Control of Multi-drug Resistant Organisms: Hospitals and Nursing Homes (RCHEs)

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Outline

- Emerging and resistant pathogens
  - MRSA
    - Evolving epidemiology (nasal and extra-nasal) and clinical relevance
    - Infection control and prevention measures
  - R-GNB
    - Epidemiology and clinical relevance
    - Cephalosporin and quinolone resistance
  - VRE
  - *C. difficile*

- Approach to preventing MDROs in nursing homes (NHs)

Impact of Multi-drug resistant organisms (MDROs)

- MDROs: one of the greatest healthcare challenge
- Responsible for
  - over 12,000 deaths
  - 3.5 billion dollars (in US)
- Prevalence estimates show an increase in MDROs
- New antibiotics ➡ Resistance
- New antibiotics not the only solution, need effective infection prevention strategies

S. aureus: Epidemiology in Hospitals

- *Staphylococcus aureus*:
  - Responsible for serious infections
  - Asymptomatic carriage predisposes symptomatic infections
  - Anterior nares primary site of *S. aureus* carriage
    - 20-50% of general population
    - 80% bacteremia are due to similar strain from patients' nares

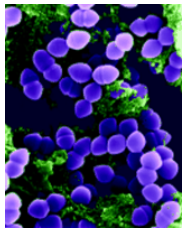
- *S. aureus* carriage at other extra-nasal sites
  - Oropharyngeal carriage – 4-60%
  - Skin carriage – 8-70%
  - Intestinal carriage – 18-100%
  - Groin carriage – 0-22%

S. aureus: healthy volunteers

Asymptomatic Carriage, N =1500 (Mertz CID, 2007)

Nares	Oroph	N (%)
+	+	343 (23)
+	-	219 (15)
-	+	245 (16)
-	-	693 (46)

Evolution of MRSA & VRE



1940 1950 1960 1970 1980 1990 2000 2010

penicillin resistance

penicillin First used

methicillin

MRSA

VISA reported in Japan

12 VRSA cases reported to date

vancomycin

streptomycin

gentamycin resistance

1988- VRE

VRSA

Successful *in vitro* Transfer of *vanA* to MRSA

MRSA

- Emerged in acute care in 1960s
- Staphylococcal infections due to MRSA
  - 1974: 2%
  - 1995: 22%
  - 2004: 63%
- Transmission

MRSA: Prevalence in NHs (RCHE)

Location	Year	No. Patients	% Colonized	Comment
St. Louis	1985	74	12	Nasal
LA	1987	170	6.0-7.3	Nasal & wound
Pittsburgh VA-ECC	1986	432	13	Nasal
Vancouver	1989	120	34	Nasal & wound
Ann Arbor (VA-ECC)	1990	120	23	Nasal & wound
Ann Arbor (VA-ECC, Co NH)	2000-1	427	17	Nasal & wound

MRSA: extra-nasal colonization

- Oropharyngeal colonization, 150 *ICU* patients,
  - Harbath S (Switzerland) 2007, J Clin Microb

Nares	Oro-pharynx	N (%)
-	-	137 (91.3)
+	+	7 (4.7)
+	-	5 (3.3)
-	+	1 (0.7)

MRSA: extra-nasal colonization

- 266 MRSA in-patients
  - Ringberg H (Sweden); Scand J Infect Dis 2006;38:888-93

Nares	Oroph	Perineum	Skin lesion	N (%)
+	-	-	-	45 (17)
-	+	-	-	46 (17)
-	-	+	-	15 (6)
-	-	-	+	68 (26)

MRSA: Hospitalized older adults

- 10,089 in-patients, Canada
  - Simor A et al, Infect Control Hosp Epidemiol 2005;26:838-41

Site	≥ 65 yr N=6613 (%)	18-64 yrs N=3476 (%)
Nares	2,919 (44)	1,219 (35)*
Groin	1,413 (21)	536 (15)*
Urine	633 (10)	219 (6)*

* $P < 0.05$

MRSA: Risk factors in NHs

- Impaired functional status
- Indwelling devices such as urinary catheters and feeding tubes
- Prior hospitalization
- Urinary incontinence
- Prior antimicrobial usage
- Wounds and pressure ulcers

MRSA: Role of Indwelling Devices

Hypothesis: MRSA carriage (both nasal and extra-nasal) would be more frequent in NH residents with indwelling devices compared with controls

- Study Facilities: 14 community NHs in Southeast Michigan
- Study Design: Cross-sectional microbial prevalence study
- Study Population:
  - All residents with an indwelling device (urinary catheter, feeding tube or PICC)
  - Randomly selected controls
- Clinical data: Age, comorbidity and functional status
- Samples obtained from
  - nares, oropharynx, groin, peri-anal, wounds (if present), skin around enteral feeding tubes (if present)

Mody L et al: J Am Geriatr Soc 2007; 55:1921-6

Methods: Molecular epidemiology

- Microbiology
  - *S. aureus* and MRSA identified using standard microbiologic methods
- MRSA sub-typing
  - Pulsed field gel electrophoresis (PFGE)
- Multiplex PCR methods to determine
  - *mec*A gene, SCC*mec* type I-V, Panton-Valentine leukocidin (PVL) toxin gene

Results

- 250 eligible residents
  - 125 with devices
  - 125 randomly selected controls
- 213 enrolled (85%)
  - 108 residents in control group
  - 105 residents in device group
    - 46 with urinary catheters only
    - 48 with feeding tubes only
    - 6 with both urinary catheters and feeding tubes
    - 5 with PICC lines only

