MDROs, CDI, and Antibiotic Selection

James McKinnell, MD

Infectious Disease Specialist

Los Angeles County Department of Public Health

Associate Professor at the David Geffen School of Medicine, UCLA

US Causes of Death

	2013	Deaths
1	Heart Disease	611,000
2	Cancer	584,000
3	Accidents	130,000
4	Stroke	129,000
5	Healthcare Associated Infections	100,000
6	Alzheimer's Disease	83,000

http://www.cdc.gov/nchs/fastats/leading-causes-of-death.htm Accessed 4/22/2015, rounded to the nearest thousand deaths.
http://www.cdc.gov/HAI/pdfs/hai/infections_deaths.pdf Accessed 4/22/2015.

The Rise of MDROs

- Methicillin Resistant *Staphylococcus aureus* (MRSA)
- Vancomycin Resistant Enterococcus (VRE)
- Multi-Drug Resistant Pseudomonas
- Multi-Drug Resistant Acinetobacter
- Extended Spectrum Beta Lactamase Producers (ESBLs)
- Carbapenem Resistant Enterobacteriaceae (CRE)
- Hypervirulent KPC (NDM)
- *Candida auris*

- CDC Report, Antibiotic Resistance Threats in the US 2013
- One of only three pathogens with an URGENT Threat Level

The Era of Pan-Resistant Pathogens

The New York Times

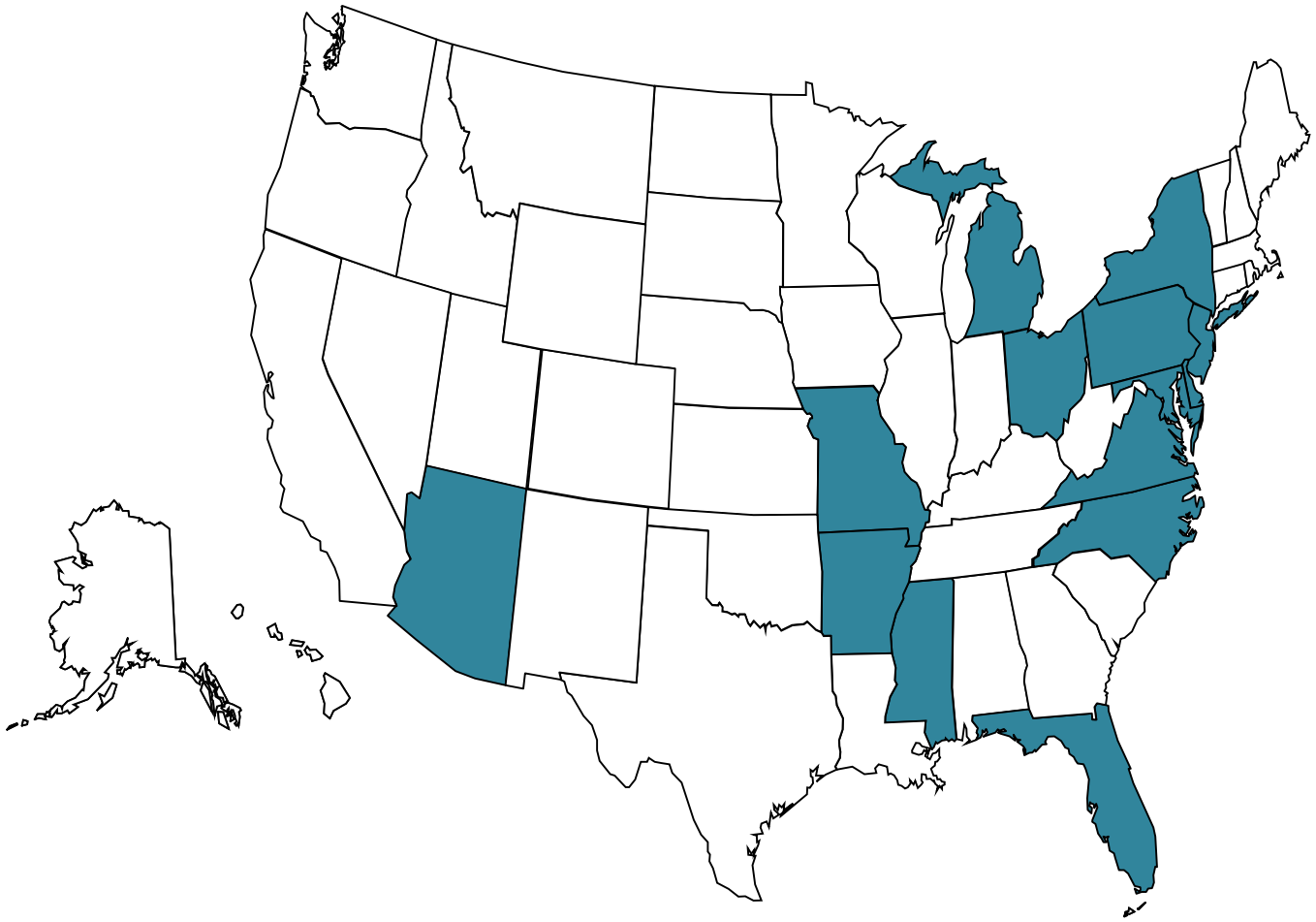
THE ORANGE COUNTY REGISTER

Los Angeles Times

San Francisco Chronicle

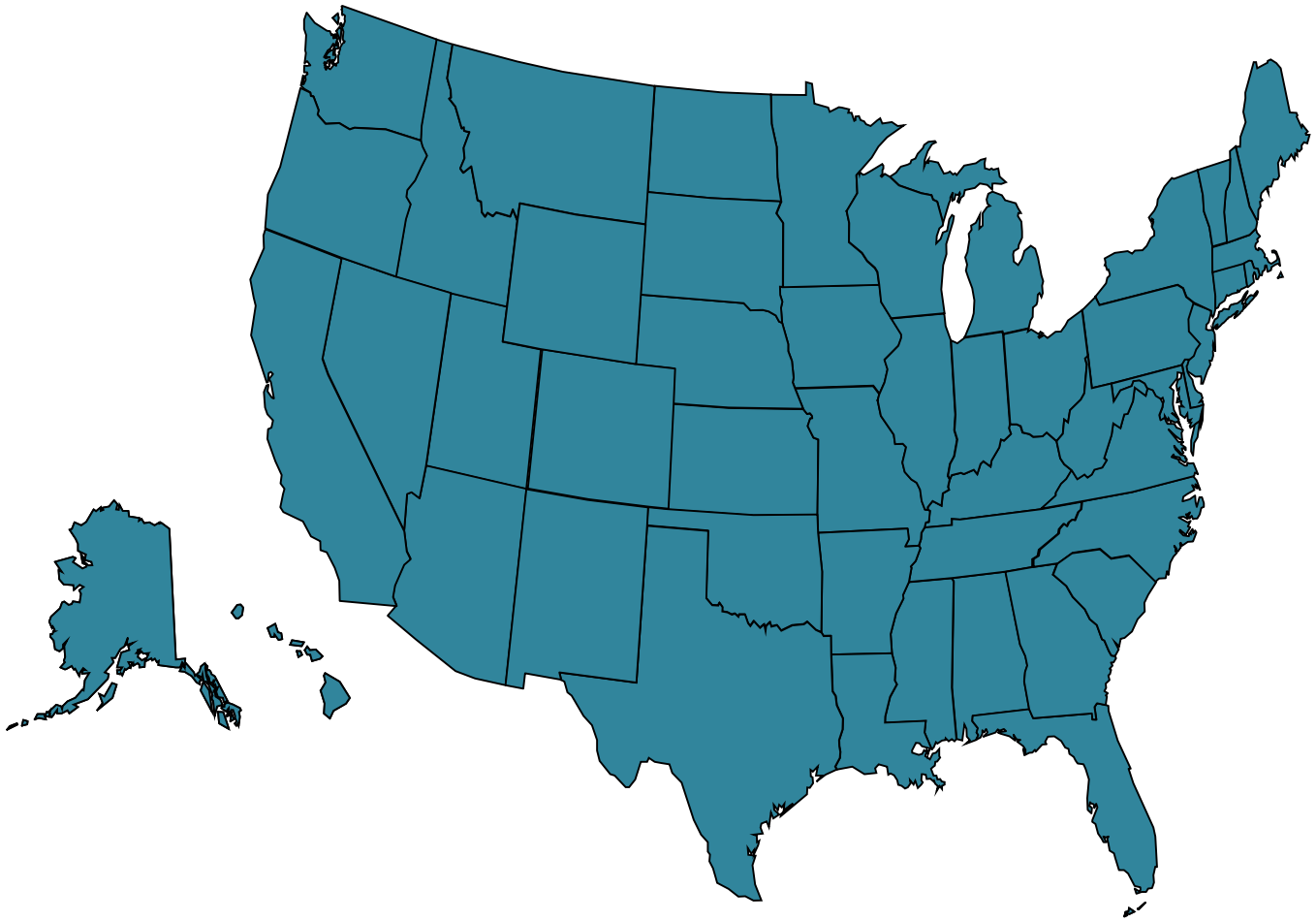
The Washington Post

Spread of CRE in US Reported to CDC in 2006



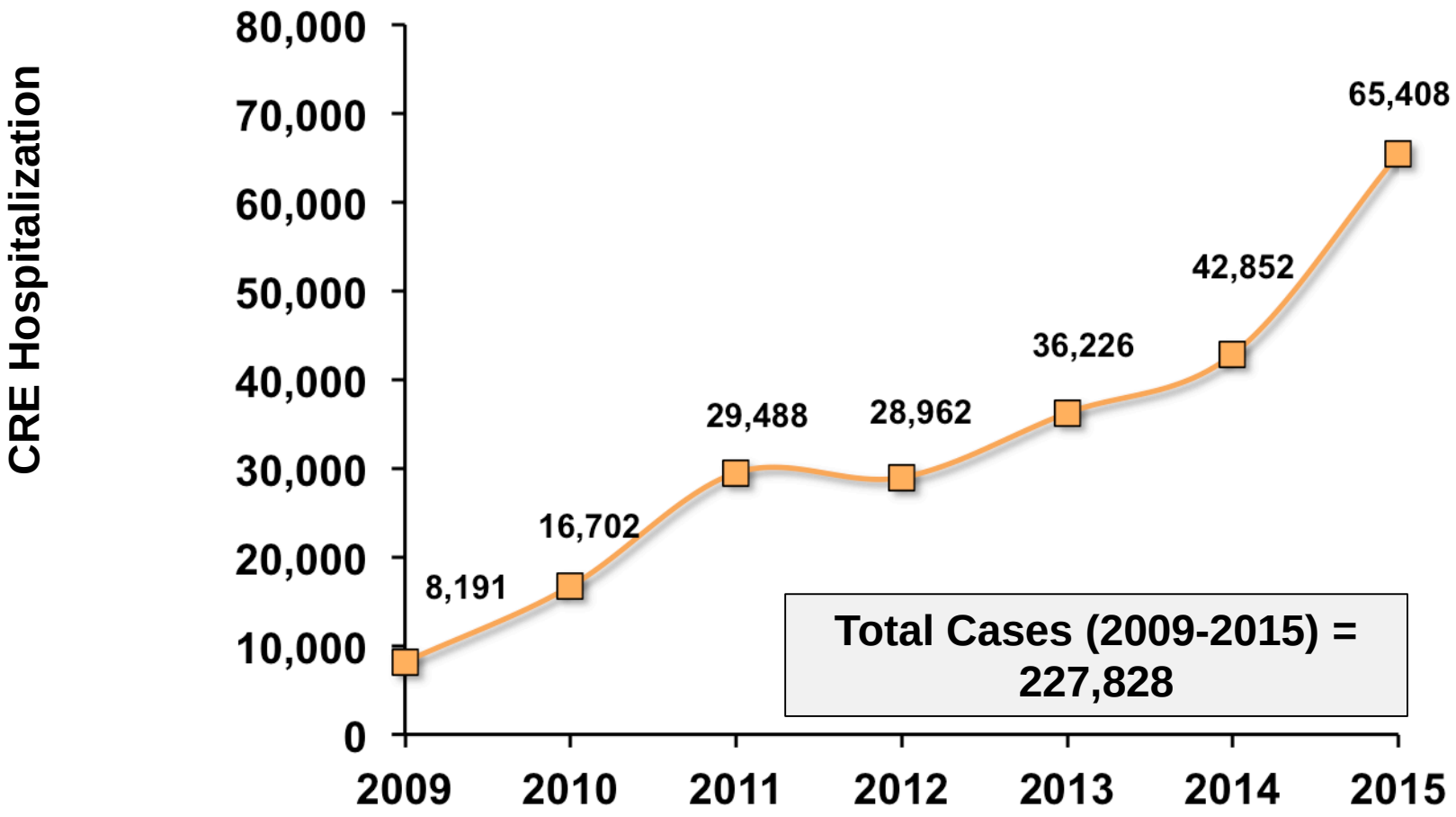
http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html

