Control of Multidrug-resistant Organisms in a Hospital Environment: Multidimensional Approach

Roy F. Chemaly, MD, MPH, FIDSA, FACP

Associate Professor of Medicine

Director, Infection Control

Director, Antimicrobial Stewardship Program

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Outline

- Impact of MDROs
- Multidimensional Approach
- Barriers
- New Strategies
- Outcomes Data

How You Define MDROs?

- No consensus definition:
  - Resistant to at least 2? or 3? complete classes of antibiotics (all beta-lactams or all aminoglycosides)
  - Resistant to the drug of choice (methicillin for *S. aureus* or vancomycin for enterococci)
  - Not antibiotic resistant but hard to kill for other reasons (*C. difficile*)
  - Epidemiologically significant

- Data on outcomes and magnitude of the problem depend on the definition used.

Consensus around the world what should be considered MDRO

- Methicillin-resistant *Staphylococcus aureus;* **MRSA**
- Vancomycin-resistant enterococci (by the vanA mechanism); **VRE**
- Extended-spectrum beta-lactamase-producing enteric Gram negatives; **ESBL**
- **Carbapenem-resistant** Gram negatives
- **Highly resistant Acinetobacter** and other non-fermenter strains
- ***Clostridium difficile***

Why are we so concerned with MDROs?

- MDROs are not necessarily more virulent but:
  - Patient outcomes are worse; acuity, mortality, LOS, toxicity of alternative antibiotics required
  - Cost per episode of care is increased: Antibiotic cost, LOS, cost of special precautions
  - MDROs are transmissible; their presence in some patients poses a risk to other patients

The Monster Amongst Us: Carbapenem-Resistant Enterobacteriaceae (CRE)

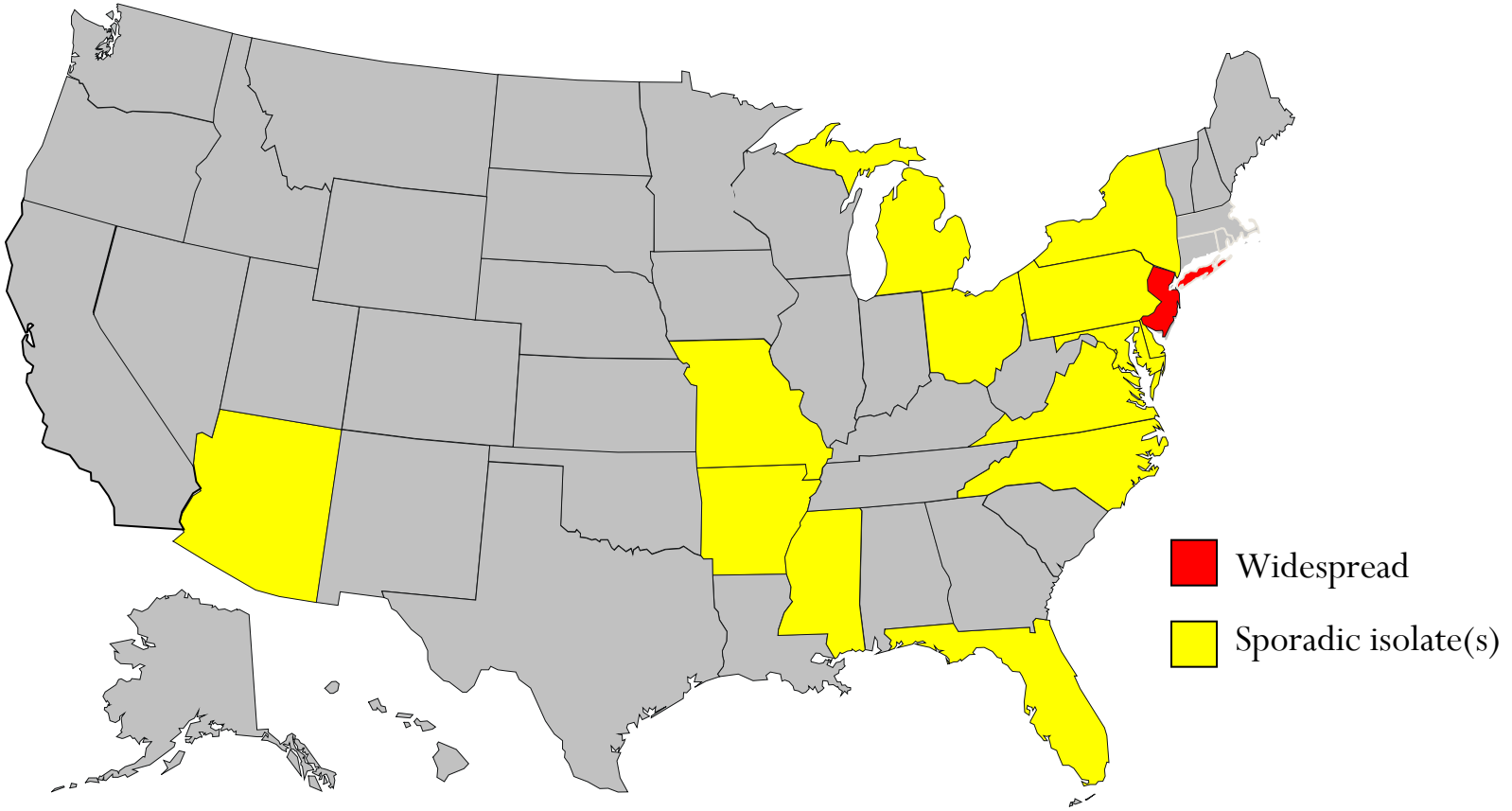
- **CRE are epidemiologically important for several reasons:**

• Association with high mortality rates (up to 50% in some studies).

• In addition to β-lactam/carbapenem resistance, CRE often carry genes that confer high levels of resistance to many other antimicrobials.

• CRE have spread throughout the world and many parts of the US and have the potential to spread more widely.

