



THE LANCET Conferences

**Healthcare-associated infections**

December 11-12, 2008, QEII Conference Centre

**Moving beyond headlines to clinical solutions**

# The role of screening and isolation

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# MRSA

## Infection Control Crew



a STEVEN SPIELBERG FILM

The true story of a real fake.

← catch me if you can →

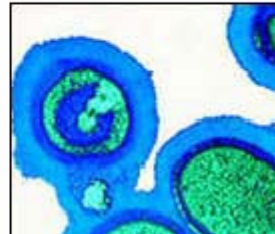
DREAMWORKS PICTURES PRESENTS A KEMP COMPANY AND SPLENDID PICTURES PRODUCTION A PARKES/McDONALD PRODUCTION A STEVEN SPIELBERG FILM  
LEONARDO DICAPRIO TOM HANKS "CATCH ME IF YOU CAN" CHRISTOPHER WALKEN MARTIN SHEEN NATHALIE BAYE DEBRA ZANE CSA DEVORAH MOSS-HANKIN  
FRANK W. ABAGNALE WITH STAN REDDING JOHN WILLIAMS MARY ZOPHRES MICHAEL KAHN A.C.E. JEANNINE OPPEWALL JANUSZ KAMINSKI ASC  
DANIEL LUPI BARRY KEMP LAURIE McDONALD MICHEL SHANE AND TONY ROMANO STEVEN SPIELBERG WALTER E. PARKES JEFF NATHANSON  
CATCH THEM IN CINEMAS STEVEN SPIELBERG DREAMWORKS PICTURES

25th October 2006

## How big a threat is MRSA really?

By Michelle Roberts  
BBC News website health reporter

During the recent election, it might have seemed as though every other story in the news was about MRSA and what should be done about it.



**BBC**  
**NEWS**

Hospital-acquired infections (HAI) are community, state, national and international problem

*Patients and the public are increasingly seeing HAI as indicators of the quality of patient care*

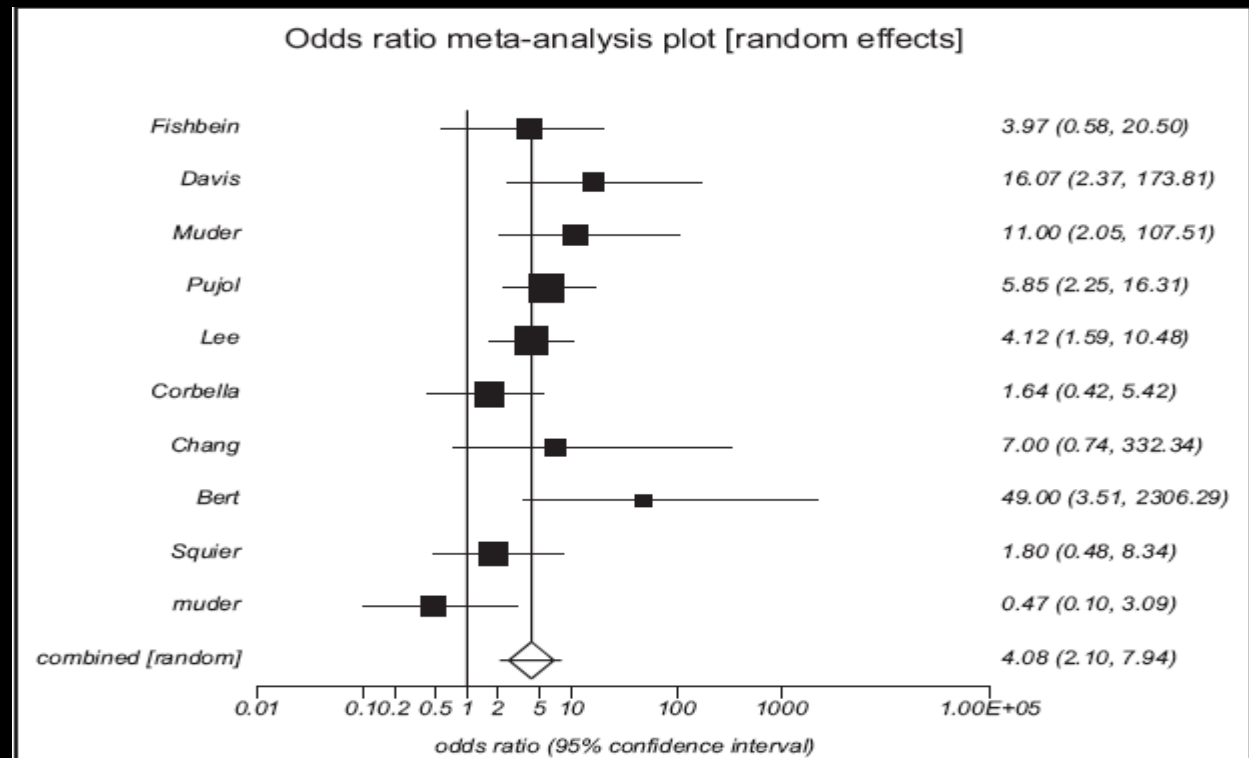
**I.** *How are healthcare professionals to decide what is the best and most effective approach to preventing transmission of HAI?*

- i. Should mandatory screening be performed?*
- ii. Should contact isolation precautions be taken with patients colonised or infected?*

**II.** *Where is the evidence?*

1° assumption:  
colonization precedes infection  
MRSA

- Nasal carriage of MRSA increases risk of MRSA infections by **4 fold**
- MRSA infections develop in **11% to 33%** of colonized patients



Mest, Anesth Analg, 1994; Jernigan, ICHE, 1995; Sadfar, Am J med 2008

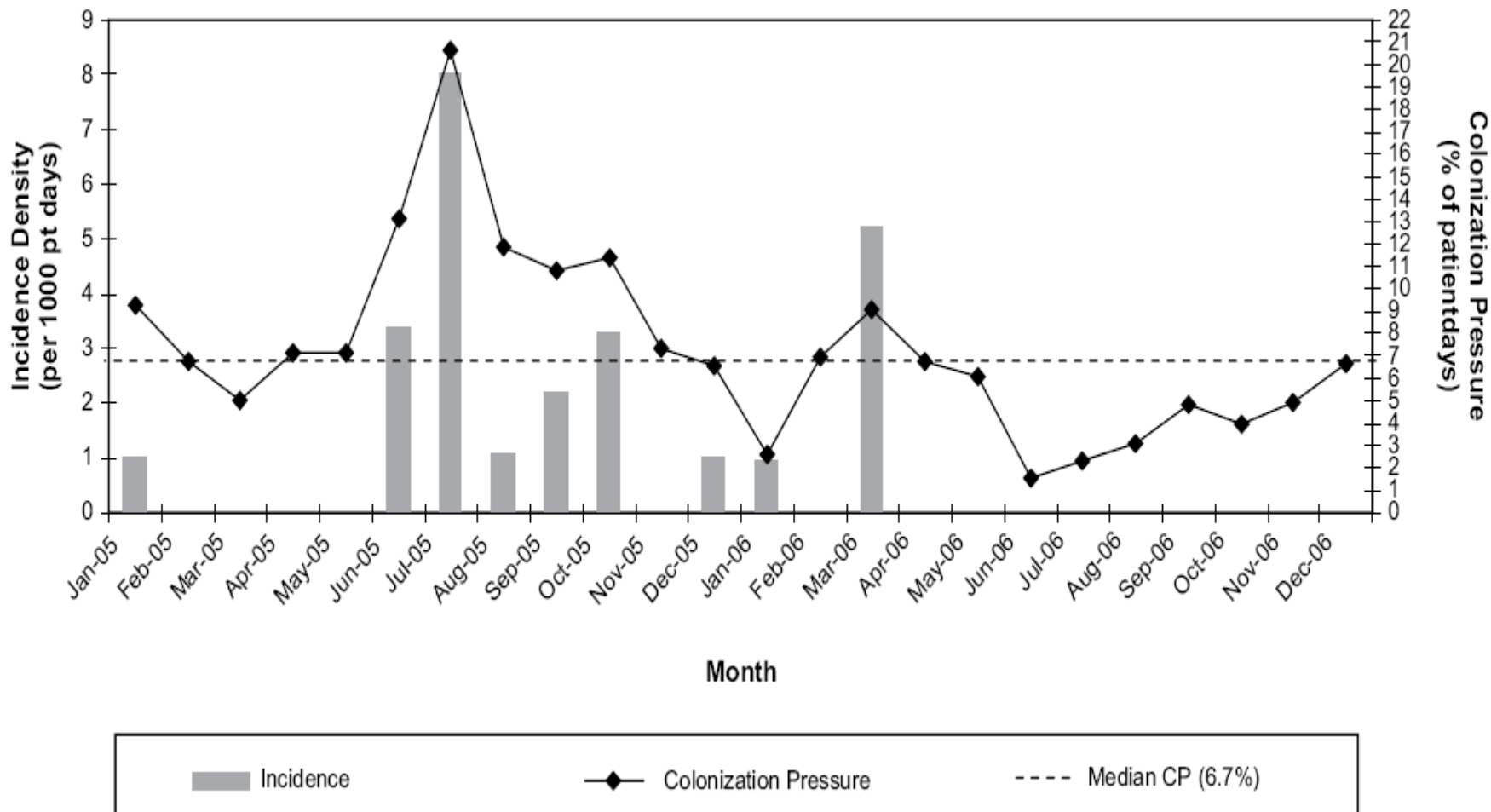
## Risk of Vancomycin-Resistant Enterococcus (VRE) Bloodstream Infection Among Patients Colonized With VRE