Growing Spread of CRE Reported to CDC in 2018



http://www.cdc.gov/hai/organisms/cre/Tracking

Steady Increase in CRE Cases in US

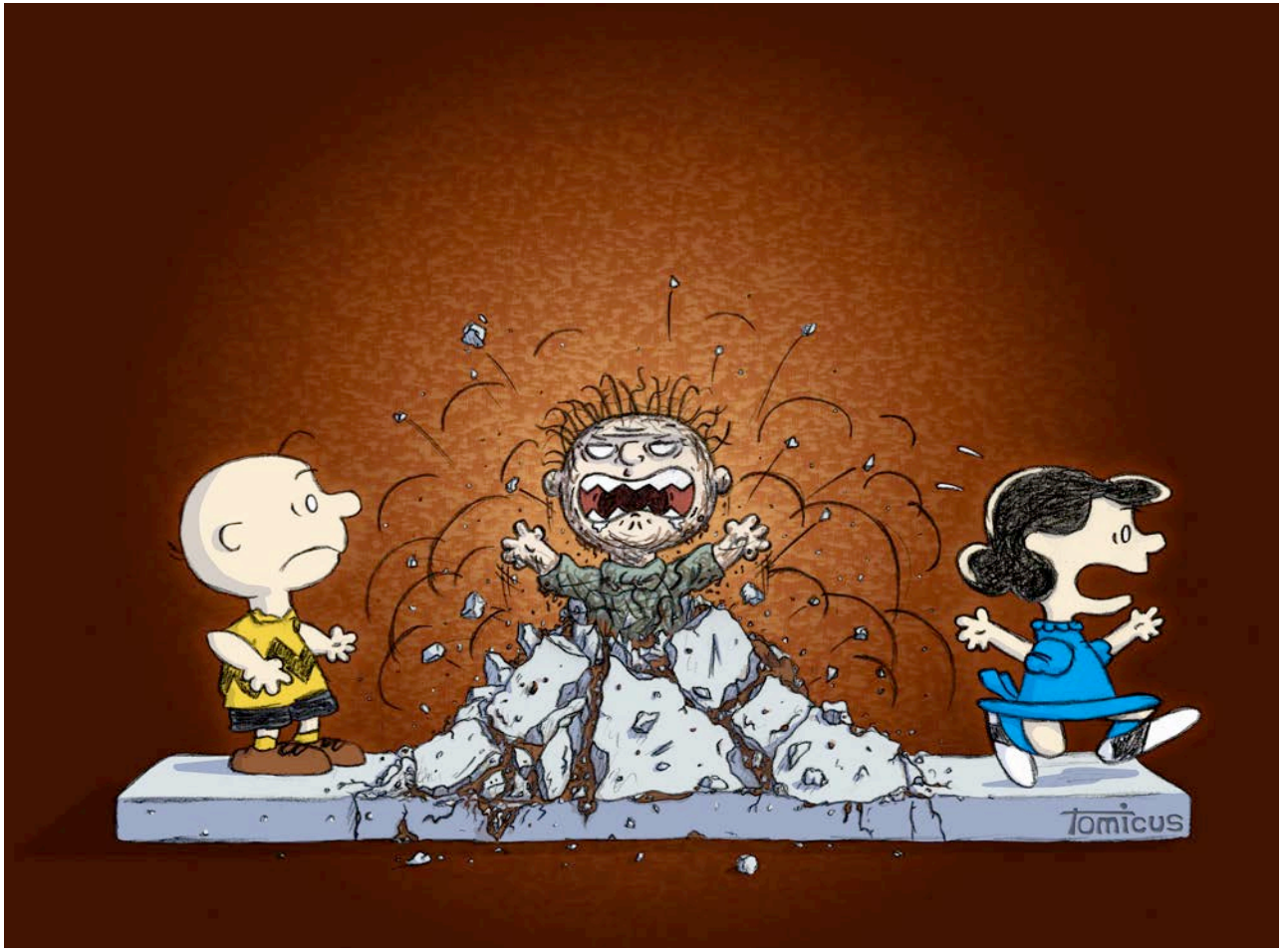


Schneider et al., SHEA 2017. Thaden et al. ICHE. 2014. Lodise et al., AAC 2017. Bartsch et al., Clin Microbiol Infect

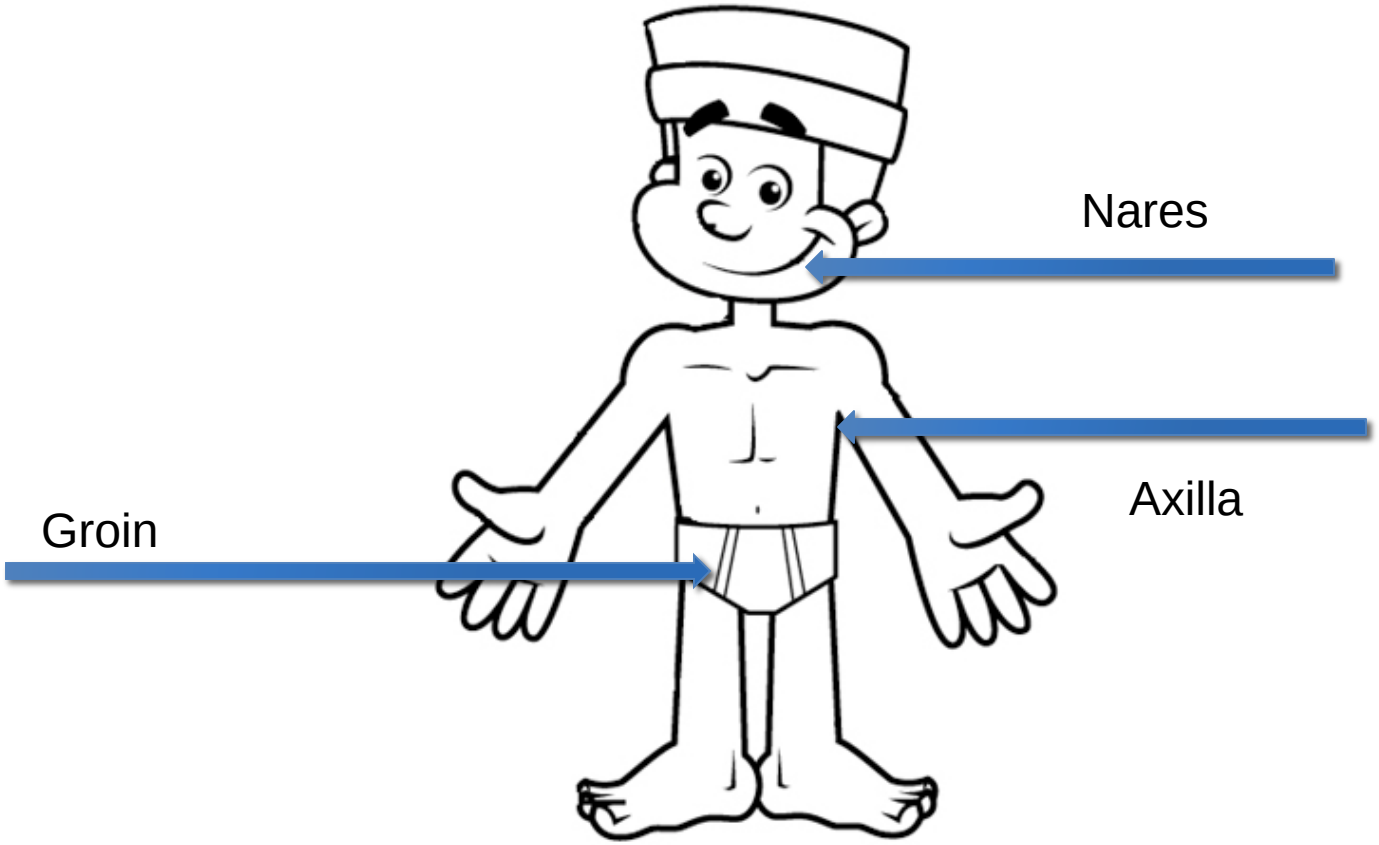
“How are CRE and Other MDROs spreading so effectively?”

The Pig Pen Principle

The Pig Pen Principle



SNF Surveillance Sites for MDRO



MultiDrug-Resistant Organism (MDRO) Body Sampling Process

- Baseline and intervention
  - Point prevalence assessment of resident MDRO carriage
- 50 randomly selected residents
- Collected bilateral nares and skin (axilla/groin) swabs
  - Nares swabs tested for MRSA
  - Skin swabs tested for MRSA, VRE, ESBL, CRE

Characteristics of PROTECT Facilities

Number of Facilities	28
Mean Age	75.32
% Male	41%
Mean Licensed Beds	113
Average Daily Census	103
Mean LOS	137
Elixhauser Comorbidity Score	4.17
% Diabetes	42%
% Chronic Lung Disease	28%
% Renal Failure	22%

MDRO Carriage in Nursing Homes

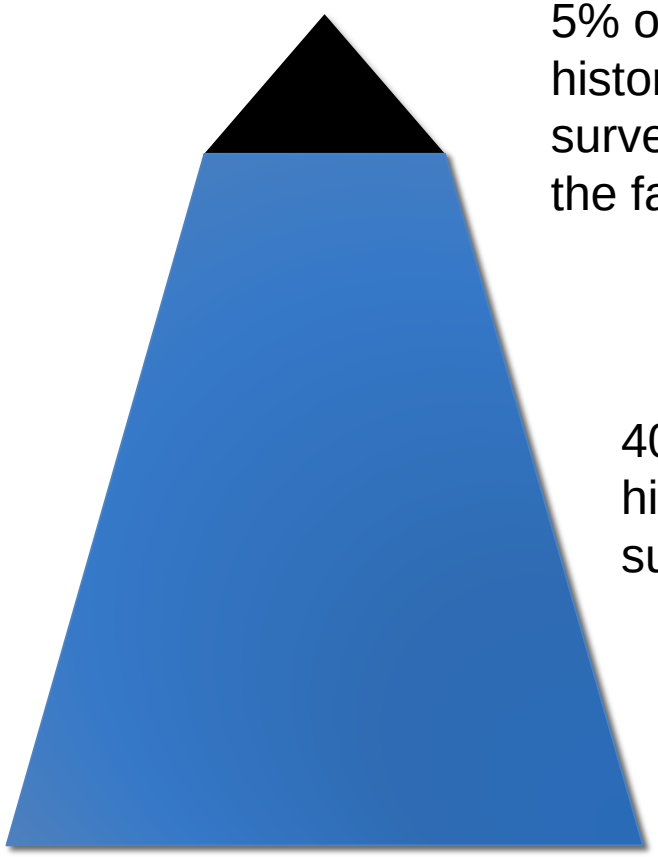
	Residents Swabbed	Any MDRO	MRSA	VRE	ESBL	CRE
Nares	1,397	29%	29%	-	-	-
Axilla/Groin	1,400	39%	24%	7%	16%	1%
All Body Sites	**1,400**	**49%**	**37%**	**7%**	**16%**	**1%**