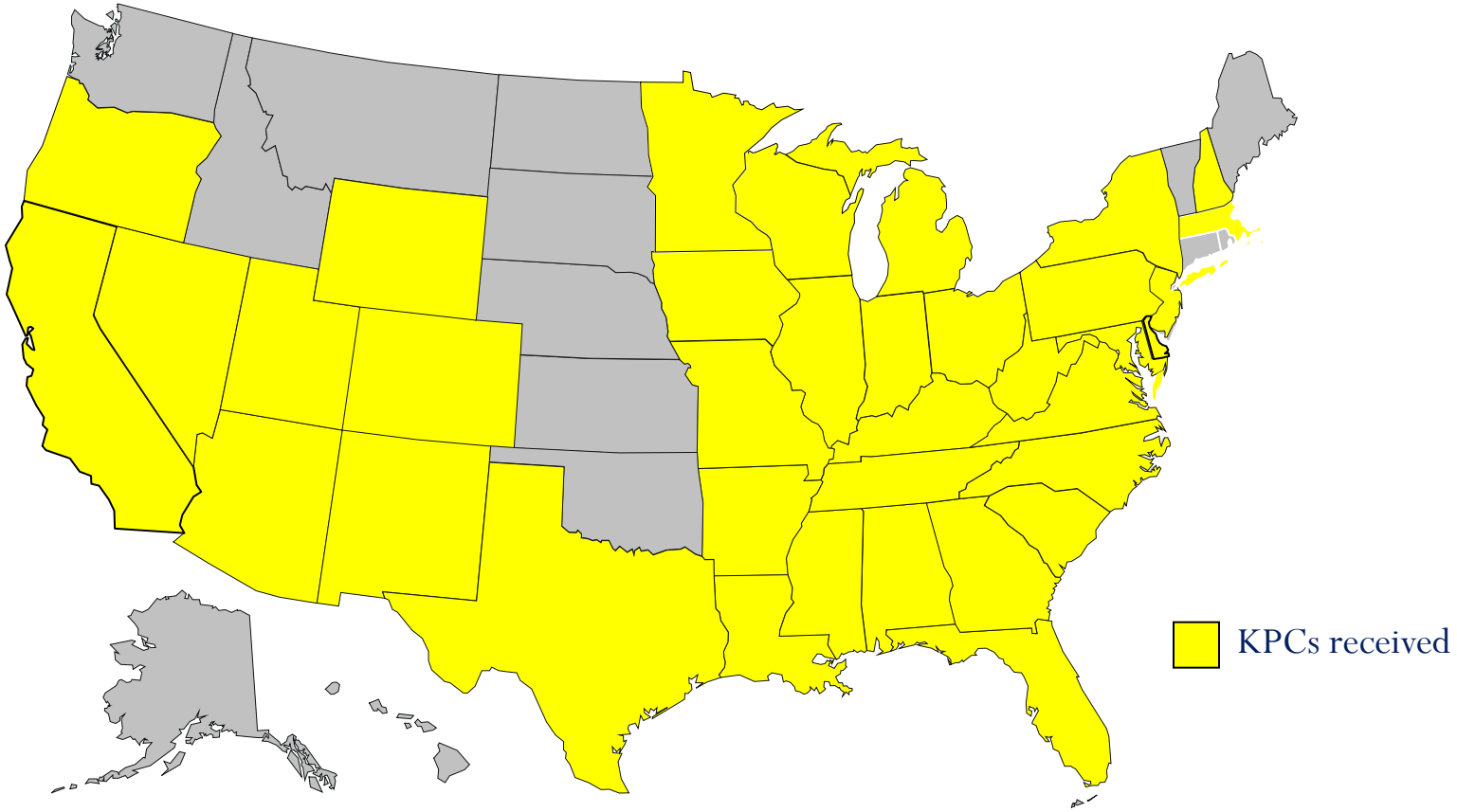
Geographical Distribution of KPC (CRE)-Producers



November 2006

Centers for Disease Control and Prevention.

Geographical distribution of extreme-drug resistant *Klebsiella* bacteria



August 2010

Centers for Disease Control and Prevention.

Can MDROs be controlled in the hospital?

WSJ 01-31-2013

When Hospitals Become Killers

By Betsy McCaughey

In 2011, the lethal germ known as CRK—short for carbapenem-resistant Klebsiella—raced through the National Institutes of Health Medical Center in Bethesda, Md. Antibiotics couldn't stop it. Infection-control precautions recommended by the Centers for Disease Control and Prevention could not contain it. Six patients died because of it, including a 16-year-old boy.

Last week, public-health researchers released alarming data in the journal Infection Control and Hospital Epidemiology showing that the same germ that swept through the NIH is invading hospitals across the country. Researchers writing this month in another medical journal, Emerging Infectious Diseases, warn that CRK poses "a major threat to public health."

Since the discovery of CRK in 2000, it has been found predominantly in New York City and the mid-Atlantic region. But Los Angeles County, one of the few places where CRK is being tracked, detected 356 cases in the second half of 2012. "Upwards of fifty percent" of patients who contract CRK die, according to NIH researchers.

Klebsiella infections generally are treated with powerful antibiotics called carbapenems, but the Jan. 25 data reveal that increasingly this medical weapon of last resort is not working. Drug resistance in Klebsiella infections is up 4,500% since 2002—from 0.1% to 4.5%, and that's just among known cases. Medical institutions are clearly moving closer to a post-antibiotic era.

A drug-resistant germ has struck even the National Institutes of Health Medical Center.

Current measures recommended by the Centers for Disease Control will not control the spread of this germ, even when hospital personnel follow the measures meticulously. That was the stunning conclusion reached by NIH researchers.

The NIH outbreak began in June 2011 when a 43-year-old woman with lung disease was admitted to the medical center from a New York hospital. Her chart alerted NIH that she was carrying CRK, so medical staff immediately isolated her and wore gowns, gloves and masks when treating her. All CDC contact and isolation precautions were followed, researchers later confirmed.

The woman recovered and left the hospital. But after three weeks, a male cancer patient in the same hospital who had no contact with the woman came down with CRK. Ten days later, a female patient with an immune disease fell victim. Both died. Week after week, more patients were hit with CRK. Researchers traced every infection back to the germ introduced into the hospital by the 43-year-old woman.

"The outbreak was finally contained by implementing tougher standards," said the NIH researchers—standards tougher than CDC guidelines.

First, to halt the outbreak, the NIH screened all patients for CRK. Patients unknowingly pick up the germ and carry it in their gastrointestinal tract for weeks without symptoms. Nurses who treat these unidentified carriers inadvertently transport the germ from bedside to bedside. The NIH used a relatively new rapid-test technology, then isolated every carrier.

Since 1991, the CDC has recommended testing all hospital patients for the AIDS virus but not for bacteria that cause hospital infections. Hospital infections kill five times as many Americans as the AIDS virus. Moreover, becoming infected with AIDS is difficult, but picking up a drug-resistant hospital germ is as easy as touching a bed rail or nurse's glove.

The second step that the NIH implemented was more rigorous cleaning than the CDC calls for. Rooms were double-cleaned with bleach and then misted with a hydrogen peroxide sprayer—another relatively new technology. Bacteria can live on equipment for days and then contaminate the hands of unsuspecting caregivers. When cleaning is inadequate, a patient assigned to a room previously occupied by the carrier of a superbug is put in danger.

