Controlling

Multidrug Resistant Drug Resistant Organisms (MDROs)

10th Annual Fleming Infection Prevention and Infectious Diseases Symposium



Carlene A. Muto, M.D., M.S University of Virginia Hospital Epidemiology/Infection Control

One day, someone in these pictures will be receiving healthcare. Potentially in your hospital or office. I don't want them (or anyone) to get an infection or die

That day is today

Do contact precautions work for the control of MDRO's? Are some pathogens more important than others?

- Vancomycin Resistant enterococci
- Staph aureus
 - MRSA
 - VISA
 - VRSA

- GNR-MDRO (Gram negative rods)
- MDR Acinetobacter
- ESBL
- CRE
 - NDM CRE

Costs of HAIs

Infection Type	Cost Estimates					
	Historical	2002	2005	2005	2005	
	Data	Stone ⁴	Stone ⁵ Min	Stone ⁵ Max	Stone ⁵ Mean	
VAP	4,947 ²	17,677	7,904	12,034	9,969	
UTI	3,8031	NS	650	1,361	1,006	
SSI	2,734 ²	15,646	1,783	134,602	25,546	
BSI	33,268 ³	38,703	1,822	107,156	36,441	
MRSA	NS	\$35,367	NS	NS	NS	

1. Claussen et al. Dissertation. Salt Lake City, Utah, 1993

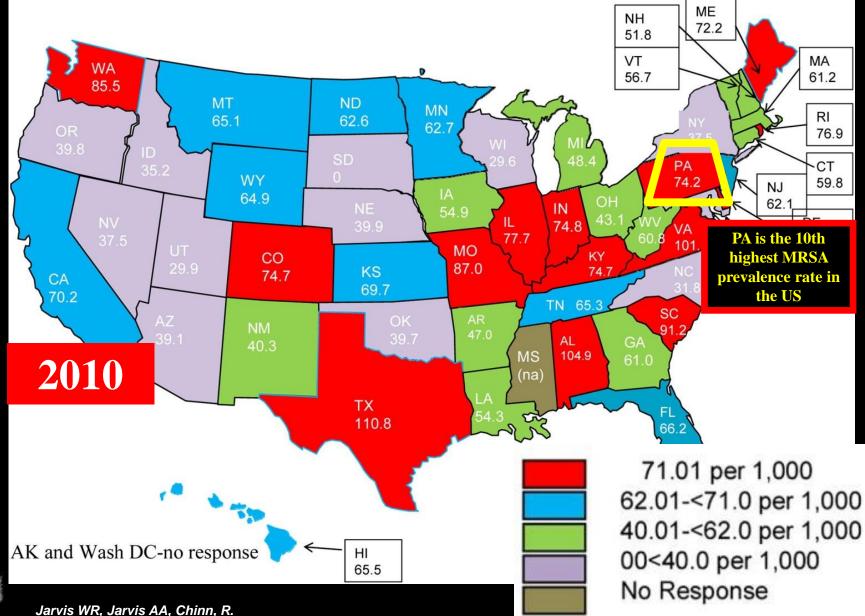
2. Haley et al. Am J Epidemiol 1985;121:206-15
3. Pittet et al. JAMA 1994;271:1598
4. Stone et al. AJIC 2002;148:30:145-52

5. Stone et al. AJIC 2005;33:501-509

U.S. MDRO Trends



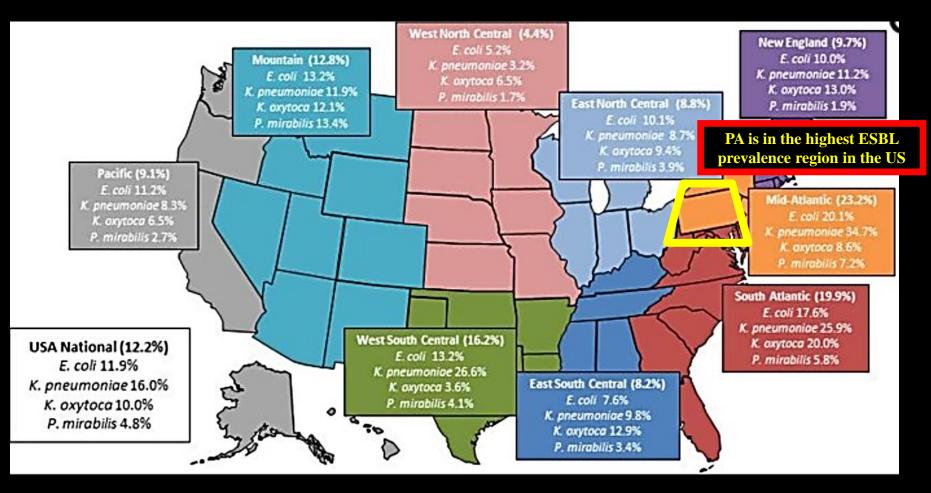
MRSA prevalence rate per 1,000 inpatients by state



American Journal of Infection Control 2012 40, 194-200DOI: (10.1016/j.ajic.2012.02.001)