49% MDRO carriers, facility range 24-70%

Among MDRO pathogens detected, only 12% known to facility

Among all residents, 45% harbored ≥1 MDRO unknown to facility

The Iceberg of MDRO Patient Colonization



5% of the NH population (75 residents) had a history of an MDRO, but Point Prevalence survey found an additional MDRO unknown to the facility

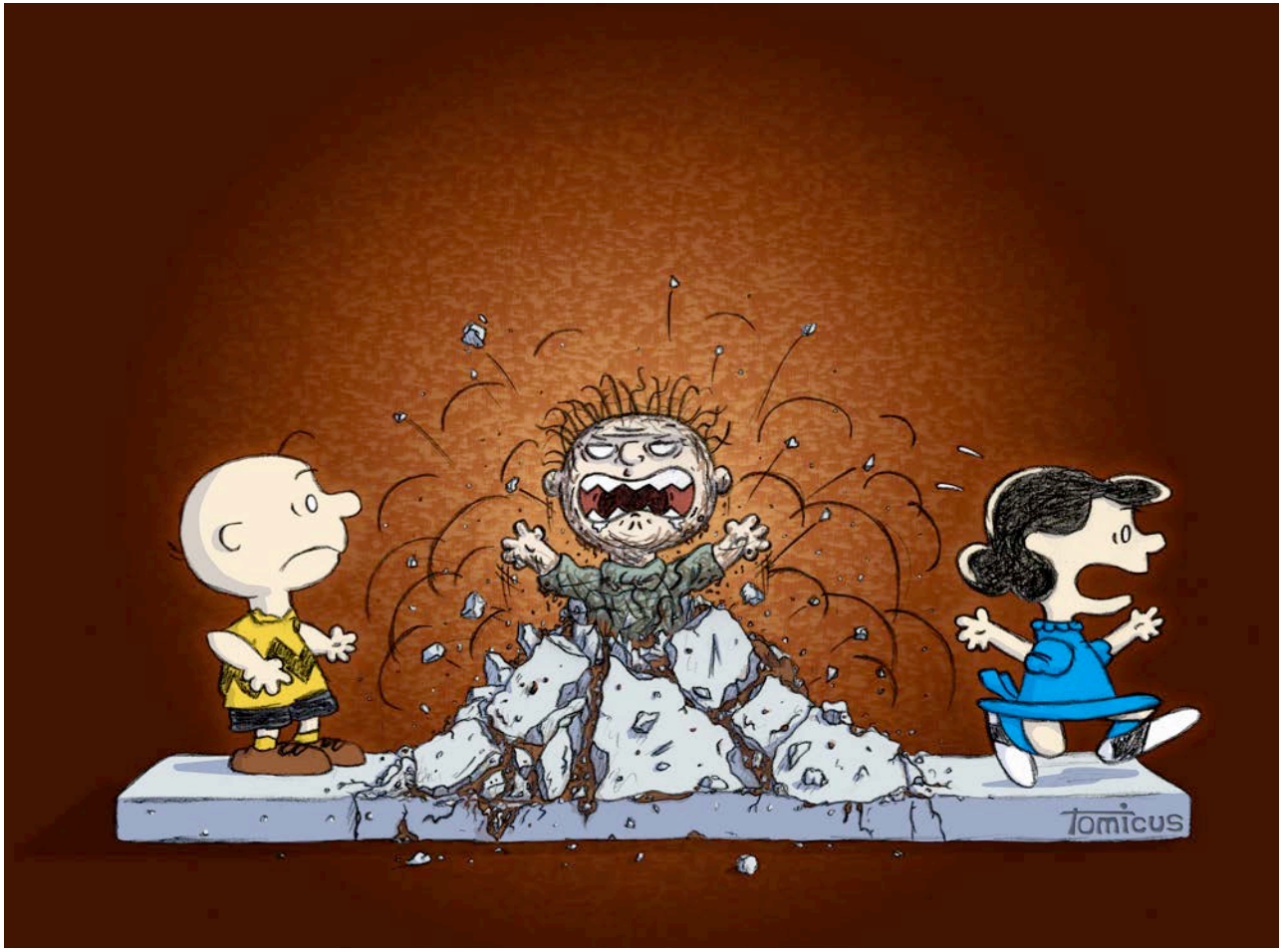
40% of the NH population (n=552) had no history of MDRO, but Point Prevalence survey Identified MDRO Carriage

MDRO Rates for Post-Acute vs Long Stay Residents

	N	Any MDRO	MRSA	VRE	ESBL	CRE
	Post Acute					
Nares	306	26%	26%	-	-	-
Axilla/Groin	306	41%	25%	15%	15%	1%
All Body Sites	**306**	**48%**	**34%**	**15%**	**15%**	**1%**

	Long Stay					
Nares	1091	30%	30%	-	-	-
Axilla/Groin	1094	38%	24%	5%	17%	1%
All Body Sites	**1094**	**49%**	**38%**	**5%**	**17%**	**1%**

The Pig Pen Principle



Prevention of Colonization and Infection by *Klebsiella pneumoniae* Carbapenemase–Producing Enterobacteriaceae in Long-term Acute-Care Hospitals

MAJOR ARTICLE

Clinical Infectious Diseases

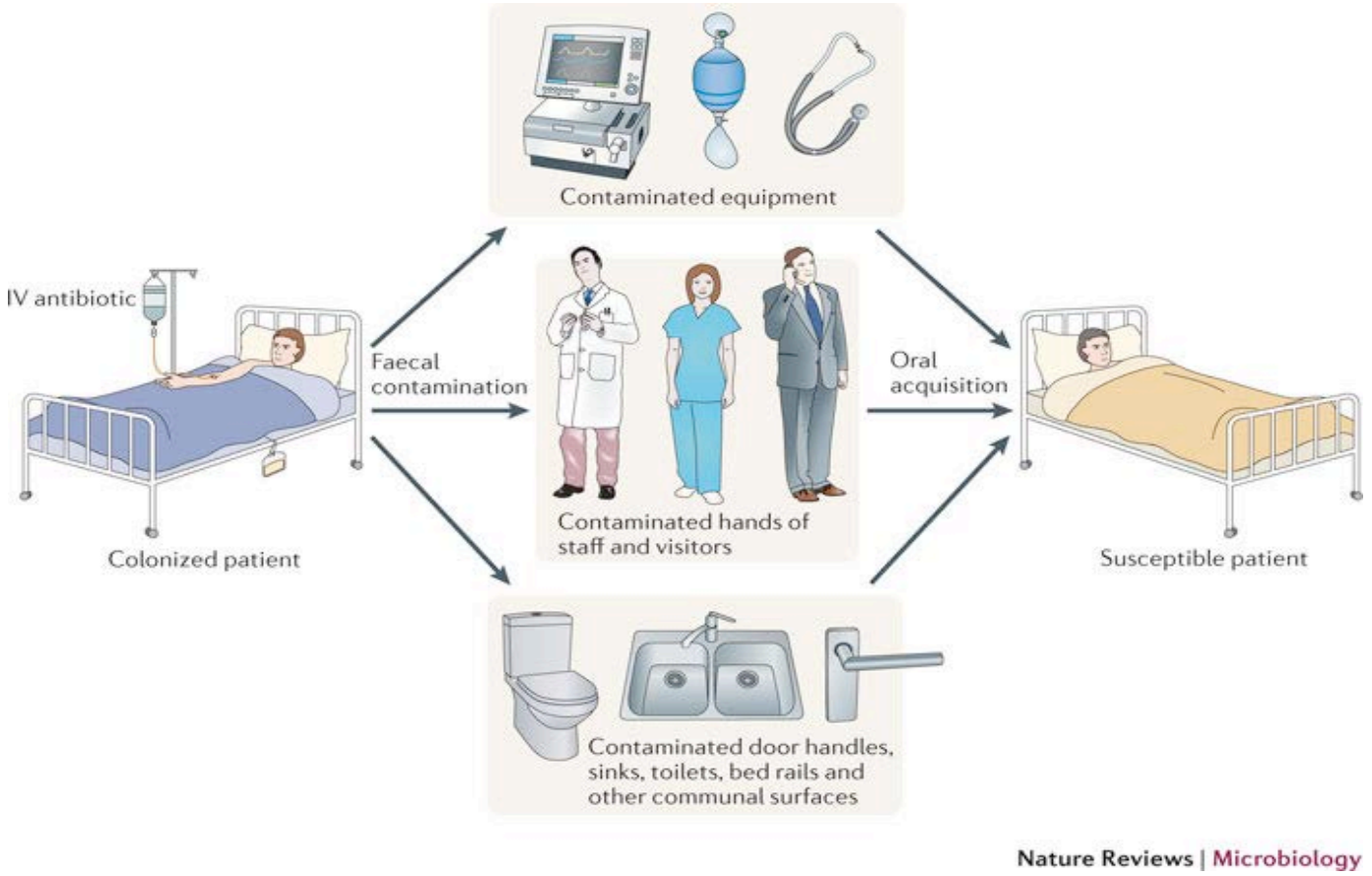
For Patient MDRO Colonization, Many feel decolonization is the answer.

Project CLEAR 2019

Protect Trial IDWeek 2019

SHIELD OC IDWeek 2019

Classical Explanation of Transmission of Hospital Acquired Infections



MDRO Environmental Sampling Process

- Baseline and intervention
  - Point prevalence assessment of object MDRO contamination
- Sampled at 28 nursing homes
  - 5 common area objects (dining hall or activity room)
  - 5 objects per resident room type
    1. ADRD* total care resident room (non-ambulatory)
    2. ADRD ambulatory resident room
    3. Short stay resident room

*Alzheimer's Disease and Related Dementia

MDRO Environmental Sampling Process

- Common Area Objects:
    1. Nursing Station Counter or Cart
    2. Table
    3. Chair
    4. Hand rail (hallway)
    5. Drinking Fountain or Drinking Station
- Resident Room Objects:
    1. Bedside Table and Bedrail
    2. Call Button and TV Remote and Phone
    3. Door Knobs
    4. Light Switch
    5. Bathroom Rail and Sink and Flush Handle

Environmental Contamination with MDROs – Common Area Objects

Object Type	# Objects Swabbed	Any MDRO	MRSA	VRE	ESBL	CRE
Nursing Station Counter or Cart	28	57%	43%	32%	0%	0%
Table*	28	54%	39%	29%	4%	0%
Chair*	28	46%	29%	18%	0%	0%
Hand Rail (hallway)	28	61%	32%	32%	4%	0%
Drinking Fountain or Drinking Station	28	32%	25%	11%	0%	0%
Any Object	**140**	**50%**	**34%**	**24%**	**1%**	**0%**

*Dining hall or activity room

Environmental Contamination with MDROs – Resident Room Objects

Object Type	# Objects Swabbed	Any MDRO	MRSA	VRE	ESBL	CRE
Bedside Table/Bedrail	84	55%	31%	29%	5%	0%
Call Button/ TV Remote/Phone	84	35%	23%	15%	1%	0%
Door Knobs	84	33%	24%	12%	1%	0%
Light Switch	84	26%	18%	8%	1%	0%
Bathroom Rail/Sink/Flush Handle	84	38%	23%	20%	5%	1%
Any Object	**420**	**37%**	**24%**	**17%**	**3%**	**0.2%**

Infection Prevention Nosocomial Infections

- Hand Hygeine
- Isolation Precautions
  - Contact
  - Airborne
  - Biohazard
- Personal Protective Equipment
- Cleaning of the Environment

For Environmental Cleaning, many opportunities still exist.