In the 1980s, the CDC, the American Hospital Association and state health departments responded quickly to the AIDS threat, revamping hospital protocols on needles, sharp equipment and bodily fluids to prevent AIDS from becoming a hospital-acquired epidemic.

Where is that determination now? The National Institutes of Health researchers urged the CDC to make CRK a reportable disease like AIDS. How can the CDC and public-health agencies control this new threat when they don't even know how many cases are occurring and where?

We have the technology to contain these drug-resistant germs. What is needed is the will to do it. Otherwise patients with cancer, organ transplants and other immune-compromised conditions may find themselves worrying: Is it safe to go to the hospital?

Ms. McCaughey, a former lieutenant governor of New York, is founder and chairman of the Committee to Reduce Infection Deaths.

Control or Elimination of MDROs in the hospital: Multidimensional Approach

1. Hand Hygiene
2. Contact Precautions
3. Optimize antibiotic use
4. Active Surveillance
5. Enhanced environmental cleaning
6. Optimal communication between key players
7. Education of Staff and Patients
8. Some might add decolonization

I. Hand Hygiene
Why are we still talking about it?

Barriers

- Compliance often sub optimal
- Measurement and monitoring systems inadequate
- Complexity of Healthcare

Successful Strategies

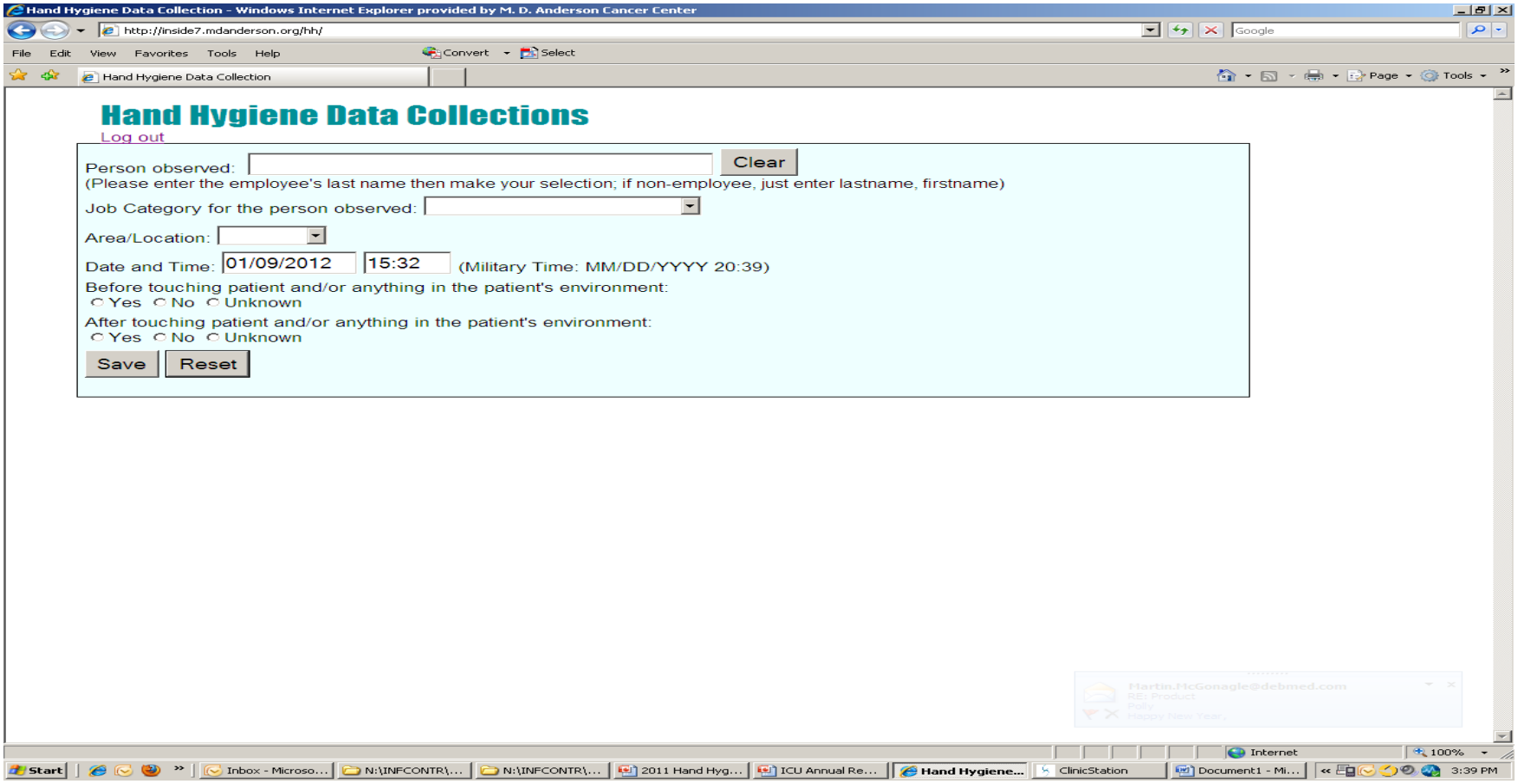
- Education
- Reinforcement
- Team work: identifying Champions
- **Culture Change**