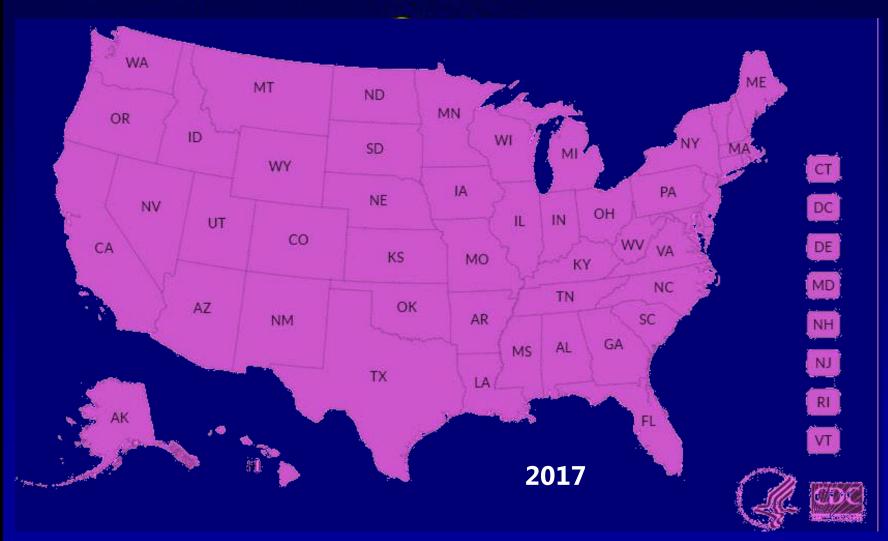
ELSEVIER

Prevalence of extended-spectrum-β-lactamase (ESBL) n the 9 U.S. Census Regions



ESBL rates among *Enterobacteriaceae* isolates collected in 72 U.S. hospitals located in the nine U.S. census regions. Castanheira M, Farrell SE, Krause KM, et al. 2013. Contemporary diversity of ß-lactamases among Enterobacteriaceae in the 9 U.S. census regions and ceftazidime-avibactam activity tested against isolates producing the most prevalent ß-lactamase groups. Antimicrob Agents Chemother. 2014;58(2):833-838.

KPC-producing CRE in the United



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

Reducing MDROs Where to Start?

- VRE
- MRSA
- VISA/VRSA
- Cdiff

- MDR Acinetobacter
- ESBLs
- CRE
- NDM CRE
- Other MDR GNRs

Where can we find MDROs?

- Hands of HCWs caring for infected/colonized patients
- Gloves of HCWs caring for infected/colonized patients
- Gowns/coats of HCWs
- Ties of HCWs
- Stethoscopes 7% of stethoscopes were contaminated with MRSA
- Computer keyboards
- Stuff in the patients room
 - 70% of MRSA rooms had MRSA recovered from the environment
 - Patient's gowns
 - Bed linens
 - BP cuffs
 - Overbed tables
 - Equipment
 - Supplies in the room

Everywhere

Boyce. ICHE. 1997;18:622.

Cohen. Fam Pract. 1997;14:446

Marinella. Arch Intern Med. 1997;157:786. Devine et Noskin et al. ICHE 1995; 16:577-581.

Devine et al. J Hosp Infect 2001; 48:72-75.

Pick Your Poison

- Do they ALL Matter
- Should they all be eliminated
- An unfocused approach is what has been done for years

 IT DOESN'T WORK
 They will try to beat you down...
- Focus, Focus, Focus
 - One by one
 - Once success is achieved/Culture Transformed
 - Move On...

Barriers to accomplishing effective Prevention

- Despite traditional and current infection control guidelines, strategies to prevent bad outcomes have not been widely and successfully implemented.
- Locations that had prevention strategies in place have decided that they are too labor intense and are not implementing them or disbanding them.

Is it just too hard. Should endemic centers just stop trying?



Consequences of MDROs

Issues

- Frequent Too Many
 - 30-60% of colonized become infected.
- TOXIC/Deadly!
- Costly
 - Increases LOS



S

Treatments

- SEVERELY limited
 - Too Few
- Less efficacious
- TOXIC/Deadly!
 - **Costly**

Cosgrove SE et al. Clin Infect Dis 2003; 36:53-59. International Society for Pharmacoeconomics/Outcome Research – 5/16/05

The Questions?

1. Do MDRO Control Measures work?

- a. For outbreaks?
- **b.** Even if they have become endemic?
- 2. Are Contact precautions necessary to control these pathogens?
- **3.** Are patients in contact precautions as safe as other patients?

Extended-spectrum beta-lactamase (ESBL)

- MDR GNR pose one of the most vexing infectious disease challenges
- β-lactamases hydrolyze the β-lactam ring and render antibiotics ineffective
- Common antibiotics like penicillins and cephalosporins don't work
- The plasmids carrying the gene encoding the ESBLs frequently carries other genes encoding resistance to aminoglycosides and TMP/S (Bactrim)
- Typically carbapenems or quinolones are used.
 - Newer reports with quinolone resistance too.