Elements of Environmental Cleaning

- Product
- Saturation
- Application
- Feedback

What does EVS Clean? What do RNs Clean?

Black Light Target

- Fluorescent marker
  - An invisible gel that glows under black light
  - An inert, non-toxic substance

Without black light

With black light

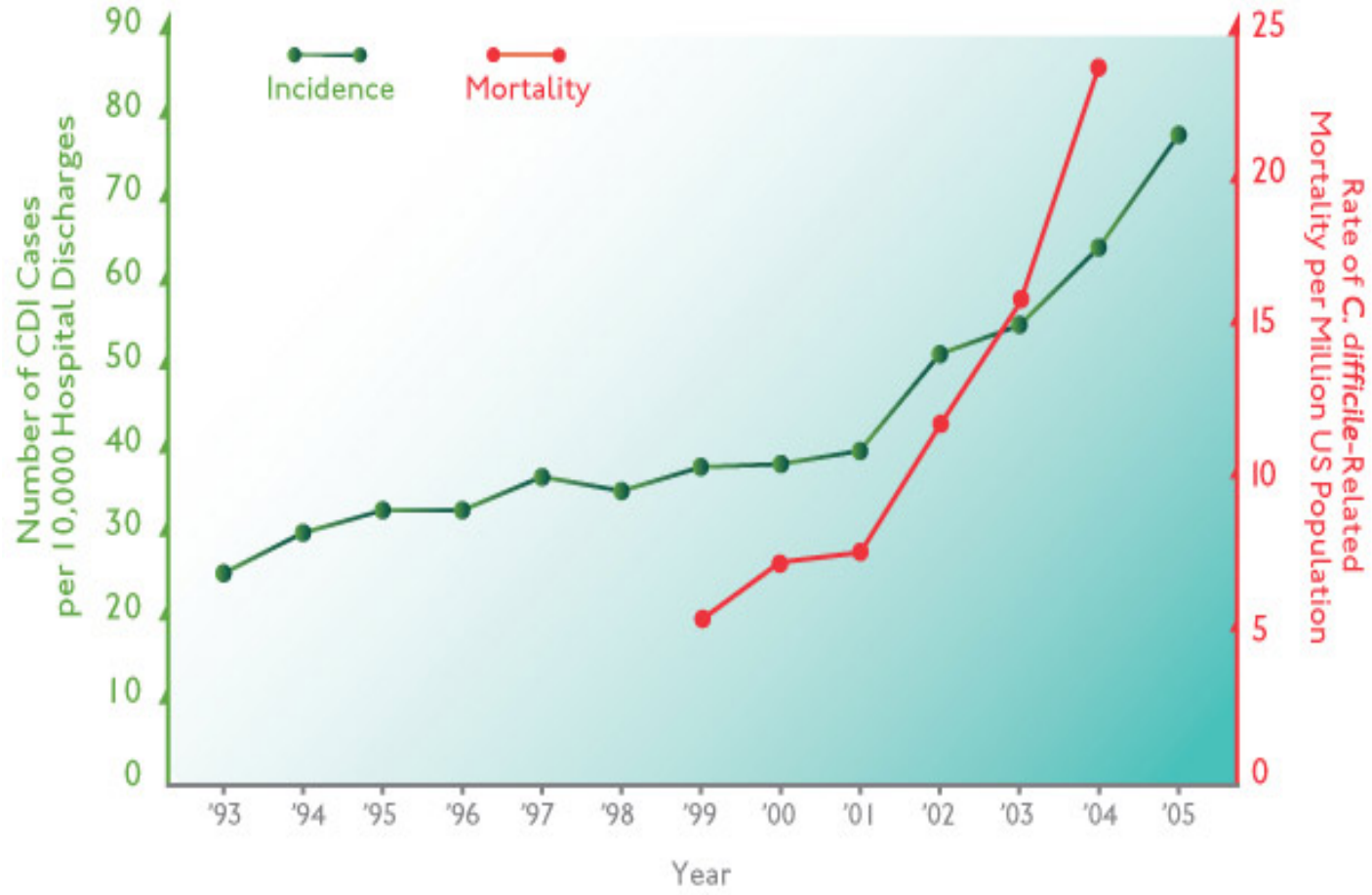
Carling PC. Clin Infect Dis 2006;42(3):385

Site A

sinks with connection between overflow cavity and drain

“CDI – it might not be Failure of Infection Prevention”

Increasing US Mortality due to C difficile

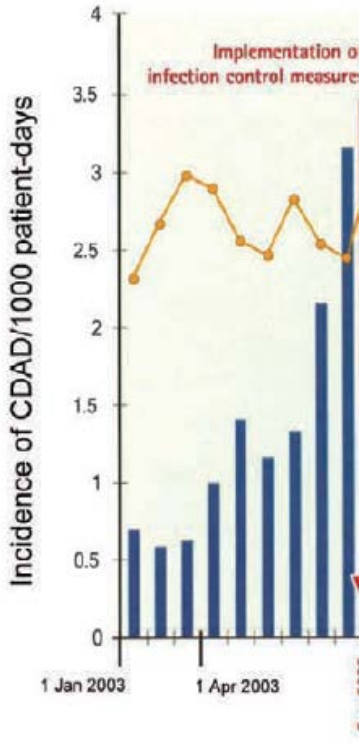


*** Daneman et al. JAC 66:2856, Dec 2011**

CDI: Impact

	Number of annual cases	Cost	Number of annual deaths
Hospital-onset, hospital acquired (HO-HA)	165,000	$ 1.3 B	9,000
Community-onset hospital acquired (CO-HA) [4 weeks of hospitalization]	50,000	$ 0.3 B	3,000
Nursing home-onset	263,000	$ 2.2 B	16,500

Houston We Have a Problem



Valiquette, et al.
Clin Infect Dis. 2007;45:S112-21

CONTACT ISOLATION PRECAUTIONS

Visitors ~ See Nurse before entering

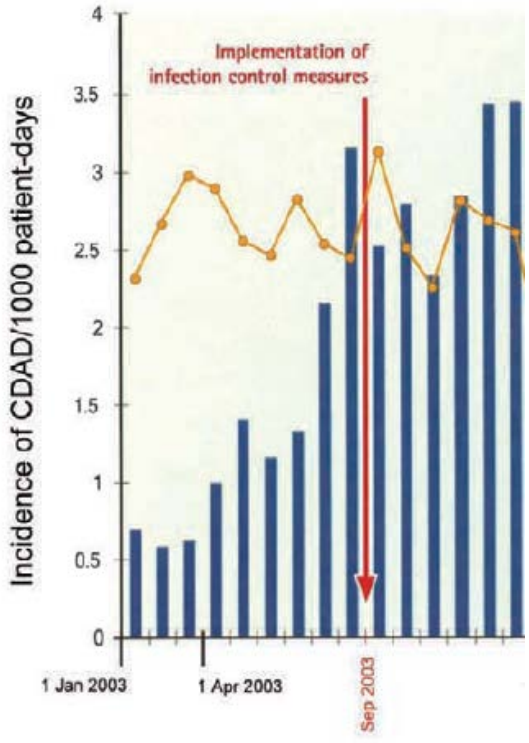
STOP

Clean Hands ~ Gown ~ Gloves

STOP

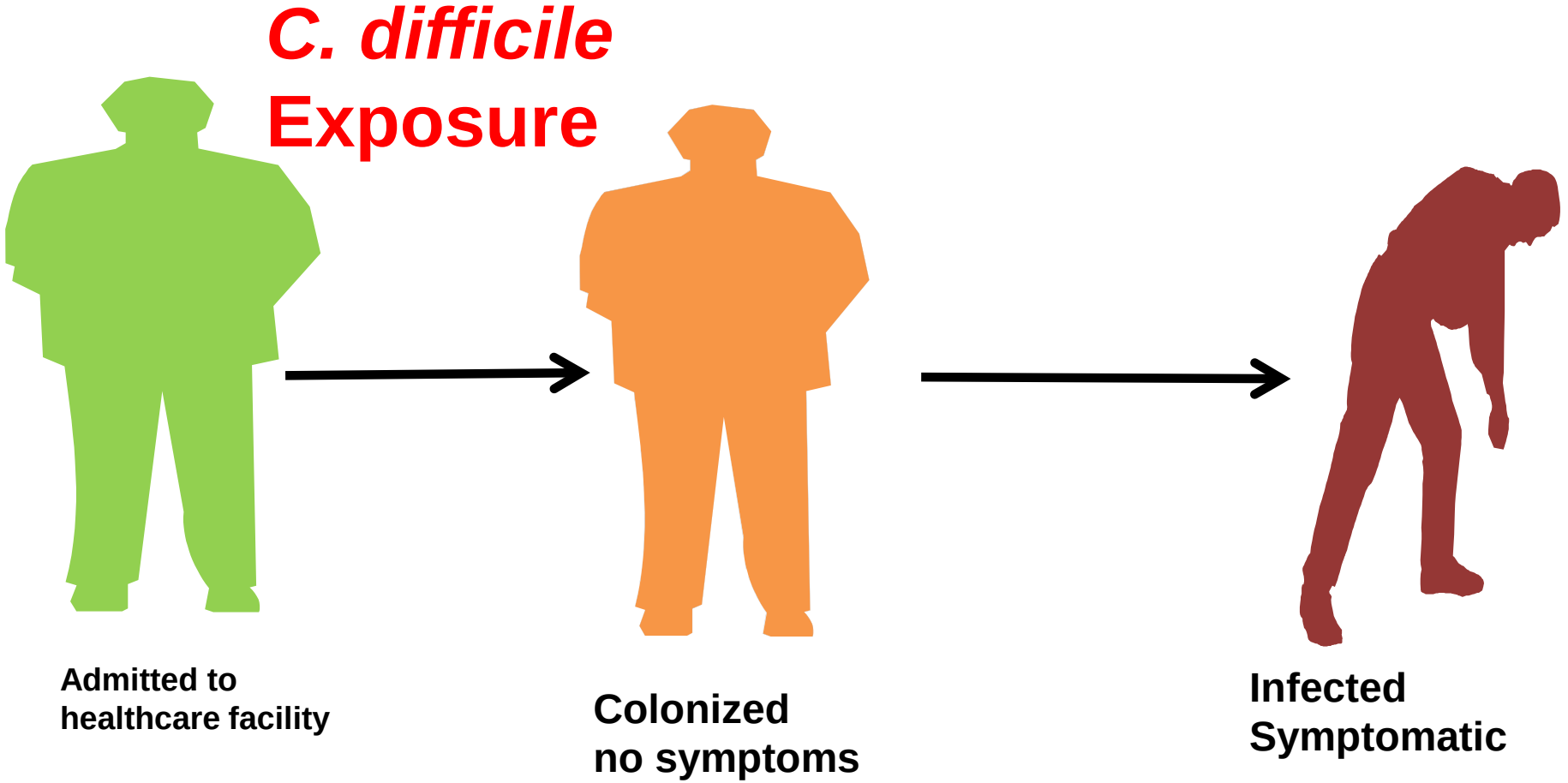
N-95 for High-Hazard Procedures (See other side)