- Colonisation with VRE is a risk factor for subsequent VRE BSI
- 4% of colonised patients developed BSI
- Independent risk factors for BSI among colonised patients were admission from a long-term care facility, infection of an additional body site, and exposure to vancomycin.

**Antibiotic Usage and Risk of Colonization and Infection with MRSA:  
a Hospital Population-Based Study**

Antibiotic	Incidence X 1000-days therapy	5 days	MRSA
<b>Carbapenems</b>	<b>13.8</b>	18.3	7.9
<i>Dyalisis</i>	29.4		
<i>Diabetes</i>	28.6		
<i>Cirrhosis</i>	20.4		
<b>Cefalolosporins 3°/4°</b>	<b>5.8</b>	5.1	2.4
<i>CRF</i>	27.3		
<i>Neoplasy</i>	15.8		
<i>HIV</i>	10.9		
<i>Cirrhosis</i>	10.6		
<i>Age &gt; 70 y.o.</i>	8.1		
<b>Quinolones</b>	<b>5.9</b>	6.6	3.1
<i>Age &gt; 70 y.o.</i>	8.3		
<b>Glycopeptides</b>	<b>9.2</b>	11.3	3.2
<i>HIV</i>	19.5		
<i>Cirrhosis</i>	15.1		
<b>Pip.-tazobactam</b>	<b>6.5</b>	11	3.5
<i>Age &gt; 70 y.o.</i>	16.2		

Characteristic	Study population (N = 439)	Patients infected or colonized with MRSA		Patients infected or colonized with ESBL-producing Enterobacteriaceae	
		Value (n = 55)	P <sup>a</sup>	Value (n = 33)	P <sup>a</sup>
Male sex	232 (52.8)	30 (54.5)	>.25	18 (54.5)	>.25
Age					
Mean ± SD, years	66.4 ± 18.3	73.9 ± 15.3	.001	64.1 ± 16.9	>.25
Median, years	69.0	75.0		66.0	
Age >69 years	207 (47.7)	35 (63.6)	.01	12 (36.4)	.18
Previous hospitalization	284 (64.7)	41 (74.5)	.10	25 (75.8)	.15
Location at time of screening			.02		>.25
Medical ward	241 (54.9)	28 (50.9)		16 (48.5)	
Surgical ward	99 (22.6)	7 (12.7)		10 (30.3)	
Rehabilitation unit	60 (13.7)	14 (25.5)	.007	3 (9.1)	
Medical or surgical ICU	39 (8.9)	6 (10.9)		4 (12.1)	
Admitted from home	407 (92.7)	48 (87.3)	>.25	32 (97.0)	>.25
McCabe score at hospital admission			.001		.04
No fatal disease	154 (35.1)	12 (21.8)		5 (15.2)	
Ultimately fatal disease	204 (46.5)	23 (41.8)		21 (63.6)	
Rapidly fatal disease	81 (18.5)	20 (36.4)		7 (21.2)	
Rapidly or ultimately fatal disease	285 (64.9)	43 (78.1)	.03	28 (84.8)	.02
Chronic health status C or D on day 30	214 (48.7)	33 (60.0)	.07	18 (54.5)	>.25
Charlson comorbidity score on day 30					
Mean ± SD	3.8 ± 2.8	4.4 ± 2.9	.05	4.5 ± 2.7	.10
Median	3.0	4.0		4.0	
Score >3	204 (46.5)	34 (61.2)	.01	17 (51.5)	>.25
Invasive device or procedure before day 30					
Surgical procedure	184 (41.9)	13 (23.6)	.004	13 (39.4)	>.25
Urinary device	208 (47.4)	26 (47.3)	>.25	17 (51.5)	>.25
Central venous catheter	89 (20.3)	12 (21.8)	>.25	9 (27.3)	>.25
Peripheral venous catheter	361 (82.2)	44 (80.0)	>.25	27 (81.8)	>.25
Nasogastric tube	93 (21.2)	10 (18.2)	>.25	8 (24.2)	>.25
Mechanical ventilation	61 (13.9)	10 (18.2)	>.25	6 (18.2)	>.25
Antimicrobial drugs received before day 30					
Any	350 (79.7)	44 (80.0)	>.25	28 (84.8)	>.25
Amoxicillin-clavulanate	140 (31.9)	14 (25.5)	>.25	15 (45.5)	.08
Fluoroquinolone(s)	106 (24.1)	20 (36.4)	.02	9 (27.3)	>.25
3rd-generation cephalosporin(s)	81 (18.5)	14 (25.5)	.15	8 (24.2)	>.25
Amoxicillin	45 (10.3)	8 (14.5)	>.25	1 (3.0)	>.25



# The role of screening

## i. Who?

All admissions

High risk patients

## ii. Where?

ICU

High-risk wards

All wards

## iii. When?

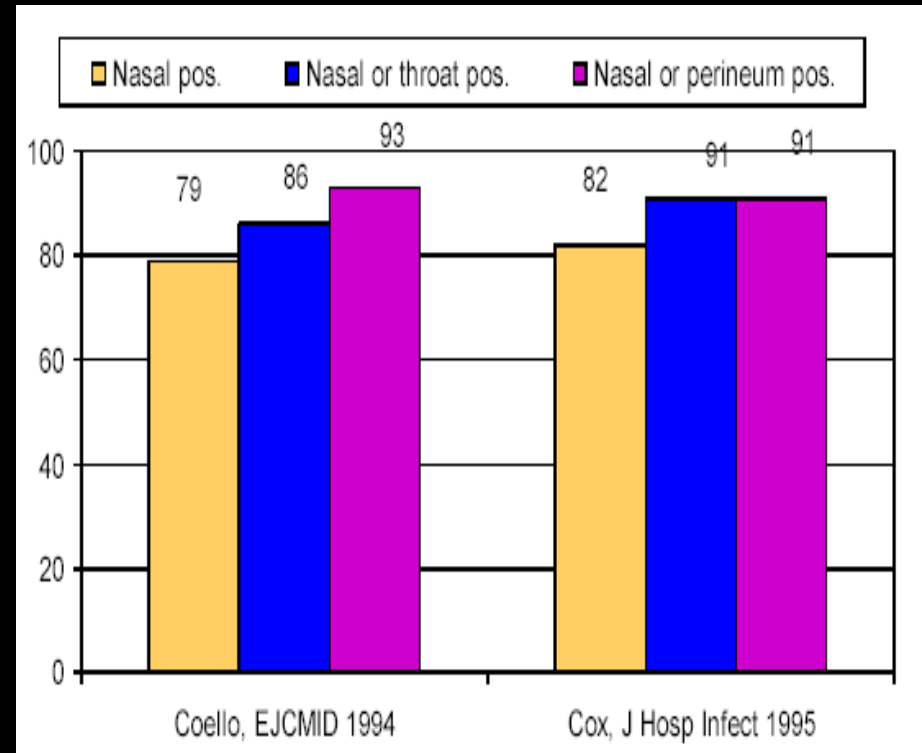
Hospital admission

Weekly during hospitalization

Discharge

# Sites to be screened (sensitivity)

- Anterior nares (78-93)
- Axilla (25)
- Groin /perineum (39)
- Nasal + wounds (100)
- Nasal + throat + perineum (99)
- Nasal + skin (92)
- Nasal + clinical (87)
- Clinical infection:
  - 60% nasal / 53% rectal
- Sites of catheters
- Traheostomy
- Sputum (if productive cough)