Last Update: 6/04/15 1:	37 PM L	URINE CULTURE
Collected: 5/29/15 11	:39 PM	Accession Num: F7154728 Status: Final
Specimen Desc: Urine from	n foley	Special Request: None
Culture: >100,000 col/r	nL Proteus m	nirabilis
>100,000 col/r	nL Escherich	nia coli Extended spectrum beta lactamase producer (ESBL). Treat with
Carbapene	em or Quinolo	one if susceptible. Patient isolation required.
ESCHERICHIA COLI		
	C (mcg/mL) M	IIC Interpretation
Amikacin	<=16	Sensitive
Ciprofloxacin	>2	Resistant
Gentamicin	. <=4	Sensitive
Imipenem		Sensitive
Levofloxacin		Resistant
Meropenem	<=1	Sensitive
	<=32	Sensitive
Nitrofurantoin		
Nitrofurantoin Sulfa/Trimethoprim	. >2/38	Resistant

ESBL Clinical Impact

- Mortality (42%)
 - Higher in patients ESBL bacteremia
 - Did not receive appropriate antibiotic therapy
- Duration of hospital stay/hospital charges
 - Higher in patients ESBL infections than with non-ESBL-producing organisms of the same species.
 - Median length of hospital stay post infection of 29 days vs 11 days in those with non-ESBL-producing KP infection.
 - Brooklyn Antibiotic Resistance Task Force

Schwaber MJ, et al. Mortality and delay in effective therapy associated with extended-spectrum beta-lactamase production in Enterobacteriaceae bacteraemia: a systematic review and meta-analysis. J Antimicrob Chemother2007; 60:913–20.

Tumbarello M. et al. Costs of bloodstream infections caused by *Escherichia coli* and influence of extended-spectrum-β-lactamase production and inadequate initial antibiotic therapy. Antimicrob Agents Chemother 2010; 54:4085–91.

Anonymous. 2002. The cost of antibiotic resistance: effect of resistance among *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudmonas aeruginosa* on length of hospital stay. Infect. Control Hosp. Epidemiol. 23:106-108

Lautenbach, E., J. B. Patel, W. B. Bilker, P. H. Edelstein, and N. O. Fishman. 2001. Extended-spectrum beta-lactamase-producing *Escherichia* coliand *Klebsiella pneumoniae*: risk factors for infection and impact of resistance on outcomes. Clin. Infect. Dis. 32:1162-1171.

ESBL Risk Factors



- Seriously ill patients
- Prolonged hospital stays
- Invasive medical devices
 - Urinary catheters
 - Endotracheal tubes
 - Central Lines
 - Especially if prolonged duration.
- Heavy antibiotic use

ESBL Transmission within health-care

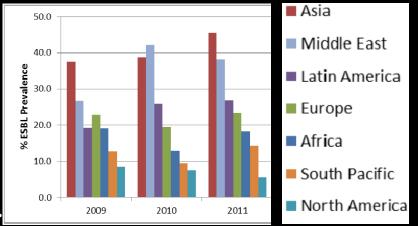
- Acute to nursing home (NH)
- NHs to acute Chicago Long-term Care
 - 46% of residents were ESBL colonized (all *E. coli*)
 - All had been in the NH, without intercurrent hospitalization > 6 months.
 - Patients from 8 NHs served as a reservoir for ESBL introduction into acute-care

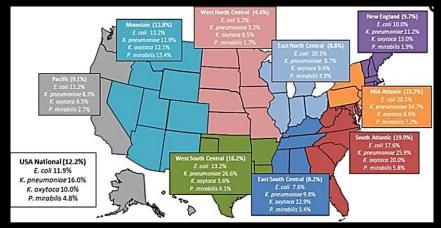


Study for Monitoring Antimicrobial Resistance Trends (SMART)

- Studies resistance patterns worldwide from 2002 to 2011
 - 92,086 intra-abd infections
 - 24,705 UTIs
 - Significant increases in ESBL infections across all continents, except Africa.
 - >40% of isolates from Asia were ESBL in 2011.
 - Latin America, the Middle East, Africa, Europe, and the South Pacific displayed a prevalence of ESBL of ~ 10%–35%.
- US data 2012 SENTRY

- ESBL *E.coli*, *Klebsiella* species, and *Proteus* collected from 72 hospitals across 9 US regions
 - 12.2% (701/ 5739) of isolates were ESBL
 - Highest region NE
 - Overall at 23%
 - 35% of KP were CRE





ESBL Transmission Data

- In 100% of the > 50 studies at least 2 patients were colonized or infected with genotypically similar strains
 - Implies patient-to-patient transmission.
- A number of outbreaks have been described with dissemination of a single clone of genotypically identical ESBL
 - Clones have been found to persist for more than 3 years

French, G. L. et al., J. Clin. Microbiol. 1998.34:358-363.Gniadkowski, M. et al. Antimicrob. Agents Chemother. 1998. 42:514-520.

Gaillot, O. et al. J. Clin. Microbiol. 1998.36:1357-1360.

Neuwirth, C. et al. Antimicrob. Agents Chemother. 2001. 45:3591-3594.

ESBL Modes of Spread (Same as all other MDROs)

- Health-care Workers
 - Hands
 - Clothing, uniforms, laboratory coats, or isolation gowns
 - Can become contaminated with pathogens after care of a patient colonized/ infected with an infectious agent
 - New in the CDC isolation guidelines (HICPAC), 2007; 1-219. cannot re-use same isolation gown even on same patient

Common environmental sources

- Ultrasonography Coupling Gel
- Bronchoscopes
- Blood Pressure Cuffs
- Thermometers (Axillary)
- Cockroaches
- Patients' Soap
- Sink Basins
- Babies' Baths

IMPORTANT - Patients may have asymptomatic colonization with ESBL-producing organisms without signs of overt infection.

