Antibiotic Stewardship in Long-Term Care: The Path of Least Resistance

Indiana
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Disclosures

- Premier
- American Institutes of Research
- Severson & Werson, LLP
- Natural Resources Defense Council
- Sutter Tracy Community Hospital

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Objectives

- Understand the rationale for antibiotic optimization in long-term care
- Learn the current regulatory messages and requirements regarding antibiotic use in long-term care
- Describe examples of antibiotic stewardship programs in long-term care facilities

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Rationale for Antimicrobial Use Optimization

- Antimicrobial resistance
  - Inherent
  - Antimicrobial exposure
- Patient safety
  - Arrhythmias, rhabdomyolysis, nephrotoxicity, *Clostridium difficile* infections, death
- Cost
  - Unnecessary use, switching from IV to PO, broad-spectrum to pathogen-directed therapy

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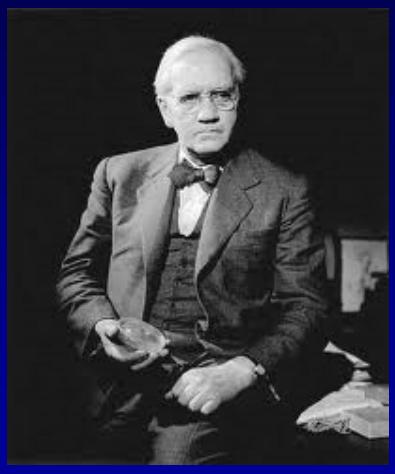
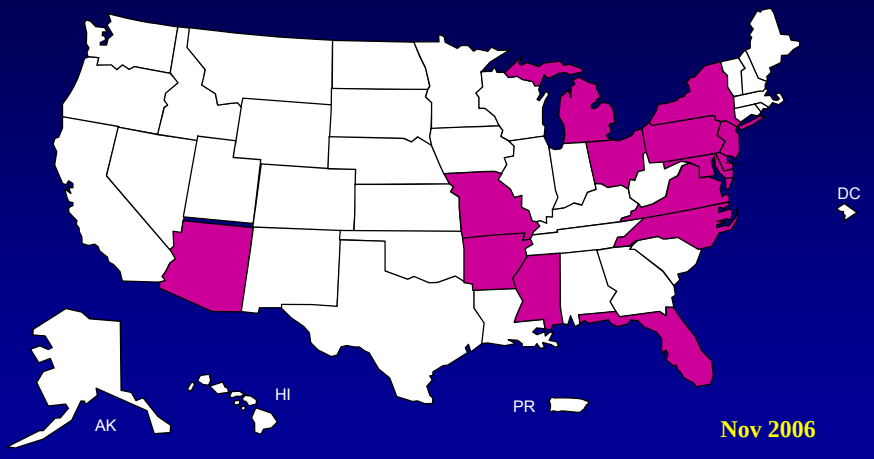
Sir Alexander Fleming



"The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily under dose himself and, by exposing his microbes to non-lethal quantities of the drug, educate them to resist penicillin."

Nobel lecture, 1945

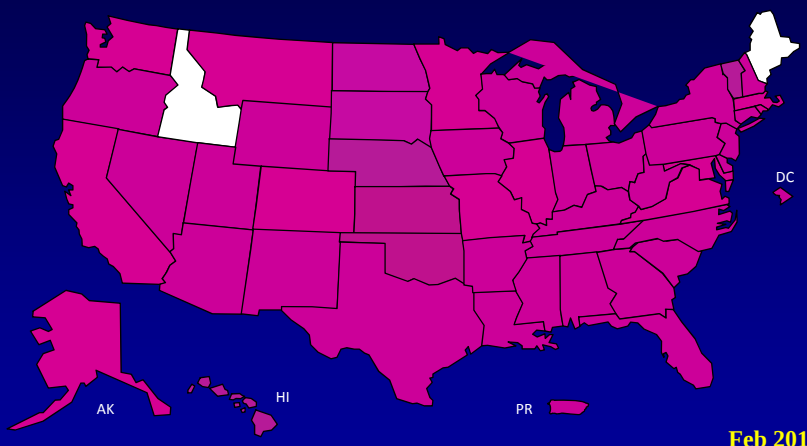
Carbapenemase-producing CRE in the United States