Clinical Characteristics

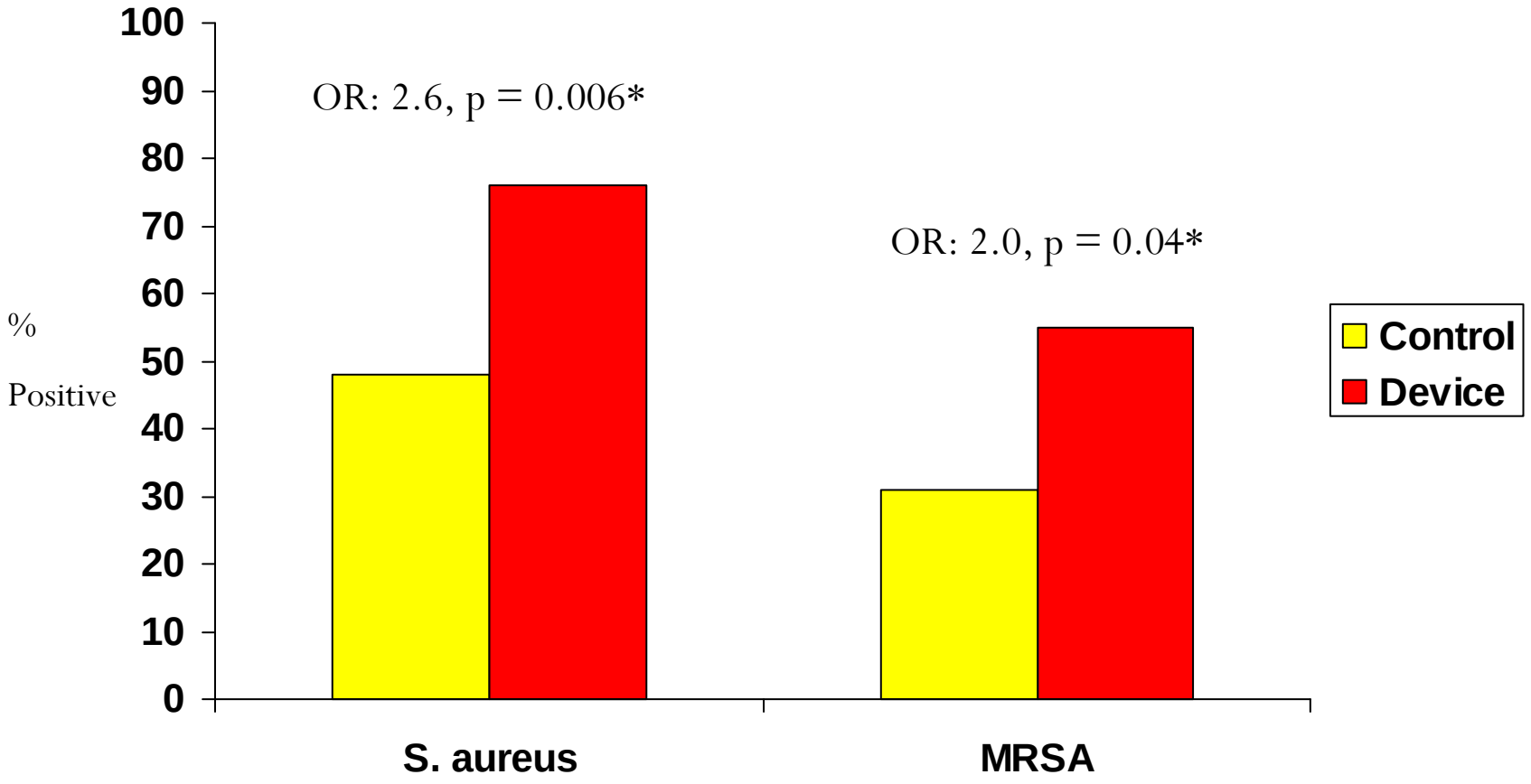
	Device Group (N = 105)	Control Group (N=108)	P value
Mean Age	78 (74-79)	81 (79-83)	0.04*
Female	60%	67%	0.16
Functional Status[#]	26 (24, 27)	20 (18, 21)	0.001*
Co-morbidity Score[‡]	3.0 (2.5, 3.3)	2.5 (2.1, 2.7)	0.04*

[#] Functional Status measured using Lawton and Brody's physical self maintenance scale