- These patients represent an important reservoir of organisms.
- For every patient with clinically significant ESBL infection at least one other patient exists in the same unit with GI colonization with an ESBL

ESBL Infection Prevention Measures

- i. **Active Surveillance (**nerirectal Testiv swal colonized
- Evaluation for the proii. common environmental sour
- iii. Campaign to improve hand hygiene
- **Contact isolation for patients** iv. found to be colonized or infected

- **Close attention to practices that** \bullet may lead to breakdowns in good
 - Audit for compliance
 - **Changes in antibiotic policy Reduce antibiotic consumption**
- The "IREALLY MEAN IT'S APPROACH **Stazidime restriction alone is** to control continued CRLis
 - Some forced to withdraw cephalosporins as an entire class in order to reduce ESBLs.

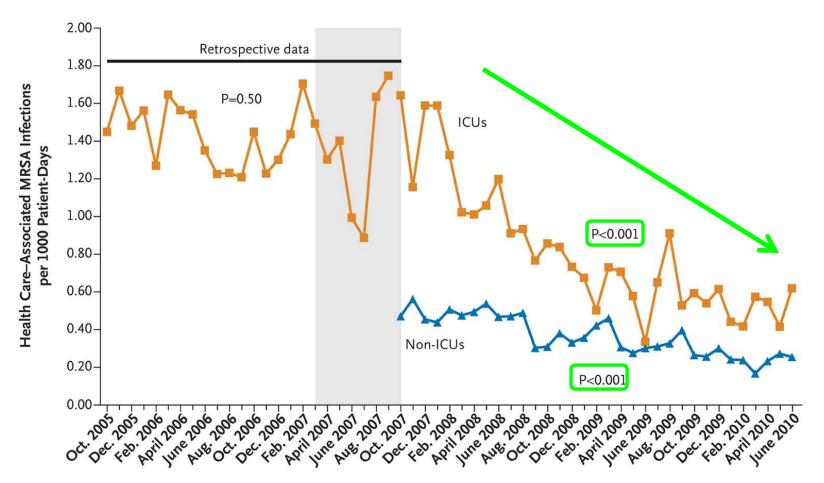


Veterans Affairs Initiative to Prevent MRSA Infections

- Implementation of a MRSA bundle was associated with a significant decline in MRSA transmission
- MRSA Bundle Components
 - Nasal surveillance for MRSA
 - Contact precautions for patients with MRSA
 - Hand hygiene (HH)
 - Institutional culture change whereby infection control was everyone's responsibility

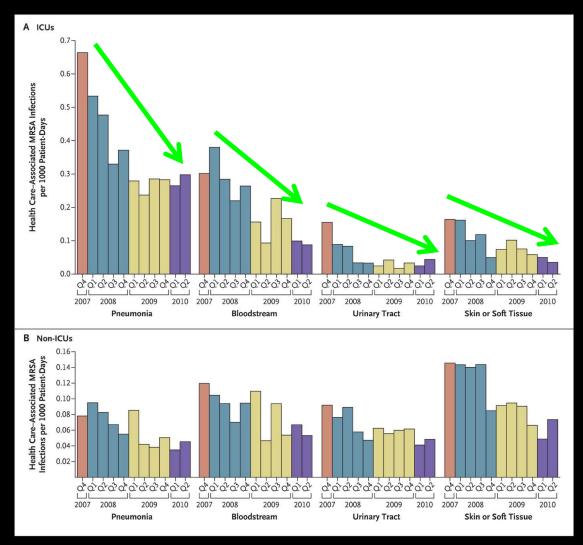


Veterans Administration (VA) National MRSA HAI Rates Facilities





Nationwide VA Quarterly Rates of HCA MRSA Infections





Acute Care vs. Long-Term Care Endemic KPC

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

2008: cluster of KPC at a Chicago LTAC

2011: REGIONAL OUTBREAK 9-fold increase in colonization prevalence among patients in area LTACs

Mary K. Hayden,^{1,2} Michael Y. Lin,¹ Karen Lolans,² Shayna Weiner,¹ Donald Blom,¹ Nicholas M. Moore,³ Louis Fogg,⁴ David Henry,⁵ Rosie Lyles,⁶ Caroline Thurlow,¹ Monica Sikka,¹ David Hines,⁷ an<mark>t Robert A. Weinstein^{1,0}</mark> for the Centers for Disease Control and Prevention Epicenters Program CID April 2015

Methods: Stepped-wedge cluster-randomized trial

			Staggered Introduction of Intervention				
		/	February 1, 2010 – November 27, 2011	November 28, 2011– February 4, 2012	February 5, 2012– April 8, 2012	April 9, 2012– June 17, 2012	June 18, 2012– June 30, 2013
u		А	0	Х	х	Х	х
	LTACH	В	0	0	х	Х	х
		D	0	0	0	Х	х
		С	0	0	0	0	Х

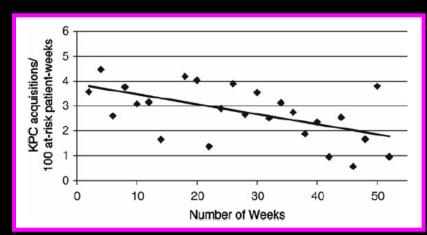
- KPC Rectal swab cultures on admission and every other week
 - Preemptive contact isolation on admits pending culture results
 - Patients with a positive screen *or* clinical cultures were presumed to remain colonized and not rescreened