1. Unit-based observer education

2. Establish unit's baseline compliance rate

3. Notification of compliance to person observed and their "one-up" (UTMDACC INSTITUTIONAL POLICY # CLN0452)

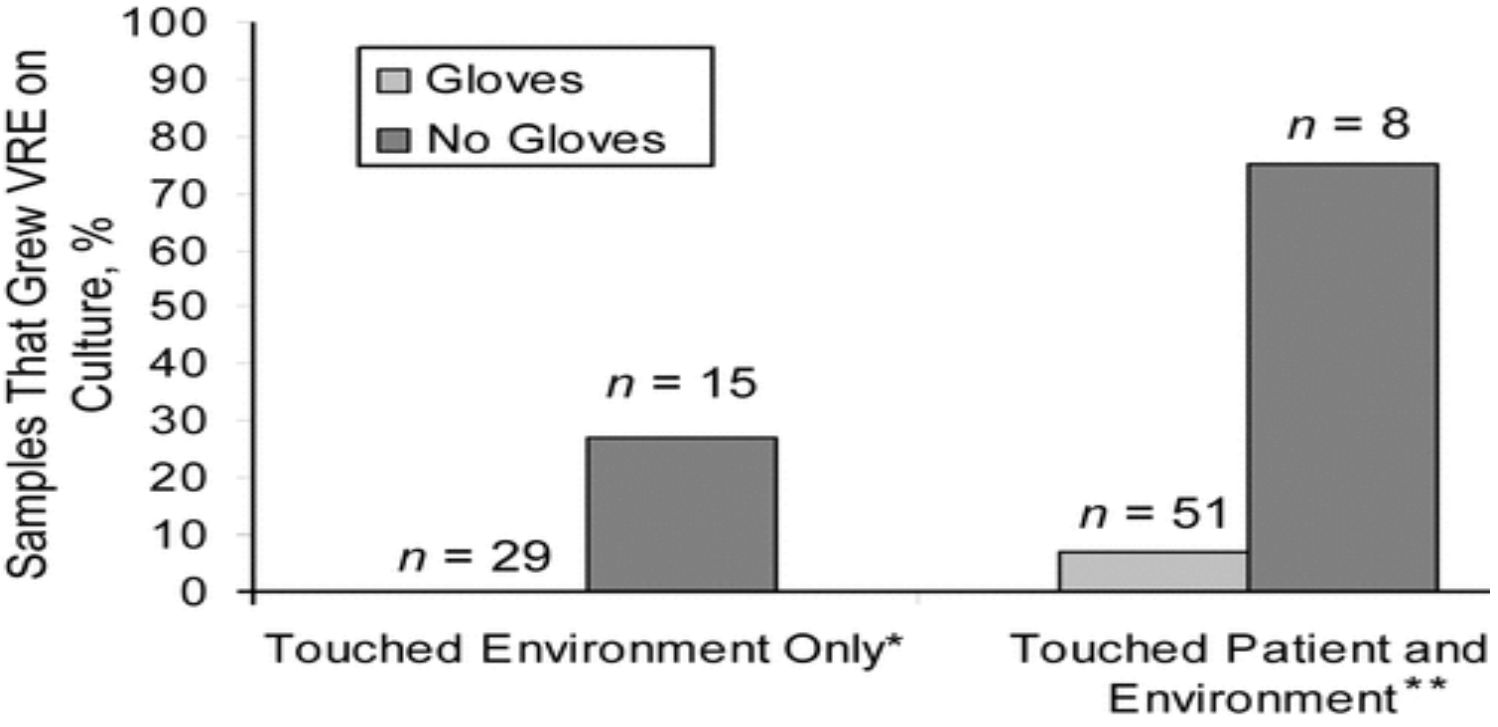
4. Using the institutional database: Web-based Data Entry



II. Contact Isolation

- High level of evidence – use of gloves
- General Agreement on need for gowns and gloves?
- Know when to remove patients from isolation
- Alternative Approach

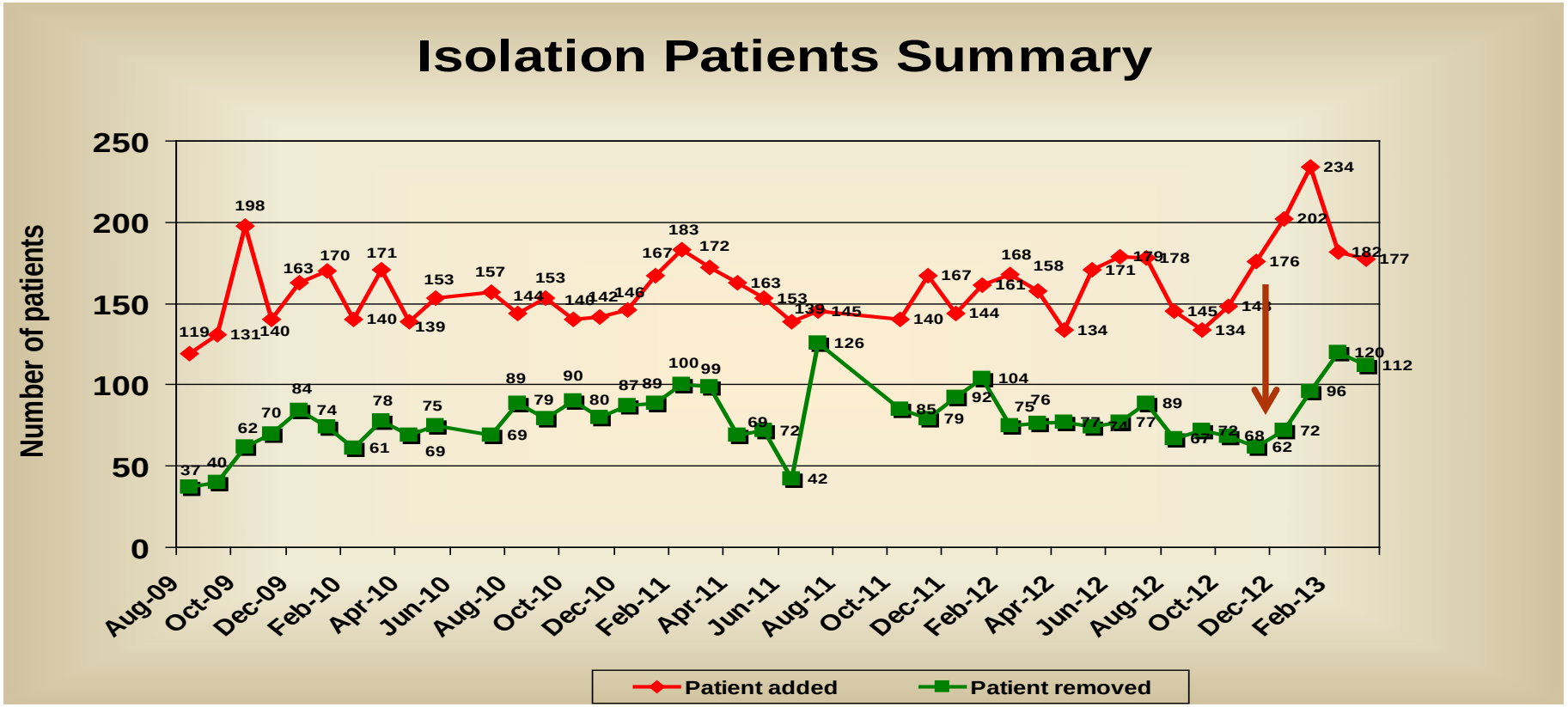
Rates of VRE contamination on HCWs' gloved and ungloved hands after touching a colonized patient and the patient's environment or after touching only the environment.