‡ Charlson's co-morbidity index

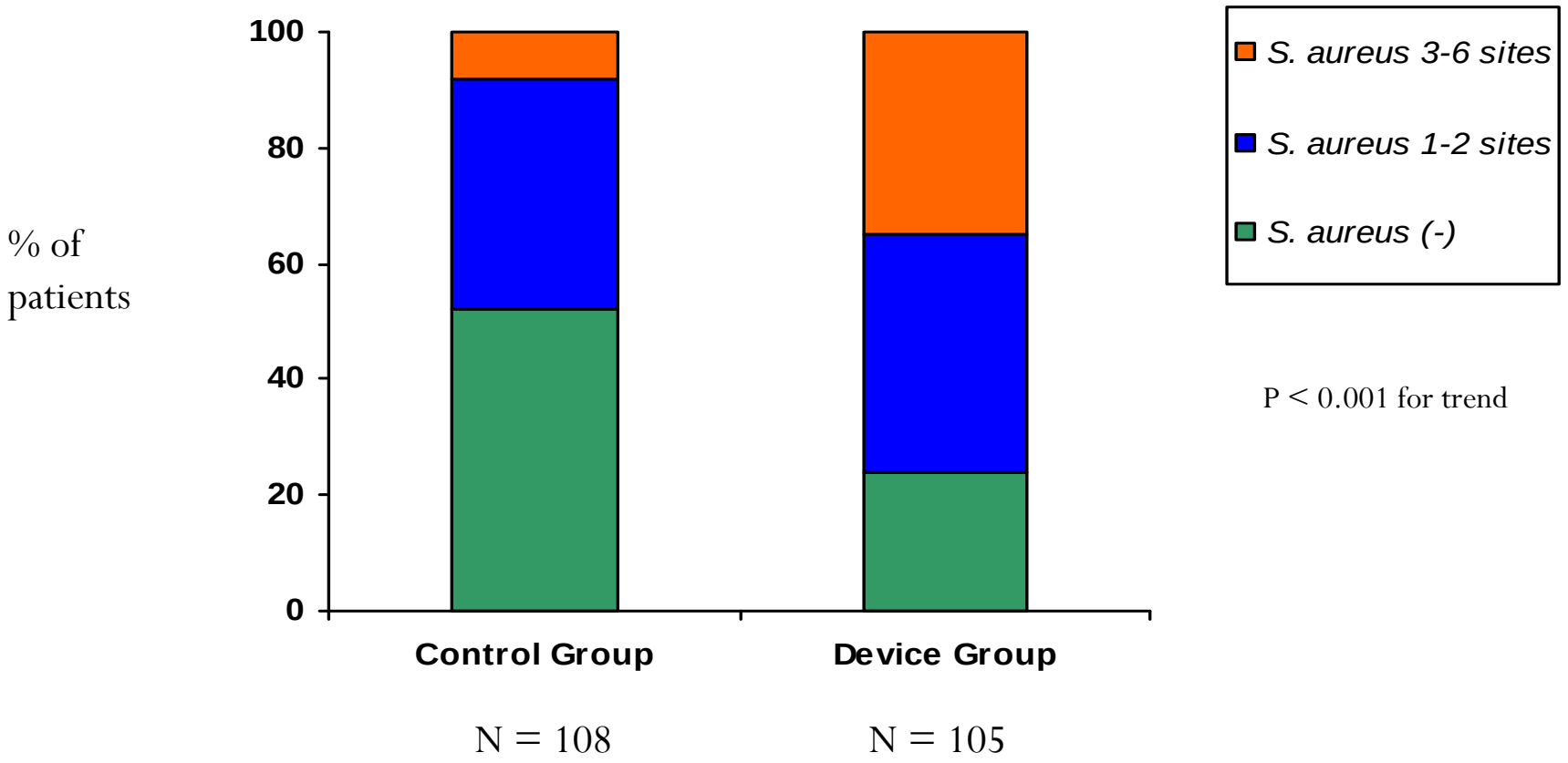
•$P < 0.05$

S. aureus and MRSA carriage

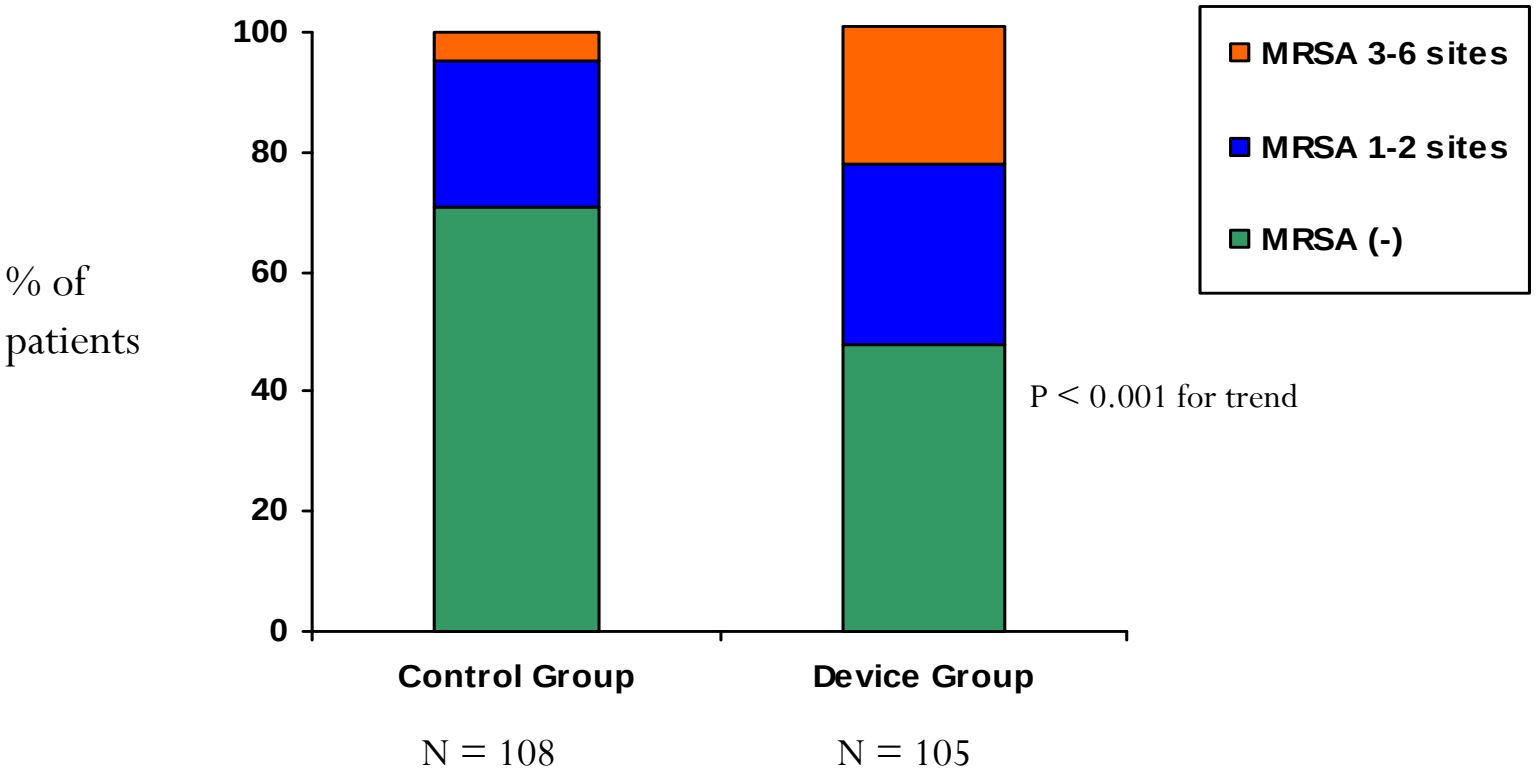


* Adjusted for age, functional status and co-morbidities

S. aureus carriage: Indwelling devices & no. of sites



MRSA carriage: Indwelling devices & no. of sites



Extra-nasal MRSA carriage

	Device Group N = 105 % pos	Control Group N = 108 % pos	OR (95% CI)	P value
Any site	52	29	2.0 (1.1,3.8)	0.04
Nares	31	21	1.8 (0.9,3.5)	0.09
Oropharynx	26	11	2.7 (1.3,5.8)	0.006
Groin	25	5	6.8 (2.4, 19.3)	< 0.001
Peri-anal	27	6	5.4 (2.1, 13.5)	< 0.001

MRSA in RCHEs: Functional Status

Ann Arbor VA ECC, N = 341

- Bradley SF et al, Annals Intern Med 1991;115:417-22.