Patel, Rasheed, Kitchel. 2009. Clin Micro News

CDC, unpublished data

KPC-producing CRE in the United States



Feb 2016

http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html

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National Injury Surveillance System (2004-2006)

- ED visits for antibiotic-related adverse effects
  - Estimated 142,000 per year (116K-168K)
  - Most prescriptions for URI, COPD, Otitis media and sinusitis
  - 78% due to allergic reactions (PCN)
  - Sulfas – highest rate of serious allergic reactions
  - 50% overall due to Sulfas and Clindamycin
  - Sulfas and quinolones associated with highest rate of neurological events

9 Shehab et al., *CID* 2008:47-735-43

Rationale for Antimicrobial Use Optimization

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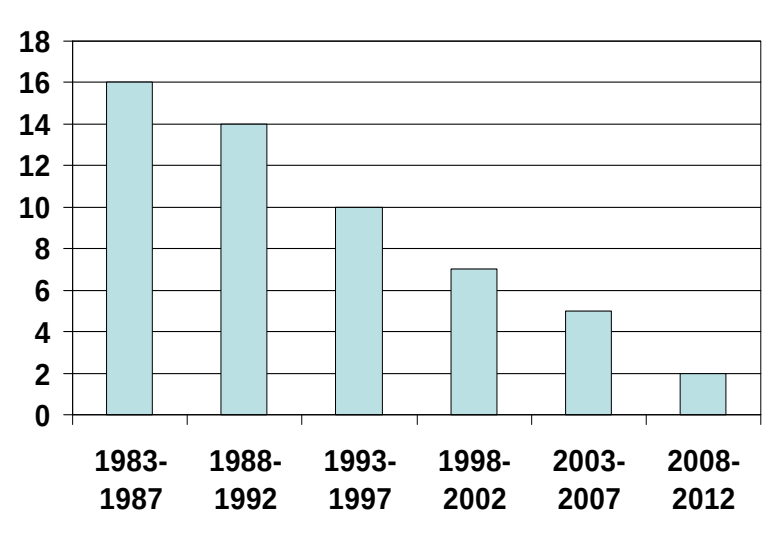
Cost of Antimicrobial-resistant Infections (ARI)

	All Patients	Patients with ARI	Patients without ARI
n (%)	1391	188 (13.5)	1203 (86.5)
APACHE II score	42.1	54.8*	40.1*
LOS (days)	10.2	24.2*	8.0*
HAI (n)	260	135*	125*
Cost per day ($)	1651	2098*	1581*
Total cost ($)	19,267	58,029*	13,210*
Death [n (%)]	70	34 (18.1)*	36 (3.0)*

*p<0.001

11 Roberts RR, et al. *CID* 2009;49: 1175-1184

New Antibacterial Agents Approved 1983-2012



Adapted from Spellberg B et al. *Clin Infect Dis*. 2004;38:1279-86.

The Pipeline is Dry

Antibiotic	Novel	Status	Activity	No or Uncertain Activity
Ceftolozane/tazobactam	N	Phase 3	ESBL	KPC, MDR PAE & Acinetobacter
Ceftazidime/avibactam	N	Phase 3	ESBL, KPC	MDR PAE & Acinetobacter
Ceftaroline/avibactam	N	Phase 2	ESBL, KPC	MDR PAE & Acinetobacter
Imipenem/MK-7655	N	Phase 2	ESBL, KPC	MDR PAE & Acinetobacter
Plazomicin	N	Phase 2	ESBL, KPC	MDR PAE & Acinetobacter
Eravacycline	N	Phase 2	ESBL, KPC	MDR PAE & Acinetobacter
Brilacidin	Y	Phase 2	ESBL	KPC, MDR PAE & Acinetobacter

Boucher HW et al. Clin Infect Dis 2013, advanced access.