Hayden et al, ICHE 2008

Assessment of Isolation at MDACC

- Implementation of an algorithm and order set for isolation removal: Patient satisfaction and cost avoidance



Alternative Approach: Red Box

III. Antimicrobial Stewardship

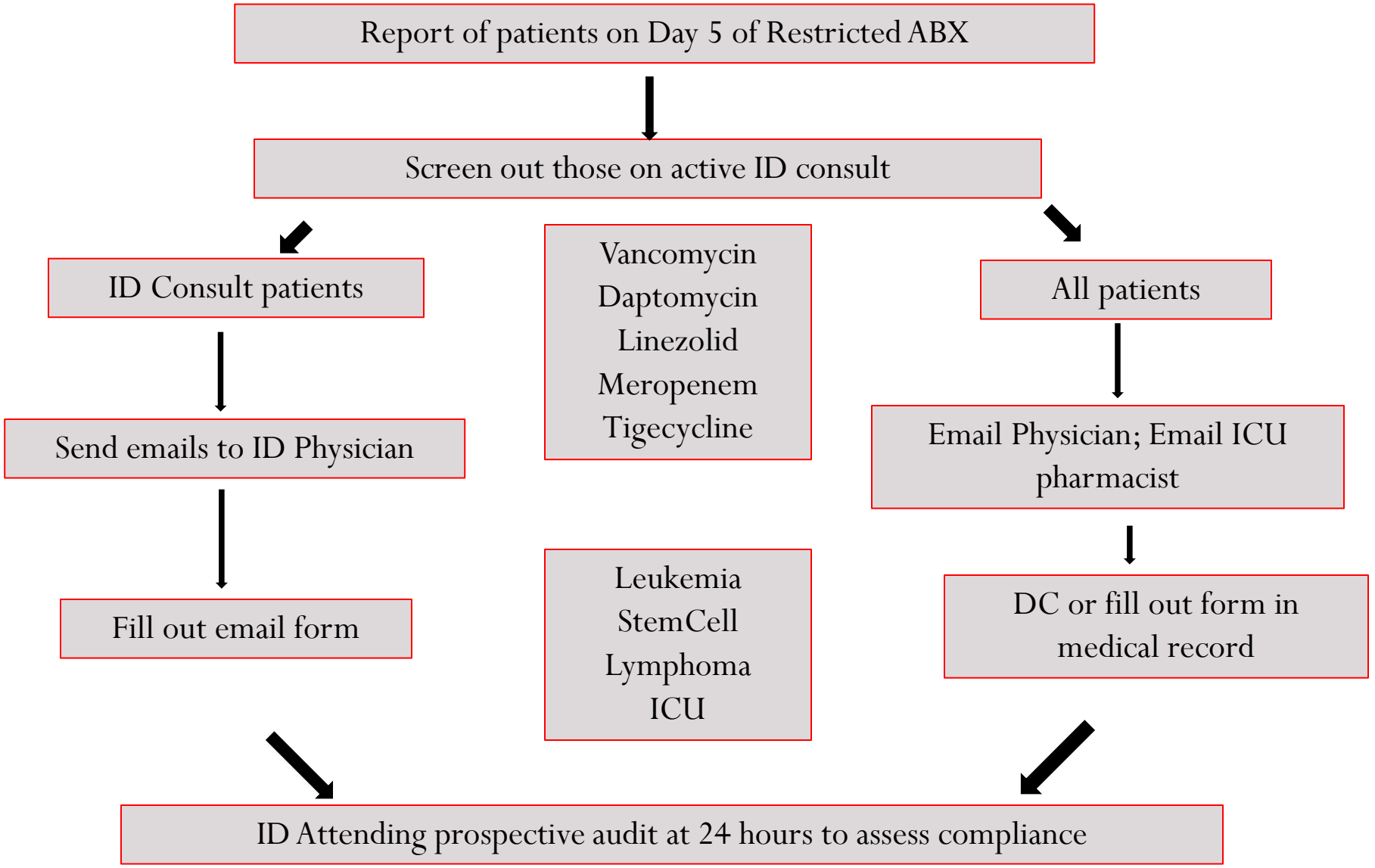
- **Increasing evidence that Antimicrobial programs are cost effective and can lead to decreased incidence and prevalence of MDROs**

- **Variety of modalities (restriction, prospective feed back, etc)**

- **Best evidence for:**
  - **Decreased resistant Gram-negative bacilli[1,5]**
  - **Decreased CDI[1-4]**
  - **Decreased VRE[1]**

Main reference:
Dellit TH et al.. Clin Infect Dis 2007 Jan 15;44(2):159-77.

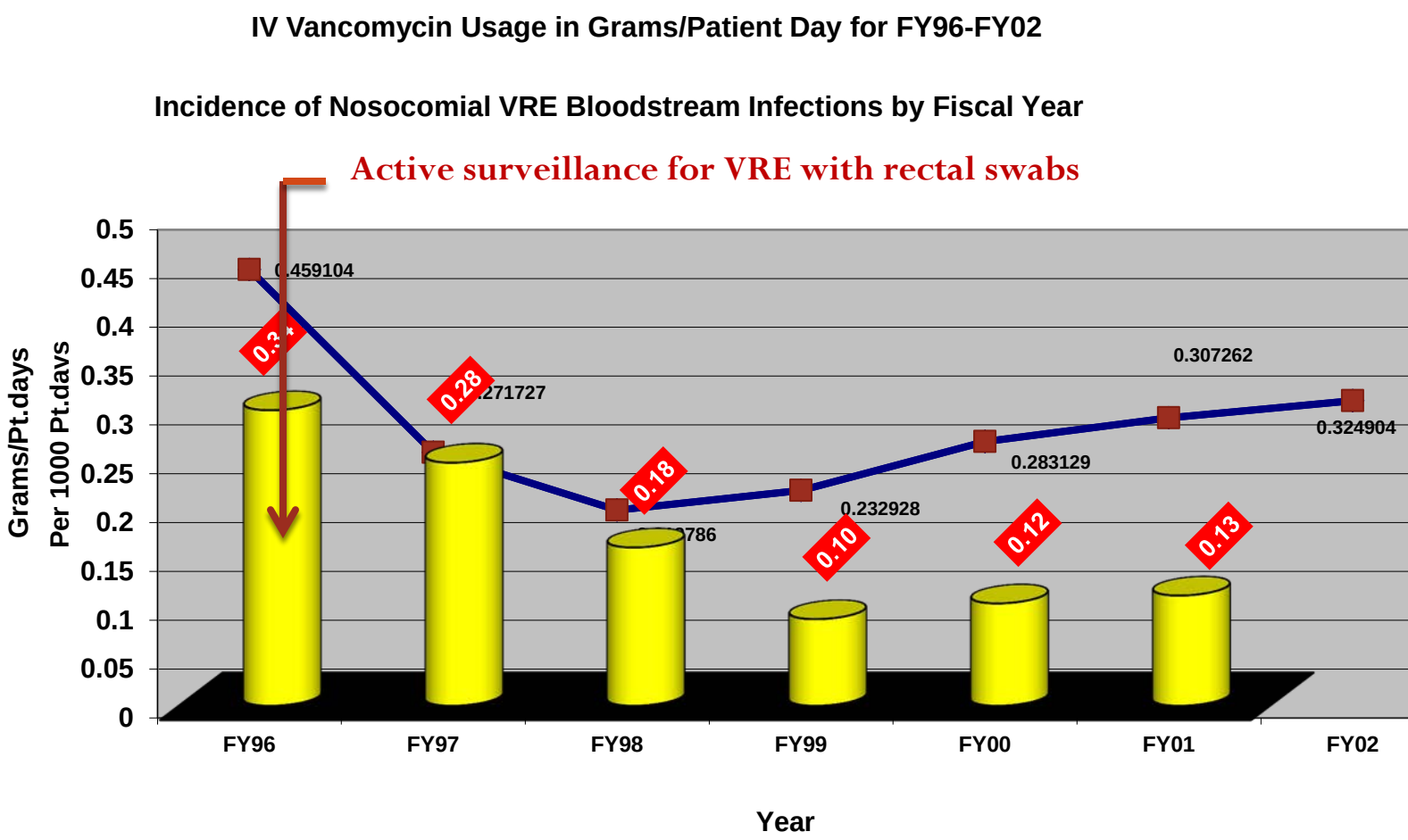
1. Carling P, et al. Infect Control Hosp Epidemiol. 2003;24(9):699-706.
2. Climo MW, et al. Ann Intern Med. 1998;128(12, pt 1):989-995.
3. Pear SM, et al. Ann Intern Med. 1994;120(4):272-277.
4. McNulty C, et al. J Antimicrob Chemother. 1997;40(5):707-711.
5. de Man P, et al. Lancet. 2000;355(9208):973-978.