Contact isolation and geographic separation of KPC + patients

- Single room or ward cohort
- Universal contact isolation of all high-acuity patients where geographic separation was not feasible
- <u>Universal daily bathing</u>
 - 2% chlorhexidine-impregnated cloths
- HCW education adherence monitoring

Results

- Compliance Adherence to intervention components was *relatively* high:
 - Swab collection, isolation >90%
 - PPE at room entry, HH at room exit, CHG bathing >70%
 - HH at room entry 25% (!)
- KPC Clinical culture positivity 32% (any source)
 KPC bacteremia 56%
- KPC Prevalence
 - Despite stable admit rate KPC prevalence \downarrow from 46 \rightarrow 34%
 - (p<.001)
 - Definite/possible KPC acquisition decreased by half (p=.004) during the intervention period



Can you teach an old Dog a New Trick?

Kirkland and Weinstein, CID 2009:

"Current use of contact isolation may be driven more by strongly held beliefs and a desire to do something to prevent HAIs than by unambiguous evidence

Weinstein RA et al, CID 2015:



000

"Implementation of a bundled intervention was associated with clinically important and statistically significant reductions in KPC colonization and infection."

Guess you can teach an old dog a new trick!!

Conclusions

Control Programs that include a BUNDLED approach

- Active surveillance testing
 - HH/Contact precautions
 - **Environmental Cleaning**

VORK to VMDROs

The Nays

STAR-ICU Study Contact Precautions: More Is Not Necessarily Better

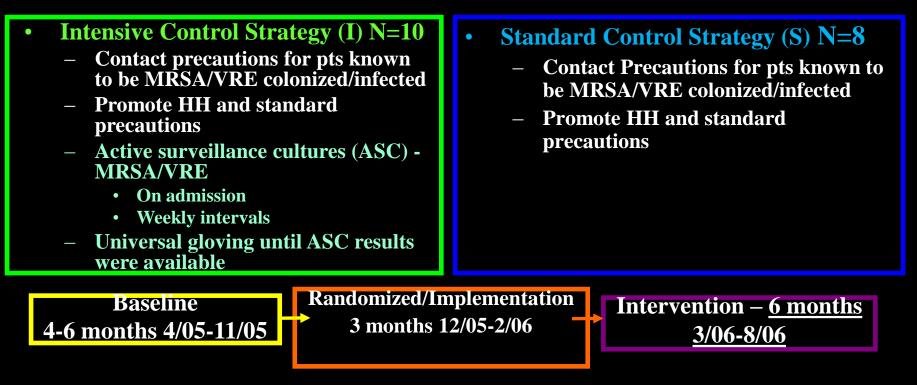
STAR-ICU 2011

Strategies to Reduce Transmission of Antimicrobial Resistant Bacteria in Intensive Care Units

Intervention to Reduce Transmission of Resistant Bacteria in Intensive Care

Study Aim

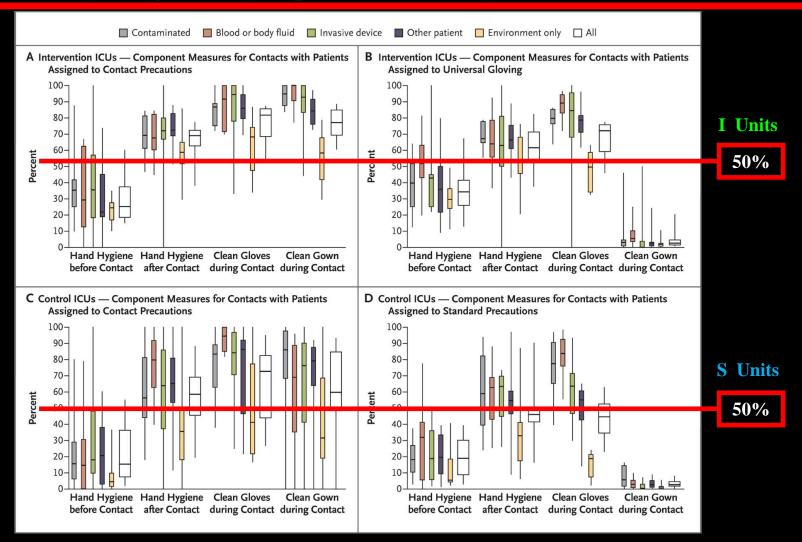
- "Is an intensive infection control strategy better than standard infection control strategy at reducing MRSA/VRE incidence in adult ICUs
 - Multicenter, cluster randomized trial



Huskins WC et al. N Engl J Med 2011;364:1407-18

Use of HH, Gloves, and Gowns by ICU HCWs

Would we study drug efficacy in patients who only received it half the time??





Results – Incidence Density of New Colonization or Infection Events

Incidence Density of New	Ι	S	P-value
Colonization or Infection Events			
MRSA and VRE	40.4	35.6	0.35
MRSA	16.0	13.5	0.39
VRE	38.9	33.4	0.53

- NO Difference
 - Results support NO effect (equal infectiveness)

1st Question - WHAT!!! 2nd Question WHY!!!