Antimicrobial Use Optimization in Acute Care and Long-Term Care

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Healthcare Continuum

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US Long-Term Care Facilities (LTCFs)

- >15,000 Nursing Homes
  - Over 4 million individuals receive care every year
  - Infection prevalence: 5% on a single day
- 21% of the population will be >65 y/o by 2040

www.aoa.gov/AoARoot/Aging_Statistics/Profile/2012/4.aspx

Rhee and Stone. *Infect Dis Clin North Am.* 2014 Jun;28(2):237-46.

16 Daneman N et al. JAMAIntMed 2013; 173:673-82.

US LTCFs

- Resistant organisms are common
  - Both infection and colonization
  - One study, >50% of patients with a resistant organism discharged to post-acute care (including LTCFs)

17 Perez F, Endimiani A, Ray AJ, et al. J Antimicrob Chemother 2010;65:1807-18.

Acute Care vs. Post-Acute Care

18

Resistant Organisms are Common in Long-Term Care Facilities

Table 2. Frequency of Culture Positivity on the Initial Study Swab for All Participants, by Study Organism

Organism	RG n/N (%)	IP n/N (%)
MRSA	26/123 (21)	29/136 (21)
ESBL-producing *Klebsiella pneumoniae*	19/114 (17)	16/117 (14)
ESBL-producing *Escherichia coli*	29/114 (25)	14/117 (12)
Vancomycin-resistant enterococci	22/114 (19)	16/117 (14)

19 *JAGS* 2004 52:2003-2009

High Rates of Multidrug-Resistant Organisms in Long-Term Care

- Frequent transfer from acute care hospitals
- Horizontal transmission of resistant organisms
- Widespread (often inappropriate) use of antimicrobials

20 Schwartz, DN et al., *J Am Geriatr Soc* 2007;55:1236-1242

Antibiotic Pressure from Hospital

Variable	Relative Risk (95% Confidence Interval)
Methicillin-resistant *Staphylococcus aureus*	
Levofloxacin receipt*	1.6 (1.1–2.2)
Third-generation cephalosporin receipt*	2.0 (1.0–4.0)
Vancomycin-resistant enterococci	
Transfer to or from another OFH unit*	1.2 (1.1–1.4)
Levofloxacin*	1.2 (1.0–1.5)
ESBL-producing *Klebsiella pneumoniae*	
Gastrostomy tube	1.2 (1.0–1.4)
ESBL-producing *Escherichia coli*	
Total dependence for activities of daily living	1.2 (1.0–1.3)
Levofloxacin receipt*	1.2 (1.0–1.4)
Third-generation cephalosporin*	1.4 (0.9–2.2)

21 *J Am Geriatr Soc* 2004 52:2003-2009; *Am J Epi* 2003 157:40-47

Horizontal Transmission

- LTCFs today can promote antimicrobial resistant infections and transmission to other high-risk residents
  - Invasive devices and procedures increased
    - Central lines, chronic resp therapy, feeding tubes, dialysis, IV antibiotics
  - Population includes more acute and subacute patients treated previously in hospitals
    - Staff not given appropriate education
  - Changing infection control provider without expertise

22 Nicolle, LE et al. Antimicrobial Use in LTCFs, *ICHE* 2000; 21: 537-545.

Antibiotic Use in LTC, Ontario, 2010

- Over a single year:
  - 75% of residents (~50,000) received an antibiotic course
  - 44% of antibiotic courses exceeded 7 days in length
- 2601 different physicians prescribed antibiotics
  - 21% of prescribers were responsible for ~80% of the antibiotic courses
- A subset of providers (n=145) were identified as "long-duration" prescribers (avg. treatment length 11.6 days)
  - Prescribing tendencies were not driven by differences in patient demographic characteristics, comorbidities, or care needs

Daneman N et al. JAMAIntMed 2013; 173:673-82

Harms from Antibiotic use in Nursing Homes

- Residents in high antibiotic use NHs had a 24% increased risk of antibiotic-related complications
  - Range: 20.4 – 192.9 antibiotic-days/1,000 resident days
  - High use: >62 antibiotic-days/1,000 resident days
  - Other predictors of antibiotic harms: recent hospitalization or ED visit, indwelling medical device, incontinence, functional dependence

Daneman N et al. JAMAIntMed 2013; 173:673-82

25-75% of systemic antimicrobial use and 60% of topical antimicrobial use in long-term care is considered inappropriate

25 Nicolle LE, Bentley DW, Garibaldi R, Neuhaus EG, Smith PW. Antimicrobial use in long-term–care facilities. *Infect Control Hosp Epidemiol* 2000;21(8):537–545.