# The Netherlands against the world

## The S&D strategy

- MRSA positive: isolation
- Hospital admission screening for high risk patients and precautionally isolated
- All pts screened in case of unexpected finding of MRSA
- All HCWs screened and furloughed from working until decontamination is achieved
- Wards will be closed for new admission when there is > 1 carrier among pts

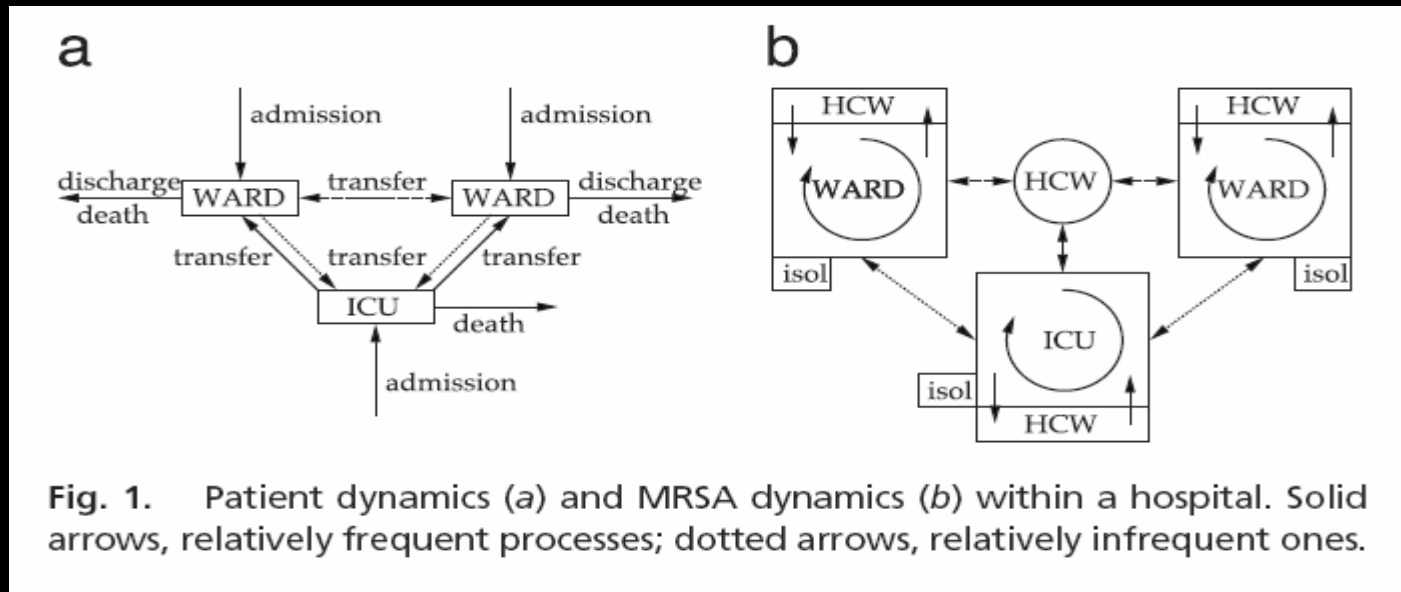


Fig. 1. Patient dynamics (a) and MRSA dynamics (b) within a hospital. Solid arrows, relatively frequent processes; dotted arrows, relatively infrequent ones.

**Table II** Yearly average cost of the MRSA search and destroy policy between 2000 and 2004 at the University Hospital Maastricht

	Cost (€)
Nursing	
1 day, all patients	570.80
1 day, MRSA patients in isolation	976.80
MRSA screening culture	
Negative culture	10.61
Positive culture	78.47
Treatment	
Mupirocin ointment/carrier	6.13
Co-trimoxazole/carrier	29.34
Flucloxacillin/MSSA BSI	60.72
Vancomycin/MRSA BSI	250.13
Vancomycin dosage	20.00
Total cost of the S&D policy	1,383,200

**Table III** Variations in the *S. aureus* treatment cost with changing MRSA/MSSA infection ratio

MRSA/MSSA ratio	MRSA BSI/year	Cost (€)			
		MRSA BSI	MSSA BSI	<i>S. aureus</i> BSI	Total MRSA
0.7/99.3	0.4	11,762	1,343,166	1,354,928	2,738,128
2/98	1.2	34,815	1,325,258	1,360,072	2,743,272
5/95	3.0	87,037	1,284,688	1,371,725	2,754,925
8/92	4.7	139,259	1,244,119	1,383,378	2,766,578
10/90	5.9	174,074	1,217,073	1,391,147	2,774,347
25/75	14.8	435,184	1,014,228	1,449,412	2,832,612
50/50	29.6	870,368	676,152	1,546,520	2,929,720

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; BSI, bloodstream infection.