Report of patients on Day 5 of Restricted ABX
Screen out those on active ID consult
ID Consult patients
Send emails to ID Physician
Fill out email form
Vancomycin
Daptomycin
Linezolid
Meropenem
Tigecycline
Leukemia
StemCell
Lymphoma
ICU
All patients
Email Physician; Email ICU pharmacist
DC or fill out form in medical record
ID Attending prospective audit at 24 hours to assess compliance

IV. Active surveillance

- Definition: Testing for colonized asymptomatic people
- Detects colonization, not infection
- Lots of extra work and expense
- Useful to control outbreaks
- Active surveillance alone, without interventions, is pointless
- Controversial outside of the outbreak setting

The use of a vancomycin order form and active surveillance program for VRE played a role in limiting the spread of VRE

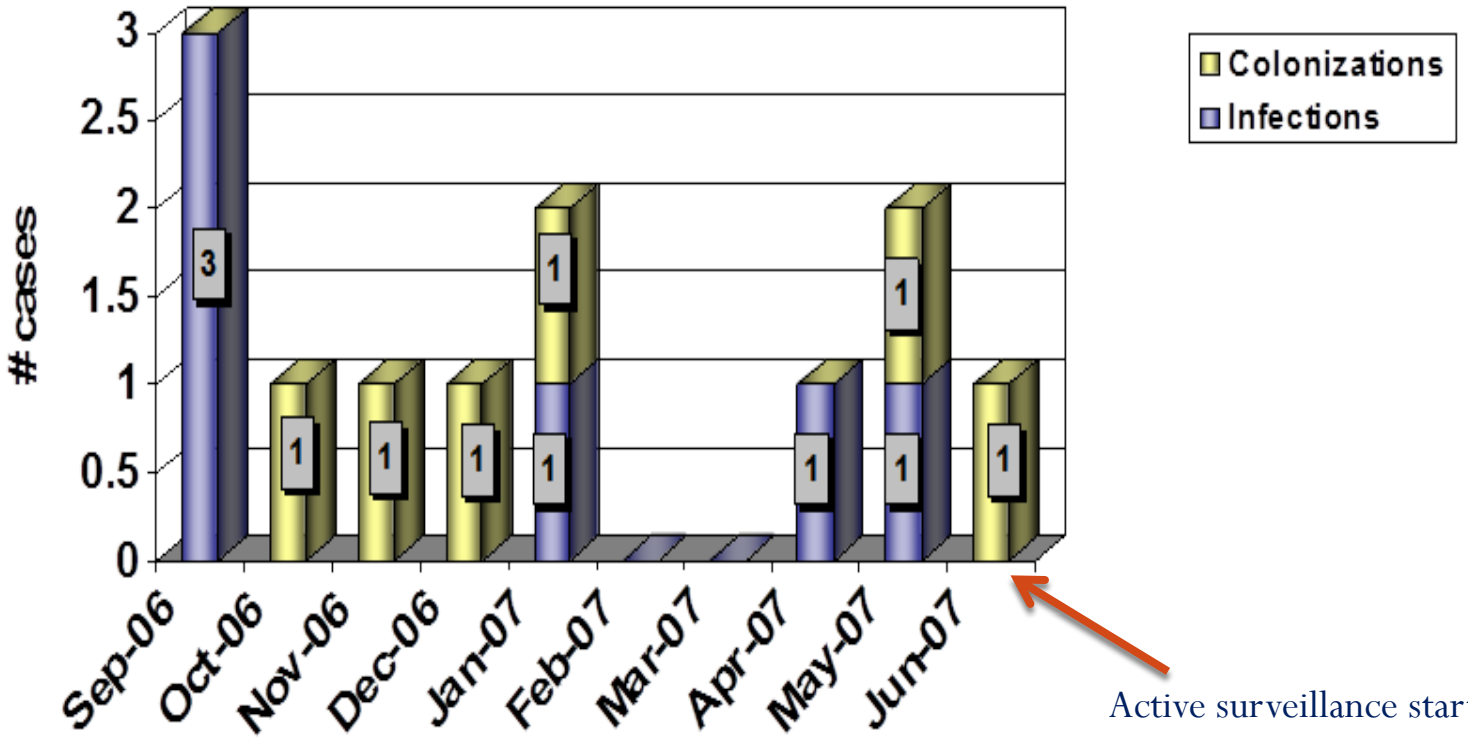


Zero outbreak of VRE after 1997

Shaikh ZH, Osting CA, Hanna HA, Arbuckle RB, Tarr JJ, Raad, II. J Hosp Infect. 2002;51(1):52-8

Active Screening at MDACC

- Rectal swabs on a weekly basis are performed to detect VRE and Pseudomonas aeruginosa colonization on the SCT, leukemia services, ICUs – but not on solid tumor services



MDR Ps aeruginosa Nosocomial Infections & Colonizations of Endemic "M" Strain

Recommendations

- If your hospital has private rooms, your HH and use of standard and special precautions are optimal, you are optimizing your use of antibiotics, you clean equipment between patients, and you do not have high or increasing rates of MDRO infections, the additional benefit of active surveillance to detect asymptomatic colonization is minimal

- I would not start an active surveillance program just because others are doing it

V. Role of the Healthcare Environment in Transmission of MDROs

- Admission to a room previously occupied by a patient known to be colonized or infected with MDRO increases the chances of acquiring these pathogens.