California Dept Public Health Investigation in LTCF: 2010

- Point prevalence study in LTCF with high rate of MDR *Acinetobacter baumannii*
  - Baseline colonization rate 19%
    - 36% colonized residents MDR (resistant to cephalosporins, FQ, aminoglycosides)
  - Implemented strict infection control practices
    - HH, cohorting, contact precautions
  - Enhanced environmental cleaning
  - Follow-up six month colonization rate remained 19%
    - 36% colonized residents negative 6 months previous
    - 71% colonized residents MDR

26 Mortensen E, KK Trivedi, J Rosenberg et al., *Infection Control Hosp Epi* 2014; 35(4):406-411

Baseline: CDPH in LTCF

- 104 residents treated for UTI were evaluated
- 8 (8%) met criteria for UTI
- Although most patients on UTI therapy did not meet consensus criteria for UTI, positive urine cultures led to antibiotic therapy
- Treatment was nurse driven

Doernberg SB, V Dudas and KK Trivedi. Implementation of an antimicrobial stewardship program targeting residents with urinary tract infections in three community long-term care facilities: a quasi-experimental study using time-series analysis. *Antimicrob Resist Infect Control*. 2015 December 1: 4:54.

27

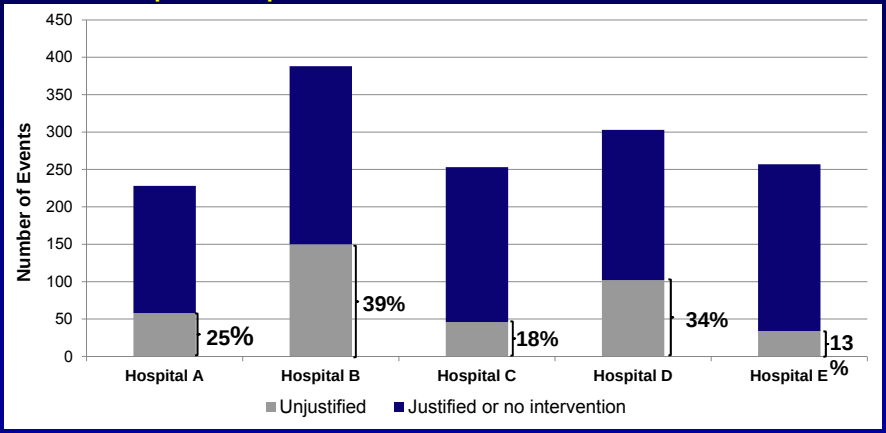
30% of antimicrobial use in acute care is either inappropriate or suboptimal

Cosgrove, SE, SK Seo, MK Bolon, et al. *Infection Control and Hospital Epidemiology* , Vol. 33, No. 4, Special Topic Issue: Antimicrobial Stewardship (April 2012), pp. 374-380.

28

Unnecessary Use of Antimicrobials

- 5 center prospective study of post-prescription review of antibiotic use



Cosgrove SE et al. Infect Control Hosp Epidemiol. 2012;33:374-80

Unnecessary Use of Antimicrobials

Reasons for modified regimens (59%)	
Organism not susceptible	9%
More appropriate agent	31%
Patient can take oral therapy	5%
Overlapping agents	15%
Reasons for stopping antibiotics (41%)	
Antibiotics no longer needed	28%
Inappropriate prophylaxis	13%

Cosgrove SE et al. Infect Control Hosp Epidemiol. 2012;33:374-80

What Can We Do?