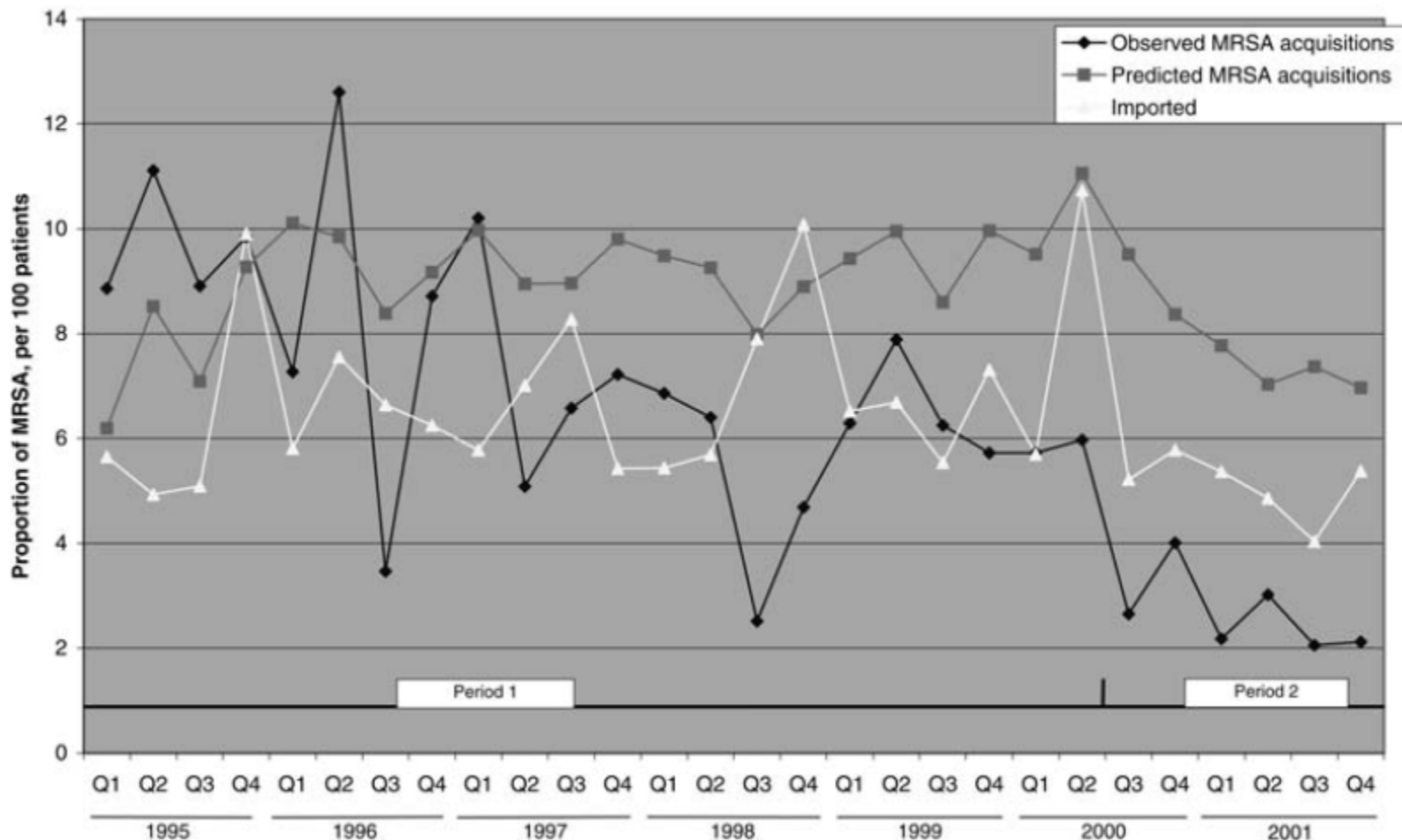
Where:  
ICU  
Who:  
All pts

In favour

Setting: ICU

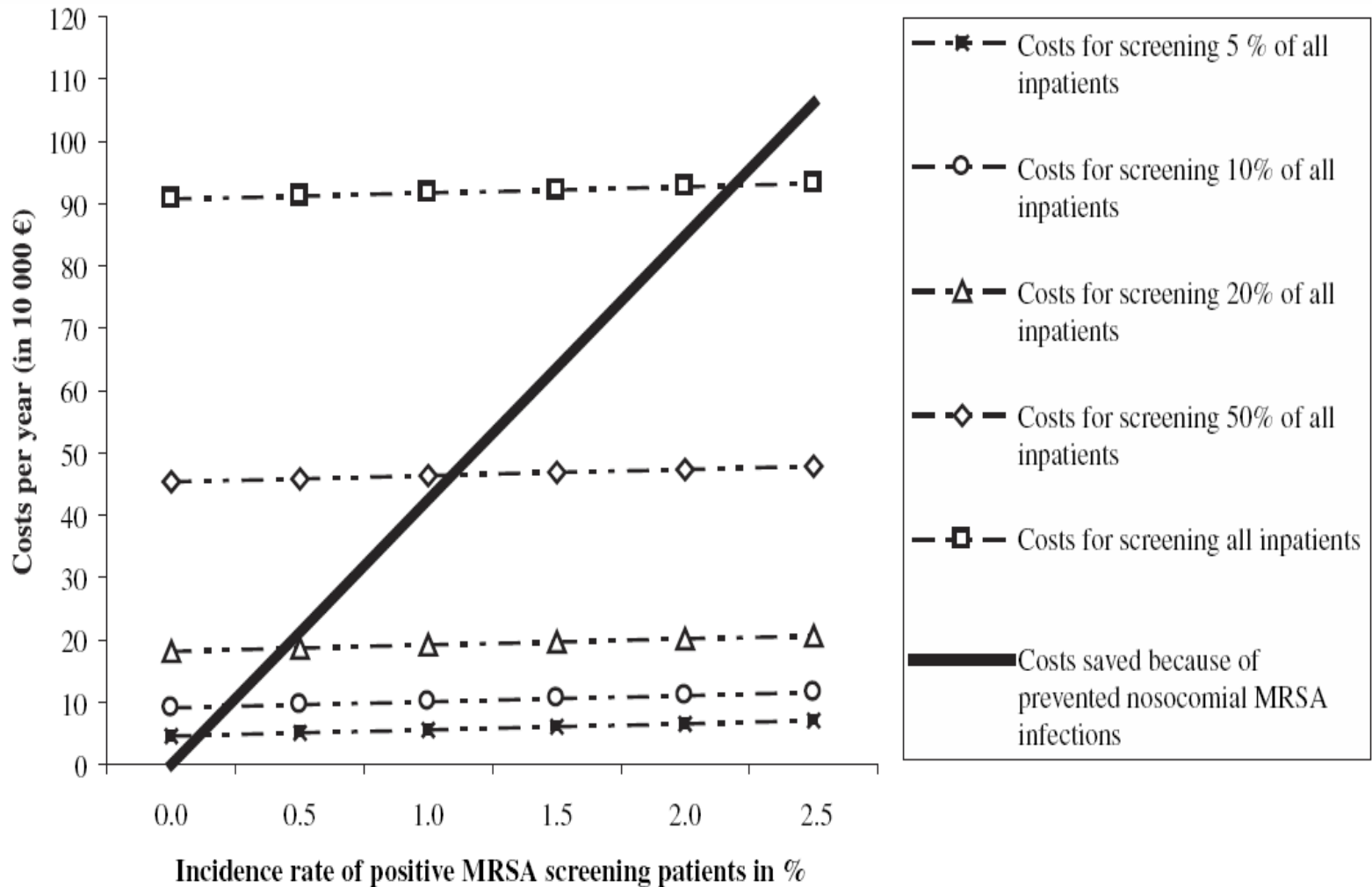
Intervention: Multiple factors including screening (all pts at admissions / weekly), CP, alcoholic handrub solution

Predictions and observation of MRSA acquisitions over a 7-year period



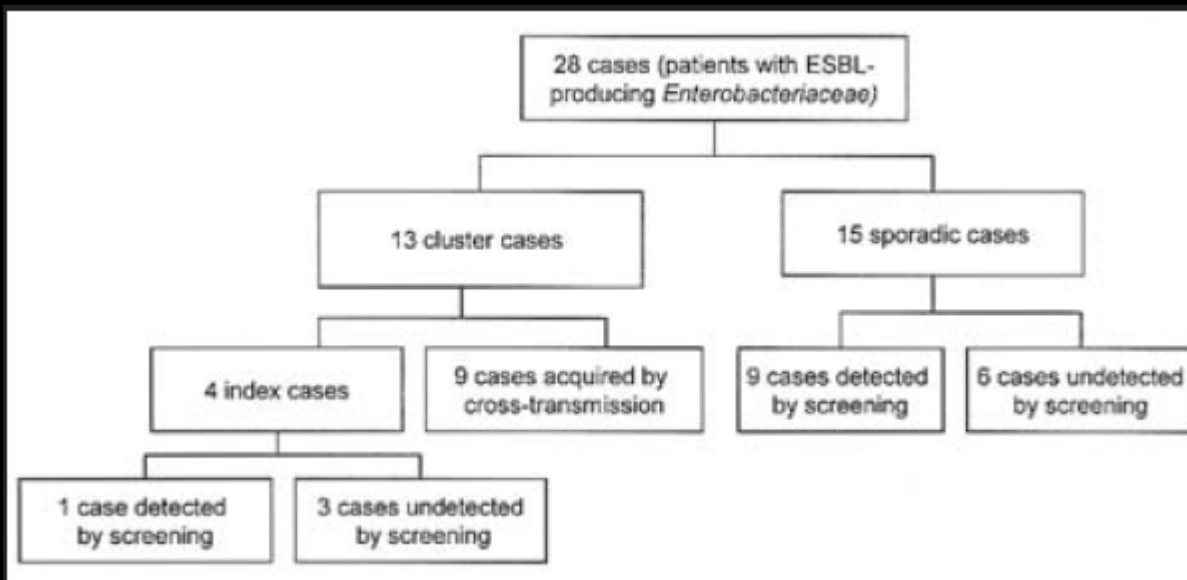
Where:  
ICU+Non-ICU  
Who:  
All pts

# Screening costs



**TABLE 4**  
**1-YEAR ACTUAL COSTS AND SAVINGS, AND THE RANGE OF ESTIMATES FOR COSTS AND SAVINGS OF ENHANCED INFECTION CONTROL STRATEGIES**