Functional Status	Total N	MRSA N (%)
I (min assist)	90	19 (21)
II (mod assist)	162	57 (35)
III (max assist)	84	41 (49)

MRSA in NHs (RCHE): Other risk factors

- NHs in Leeds, UK; N = 715; Nares culture, Barr B, ICHE 2007;28:853-9

	Proportion (%) with MRSA	P value	Crude OR	Adjusted OR
Gender				
Female	116/574 (20)			
Male	43/141 (30)	0.008	1.8 (1.2,2.8)	1.6 (1.03,2.6)
Presence of device				
No	141/673 (21)			
Yes	16/35 (38)	0.002	3.2 (1.5,6.6)	2.7 (1.3,5.7)
Use of antibiotics				
No	141/657 (22)			
Yes	16/51 (31)	0.13	1.7 (0.9,3.4)	NS
Presence of wound				
No	146/679 (22)			
Yes	11/29 (38)	0.13	1.9 (0.8,4.5)	NS

MRSA in RCHEs: Other risk factors

- NHs in Germany; N = 3,236; Nares culture
  - von Baum, Infect Control Hosp Epid 2002;23:511-15

	% with MRSA N = 36	% without MRSA, N = 3200	P value	ORa
Male	32%	26%	NS	
Use of Antibiotics	23%	8%	0.006	1.6 (0.7,3.8)
Presence of wound	19%	4%	0.001	3.3 (1.3,8.0)
Urinary catheter	36%	9.6%	0.001	2.7 (1.2,6.3)
Feeding Tube	19.4%	9.3%	0.002	1.5 (0.6,4.1)

MRSA: Evolving Epidemiology

- MRSA in 20th century
  - Acute care 1960s
  - Spill over to NHs in 1980s
  - Healthcare exposure a pre-requisite
- MRSA in 21st century
  - Can be healthcare associated or community-associated
  - Community-associated seen in schools, athletes, jails, overcrowding
  - Spill over to hospitals

MRSA: Healthcare vs. Community

Healthcare associated MRSA (HA-MRSA)	**Community associated MRSA (CA-MRSA)**
Healthcare exposure; Dialysis, indwelling devices, NH residents	No healthcare exposure; Athletes, prisoners, young children, military recruits
Nasal	Nasal & extra-nasal, evolving
Surgical wound infections, UTI, nosocomial pneumonia, blood stream	Boils, spider bites, pneumonia, septicemia
SCC*mec* type II, PVL (-)	SCC*mec* type IV, PVL (+)
Resistant to majority of antibiotics	Susceptible to several antibiotics

MRSA in NHs: Emergence of CA-MRSA?

- Finland:
  - 6.6% of 76 residents with CA-MRSA
    - Kerttula A, J Clin Microbiol 2005;43:6161-3
- Germany:
  - 7.6% of 197 residents with CA-MRSA
    - Raab U, Infect Control Hosp Epidemiol 2006;27:208-11
- Hong Kong:
  - 13 NHs
  - 2.4% of 949 residents CA-MRSA
    - Ho PL, Infect Control Hosp Epidemiol 2007;28:671-8.

CA-MRSA in MI NHs

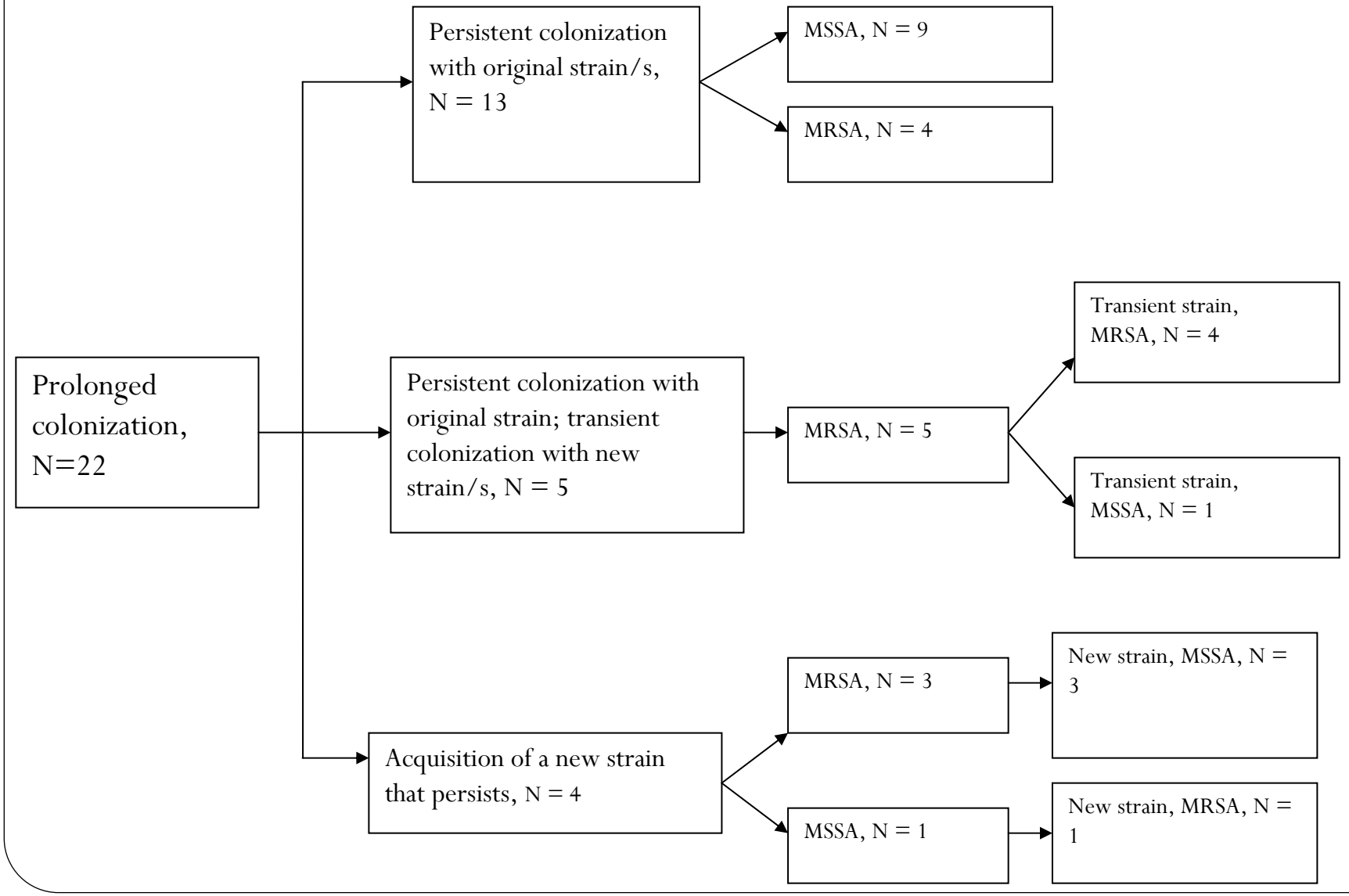
PCR	Device Group (N=55)	Control Group (n=31)
SCC*mec* type		
II (HA-MRSA)	**47**	**26**
IV (CA-MRSA)	**5**	**3**
Unknown	**2**	**1**
PVL (+)	**1**	**1**