- Sit around and wait for new antibiotics? X
- Programmatic approach: optimize use of antimicrobials
- Point-of-care approach: teach prescribers to change their views and habits
- Regulatory requirements

Antimicrobial Use Optimization

- Widely accepted in acute care settings*:
  - Improve antimicrobial resistance patterns
  - Decrease patient toxicity
  - Decrease costs
- Limited literature and few studies in long-term care
- Working together across healthcare continuum may be ideal

*SHEA/IDSA Guidelines, *CID* 2007 Jan;44(2):159-77
**Chopra T and EJC Goldstein, CID 2015; 60(S2):S72-6
32 Mortensen E, KK Trivedi, J Rosenberg et al., *Infection Control Hosp Epi* 2014; 35(4):406-411

Antimicrobial Stewardship Program (ASP)

- Coordinated interventions to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy and route of administration
- Objective:
  - Minimize acquired resistance
  - Improve patient outcomes and toxicity
  - Reduce treatment costs

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Regulatory Messages

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Dept HHS: Antimicrobial Review in Long-Term Care

- With Center for Medicare and Medicaid Services (CMS)
- Effective September 30, 2009
- Interpretive Guidelines for Long-Term Care Facilities
  - *"It is the physician's responsibility to prescribe appropriate antibiotics and to establish the indication for use of specific medications. As part of the medication regimen review, the consultant pharmacist can assist with the oversight by identifying antibiotics prescribed for resistant organisms or for situations with questionable indications, and reporting such findings…"*

http://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/som107ap_pp_guidelines_ltcf.pdf

Existing Regulations Promoting Antibiotic Stewardship in Nursing Homes

Federal Tag 441: Infection Control
- Mentions performing antibiotic review

Federal Tag 329: Unnecessary Drugs
- To optimize medication use and monitoring to appropriately minimize exposure and prevent consequences

Federal Tag 332/333: Medication Errors
- To reduce preventable errors and adverse events

Federal Tag 428: Drug Regimen Review
- Outlines role of pharmacist in scheduled reviews of medication use in high risk residents

PCAST Report: Rec 6 - Improve Antimicrobial Stewardship in Health Care

(1) CMS should use reimbursement incentives to drive antibiotic stewardship.

- By the end of 2017, CMS should have Federal regulations (Conditions of Participation) in place that will require U.S. hospitals, critical access hospitals, and long-term care and nursing home facilities to develop and implement robust ASPs that adhere to best practices.

http://www.whitehouse.gov/sites/default/files/microsites/ostp/PCAST/pcast_carb_report_sept2014.pdf

37

California Senate Bill 361(Hill)

- **1275.4.** (a) On or before January 1, 2017, each skilled nursing facility, as defined in subdivision (c) of Section 1250, shall adopt and implement an antimicrobial stewardship policy that is consistent with antimicrobial stewardship guidelines developed by the federal Centers for Disease Control and Prevention, the federal Centers for Medicare and Medicaid Services, the Society for Healthcare Epidemiology of America, or similar recognized professional organizations.
- Signed October 10, 2015

38 http://leginfo.legislature.ca.gov/faces/billNavClient.xhtml?bill_id=201520160SB361

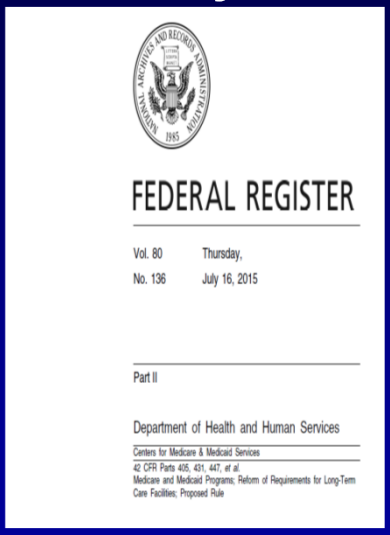
CMS Proposed Regulations for Certified Nursing Homes, July 2015

Antibiotic stewardship integrated within pharmacy and infection prevention and control (IPC):

-Expanding pharmacy medication reviews to include antibiotics for monthly review; reviews also occur for all new admissions/re-admissions, (§ 483.45)

