciprofloxacin* *Levofloxacin* *Moxifloxacin*
B-lactam/B-lactamase inhibitor	*Ampicillin/sulbactam* *Piperacillin/tazobactam*	Tetracyclines	*Doxycycline* *Minocycline*
Cephalosporins	*Cefazolin* *Cefuroxime* *Cefoxitin* *Ceftriaxone* *Cefepime*	Azole Antifungals	*Fluconazole* *Itraconazole* *Voriconazole* *Posaconazole*
Carbapenems	*Ertapenem* *Meropenem*	Lincosamide	*Clindamycin*
Macrolides	*Azithromycin* *Clarithromycin*	Nitrofurans	*Nitrofurantoin*
Sulfonamide	*Sulfamethoxazole/ Trimethoprim*	Oxazolidinones	*Linezolid* *Tedizolid*
Nitroimidazoles	*Metronidazole*	Glycopeptide	*Vancomycin IV*
Neuraminidase inhibitors	*Oseltamivir* *Zanamivir*	Lipoglycopeptides	*Telavancin* *Dalbavancin*

Agents Not Currently A Standard to Track in NHSN AUR Module

- Topical antifungals
  - Nystatin, clotrimazole, ketoconazole
- Topical antibiotics
  - Triple antibiotic, bacitracin, mupirocin
- Antibiotic-containing eye and ear drops/ointments
  - Gentamicin, tobramycin, erythromycin
- Agents that work locally in GI tract or not absorbed
  - Sulfasalazine, rifaximin
  - Exceptions: vancomycin PO, fidaxomin
- Urinary tract antiseptic / analgesic
  - Methenamine, phenazopyridine

Take Home Points

- Antimicrobial stewardship is important to:
  - Optimize antimicrobial use
  - Minimize antimicrobial resistance
  - Prolong useful “shelf-life” of available drugs
  - Minimize toxicity
- Regulations are in place requiring ASP in all healthcare settings
  - Hospitals using Joint Commission Accreditation process
  - FLEX grant requirements for CAH
  - CMS Conditions for Participation for LTCFs
- Antibiotic use data are important to
  - Show ASP efforts
  - Determine areas requiring interventions
  - Drive strategies to improve use

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