Mody L et al, Clin Infect Dis 2008-, in press

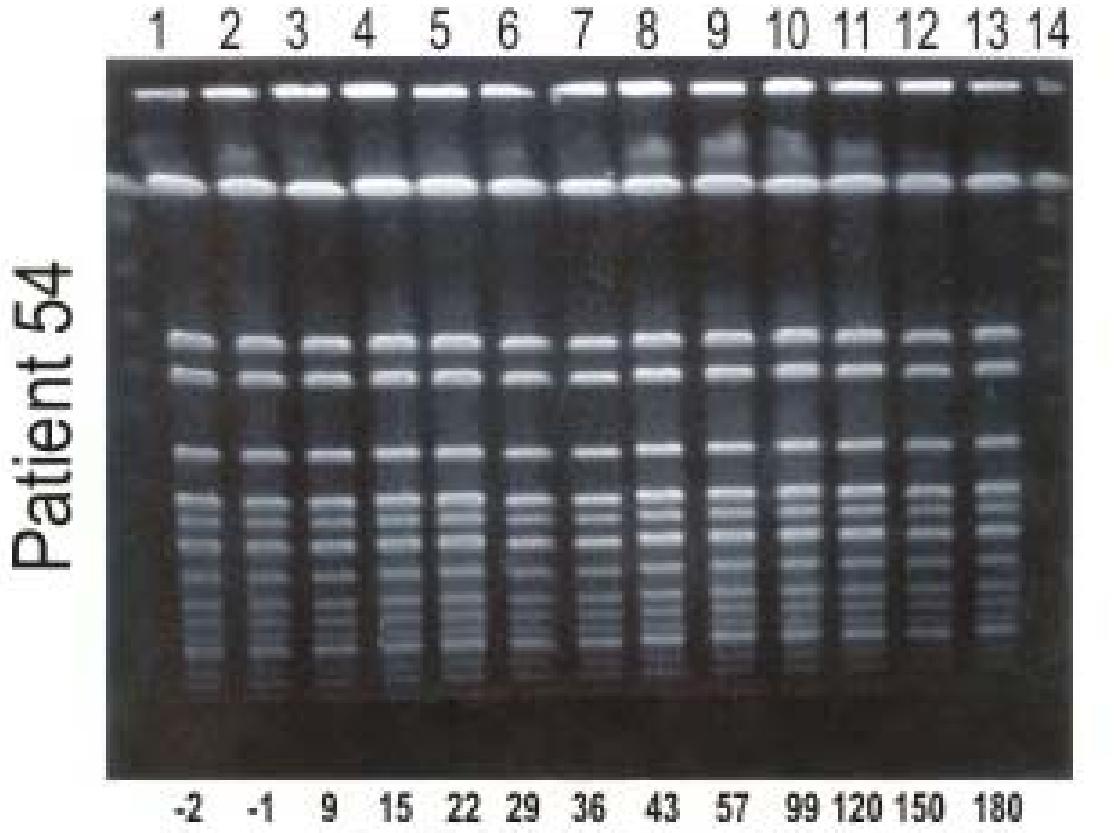
MRSA: Natural history in NHs

- Transfers from acute care
  - 2-25% of new residents colonized
- Persist and spread
  - Enclosed environment, poor functional status, presence of devices
  - HCW to resident and resident to resident spread
  - Serial studies show persistence

MRSA in NH (RCHEs): Persist and Spread



MRSA persistence



Mody et al ICHE 2006; 27:212-4

MRSA Infections

- 3-25% of MRSA carriers develop infections
- Skin & soft tissue, urinary tract infections, respiratory infections
- Atypical presentation