Draconian Infection Control Measures



Valiquette, et al.
Clin Infect Dis. 2007;45:S112-21

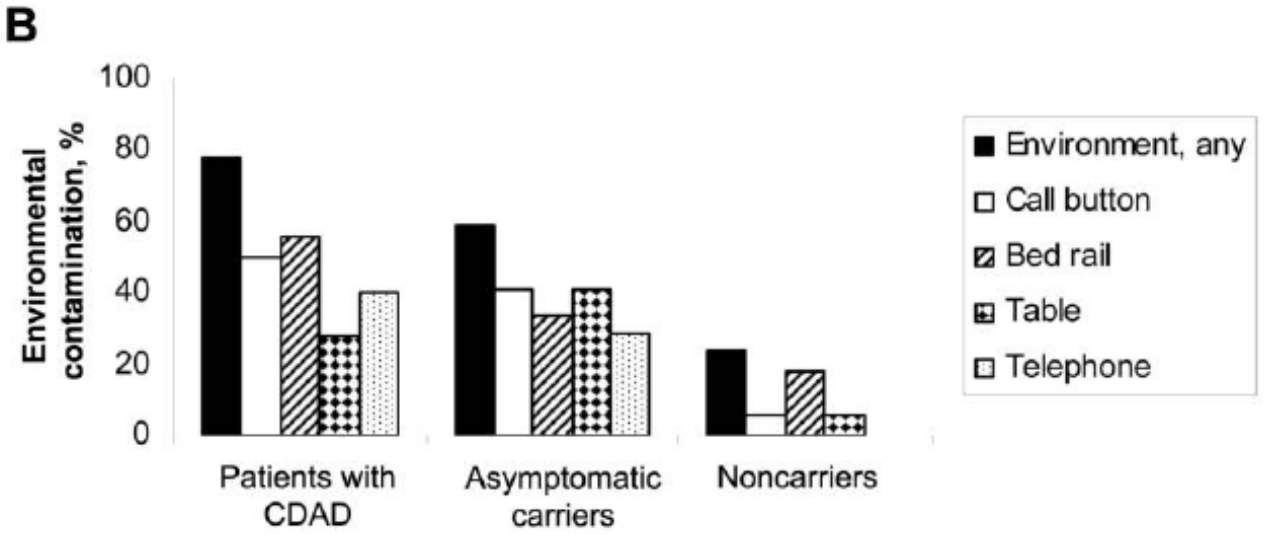
CDI Pathogenesis



Asymptomatic carriers are a potential source for transmission of Clostridium difficile

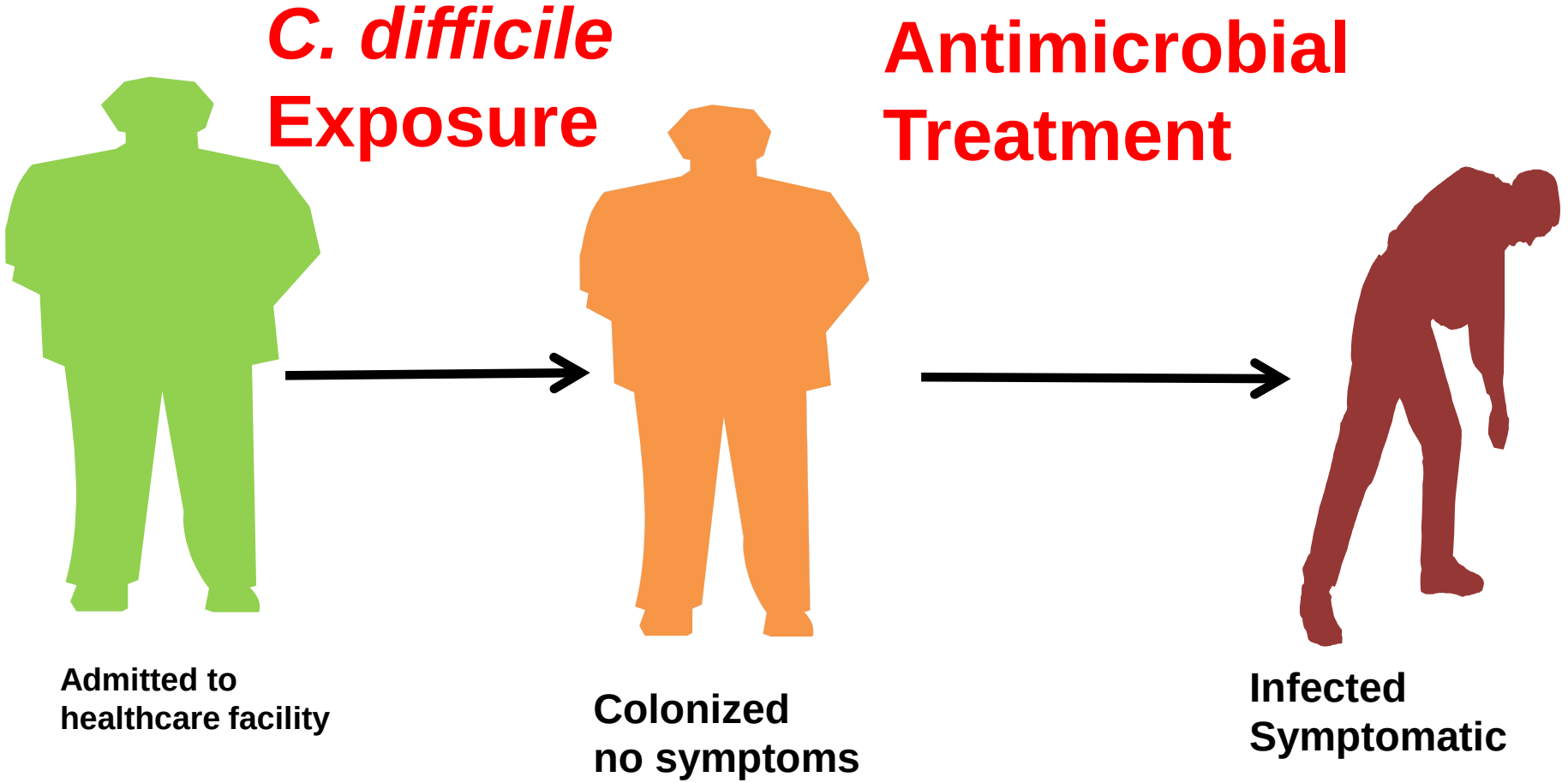
3-month study in LTCF with 73 residents
Five (7%) patients had CDI
35 (51%) were asymptomatic carriers (nine had a prior history of CDI)

Asymptomatic carriers associated with significantly higher rates of skin (61% vs. 19%) and environmental contamination (59% vs. 24%) than non-carriers



Riggs et al Clin Infect Dis 2007 **45**:8, 992-8

CDI Pathogenesis



Antimicrobials Predisposing to CDI

Very commonly related	Less commonly related	Uncommonly related
Clindamycin Ampicillin Amoxicillin Cephalosporins Fluoroquinolones	Sulfa Macrolides Carbapenems Other penicillins	Aminoglycosides Rifampin Tetracycline Chloramphincol

More on why Cipro, Levo, and Moxi are problematic

Antibiotics and CDI

Risk of CDI compared to resident on 1 antibiotic

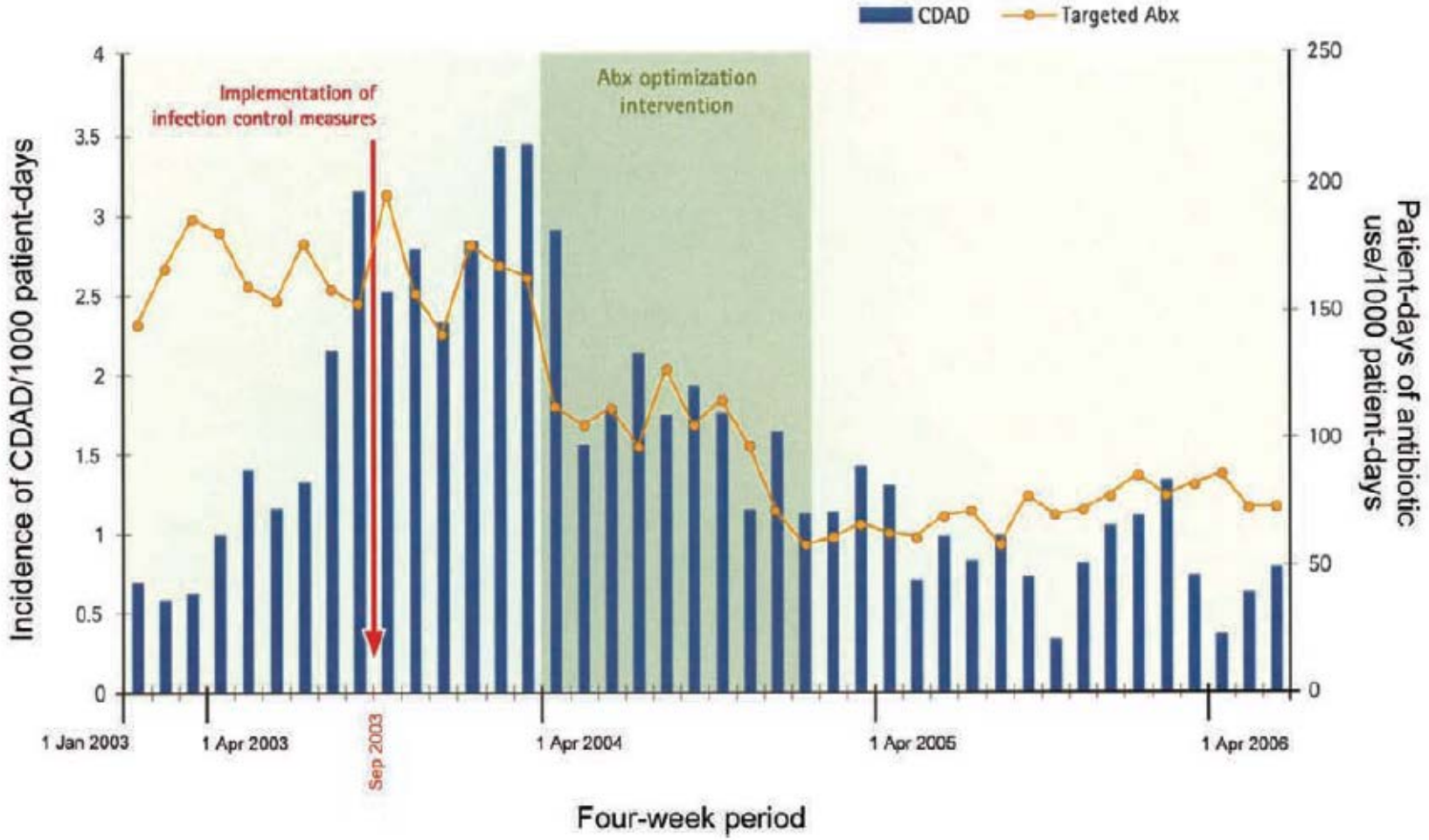
	Number of ATBs	
2 ATBs	**3-4 ATBs**	**5+ ATBs**
2.5 times higher	3.3 times higher	9.6 times higher

Risk of CDI compared to resident on ATBs for <4 days

	Days of Antibiotic	
4-7 days	**8-18 days**	**>18 days**
1.4 times higher	3 times higher	7.8 times higher

15. Epson,E. Orange County CDI Prevention Collaborative: Antimicrobial Stewardship. CDPH. November 5, 2015. Permission granted for use of this slide by Dr. Erin Epson.
Original slide reference: Stevens,et al. Clin Infect Dis. 2011;53(1):42-48

Targeting High-Risk Antibiotics Reduces CDI



Valiquette, et al.
Clin Infect Dis. 2007;45:S112-21

Effects of control interventions on *Clostridium difficile* infection in England: an observational study

*Kate E Dingle, Xavier Didelot, T Phuong Quan, David W Eyre, Nicole Stoesser, Tanya Golubchik, Rosalind M Harding, Daniel J Wilson, David Griffiths, Alison Vaughan, John M Finney, David H Wyllie, Sarah J Oakley, Warren N Fawley, Jane Freeman, Kirsti Morris, Jessica Martin, Philip Howard, Sherwood Gorbach, Ellie J C Goldstein, Diane M Citron, Susan Hopkins, Russell Hope, Alan P Johnson, Mark H Wilcox, Timothy E A Peto, A Sarah Walker, Derrick W Crook, the Modernising Medical Microbiology Informatics Group**

- Incidence of C. difficle in UK dropped by 80% after 2006
- Decline was due to multiple interventions
- However, Fluoroquinolone reduction is thought to be the primary driver for change

Dingle et al. Lancet ID. 2017

Antimicrobial Stewardship Structure

- CMS Survey Guidance

  Survey Resources, CMS-20054

https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/GuidanceforLawsAndRegulations/Nursing-Homes.html

CMS Requirement #1

- Written antibiotic use protocols on antibiotic prescribing, including the documentation of the indication, dosage, and duration of use of antibiotics

CMS Requirement #2

- Protocols to review clinical signs and symptoms and laboratory reports to determine if the antibiotic is indicated or if adjustments to therapy should be made and identify what infection assessment tools or management algorithms are used for one or more infections (e.g., SBAR tool for urinary tract infection (UTI) assessment, Loeb minimum criteria for initiation of antibiotics);

Nursing Assessment is Paramount

- Physicians may not be in the building
- Nursing assessment will frequently drive the clinical decisions
- When there is doubt, patients are routinely sent to the hospitals for “a REAL” assessment of the patient.