Methodology Flaws

- Too Low Too Long Too Short
- Sensitivity of Assay Too Low
 - No chromogenic media/ or PCR
- Prolonged time to ASC positivity Too Long
 - **(5.2.** lays after culture +/- 2 days to obtain culture
 - Entered into password protected site
 - Investigator had to actively get results and forward to the patient care
 - > Average LOS (4.9 days)
 - 58% of patients were discharged prior to ASC results!
- Barrier Compliance Too Low
 - Observations only done 8A 8P
 - Intervention <u>NEVER</u> fully implemented
- Time of intervention 6 months Too Short
 - Many studies have shown that reductions are not linear
 - Reductions often not realized until > 6 months

A 2.7-year study of AST and isolation in VA hospitals by Jain/Muder et al. showed significant control hospital-wide.

The flaws of the study design prohibit assessment of Intensive Control Strategy

Contact Precautions: More Is Not Necessarily Better

S Dhar, et al . Infection Control And Hospital Epidemiology March 2014, Vol. 35, No. 3

How Do You Measure BETTER?



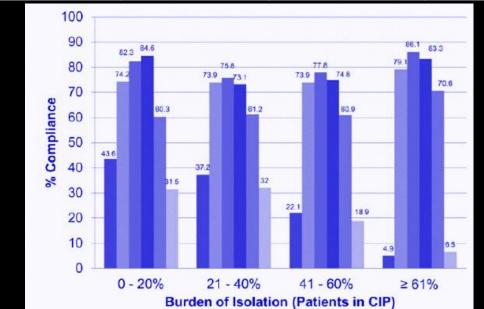
Study Features

- Objective
 - To determine whether increases in contact isolation precautions are associated with decreased adherence to isolation practices among healthcare workers (HCWs).
- Design
 - Prospective cohort study from 2/09 10/09 (9 Months)
- Setting
 - 11 teaching hospitals
- Methods
 - 1,013 observations conducted on HCWs.
 - Additional data included:
 - *#* of persons in isolation
 - Types of HCWs
 - Hospital-specific contact precaution practices
- Outcome measures Compliance with individual components of contact isolation precautions during varying burdens of isolation
 - Hand hygiene (HH) before and after patient encounter
 - Donning of gown and gloves upon entering a patient room
 - Doffing of gown and gloves upon exiting
 - Composite compliance (all 5 measures together)

BURDEN of ISOLATION

Isolation Density

			Overall	≤20%	>60%	
Outcome Measure		% Compliance				
	■ HH Pre		37.2	43.6	4.9	
	∎ Gwn		74.3	74.2	79.1	
	■ Glv		80.1	82.3	86.1	
	■ Gwn/Glv Doffing		80.1	84.6	83.3	
	■ HH Post		61.0	60.3	70.6	
	≡All 5		28.9	31.5	6.5	

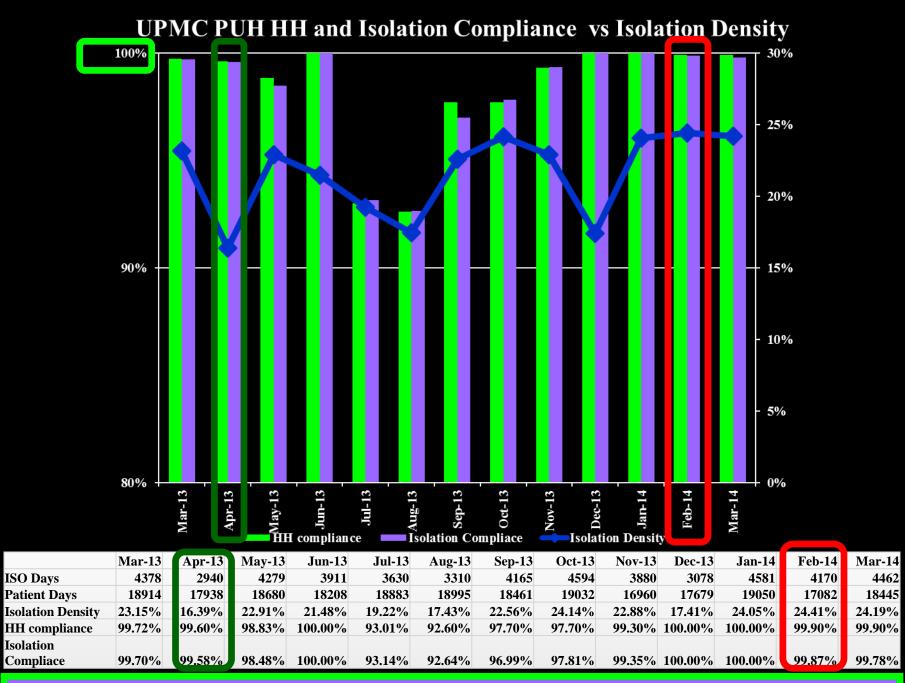


Results

Some Issues

Total HH obs = 1,013Total Sites = 11**Total Number of months = 9 Total Iso obs/month** = **93 HH obs/month per facility** = 10Iso Obs/month per facility <1

And how is this helpful??