- In light of these findings, terminal disinfection following patient discharge should be improved.

Challenges in Improving Environmental Cleaning

- Environmental Services (EVS) has not traditionally been an integral part of the Infection Prevention team
- Many healthcare institutions run at or near 100% capacity: Room turnover, quick discharge and admission of new patients is a priority
- Outcome data is not usually shared with EVS staff

What has been done?

- Educational campaigns
- The use of fluorescent or other markers after cleaning to improve compliance with cleaning regimens
- Issues:
  - Even aggressive cleaning protocols may not be sufficient to remove contamination with some pathogens
  - The impact of educational campaigns is difficult to sustain.

Environmental Cleaning Intervention and Risk of Acquiring MDROs From Prior Room Occupants

- **Setting:** ICU rooms
- **The intervention:** targeted feedback using a black-light marker, cleaning cloths saturated with disinfectant via bucket immersion, and increased education regarding the importance of repeated bucket immersion during cleaning.
- **Aim:** Evaluation of the effect of this intervention on the risk of acquiring MRSA and VRE from prior room occupants.

Datta, R. et al. Arch Intern Med 2011;171:491-494.

Predictors of MRSA and VRE Acquisition

Table 2. Predictors of MRSA and VRE Acquisition

Model[a]	Odds Ratio (95% Confidence Interval)	*P* Value
MRSA		
Pre-ICU length of stay	1.2 (1.1-1.3)	<.001
Duration of room vacancy between occupants	0.9 (0.8-1.0)	.03
Age per decade increase	1.1 (1.0-1.2)	<.001
End-stage liver disease	1.8 (1.2-2.9)	.008
Prior occupant status and intervention interaction		
Baseline		
MRSA-negative	1 [Reference]	
MRSA-positive	1.3 (1.0-1.8)	.04
Intervention		
MRSA-negative	0.6 (0.5-0.7)	<.001
MRSA-positive	0.5 (0.3-0.8)	.006
VRE		
Pre-ICU length of stay	1.4 (1.3-1.6)	<.001
Age, in decades	1.1 (1.1-1.2)	<.001
Male sex	0.8 (0.7-1.0)	.05
Surgical ICU (vs medical)	0.5 (0.3-0.7)	<.001
Diabetes mellitus	1.3 (1.1-1.6)	.004
End-stage renal disease	1.5 (1.1-2.0)	.008
Hematologic malignant neoplasm	1.4 (1.0-1.8)	.04
Prior occupant status and intervention interaction		
Baseline		
VRE-negative	1 [Reference]	
VRE-positive	1.4 (1.0-1.8)	.04
Intervention		
VRE-negative	0.6 (0.5-0.8)	<.001
VRE-positive	0.9 (0.6-1.2)	.35

Abbreviations: See Table 1.

[a] Adjusted for age, sex, comorbidities, pre-ICU length of stay, prior occupant length of stay, duration of room vacancy before occupancy, and clustering by ICU ward. Measured comorbidities included diabetes mellitus, end-stage renal disease, end-stage liver disease, solid cancer, immunocompromised noncancer, and hematologic malignant neoplasm.

Datta, R. et al. Arch Intern Med 2011;171:491-494.

In Conclusion

- The thorough environmental cleaning eliminated the increased risk of MRSA acquisition from an MRSA-positive prior room occupant but did not eliminate the increased risk of VRE acquisition from a VRE-positive prior room occupant

- ? Higher burden of VRE contamination in the environment and/or a greater difficulty in eliminating VRE contamination.

Datta, R. et al. Arch Intern Med 2011;171:491-494.

Adaptation of New Technologies
&
Objective Quantitative Assessment

Enhanced Room Disinfection Systems

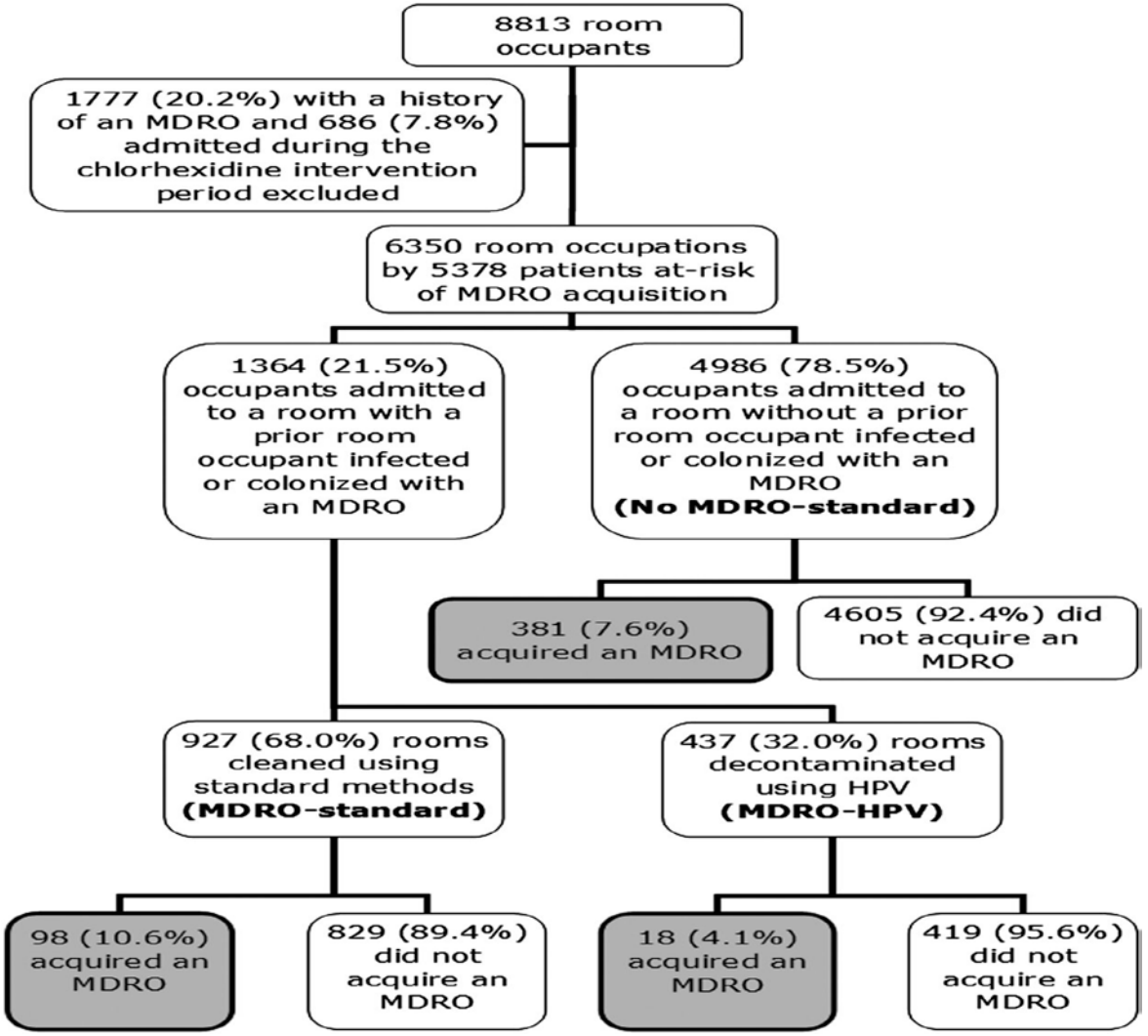
- Automated systems do not rely on the operator to ensure all surfaces are disinfected and adequate contact time is achieved
- However, automated methods must be applied in addition to standard cleaning
- Require areas to be temporarily vacated of patients and staff (potentially leading to delays in bed availability), and incur additional expense.