Red
Hot
Tender
Swollen
Knee Day 1

Red
Hot
Tender
Swollen
Knee Day 2

McGeer Criteria are the Wrong Criteria for Antimicrobial Stewardship

- 78 yo resident with Temperature of 99.6 Degrees, Heart Rate of 132, Blood Pressure of 90/40, White Blood Cell Count of 13,500 and no localizing signs of infection

- 78 year old resident complaining of dysuria, urgency, Frequency, CVA tenderness, suprapubic pain, no evidence of fever, heart rate of 88, blood pressure of 120/80

CMS Requirement #3

Periodic review of antibiotic use by prescribing practitioners

- "When the resident is **new to the facility**, when a **prior resident returns** or is transferred from a hospital or other facility,"

- **"during each monthly drug regimen review** when the resident has been prescribed or is taking an antibiotic, or any antibiotic drug regimen review as requested by the QAA committee"

Antibiotic Time Out

- Appropriateness of Treatment
- Drug Selection
- Dose
- Duration
- Contra-indications or Drug Interactions

CMS Requirement #4

- Protocols to optimize the treatment of infections by ensuring that residents who require antibiotics are prescribed the appropriate antibiotic

Organism	No. Isolates	Penicillins			Cephalosporins				Carbapenems			Aminoglycosides			Fluoro-quinolone	Other	
		Ampicillin	Ampicillin-sulbactam	Piperacillin-tazobactam	Cefazolin	Cefepime	Ceftazidime	Ceftriaxone[1]	Ertapenem	Imipenem	Meropenem	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Trimethoprim–sulfamethoxazole	Colistin
Citrobacter freundii	40	R[2]	R	88	R	93	—[3,4]	—[4]	90	93	95	99	83	93	85	73	99
Enterobacter aerogenes	63	R	R	79	R	95	—[4]	—[4]	98	95	99	99	99	99	98	98	99
Enterobacter cloacae	172	R	R	81	R	92	—[4]	—[4]	95	99	99	99	98	98	97	91	79
Escherichia coli	441	41	50	92	59	84	83	79	98	99	99	98	79	81	58	55	99
Klebsiella oxytoca	102	R	66	91	31	95	95	92	98	99	99	99	95	97	96	91	99
Klebsiella pneumoniae	299	R	72	88	71	86	84	82	93	93	93	94	90	87	85	76	98
Morganella morganii	29[5]	R	R	97	R	99	—[4]	—[4]	99	—	99	99	76	90	69	66	R
Proteus mirabilis	117	74	87	99	34	95	97	92	99	—	99	99	87	93	71	70	R
Serratia marcescens	99	R	R	98	R	99	—[4]	—[4]	99	97	99	99	99	99	93	99	R
Acinetobacter baumannii	49	R	69	49	R	63	61	—	R	74	71	74	65	69	63	67	94
Pseudomonas aeruginosa	498	R	R	87	R	89	90	R	R	80	86	95	92	96	78	R	99
Stenotrophomonas maltophilia	53	R	R	R	R	—	32	R	R	R	R	R	R	R	—	94	45
Burkholderia cepacia complex	12[5]	R	R	R	R	R	42	R	R	R	42	R	R	R	58	92	R

[1] Cefotaxime and ceftriaxone have comparable activity against *Enterobacteriaceae.*

[2] R = intrinsic resistance.

[3] — = Not routinely tested and/or not applicable.

[4] 3rd generation cephalosporins should not be used for serious infections.

[5] Calculated from fewer than the standard recommendation of 30 isolates.

http://www.pathnet.medsch.ucla.edu/department/cliniclab/microbio/amic.pdf
Accessed 11/22/2017

CMS Requirement #5

- A system for the provision of feedback reports on antibiotic use, antibiotic resistance patterns based on laboratory data, and prescribing practices for the prescribing practitioner.

Prescribing Patterns of the Highest Antibiotic Prescribers

Prescriber	Antibiotic Orders (n)	Ave DOT	FQ Orders	non-FQ Orders	FQ ave DOT
Doctor	48	7.6	12.5%	87.5%	6.7
Doctor	21	7	33.3%	66.7%	6.6
Doctor	21	6.3	9.5%	90.5%	8.5
Doctor	20	6.2	40.0%	60.0%	7.3
Doctor	20	6.3	35.0%	65.0%	4.6
Doctor	15	8.4	20.0%	80.0%	10.3

LA County DPH SNF Interviews

- Random Selection of 50 nursing facilities licensed in LA County
- Randomization stratified by >99 Beds and ≥100 Beds
- Questions Based off CDC checklist for Antimicrobial Stewardship in California (mirrors State toolkit)
- Telephone based survey process

Element 1. Leadership Commitment

SNF leadership commitment support helps ensure adequate funding and staffing of the ASP, and facilitates buy-in among clinicians.

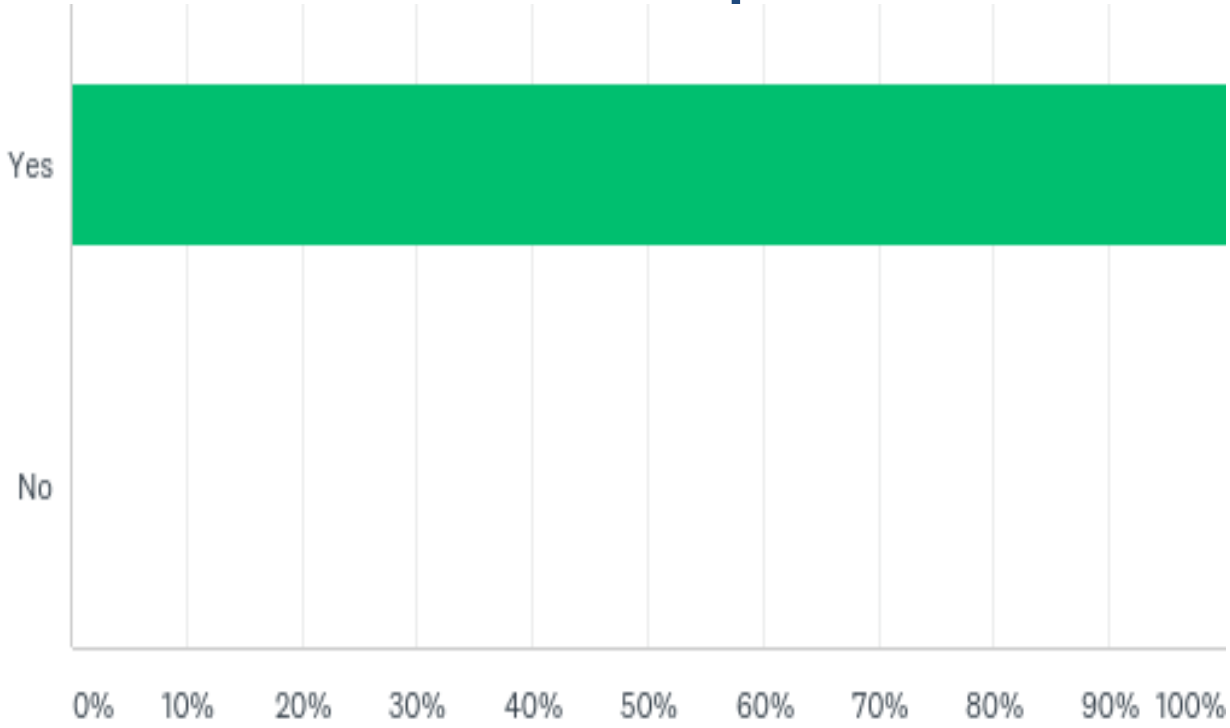
- Create a written statement in support of ASP
- Establish antibiotic stewardship as a Performance Improvement Program under QAPI
- Routinely review ASP activities during the facility quality improvement committee meetings

Element 2. Accountability

A SNF leader should be accountable for ASP outcomes and their effectiveness assessed through clear performance standards. ASP leaders serve as liaisons and champions to promote stewardship education and practices across disciplines.

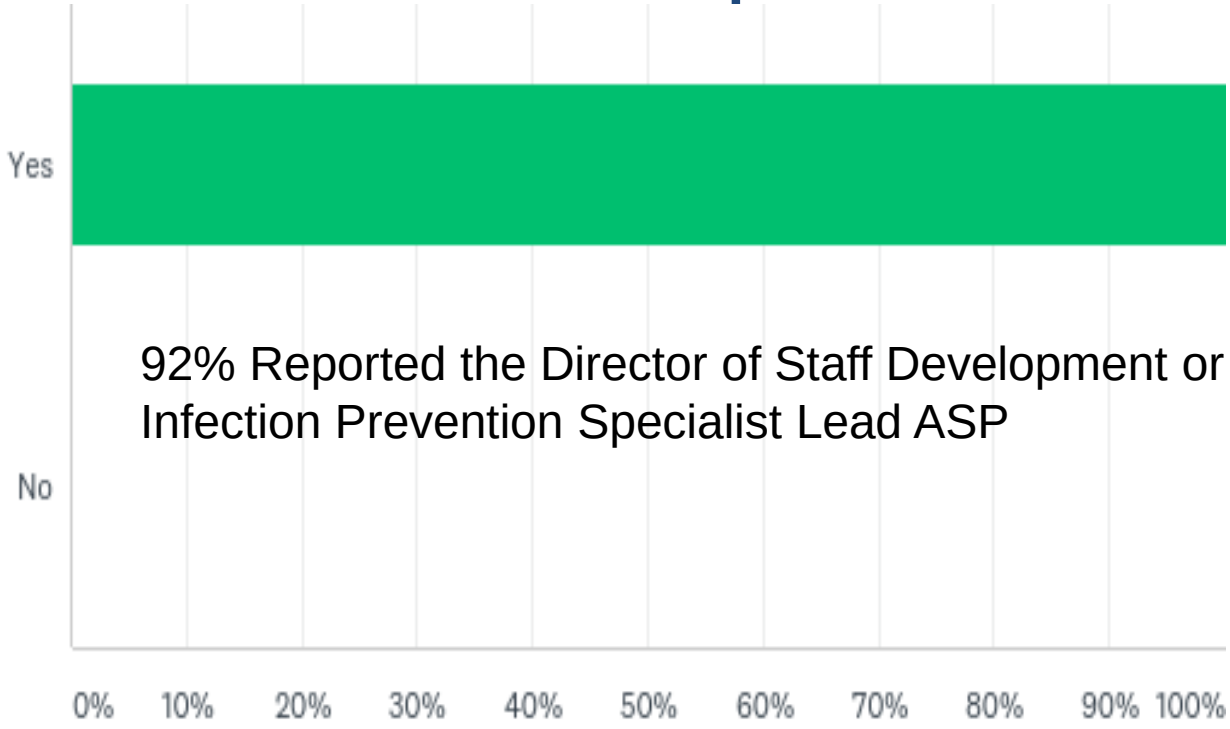
- Convene a **physician-supervised** multidisciplinary antibiotic stewardship committee, subcommittee, or workgroup

Has your facility identified a lead(s) for antibiotic stewardship activities?