<b>Cost Components</b>	<b>Cost (1995 Dollars)</b>	<b>Range of Estimates (1995 Dollars)</b>	<b>Reference for Estimate</b>
Nurse assistant*	68,202	49,725-93,600	†
Microbiologist	14,040	14,040-19,188	‡
Gowns	15,276	15,276-21,994	§
Gloves	3,864	3,765-4,116	§
Surveillance cultures supplies	4,137	4,137 <sup>l</sup>	
Admitting personnel time	704	704 <sup>ll</sup>	
Nurse for surveillance cultures, patient education, and antimicrobial control	10,292	10,292 <sup>ll</sup>	
<b>Total cost</b>	<b>116,515</b>	<b>97,939-148,883</b>	
<b>Savings Components</b>	<b>Actual Savings (1995 Dollars)</b>	<b>Range of Estimates (1995 Dollars)</b>	<b>Reference for Estimate</b>
Fewer patients with VRE BSI	123,081	118,587-143,247 <sup>ll</sup>	SPARCS <sup>ll</sup>
Gown and gloves	2,755	2,742-3,760	§
Reduction in antimicrobial use	130,600	93,393-216,104 <sup>#</sup>	Reference 9
Administration of antimicrobials	49,397	49,397 <sup>l</sup>	
<b>Total savings</b>	<b>313,525</b>	<b>271,531-421,461</b>	



**TABLE 2**  
RESULTS OF SCREENING CULTURES IN BOTH INTENSIVE CARE UNITS

ICU	No. of Admitted Patients	No. (Rate) of Specimens Screened	No. (Rate) of Patients With Positive Results on Screening Test	No. of Carriers Identified
Medical	1,825	1,475 (80.8%)	20 (1.35%)	10 (0.68%)
Surgical	1,853	1,408 (76.0%)	8 (0.57%)	3 (0.21%)
Total	3,678	2,883 (78.4%)	28 (0.97%)	13 (0.45%)

ICU - intensive care unit.

**TABLE 3**  
ANALYSIS OF THE CLUSTERS OF EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING ENTEROBACTERIACEAE

Cluster	No. of Patients	Species	ICU	Date of Stay of Patients in the Cluster	Detection of the Probable Index Case* of the Cluster by Screening Culture
1	3	<i>Enterobacter cloacae</i>	Surgical	5/1 to 5/20/1999	Yes
2	4	<i>Enterobacter aerogenes</i>	Medical	10/10/1999 to 1/27/2000	No
3	4	<i>Enterobacter aerogenes</i>	Medical	3/7 to 4/17/2000	No
4	2	<i>Escherichia coli</i>	Medical	8/21 to 9/20/2001	No

# High risk carriage

## Targeted screening

### Evidence

- Previous infected or colonised
- Frequent hospitalizations
- Transfers from other hospitals or LTCF
- Dyalised
- Eczema, psoriasis, dermatitis
  
- IVDA
- HIV
- Professionanl contact sport teams
- High risk wards
  - Orthopedic
  - Cardiosurgery
  - Transpalntation

# Target screening

**Table 2.** Variables Associated with Newly Identified MRSA Carriage at Admission to Surgery Department, Excluding Formerly Known MRSA Carriers (Derivation Cohort)

Risk factor	Odds ratio (95% CI)	
	Bivariate	Multivariate
Male gender	1.5 (0.8–2.7)	
Age 75 years or older	2.3 (1.3–4.1)	1.9 (1.0–3.8)
Emergency admission	0.8 (0.4–1.5)	
Previous hospitalization (past 12 mo)	5.6 (2.7–11.7)	2.7 (1.1–6.4)
Previous operation (past 12 mo)*	3.6 (1.9–6.8)	
Previous stay in longterm care	3.1 (1.2–7.9)	
Charlson score (per 1-point increment)	1.1 (1.0–1.3)	
Ultimately or rapidly fatal disease	1.1 (0.5–2.3)	
Ischemic heart disease	3.1 (1.3–7.7)	
Diabetes mellitus	1.5 (0.7–3.3)	
Malignancy	1.0 (0.4–2.5)	
Chronic renal disease	1.6 (0.5–4.7)	
Recent antibiotic therapy (< 6 months)	7.7 (3.7–16.0)	4.5 (2.0–10.1)
Origin of patient		
Home	0.8 (0.3–1.7)	
Nursing home	1.3 (0.3–4.6)	
Intrahospital transfer	2.0 (0.2–22.1)	
Presence at admission of		
Peripheral catheter	1.3 (0.3–6.6)	
Central venous catheter	4.0 (0.3–63.9)	
Urinary catheter	5.3 (0.9–32.7)	
Open skin lesions	1.9 (0.7–5.4)	

# VRE positive patients at hospital admission

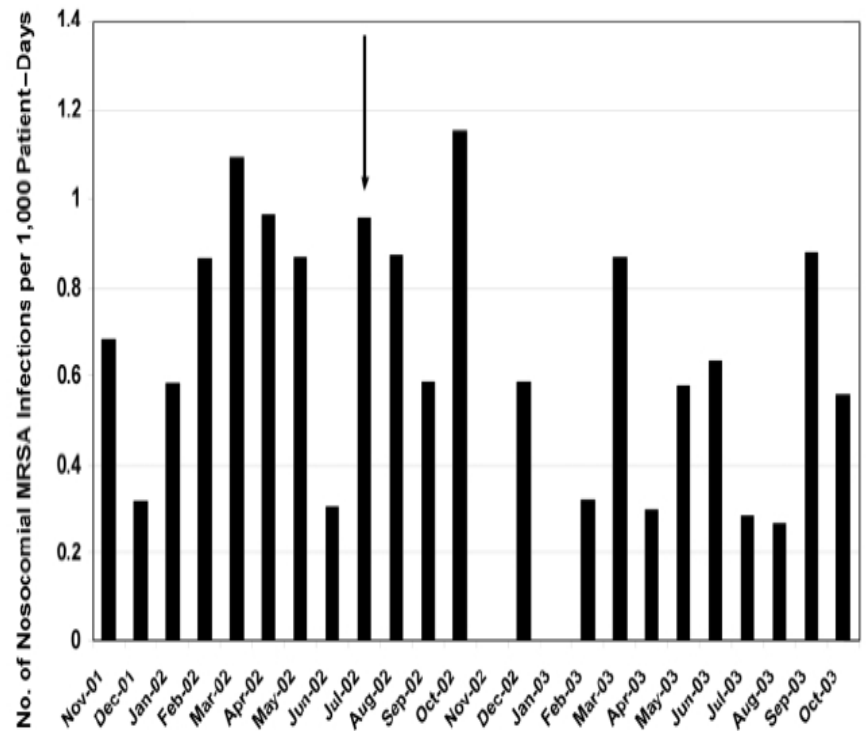
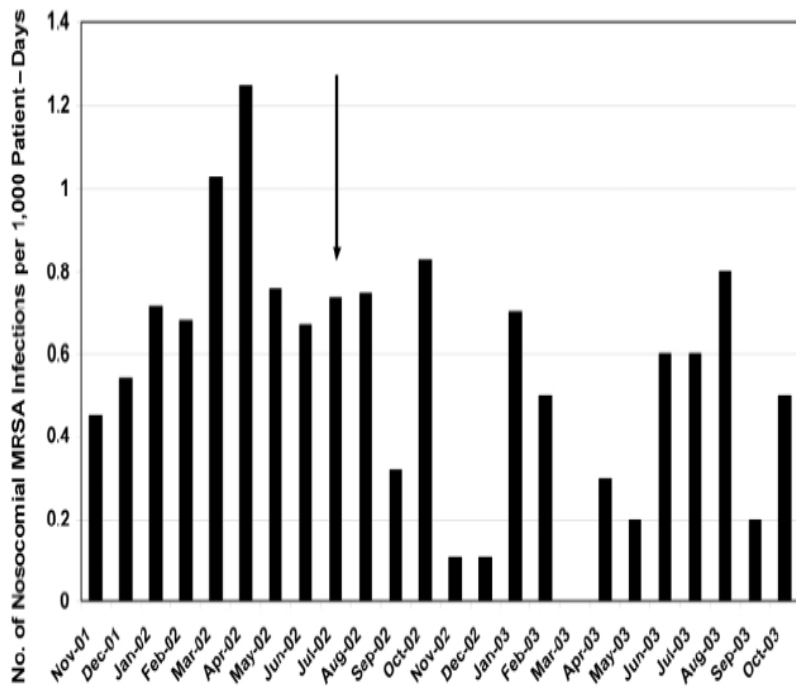
**Table 3. Risk index score for recovery of vancomycin-resistant enterococci at hospital admission, by associated risk factor.**