-Antibiotic use protocols and monitoring included in IPC (§ 483.80)

-Integrating IPC and antibiotic stewardship into QAPI activities (§ 483.75)



FEDERAL REGISTER

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Part II

Department of Health and Human Services

Centers for Medicare & Medicaid Services

42 CFR Parts 405, 431, 447, et al.
Medicare and Medicaid Programs; Reform of Requirements for Long-Term Care Facilities; Proposed Rule

CMS Proposed Rule: Reform of Requirements for LTCFs

- Proposed July 2015
- 7000+ comments submitted awaiting CMS response

https://www.federalregister.gov/articles/2015/07/16/2015-17207/medicare-and-medicaid-programs-reform-of-requirements-for-long-term-care-facilities

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ASP Implementation

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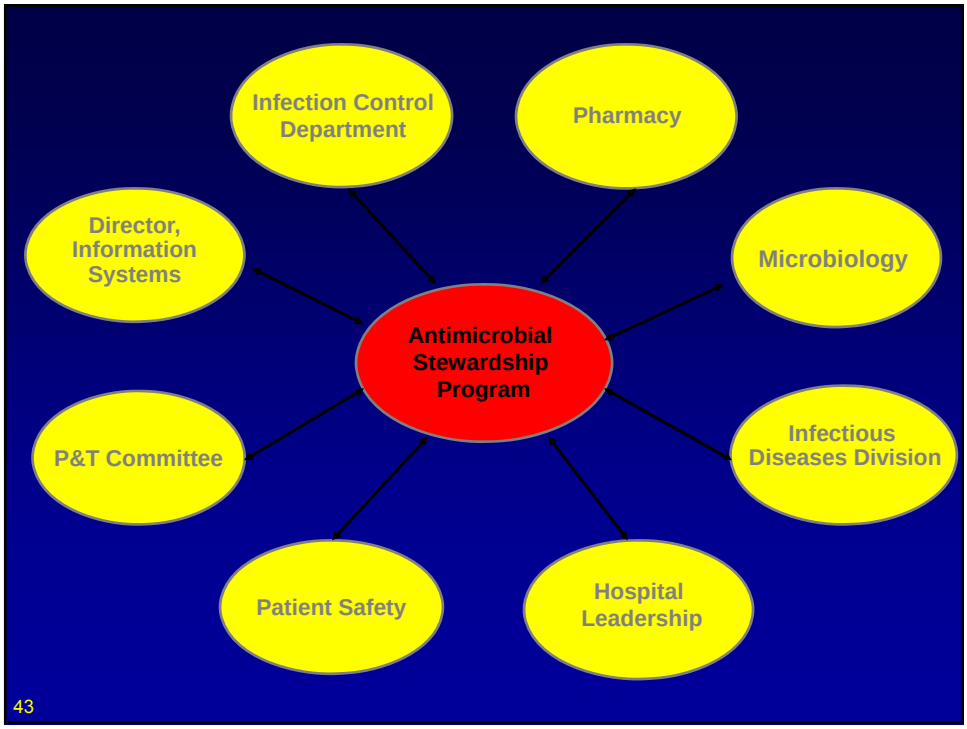
Differences in ASP Implementation

- Many acute care hospitals have developed ASPs due to:
  - Increasing prevalence of HAIs coupled with decreased reimbursement and public reporting
  - Lack of new antimicrobials under development
- LTCFs have been slower to adopt ASPs due to:
  - Lack of necessary personnel
  - Funding
  - Paucity of well-validated strategies specific to LTCFs

Jump RLP, DM. Olds, N Seifi, et al. *Infection Control and Hospital Epidemiology* , Vol. 33, No. 12 (December 2012), pp. 1185-1192

42



ASP Strategy Selection

- Facility dependent
  - Beds and acuity of care
  - Dedicated personnel
  - Funds
  - Pharmacy support
  - Electronic systems
  - Laboratory support

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Stewardship Hierarchy in LTCF