Total Isolation Days = 51,378

Total patient Days = 238,327

Conclusions/Discussion

- Placing 40% of patients under contact precautions represents a tipping point for noncompliance with contact isolation precautions measures in these hospitals.
- Translation
 - It is TOO DAMN HARD to uphold patient safety measures when there are more people at risk.

REALLY!!!

Perhaps they should spend more time and effort on increasing HH compliance before setting out to study effects of other parameters.

Sorry we are VERY Busy Today. Our Parachute Density is >60%

I am afraid we won't be offering you parachutes.

Conclusions of the Paper

• Providers/IP programs should consider the negative impact of the burden of isolation on compliance with contact isolation precautions when developing infection control policies/practices.

- We do BUT still expect compliance to be near perfect

- Indiscriminately placing patients in contact precautions might have the adverse effect of decreasing the efficacy of contact isolation precautions in controlling the spread of MDROs.
 - Define Indiscriminately?
 - Efficacy is not decreased in hospitals that practice consistent infection prevenion
- Burden of isolation of 40% may represent a tipping point, above which compliance with contact isolation precautions drops significantly.

YIKES!!

Hard to imagine isolation density of 40% but if isolation practices are hard wired density should not result is decreased compliance.

The Infamous Stelfox Study Safety of Patients Isolated for Infection Control

- Nonrandomized study
- "Adverse events" were higher in patients on CP than those not on CP
 - Absolute terms and adjusted for length of stay.
- A rate of 31 versus 15 adverse events/1000 days was observed in isolated vs nonisolated patients (*P* < .001).
- General process of care measures were worse in CP patients.
 - Inappropriate documentation of vital signs (14% vs 9%, respectively, *P* < .001)
 - Days without a physician note (26% vs 13%, respectively, P < .001)
 - Days without a nursing note (14% vs 10%, respectively, P < .001)
- CHF specific process measures were worse in CP patients.
 - Stress testing (14% vs 45%, P < .001)
 - Evaluation of left ventricular function (57% vs 69%, P = .049),

THE STUDY FOUND <u>NO SIGNIFICANT INCREASES</u> IN <u>MORTALITY</u> DIAGNOSTIC, OPERATIVE, ANESTHETIC, MEDICAL PROCEDURE, OR ADVERSE DRUG EVENTS.

Stelfox HT, Bates DW, Redelmeier DA • JAMA 2003; 290:1899-1905

Bottom Line

- If neglect of isolated patients is associated with adverse effects
 - Facilities should spend time correcting bad behavior instead of measuring outcomes of this tolerance
- Inexcusable behavior by medical professionals should not be used as justification for avoiding use of effective control measures and allowing, no promoting, transmission of lethal infections.

What Are Others Doing?

TABLE 1. Contact Isolation Practices for Multidrug-Resistant (MDR) Bacteria, Reported by Society for Healthcare Epidemiology of America Research Network Members

		VDE	ESBL-producing	CDE	MDR ^a	MDR ^a
	MRSA	VRE	bacteria	CRE	Pseudomonas	Acinetobacter
Isolate patients with this organism $(n = 66)$	93.9	93.9	74.2	93.9	81.8	84.9
United States $(n = 46)$	100.0	100.0	87.0	95.7	87.0	89.1
International $(n = 20)$	80.0	80.0	45.0	90.0	70.0	75.0
Duration of isolation	(n = 62)	(n = 62)	(n = 49)	(n = 62)	(n = 54)	(n = 56)
During active illness	6.5	9.7	8.2	6.5	7.4	7.1
Duration of hospitalization	12.9	11.3	26.5	12.9	27.8	28.6
Until negative surveillance cultures	64.5	50.0	32.7	29.0	35.2	33.9
Indefinitely	11.3	24.2	34.7	43.5	31.5	33.9
	75.8	74.2	67.4	72.5	66.7	67.8
How soon cultures may be obtained ^b	(n = 40)	(n = 31)	(n = 16)	(n = 18)	(n = 19)	(n = 19)
After completion of antibiotics	45.0	54.8	37.5	44.4	42.8	42.1
After hospital discharge	15.0	19.4	25.0	22.2	14.3	21.1
<3 months	12.5	19.4	12.5	27.8	28.6	26.3
≥1 year	7.5	6.5	0.0	5.6	0.0	5.3
Isolate readmitted patients	(n = 62)	(n = 62)	(n = 49)	(n = 62)	(n = 54)	(n = 56)
Yes	77.8	74.6	55.6	72.1	53.2	58.1
Allow cohorting $(n = 66)$	54.5	42.4	21.2	18.1	19.7	21.2
	54.5	42.4	21.2	1011	17.0	
Perform active surveillance in at least one	54.5	42.4	21.2	1011	17.0	
Perform active surveillance in at least one area of hospital $(n = 66)$	75.8	34.8	18.2	21.2	7.5	15.2

NOTE. Data are % of facilities. CRE, carbapenem-resistant Enterobacteriaceae; ESBL, extended-spectrum β -lactamase; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant enterococci.

^a As defined by the respondent for isolation/infection control purposes.