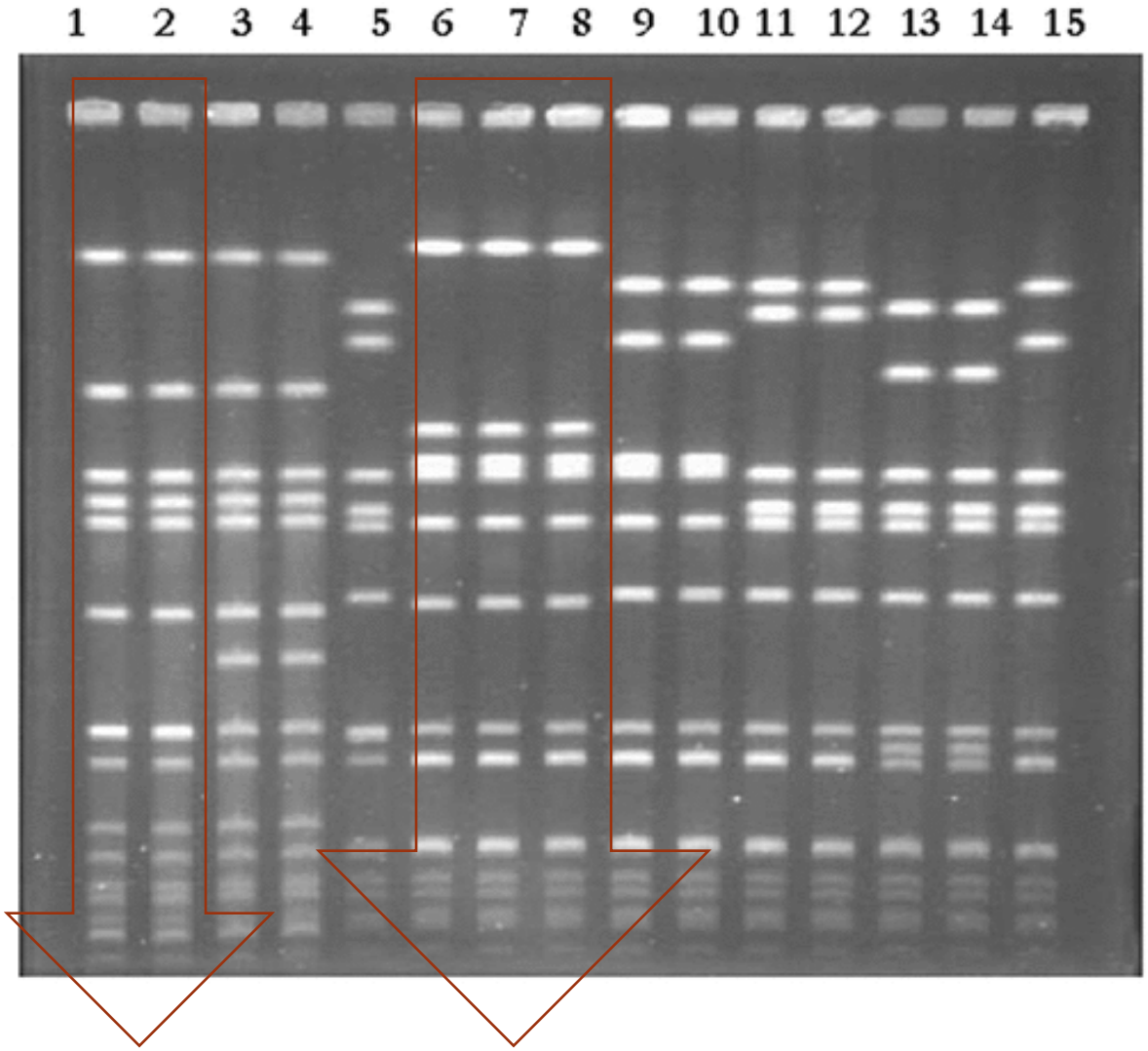
MRSA not the only MDRO…

Environmental sampling

MRSA	VRE	MDRGN	*C. difficile*
Pagers	Stethoscopes	Bedrails	Bed frames
White coats		Sinks	
Blood pressure cuffs		Ventilator water	
		Computer keyboards	

Adapted from: Hebert and Weber, Infection Prevention and Control in the Hospital, 2011

MRSA from environmental cultures



Quinolone Resistance

- Frequent use to treat NH infections
- Resistance in GNB
  - *E. coli*: 5-41%
  - *P. aeruginosa*: 27- 67%
  - *K. pneumoniae*: 7-14%
  - *P. mirabilis*: 38-57%
    - Viray M, Infect Control Hosp Epidemiol 2005;26:56-62
    - Bonomo R, Clin Infect Dis, 2000;31:1414-22
- Antibiotic pressure

β-lactam resistance in GNBs

- GNB carry extended spectrum β-lactamases (ESBLs)

Outbreaks:

- Massachusetts Chronic Care Facility: 1990
  - 25 patients over 4 months
  - Ceftazidime use
- Chicago: 1992
  - 55 hospitalized patients with CTZ-R
  - 31/55 from 8 NHs with CTZ-R
  - Point prevalence study in 1 NH: 18/39 CTZ-R GNB

Bonomo R, Clin Infect Dis, 2000;31:1414-22

Resistant GNB: VA ECC experience

	Ann Arbor	Portland	Pittsburgh
Ceftriaxone -R	27/286 (9.4%)	26/311 (8.4%)	5/754 (0.7%)
Ceftazidime- R	33/349 (9.5%)	7/121 (5.8%)	20/876 (2.3%)

Mody L et al Infect Control Hosp Epidemiol; 2001

Indwelling Devices: R-GNB

Outcome	Devices % (+)	Controls % (+)	ORa	*P-value*
MRSA	55	29	2.0 (1.01,3.8)	.04*
VRE	9	9	1.1	.88
CTZ-R GNB	24	5	5.6 (1.8,17.0)	.003*

* Adjusted for age, co-morbidities and functional status

Risk Factors for R-GNB

- Indwelling devices
- Poor functional status
- Pressure ulcers/wounds
- Quinolone use
- Prior hospitalization

VRE (Vancomycin Resistant Enterococci)

- VRE a relatively recent discovery
  - But widespread, esp. in hospitals with significant mortality and morbidity
- VRE accounts for ~ 30% of ICU isolates of *Enterococcus* in the United States
  - NHs (RCHE)
  - Prevalence varies from 5-20%

Commonality of risk factors: MRSA, R-GNB, *C. difficile*

- Use of indwelling devices
- Prior hospitalization
- Functional impairment
- Prior antimicrobial usage
- Presence of wounds

Infection Control Strategies in NHs

- Progress in LCTFs infection control
  - Guidelines from various national societies
- Immense variations in practice
  - Do-nothing to do-everything
  - No controlled trials
- Issues to remember
  - NHs are not hospitals
  - Rehab and socialization critical
  - Screening cultures require infrastructure
  - NHs may not want to or need to know their MRSA status (although this is changing)

Infection Control Strategies: MRSA

- Hand Hygiene
- Active Surveillance
  - Nares or multi-site
  - All residents or high risk residents such as new admits or those with indwelling devices
- Mupirocin
  - Effective in eradicating for up to 6 months
    - (Mody, Kauffman, Bradley et al Clin Infect Dis 2003;37:1467-74)
  - Re-colonization risk
  - Mupirocin resistance a concern
  - Reduction in infections needs to be established
- Chlorhexidine baths
  - Some data in acute care, no studies in NHs

Hand Hygiene Products

Hand Hygiene adherence

Year of Study	Adherence Rate	Hospital Area
1994 (1)	29%	General and ICU
1995 (2)	41%	General
1996 (3)	41%	ICU
1998 (4)	30%	General
2000 (5)	48%	General

1. Gould D, *J Hosp Infect* 1994;28:15-30.
2. Larson E, *J Hosp Infect* 1995;30:88-106.
3. Slaughter S, *Ann Intern Med* 1996;3:360-365.
4. Watanakunakorn C, *Infect Control Hosp Epidemiol* 1998;19:858-860.
5. Pittet D, *Lancet* 2000:356;1307-1312.

Hand cleansing in NHs

- Thompson et al, MMWR 1993;42:672-75
  - Hand cleansing
    - 32% before interaction
    - 64% after interaction
  - Glove usage
    - 84% compliance
    - Changed only 15% of times

Hand cleansing in NHs

What do healthcare workers carry on their hands?

Does alcohol gel reduce these pathogens?

Does alcohol gel increase hand hygiene compliance?