ANSWER CHOICES	RESPONSES	
Yes	100.00%	35
No	0.00%	0
TOTAL		35

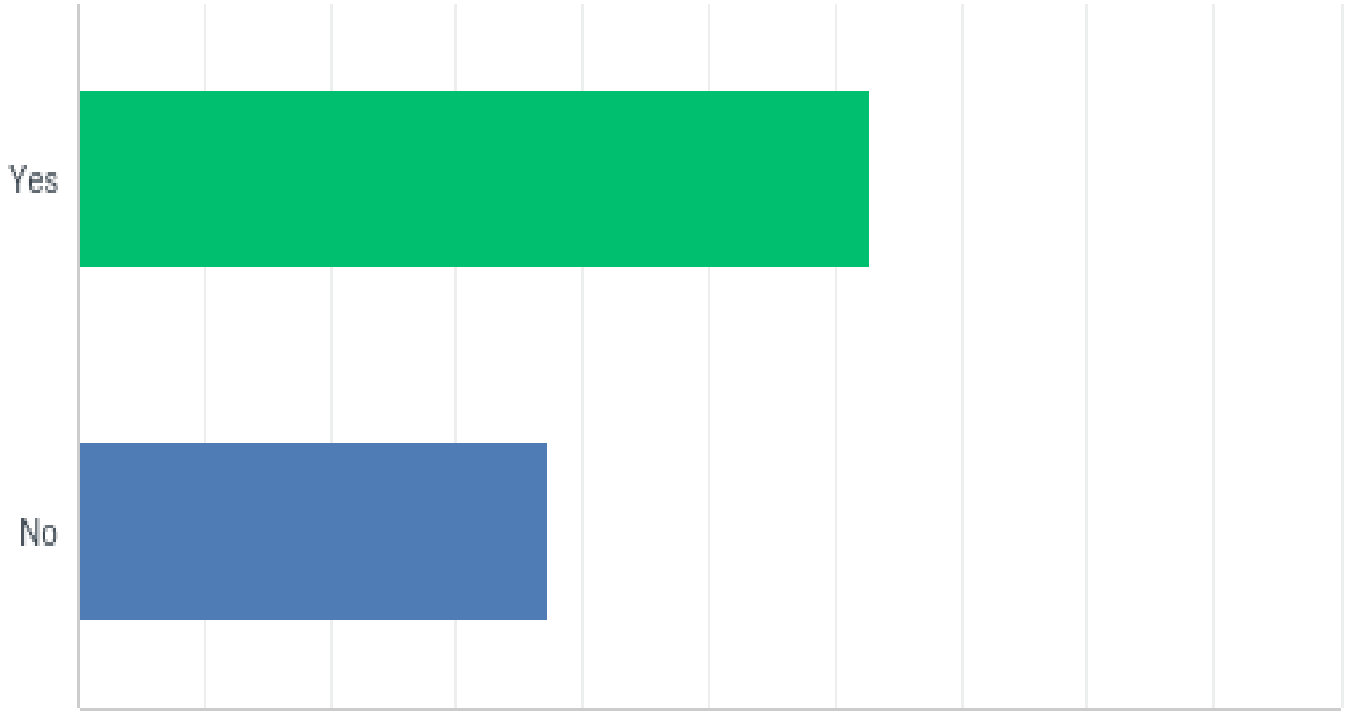
Has your facility identified a lead(s) for antibiotic stewardship activities?



92% Reported the Director of Staff Development or Infection Prevention Specialist Lead ASP

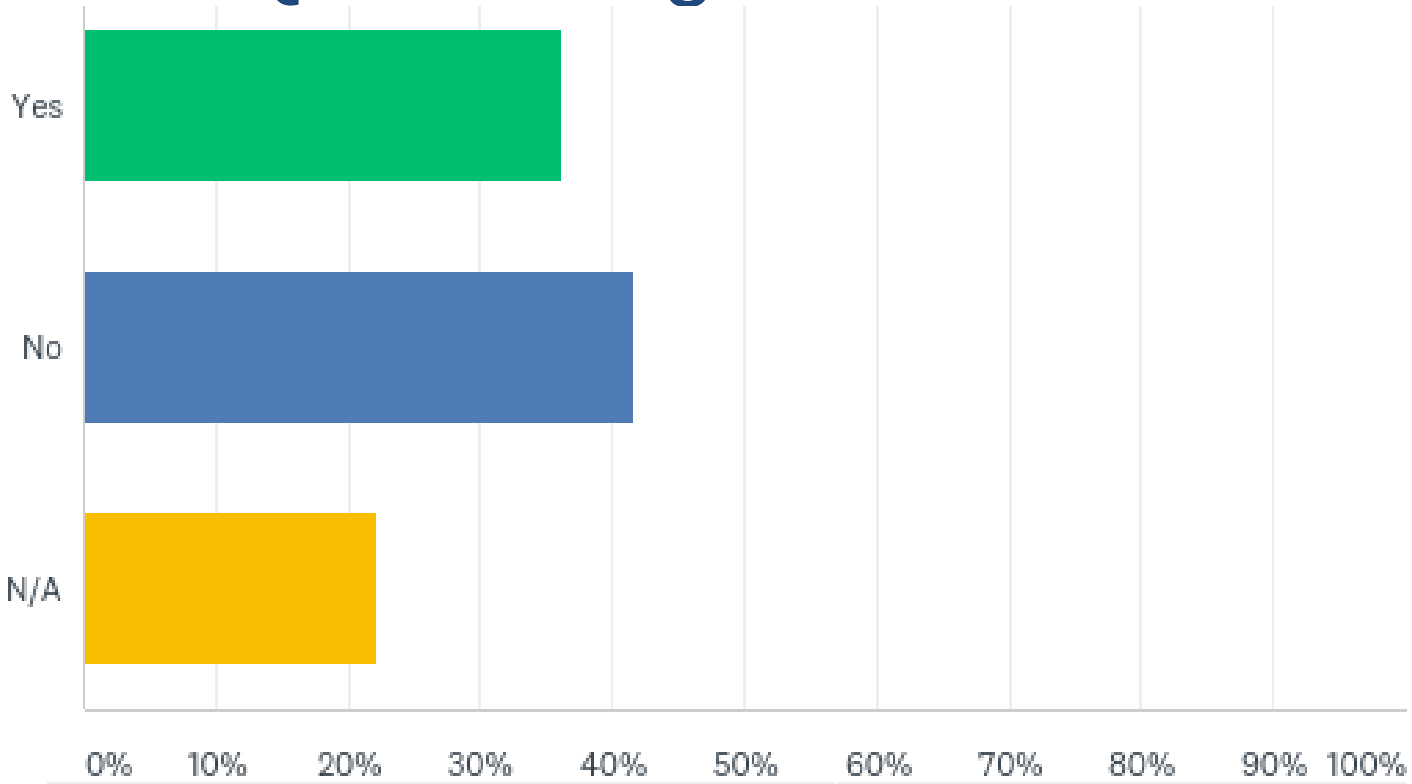
ANSWER CHOICES	RESPONSES	
Yes	100.00%	35
No	0.00%	0
TOTAL		35

Do you have a physician lead for ASP?



ANSWER CHOICES	RESPONSES	
Yes	62.86%	22
No	37.14%	13
TOTAL		35

Does the physician lead spend time outside QA meetings on ASP?



ANSWER CHOICES	RESPONSES	
Yes	36.11%	13
No	41.67%	15
N/A	22.22%	8
TOTAL		36

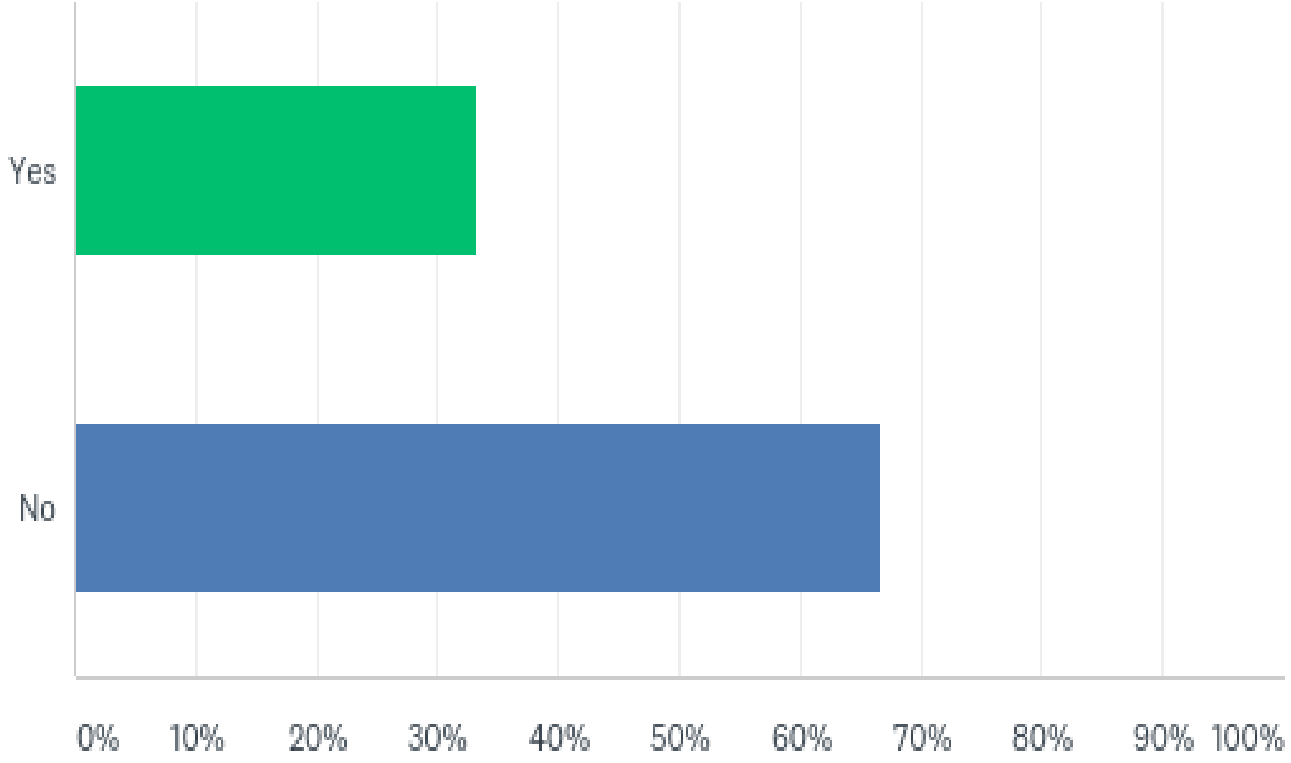
Element 3. Drug Expertise

SNF should establish access to individuals with antibiotic expertise to implement antibiotic stewardship activities. Suggestions:

- Obtain ASP support from a physician or pharmacist who has attended specific training on antibiotic stewardship. The trained physician or pharmacist may be consultant pharmacy staff trained or experienced in antibiotic stewardship, an external infectious disease stewardship consultant, or part of the stewardship team at a referral hospital

