Effectiveness of MDRO decolonization: challenges and determinants

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Disclosures

- Speakers' bureau: bioMérieux and Pfizer
- Advisory board: Destiny Pharma, DaVolterra, bioMérieux
- Support for MDRO research activities: B.Braun, Pfizer, UniGe/HUG, European Commission

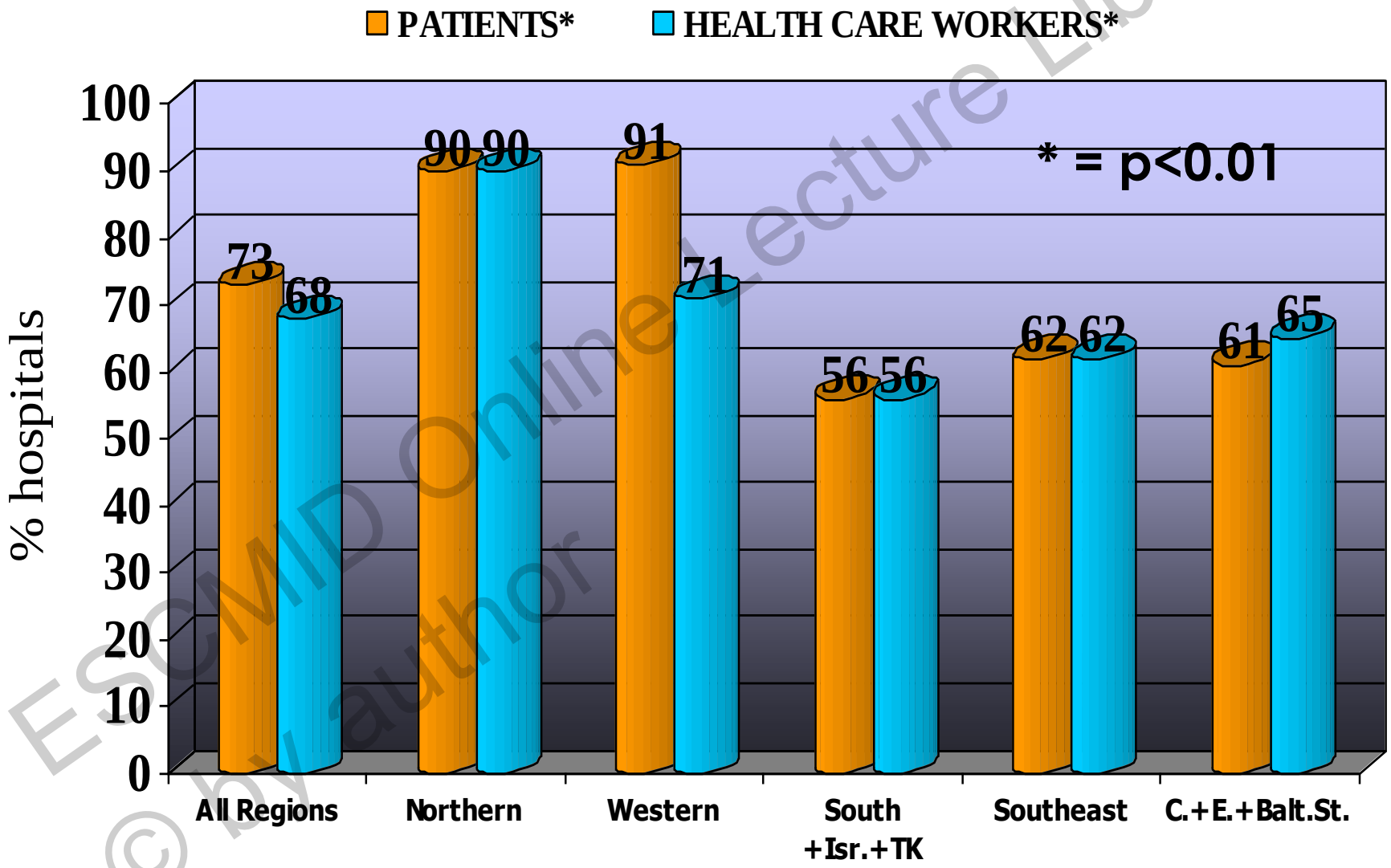
Thanks to Kalis Marimuthu for help.