Risk factor	Point value
Previous recovery of MRSA <sup>a</sup>	4
Long-term hemodialysis	3
Transfer from LTCF or hospital	3
Exposure to $\geq 2$ antibiotics <sup>b</sup>	3
Previous hospitalization <sup>a</sup>	3
Age >60 years	2

## Hospital-wide

## Targeted screening:

- (1) transfers from other hospitals or LTCF;
- (2) hospitalization within 30 days;
- (3) admission to a nephrology service



# The role of isolation / cohorting

"There was evidence that intensive concerted interventions that include isolation can substantially reduce MRSA. Little evidence was found to suggest that current isolation measures recommended in the UK are ineffective, and these should continue to be applied until further research established otherwise"



Cooper, HTA, 2003

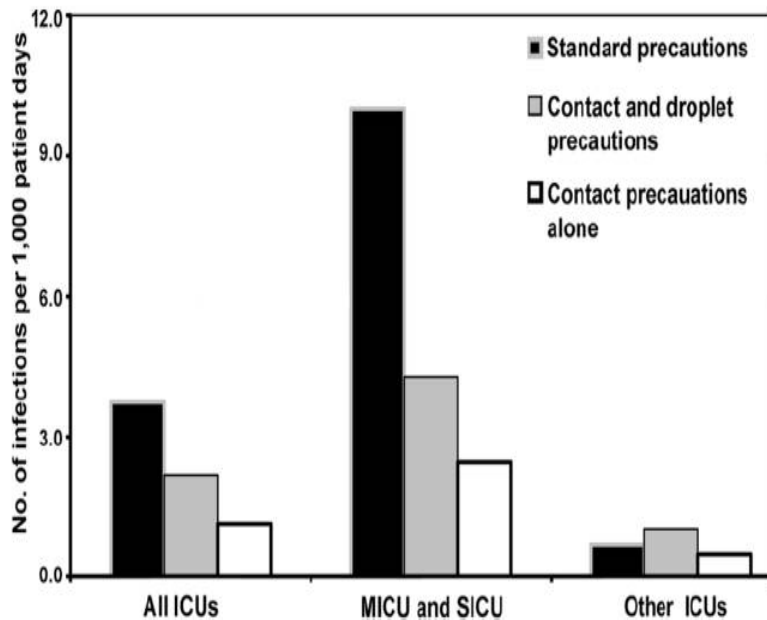


FIGURE 2. Rates of hospital-acquired methicillin-resistant *Staphylococcus aureus* infection in intensive care units (ICUs) during the use of standard precautions, use of contact and droplet precautions, and use of contact precautions alone. MICU, medical ICU; SICU, surgical ICU. See Methods for other ICUs analyzed.

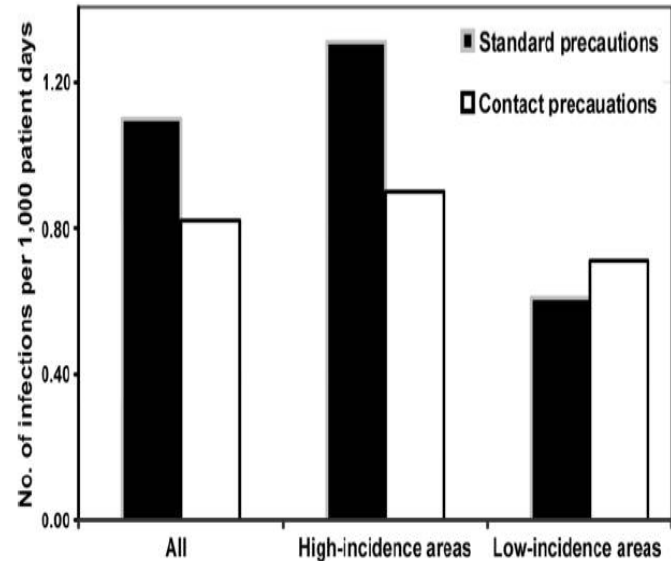
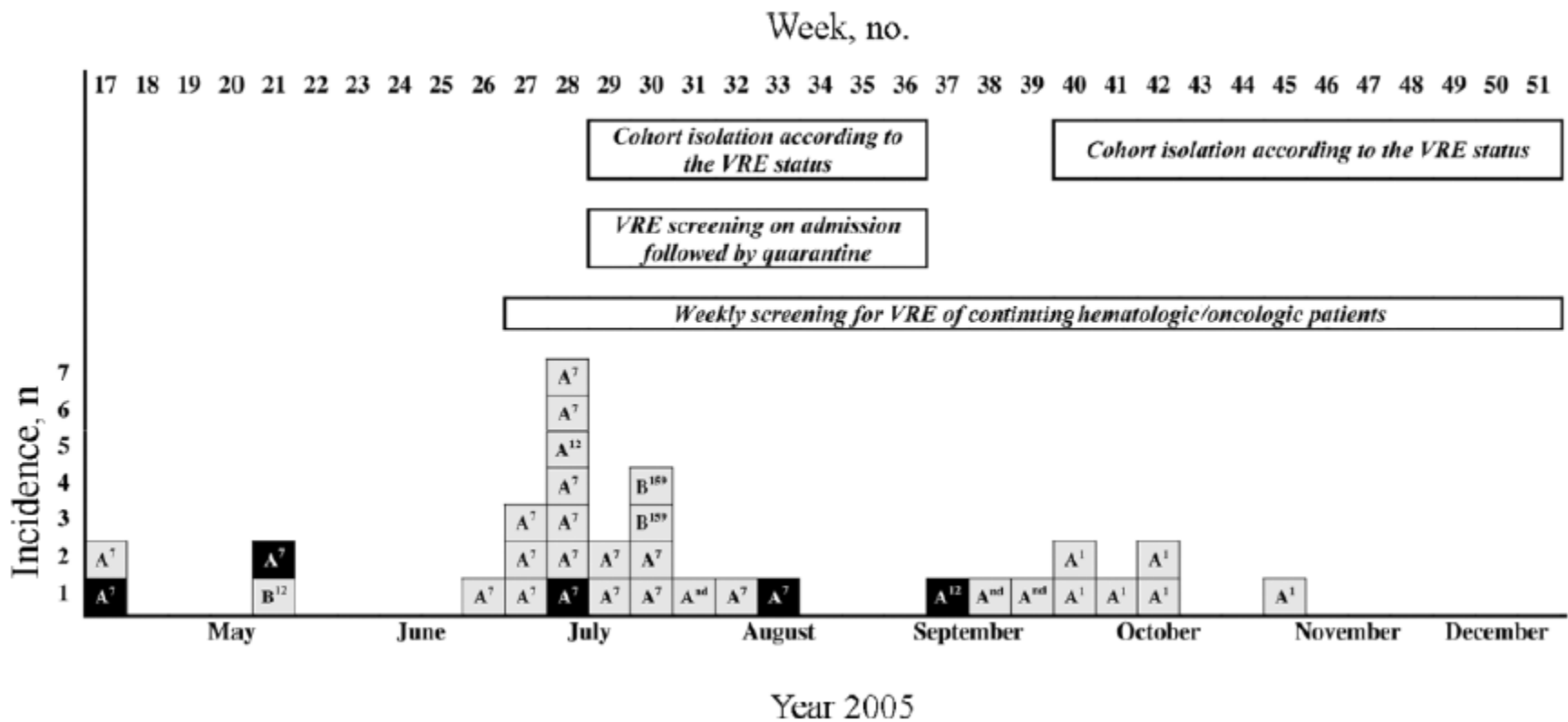


FIGURE 3. Rates of hospital-acquired methicillin-resistant *Staphylococcus aureus* infection in patient-care areas outside the intensive care units during the use of standard precautions and during the use of contact precautions alone. High incidence was defined as more than 1.0 infection per 1,000 patient-days.