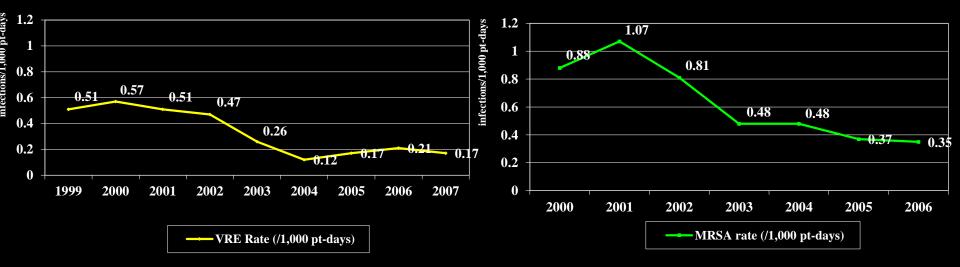
^b If negative surveillance cultures required.

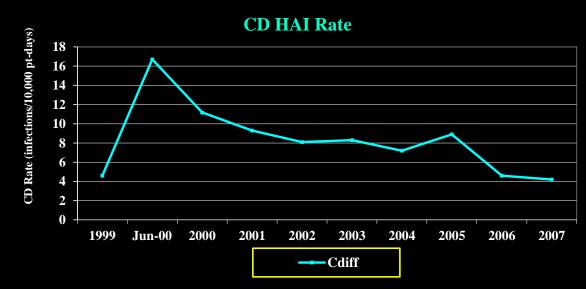
University of Pittsburgh Experience

RESULTS - Sustained MDRO Reduction

VRE HAI Rates

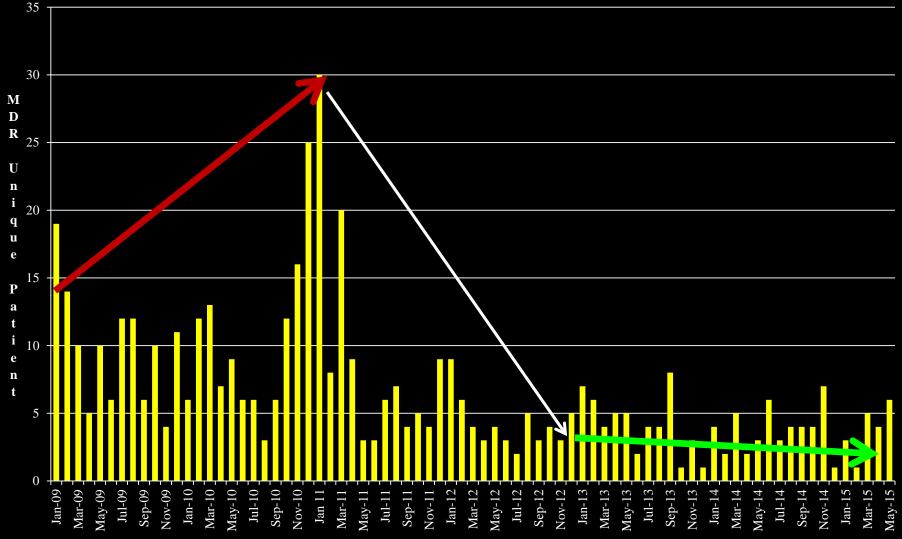
MRSA MICU HAI Rates



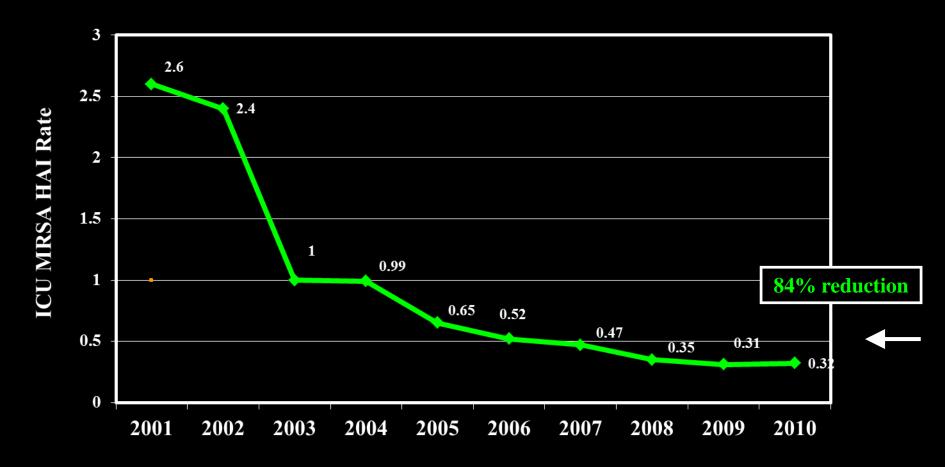


Acinetobacter baumanii (ACAT) MDR by Unique Patient at PUH Jan 2009 to May 2015

Source: Antibiotic Management Program - Clinical Analyst



MRSA Whole House HAI Rates



SUSTAINED REDUCTION

University of Pittsburgh Summary Annual Estimated Benefits of MRSA Control (02-10)

Avoided MRSA HAI	87			
Lives Saved	21			
Avoided Costs	\$3.1M			
Sending Patients Home Alive and WellPriceless!!				

Conclusions

(1) Do MDRO Control Measures work?	YES without question (when done correctly)
(2) Are Contact precautions necessary to for MDRO control?	YES
(3) Are patients in contact precautions as safe as other patients?	YES (when not neglected)
(4) Can we use conclusions of studies without analysis of methods?	OF COURSE NOT

MRDO Prevention

Questions?