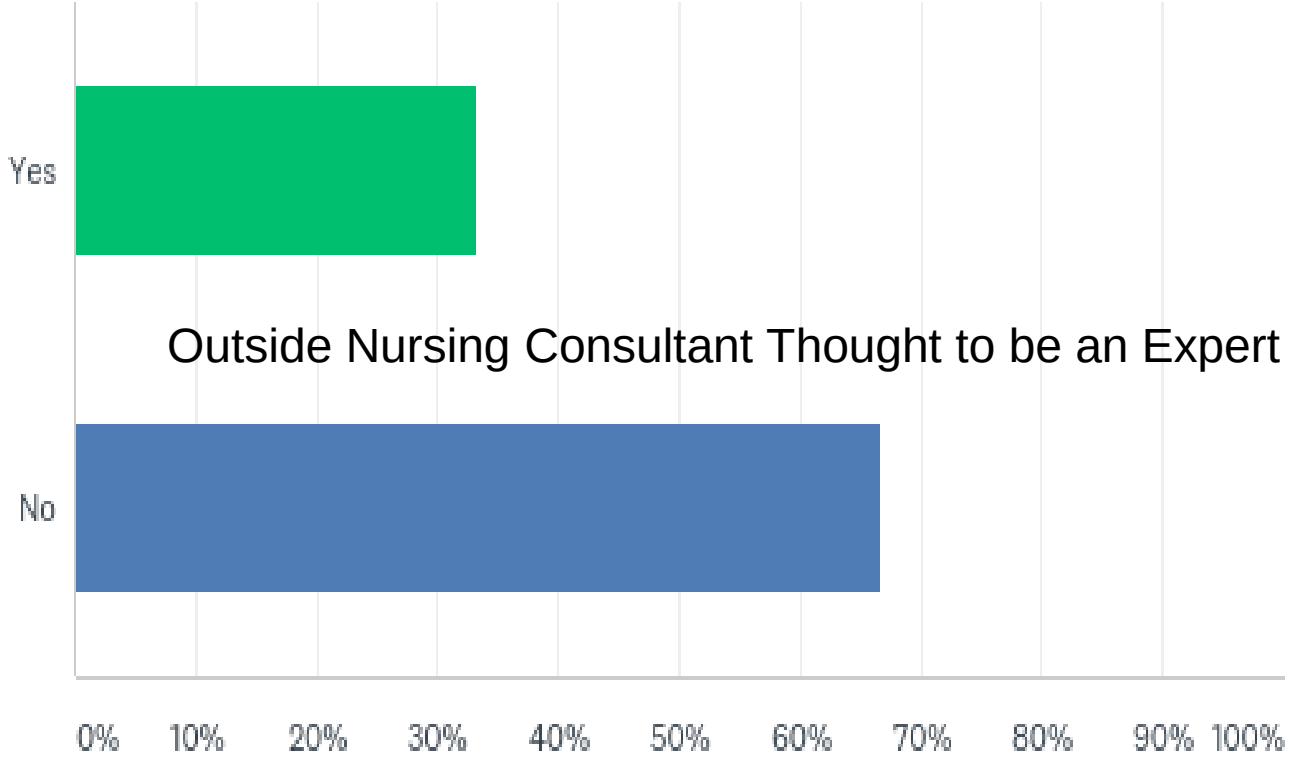
- CDC, SHEA, IDSA, IDAC, etc.

Access to individual(s) with antibiotic stewardship expertise?



ANSWER CHOICES	RESPONSES	
Yes	33.33%	12
No	66.67%	24
TOTAL		36

Access to individual(s) with antibiotic stewardship expertise?



ANSWER CHOICES	RESPONSES	
Yes	33.33%	12
No	66.67%	24
TOTAL		36

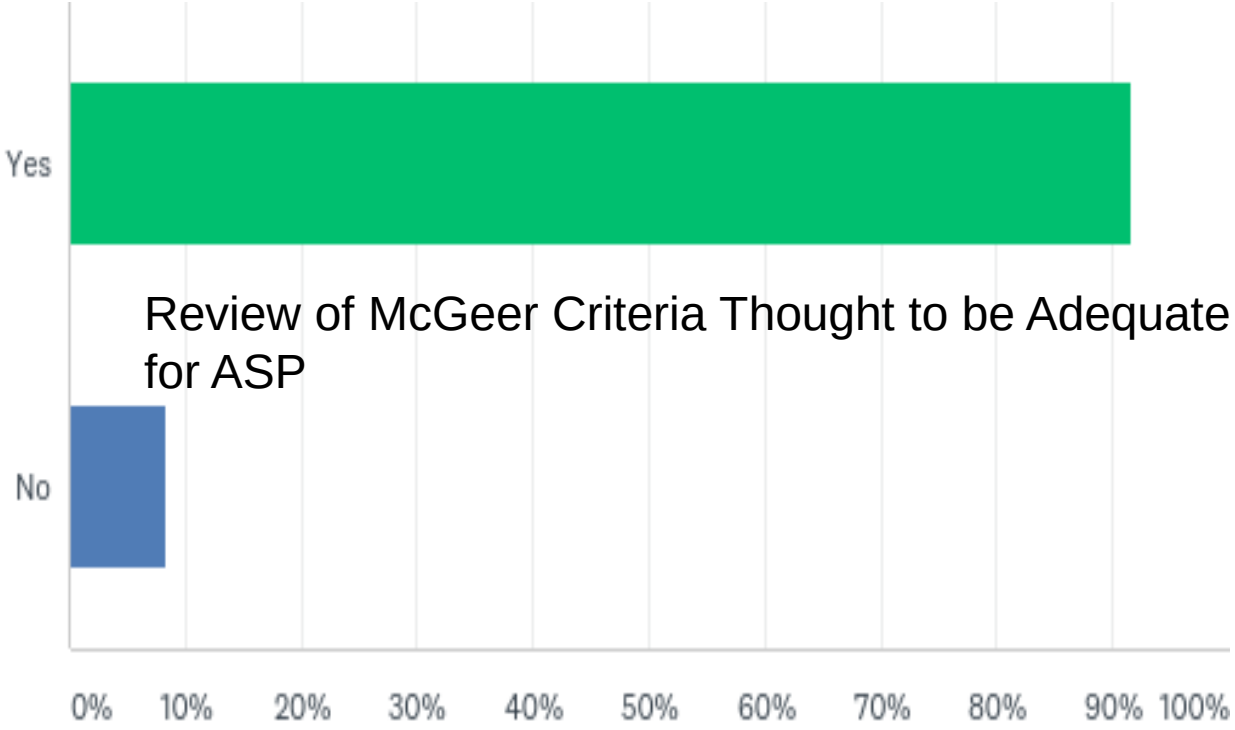
Element 4. Action

SNF should implement at least one intervention to improve antibiotic use.

- New policies and procedures should be introduced in a step-wise fashion.

- Prioritize interventions based on the prescribing and resistance patterns or most prevalent antibiotic adverse events (e.g., Clostridium difficile infections) at the facility.

Implemented practices to improve antibiotic use?



ANSWER CHOICES	RESPONSES	
Yes	91.67%	33
No	8.33%	3
TOTAL		36

Element 5. Tracking

SNF should monitor both antibiotic use practices and outcomes related to antibiotics to guide practice changes and track the impact of new interventions.

Tracking Continued

- Monitor outcomes of antibiotic use.
  - Rates of C. difficile infection
  - Rates of antibiotic-resistant organisms
  - Rates of adverse drug events due to antibiotics

Tracking Continued

- Monitor measures of antibiotic use.
  - Adherence to clinical assessment documentation (e.g., signs/symptoms, vital signs, physical exam findings)
  - Adherence to prescribing documentation (e.g., dose, duration, indication)
  - Adherence to facility-specific treatment recommendations
  - Rates of new antibiotic starts per 1000 resident-days
  - Rates of antibiotic days per 1000 resident days.

Element 6. Reporting

Regular reporting of information on antibiotic use, including adherence to antibiotic prescribing policies, to physicians, nurses, and relevant staff engages and motivates them to meet ASP goals.

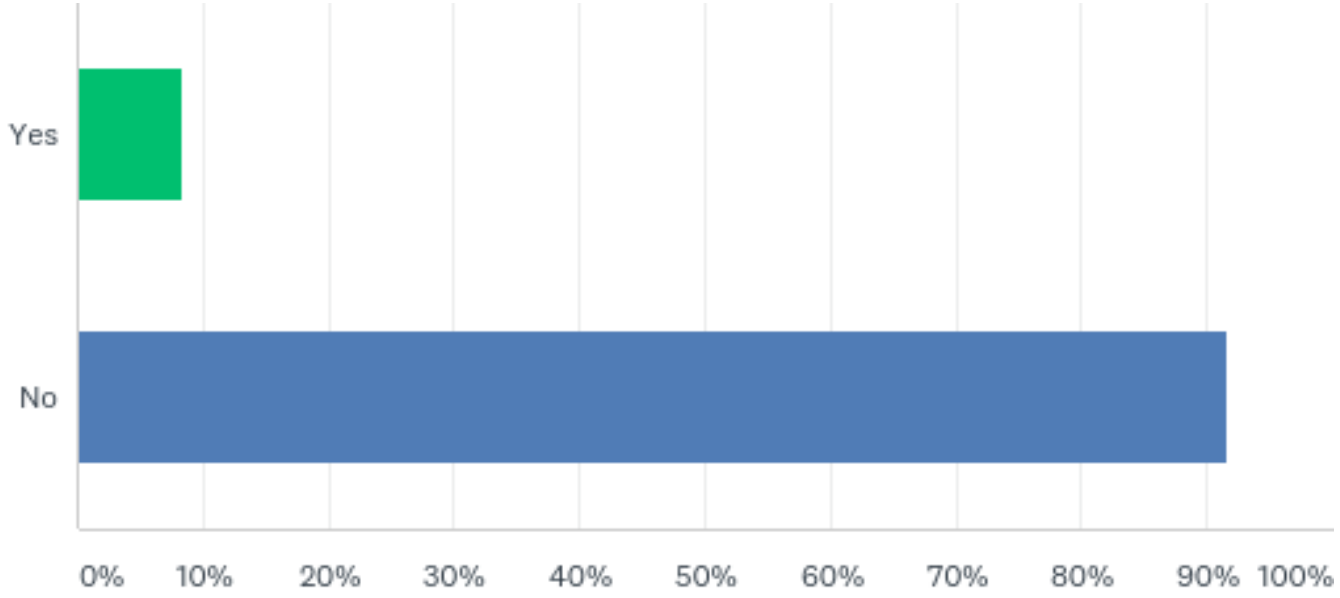
- Regularly provide written summaries of antibiotic stewardship goals, antibiotic use, and outcome measurements to prescribers and nursing staff
- Conduct real-time audits/reviews of individual prescriber practices and provide personalized feedback to clinical providers

Element 7. Education

SNF ASP should educate both **clinical providers** and **nursing staff** on the rationale and goals of antibiotic stewardship interventions, and the responsibility of each group for ensuring implementation. SNF should also **engage residents and their family members** in antibiotic use and stewardship education to ensure their support when clinicians make appropriate antibiotic use decisions.

- Regularly provide education and updates about antibiotic resistance and opportunities for improving use to clinical providers, nursing staff, residents, and families

Did you have any antibiotic stewardship deficiencies?



ANSWER CHOICES	RESPONSES	
Yes	8.33%	3
No	91.67%	33
TOTAL		36

ASP Confusion

- Nursing Homes are confusing Infection Prevention with Antimicrobial Stewardship
  - Structure of program is wrong
  - Insufficient expertise
  - Incorrect application of clinical criteria
- Some facilities may meet the regulations with paper compliance, but still fail to have a robust program
  - Few deficiencies have been issued to date
- Great need still exists for more robust ASP programs for our most vulnerable patients