**Table II** Cost of extended-spectrum  $\beta$ -lactamase (ESBL) infection control measures at The Ottawa Hospital, 2002–2005

	<i>N</i>	Unit	Newly detected ESBL cases	Readmitted known ESBL	Total CN\$ (% total cost)
No. of ESBL admissions	173		89 (52%)	84 (48%)	
Total days of contact precautions (no. of patients)	1442 (69)		1037 (44)	405 (25)	
Total days in private room (no. of patients)	2350 (134)		1294 (62)	922 (72)	
<i>Cost of private room</i>		\$200.00/day	\$258 600.00	\$211 400.00	\$470 200 (85%)
<i>Cost of contact precautions</i>					
Nursing costs:		\$30.00/h			
Time to don and remove gowns/gloves		1 min			
No. of contacts/patient/day		50			
Total nursing costs		\$25.00/ patient/day	\$25 925.0	\$10 125.00	\$36 050.00 (6.9%)
Supply costs:					
Gowns/gloves		\$0.46–\$0.14			
No. of contacts/patient/day		50			
Total supply costs		\$30.00/ patient/day	\$31 110.00	\$12 150.00	\$43 260.00 (7.8%)
<i>Infection control costs</i>		\$31.00/h			
Time spent on new ESBL case		20 min/case			
Time spent on known ESBL case		10 min/case			
Total infection control costs			\$919.67	\$434.00	\$1353.67 (0.2%)
<i>Housekeeping costs</i>					
Isolation room cleaning:					
Time (114 min @ \$24.04/h)		\$45.68			
Supplies		\$8.84			
Regular room cleaning:					
Time (62 min @ \$24.04/h)		\$24.84			
Supplies		\$7.61			
Total housekeeping costs (cost difference)		\$22.07/case	\$971.08	\$551.75	\$1522.83 (0.3%)
<i>Total cost of infection control measures</i>			\$317 525.75 (58%)	\$234 660.75 (42%)	\$552 186.50
<i>Cost of control measures/patient</i>			\$3567.71	\$2793.58	\$3191.83

# Not in favour

## Setting : ICU

- Intervention: daily micro alone
  - Intervention: admission and
  - 10-week
  - Setting
  - Surveillance of MRSA in a cross-sectional study of ICU patients.
- “At the end of the day a single randomised controlled trial, whether the results are positive or negative, is just one study, and no single epidemiological study should be considered definitive.
- One should always weight all available evidence”
- Farr, ICHE 2006
- Reporting culture results and isolating patients, as suggested by some GL, would have falsely suggested the success of such ICU policies
- to single cross-section of ICU

# Adverse effects of contact isolation

Timing of handwashing	Patients in contact isolation (n=29)	Controls (n=88)	p
Before and after encounter	2 (7%)	8 (9%)	1.0
Before only	0	4 (5%)	0.6
After only	24 (83%)	30 (34%)	<0.001
Not at all	3 (10%)	43 (49%)	<0.001

NS=not significant.

	Patients in contact isolation	Controls	p
Mean (range) room entries/h	3.9 (0-8)	7.9 (1-26)	0.06
Mean (range) contacts/h	2.1 (0-6)	4.2 (1-13)	0.03
Mean (range) duration of interaction (min)	4.5 (0.08-30)	2.8 (0.08-18)	0.6

Lancet, 1999

## Legislative mandates for use of ASC to screen for MRSA and VRE Position statement from the Joint SHEA and APIC Task Force

- Legislation aimed at controlling ARP through use of ASC to screen hospitalized pts has been introduced in at least 2 US States
  - On the grounds of lack of evidence of clinical and cost-effectiveness, routine screening of all admission to hospital is not advocated
  - --welcome private, local, state efforts to focus attention on prevention of infections due to ARP..
  - ..support stronger collaboration between state and experts...

# DECOLONISATION

The British Experience  
Since 1945

NICHOLAS J. WHITE

SEMINAR STUDIES

IN HISTORY



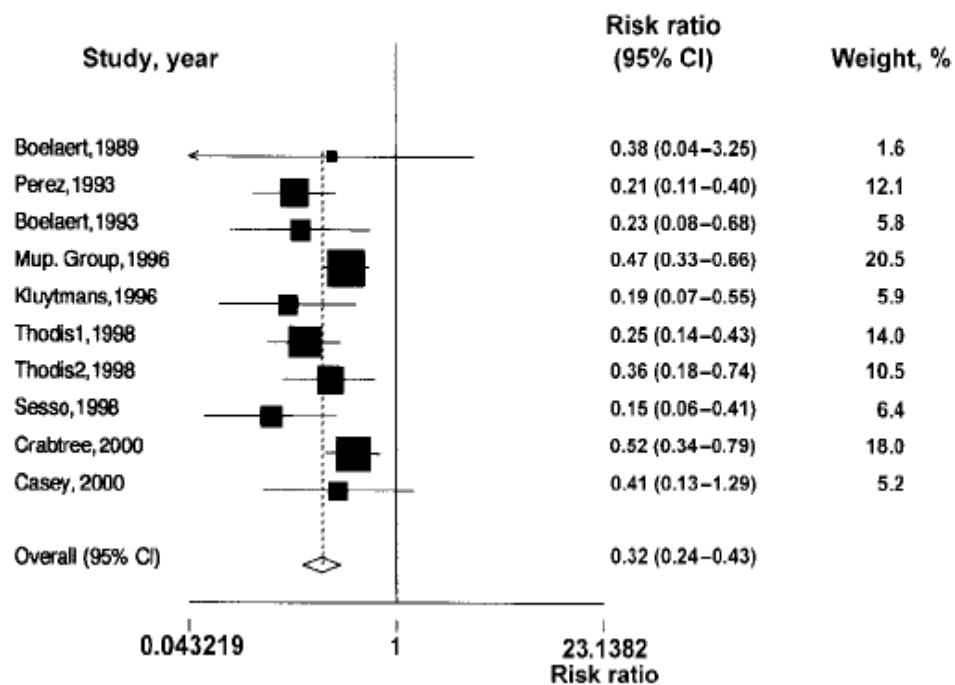
## Decolonisation

- How?
- How long?
- Who?
  