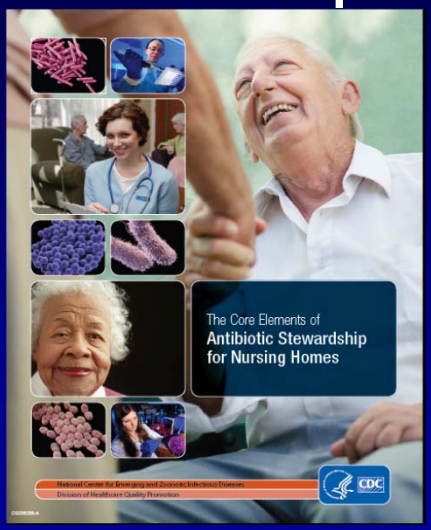
Most Intrusive
Requires most expertise, effort and expertise.

Least Intrusive
Requires least expertise, effort and expense

"Back End" approach – Review of already prescribed antibiotics	Individual cases are concurrently reviewed for appropriateness, usually by an expert, with feedback to the provider. Individual use data with comparators and benchmarks is provided to prescribers regarding appropriate use.
"Front End" approach—Active direction of antibiotic selection	Preauthorization of antibiotics based upon predetermined criteria. Review of case and immediate feedback on choice of antibiotics at initiation.
"Front End" approach—Passive direction of antibiotic selection	Guidelines, treatment algorithms, antibiotic formulary, antimicrobial order forms
Education	Classes or training sessions regarding antibiotic resistance, stewardship practices, etc. offered to LTCF employees or staff. Small group sessions with prescriber feedback and case discussions.
Passive monitoring	Measuring types and quantities of antibiotics used in the facility, and the presence of antimicrobial resistance in cumulative laboratory culture and sensitivity reports.

45 Smith, PW, Van Schooneveld TC. *Ann Long-Term Care*. 2011;19:20-25.

CDC Core Elements of Antibiotic Stewardship



http://www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html

CDC Core Elements of ASPs in Nursing Homes

- Adaptation of Core Elements for Hospital ASPs into practical ways to initiate or expand antibiotic stewardship activities in nursing homes
- Nursing homes are encouraged to work in a step-wise fashion, implementing one or two activities to start and gradually add new strategies from each element over time

47 http://www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html

CDC Core Elements of Antibiotic Stewardship in Nursing Homes

- Leadership Commitment
- Accountability – physician, nursing and pharmacy leads
- Drug Expertise
- Action – implement at least one policy or practice
- Tracking – monitor at least one process and at least one outcome measure
- Reporting – regular feedback
- Education – to clinicians, nursing staff, residents and families

48 http://www.cdc.gov/longtermcare/prevention/antibiotic-stewardship.html

SHEA/IDSA: ASP Implementation Guidelines

26. In nursing homes and skilled nursing facilities, we suggest implementation of antimicrobial stewardship strategies to decrease unnecessary use of antimicrobials and improve clinical outcomes [Good practice recommendation]

- Comment: Implementing ASPs at nursing homes and SNFs is important and must involve point-of-care providers to be successful. The traditional physician-pharmacist team may not be available on-site and facilities might need to investigate other approaches to review and optimize antibiotic use, such as obtaining infectious diseases expertise through telemedicine consultation.

Barlam TF, SE Cosgrove, LM Abbo et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis*. 2016 Apr 13.

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Examples

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Education Can Work to Reduce Treatment of Asymptomatic Bacteriuria

	3-Months Pre-intervention	7 to 30 Months Post-intervention
Total urine cultures sent/ 1000 patient days	3.7 (2.8 – 4.9)	1.3 (1.1 – 1.5)
Inappropriate cultures, n (%)	34 (69%)	75 (46%)
ASB treated, n. (%)	23 (68%)	33 (44%)
ASB treated/ 1000 patient days	1.7 (1.1 – 2.6)	0.3 (0.2 – 0.4)
Antimicrobial days of therapy/1000 patient days	167.7	109

Am J Infect. Control 2008 Sep; 36 (7): 476-80.