Hydrogen Peroxide Vapor decontamination

- Use of HPV to eradicate micro-organisms from the environment

Source: http://www.bioquell.com/services/bioquell-room-bio-decontamination-service-rbds/

Flowchart of the patient cohort admitted to any study unit by exposure and intervention.



Passaretti C L et al. Clin Infect Dis. 2013;56:27-35

Hydrogen Peroxide Vapor decontamination

- Reduced the risk of MDRO acquisition among high-risk patients when patients are admitted to a room previously occupied by a patient infected or colonized with an MDRO

- These findings suggest that HPV should be considered for decontamination of MDRO patient rooms.

- HPV in addition to a thorough infection prevention program could be implemented in high-risk environments to maximize patient safety.

Drawbacks

- The time for disinfection is on average 2 to 4.5 hours.
- At an average of 15 rooms per day, HPV costs around $262.19 per room

Enhanced Room Disinfection Systems

- APIC 2013 Guide to Preventing *Clostridium difficile* infections
  - "Ultraviolet irradiation and vaporized hydrogen peroxide have been shown to perform well"
  - States the Mercury-based ultraviolet takes 45 minutes for efficacy against *C. diff* and does not evaluate other means of producing UV

Pulsed Xenon Ultraviolet Light (PX-UV)

PX-UV produces broad-spectrum UV irradiation, including large amounts of energy in the germicidal spectrum and in the UVA, UVB and visible spectrums using a xenon gas flash lamp.

Shown to be effective in killing a variety of microbial pathogens, including endospores of *C. difficile*, vegetative bacteria and viruses.

The device is typically operated by housekeeping personnel and includes safety features such as motion sensors.

The average operating time is 5 minutes per position for a total of 3 positions based on the average size of each room.

Evaluation of a PX-UV room disinfection device for impact to hospital operations and microbial reduction at MDACC

- We compared the use of a PX-UV disinfection system to the standard room terminal cleaning process

- We assessed the level of room microbial contamination before and after applying each method and the degree to which hospital operations (i.e. room turnaround time) were affected by the use of each approach.

Stibich M, et al. Infect Control Hosp Epidemiol. 2011 Mar;32(3):286-8.

Comparison of Room Cleaning Status HPC (cfu/inch)^2

Room Status	# of samples	# positive (%)	min	mean	median	max	iqr
Pre-clean	18	14 (77.8)	0	199.7	60	780	370
Post Standard terminal clean	21	12 (57.1)	0	74.5	10	860	50
Post PX-UV treatment	19	2 (10.5)	0	3.9	0	40	0

Comparison of VRE Positive Surfaces by Room Cleaning Status

	Phase 1		Phase 2		Combined	
Room Status	**# of samples**	**# (%) of VRE**	**# of samples**	**# (%) of VRE**	**# of samples**	**# (%) of VRE**
Pre-clean	55	15 (27.3)	18	2 (11.1)	73	17 (23.3)
Post Standard terminal clean	28	3 (10.7)	21	1 (5.3)	49	4 (8.2)
Post PX-UV treatment	56	0 (0)	19	0 (0)	75	0 (0)

Hospital Operational Statistics for 8 PX-UV Treated Rooms

Activity	Minutes
PX-UV travel time to room	3:48
Preparing the room	:15
PX-UV emittance	12:00
Safety countdown	1:30
Repositioning the PX-UV device	:31
Room exit	:44
Total PX-UV Disinfection Time	**18:48**

Stibich M, et al. Infect Control Hosp Epidemiol. 2011; 32(3):286-288

Equivalency trial of bleach versus PX-UV light for reducing environmental *C. difficile* contamination on high-touch surfaces in *C. difficile* isolation rooms

Arm	Observations	Mean CFU before	Mean CFU after	% reduction
Bleach	74	2.39	0.72	70%
PX-UV	25	3.56	0.12	97%

Chemaly RF, et al. Submitted.

In Conclusion

- The PX-UV system showed a statistically significant reduction in microbial load and eliminated VRE on sampled surfaces when using a 12-minute multi-position treatment cycle
- It was equivalent to bleach for *C. diff* elimination from contaminated rooms.
- At an average of 5 rooms per day, the cost is $6 per room

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How – One quick swab provides a rapid, objective measurement that accurately quantifies surface cleanliness.

Environmental, Health & Safety sampling and adapted data to unit measurements

Environmental Sampling				
Clean Trace (RLU) Range	EH&S Culture Sampling (Average CFU)	APPA Standards	Performance Criteria	
0-99	5 CFU	1	Exceeded – Pass	89%
100-399	10 CFU	2	Substantial Exceeds – Pass	
400-699	15 CFU	3	Meets – Caution /Re-clean	7%
700-1000	21 CFU	4	Unacceptable – Fail /Re-clean	4%
1001 and Up	22 and Up	5	Unacceptable – Fail/Re-clean	
RLU - Relative Light Units **CFU - Colony Forming Units** **APPA – Assoc. of Physical Plant Administrators**				

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Conclusion

- MDROs are a world wide problem
- The answer is not a single approach
- We must blend technical knowledge with socio-adaptive skills
- We must create a vision where prevention of harm, quality and safety is everyone's responsibility

Infection Control Preserves, Protects and Defends

- Director, Roy Chemaly, M.D., M.P.H. (center).
- To his left are Linda Graviss, Cecile Arcilla, Polly Williams and Susan Conley.
- To his right are Sherry Cantu, Kim Nguyen, Cheryl Perego, Supervisor, and Cindy Good.


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