- Limits
  
- Role of HCW decolonisation
  
- Role of environmental decontamination

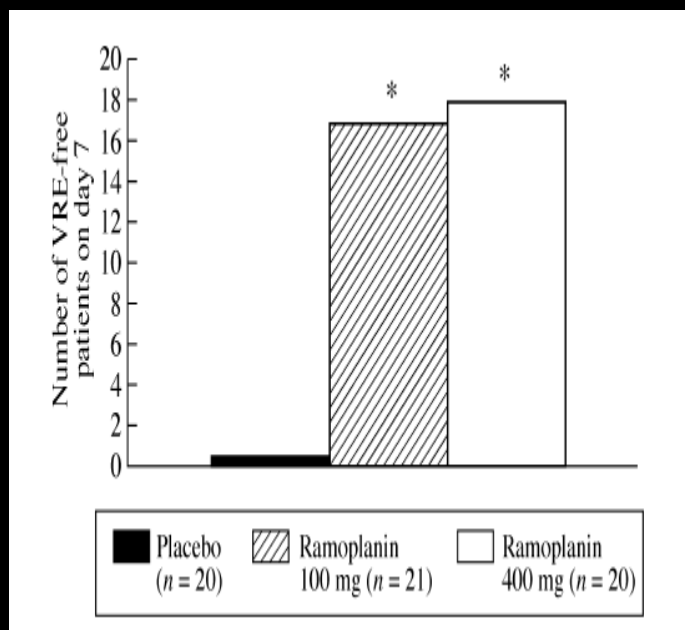
# Protocols MRSA

- **2% mupirocin ointment intranasally alone or:**
  - 2% chlorhexidine or octenidine dihydrochloride washes or 7% povidone-iodine or 2% triclosan *and* oral **rifampin and/or doxycycline** or **trimethoprim-sulfamethoxazole**
  - oral vancomycin (250 mg q6h, 2002)
  - arbekacin inhalation + trimethoprim-sulfamethoxazole (800 mg/160 mg, twice daily)
  - tea tree topical preparation
- **Paediatric (3-step-protocol):** mupirocin + oral rifampin (20 mg/Kg/die) + fusidic acid (50 mg/kg/die) + chlorhexidine for washing x 5 days; **teicoplanin** for (10 mg/kg 12 h x 3 doses then once daily for 9 days) **for persistent carriage (2007)**
- Gentian violet
- **Duration of therapy: 5-7 days**

## All patients



# VRE decolonisation Protocols



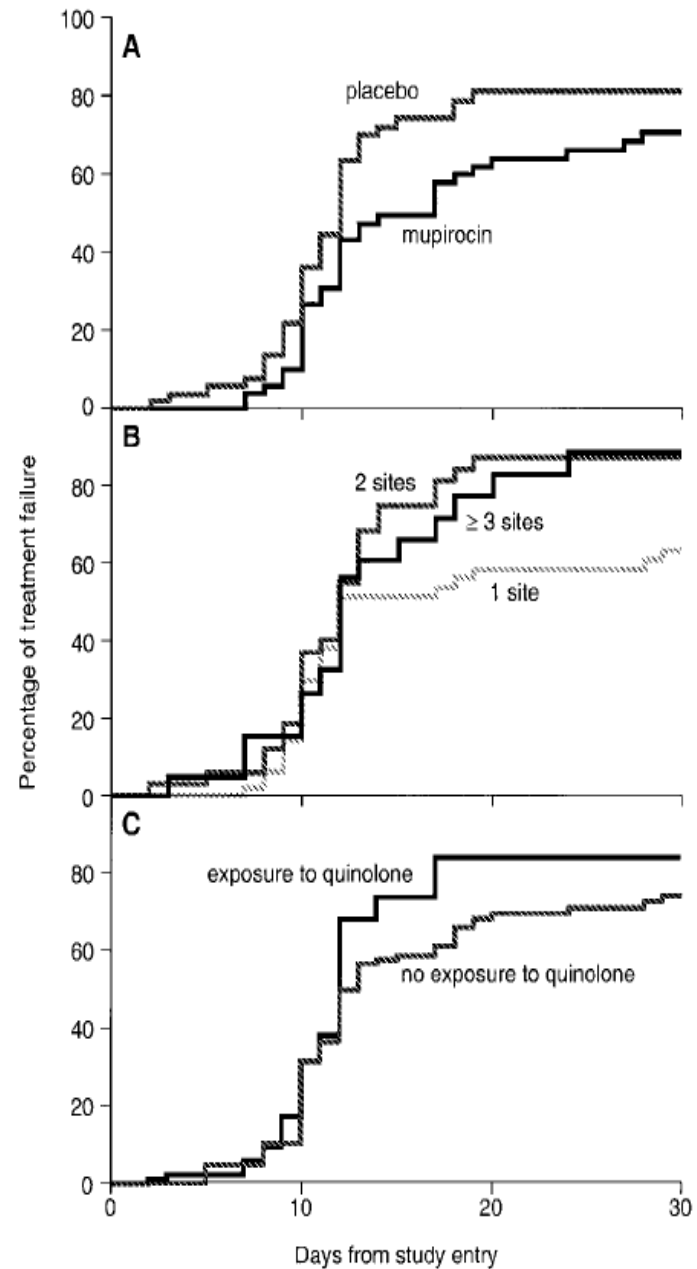
Wong, CID, 2001

- Bacitracin solution (75.000 U 4 time daily) + doxycycline x 14 days
- Bacitracin solution + oral gentamicin (80 mg) x 14 days
- Zinc bacitracin capsules
- Novobiocin plus
  - Rifampicin or tetracycline or doxycycline
- **Ramoplanin**

Kauffmann, JAC, 2003; Montecalvo, JAC, 2003

## Limits of decolonisation

- Persistent carriage
  - Multisite MRSA (> 2) and previous therapy with quinolones were associated with mupirocin failure
- Development of resistance



# Decolonisation Health care workers (HCW)

## Prevalence of MRSA

- Geographical regions
  - Eastern Europe 1.6%
  - Africa 15.5%
- Location
  - ICU 4.7%
  - General wards 6.3%
- Type of HCW
  - Nurse 8%
  - Medical 7.4%
- Type of room
  - Private / cohorting 2.4%
  - No private / no cohorting 7.7%
- Contact precautions
  - Yes 3.3%
  - No 5.6%

# Staff screening

- Controversial
- Time-consuming and costly
- Emotional implications
- Little evidence to suggest that the exclusion of MRSA-positive HCWs improves the control of MRSA
- Low / High prevalence
- Only staff members with colonised or infected hand lesions should be off work while receiving courses of clearance therapy
- Sampling sites: nose, throat, areas of abnormal or broken skin, groin/perineum
- 3 screens at weekly intervals

Simpson, Bone Joint Surg, 2007  
Kaminski, J Bone Joint Surg, 2007  
Cookson, J Clin Micr, 1989

# Rapid diagnosis of MRSA

- Costly
- Benefit may vary
- Different methods available (PNA-Fish, PCR etc)
- Techniques differ in terms of:
  - sample source (nasal only): missing 17%
  - risk of systematic errors: SCCmec types
  - technician experience

Table 2 Sensitivity, specificity, positive and negative predictive values of PCR, culture and enrichment

	PCR	Blood agar	Blood agar + enrichment	CHROMagar MRSA	CHROMagar MRSA + enrichment
Sensitivity	86.7%	40%	40%	80.0%	93.3%
Specificity	88.4%	99.4%	98.7%	100.0%	98.7%
PPV	56.5%	87.5%	77.8%	100.0%	87.5%
NPV	80.6%	95.1%	95.1%	98.1%	99.4%

PPV, positive predictive value; NPV, negative predictive value.

Rajan , J Infect, 2007

Table 1. Sensitivity and specificity of the GenoType MRSA Direct assay in comparison with culture for the detection of methicillin-resistant *Staphylococcus aureus*

Culture	GenoType MRSA Direct		Compared with culture			
	MRSA-positive	MRSA-negative	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Positive	35	2	94.59	98.73	85.37	99.57
Negative	6	465				

PPV, positive predictive value; NPV, negative predictive value.

Holfelder , CMI, 2006

# Conclusions

- Intensive promotion of alcohol-based hand rubs and behavioural change interventions represent a more cost-effective approach compared with universal screening policies.
- Rapid molecular test for MRSA screening is realistic only when combined with adequate infection control measures. No evidence supports wide use of new molecular tests for MRSA.
- Multi-institutional research is required. Advancing the use of mechanistic models to improve the interpretability and, possibly, validity, of statistical analyses of epidemiological data is important.