CDPH: ASP in LTCF Study 2011-2012

- Goal: characterize the benefit of implementing a formal ASP in LTCF
- Establish ASP in three LTCFs
  - Post-prescriptive review and feedback with pharmacist and ID physician
  - Establish feasibility and effectiveness
  - Specify effects of ASP on antimicrobial utilization, susceptibility patterns and rates of *Clostridium difficile* over time

52 Doernberg, S et al., unpublished

Intervention Results

- Recommendations were made in 43 (41%), and 10 (23%) were accepted
- Recommendations were not made in 61 (59%) due to 20 (33%) on appropriate therapy and 41 (67%) who completed therapy between evaluations.
- None in whom recommendations were accepted experienced fever, leukocytosis, escalation of therapy, or death at 30 days.

53 Doernberg SB, V Dudas and KK Trivedi. *Antimicrob Resist Infect Control*. 2015 December 1; 4:54.

Measure	Pre[5]	Post	IRR (95% CI)
All antibiotic starts	5.5	3.8	**0.69 (0.60-0.80)**
Antibiotic starts for UTI	2.5	1.6	**0.65 (0.50-0.86)**
Resistant organism[1]	6.0	4.5	0.75 (0.55-1.01)
Clostridium difficile	2.2	1.5	0.68 (0.33-1.37)
ESBL, urine[2]	1.6	1.1	0.65 (0.31-1.37)
ESBL, all sites	1.6	1.2	0.76 (0.37-1.54)
FQ-R *P. aeruginosa*, urine[3]	1.1	0.7	0.66 (0.25-1.73)
FQ-R *P. aeruginosa*, all sites	1.7	1.0	0.58 (0.27-1.32)
VRE, urine[4]	0.5	0.8	1.57 (0.67-3.63)
VRE, all sites	0.5	0.8	1.56 (0.67-3.63)

[1]Includes *Clostridium difficile*, extended-spectrum β-lactamase (ESBL) producing organism, fluoroquinolone (FQ)-resistant *Pseudomonas aeruginosa (P. aeruginosa)*, and vancomycin-resistant Enterococci (VRE) from any site
[2]ESBL – extended-spectrum β-lactamase (ESBL) producing organism
[3]FQ – fluoroquinolone
[4]VRE – vancomycin-resistant Enterococci
[5]N/1000 patient-days for antibiotic measurements; N/10,000 patient-days for resistant organism measurements

54 Doernberg SB, V Dudas and KK Trivedi. *Antimicrob Resist Infect Control*. 2015 December 1; 4:54.

NY Antimicrobial Stewardship Project 2009

- Greater NY Hospital Association, United Hospital Fund, NY State Department of Health
- Objectives:
  - Establish ASPs in 3 LTCFs using existing personnel through collaboration with acute care hospital partners
    - Emphasis on implementing strategies without expending significant new resources
  - Develop and pilot tools and materials for ASP development and implementation

55 Calfee DP, et al. SHEA Annual Meeting. 2011; poster presentation

NY Antimicrobial Stewardship Project 2009

- All LTCFs identified inappropriate treatment of asymptomatic bacteriuria
- 2/3 LTCFs reported qualitative improvement
- Successful implementation associated with:
  - Motivated team, support from administration and medical leadership, collaboration with hospital partner, ability to provide antimicrobial use and resistance data

56 Calfee DP, et al. SHEA Annual Meeting. 2011; poster presentation

Conclusions

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ASPs in Long-Term Care

- Essential:
  - High rates of resistance, variable infection control, overuse of antimicrobials
- CMS established regulatory guidance to prioritize optimizing antimicrobials
  - California may require ASPs in every nursing home
- Implementation of ASPs difficult
  - Elderly population complex
  - Guidelines, expertise is sparse
  - Resources are limited

ASPs in LTCF

- Criteria such as syndromic approach may be "low hanging fruit"
  - E.g., Pneumonia or UTI
- Education strategies must include nurses, patients, and their families
- ASP interventions must be tailored to the environment

Recommendations: Partnership

- Goal is a standardized regional approach to ASP implementation and infection control
- Acute care and long-term care must work together
  - Provide drug expertise
  - Improve interfacility communication
  - Share resources

Questions/Comments

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