Mody L et al *Infect Control Hosp Epidemiol*; 2003:24:165-171

Study Methods

- Quasi-experimental study
- Two 36-bed wards
- Cultured hands of healthcare workers
  - Baseline
  - After an educational intervention
  - After introducing alcohol gel on intervention ward
- Standard microbiologic tests to identify
  - *S. aureus*,
  - Gram-negative pathogens
  - Yeast, VRE

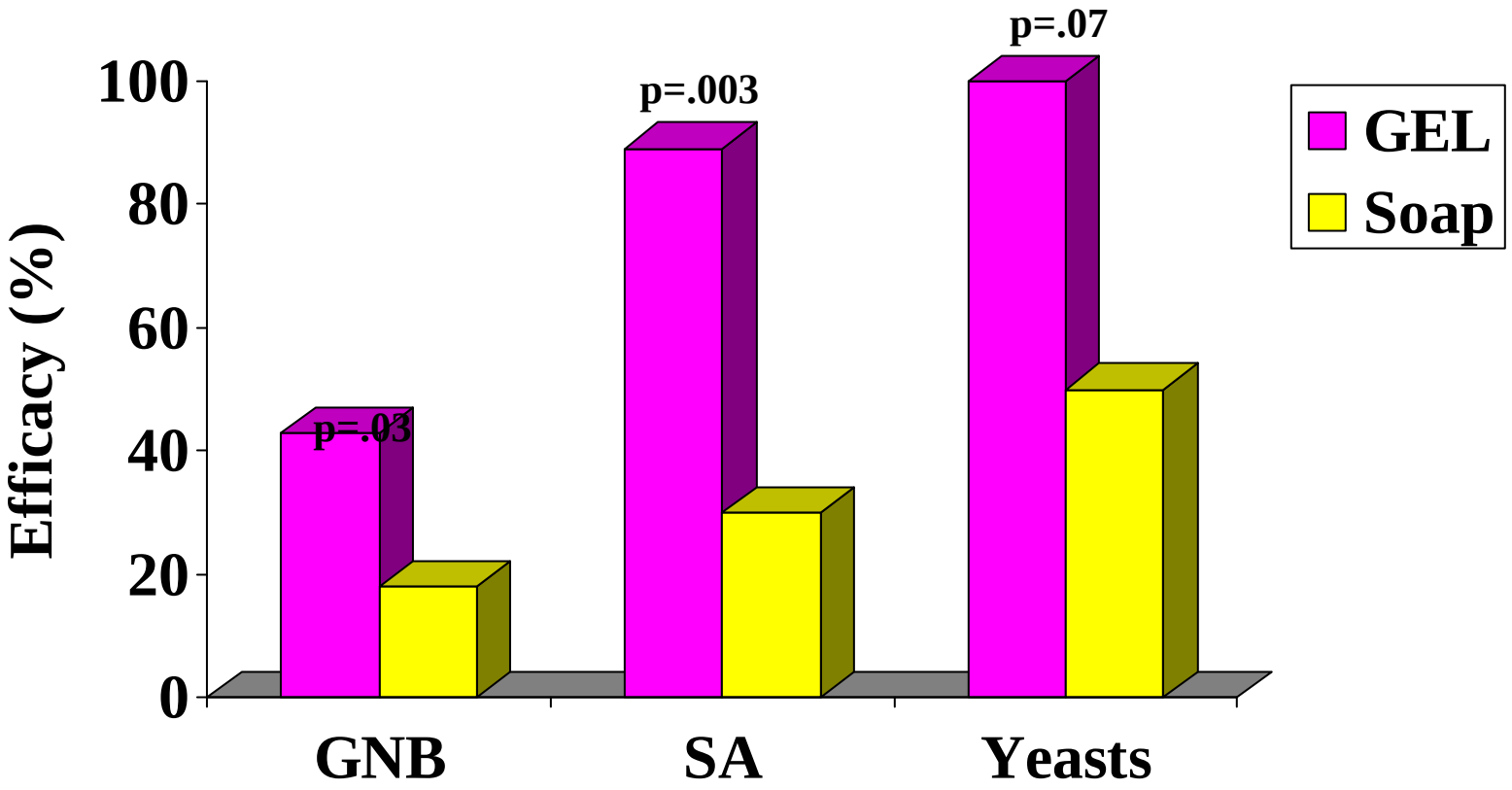
Demographics

	Ward A (GEL)	Ward B (Soap & Water)
No. of HCWs	23	23
F:M	23:0	21:2
RN:Nursing Aide	6:17	7:16
Nail Polish	4	3
Artificial Nails	5	3

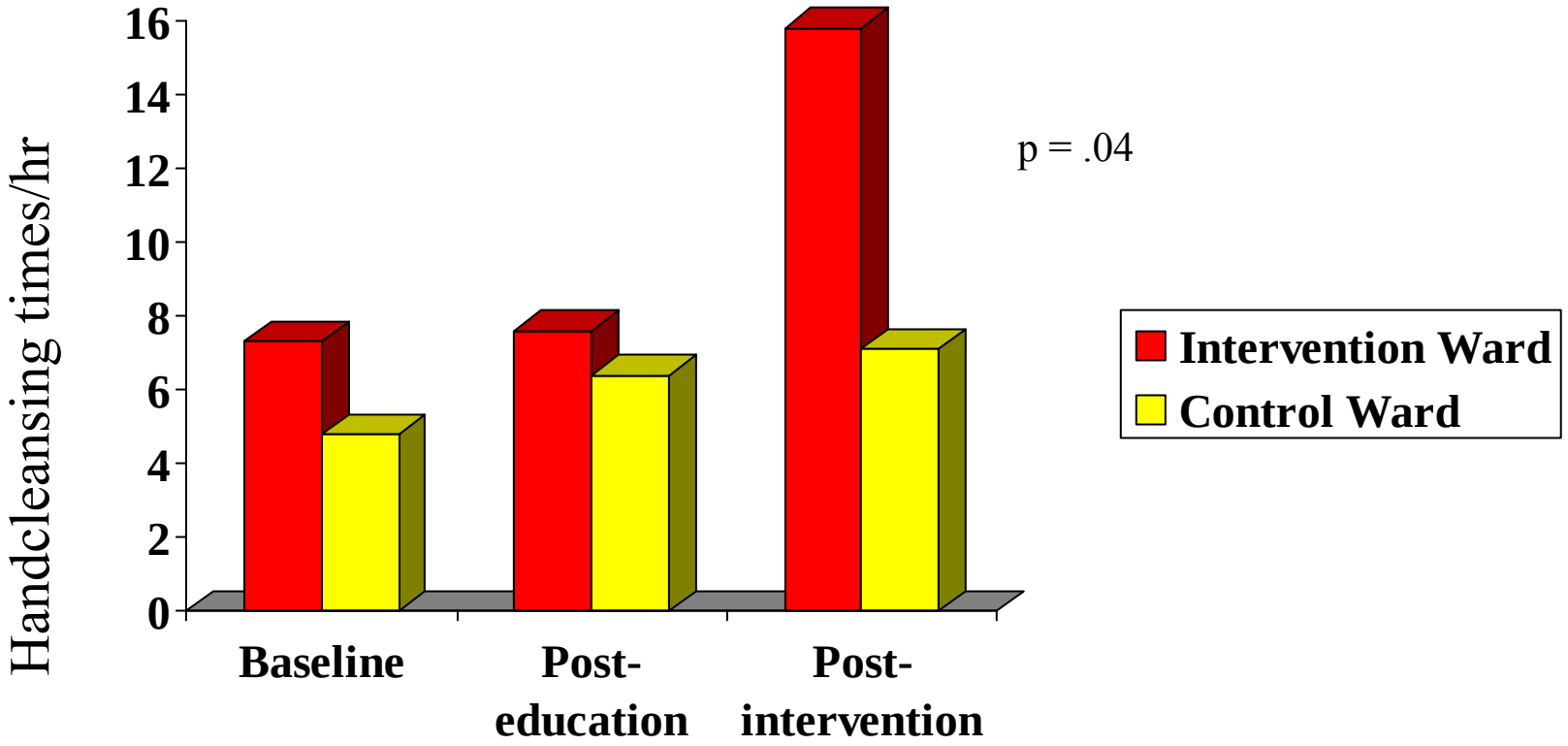
HCWs Hands: What do they grow?

Organism	N (%)
GNB	30 (65)
Yeasts	18 (39)
S. aureus	9 (20)
VRE	4 (9)

Efficacy of Soap vs GEL in eliminating pathogens from the hands of HCW



Effect of an educational intervention & introduction of GEL on hand cleansing frequency



Oro-pharyngeal Decolonization

- Cardiothoracic Surgery
  - Does peri-operative decontamination lead to reduced infections?
    - 991 patients randomized to Chlorhexidine Gluconate or placebo
    - Nosocomial infection rate: 19.8% in Rx group; 26.2% in placebo group
    - NNT: 16 patients needed to be treated to prevent 1 infection
    - Documented significant reduction in *S. aureus*

      - Segers P et al JAMA 2006;296:2460-6

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  - Re-colonization risk
  - Reduction in infections needs to be established
- Chlorhexidine baths
  - Some data in acute care, no studies in NHs

Infection Control: Other MDROs

- Control of transmission
  - Preventing the spread of resistant organisms principally via the hands of healthcare workers
    - Transient vs. Resident flora on hands
  - Preventing environmental contamination
- Antibiotic Stewardship

Hand Hygiene

- VRE:
  - Can easily pass on HCW hands and contaminate environment
  - Documented on 13-41% of HCWs
  - Can persist for up to an hour
  - Can be successfully removed with soap and water or alcohol based hand rub
- R-GNB
  - Commonly found on environmental surfaces as well as HCW hands
  - Survive longer on inanimate objects than hands
  - Artificial finger nails a risk factor
  - Hand hygiene adherence shown to reduce MDR colonization
- *C. difficile*
  - form spores
  - Isolated from environment; survives for prolonged period
  - Antiseptic hand rubs may not be as effective
  - Physical removal of spores by soap and water required
  - Bleach cleaning for environment

Isolation precautions and PPE

- Isolation precautions one of the oldest form of infection control
- Modern medicine moving away from strict isolation to use of personal protective equipment (PPE)
- Gloves: reduces risk of hand contamination
- VRE: current guidelines recommend isolation
  - few well designed studies; significant circumstantial evidence in favor of using gowns and gloves to prevent transmission
  - Gown free period shown to increase transmission
- R-GNB
  - Few studies to support active surveillance and isolation
  - Some data supporting the use of gowns and gloves in reducing transmission
  - Well-designed studies lacking
- C. difficile
  - If diarrhea, then contact precautions as well as gowns and glove use
  - Several studies now support this approach

Challenges to Isolation Precautions in NHs

- Can compromise quality of care
- Concerns about reduce nurse and physician oversight
- Potential for depression and anxiety especially in older adults

Active surveillance

- MRSA
  - Targeted surveillance for MRSA useful in acute care setting
  - Routine surveillance in ICU with appropriate infection control measures, shown to be useful
  - Universal hospital surveillance can also reduce MRSA
- VRE
  - A large proportion undetected by clinical cultures
  - Some evidence showing active surveillance can reduce VRE bacteremia
  - Can consider surveillance in high-risk patients
- R-GNB
  - Active surveillance not well-studied
  - Heterogeneity of GNB a major challenge
  - Active surveillance can increase appropriate antibiotic usage, but research is lacking
- C. difficile:
  - A significant proportion of asymptomatic carriage
  - Active surveillance generally not recommended

Challenges to Active Surveillance in NHs (RCHE)

- At any given time:
  - 30% colonized with MRSA
  - 10-20% with VRE
  - 35-40% with CIP-R GNB
- Issues to consider
  - Is it practical to culture 1.5 million residents?
  - Can we define specific high risk groups?
  - Multi-anatomic site cultures? Nares alone may not suffice
  - How often should they be cultured?
    - Short-stay: 2-3 months; Long-stay: 3-4 yrs
  - If positive then…?

Antimicrobial Stewardship

- Rational use of antibiotics critical
- Balance between effective treatment and avoidance of resistance
- Two major approaches:
  - Prospective auditing/feedback
  - Pre-authorization
- Leads to effective therapy and cost savings
- Computerized decision support emerging
- Research in NHs lacking

Antimicrobial Stewardship: Limitations

- Lack of research to demonstrate sustained decrease in overall burden of MDROs
- Research lacking in NHs
- Only antimicrobial stewardship without other infection control approaches may fail
- Difficult to predict which antibiotic to restrict

Summary

- Epidemiology of MRSA in NHs is evolving
  - more studies required
- GNB resistance to quinolones and cephalosporins frequent
- Goals of infection control in NHs different
- Need for Infection prevention and MDRO transmission research in NHs

"PENICILLIN IS CALLED A "WONDER DRUG" BECAUSE ANY TIME THE DOCTOR WONDERS WHAT YOU'VE GOT, THAT'S WHAT YOU GET."