Agenda

- Microbiological determinants: Resistance to antiseptic agents
- Clinical challenges
- Health-economic determinants

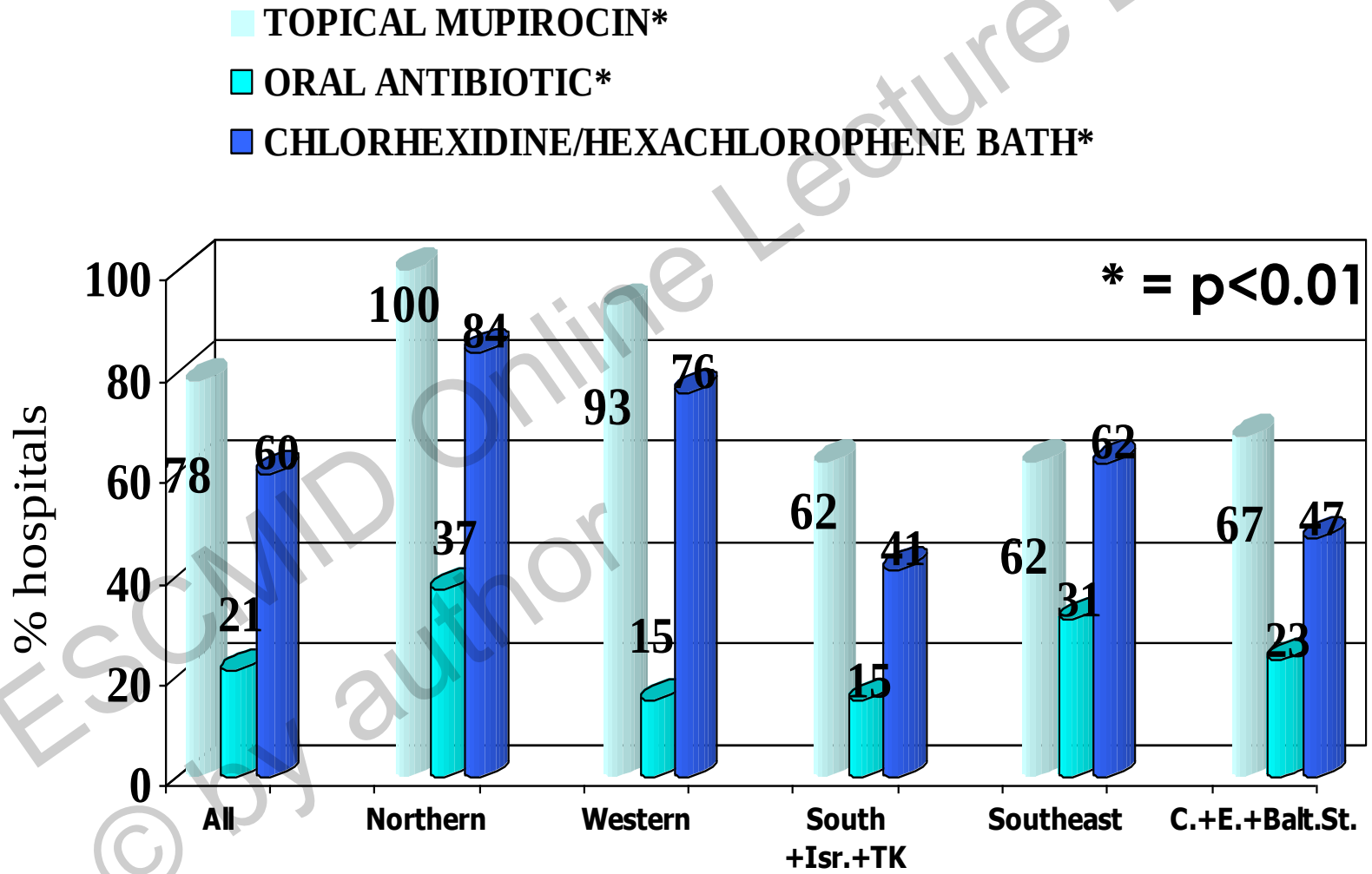
→ **Will focus on <u>MRSA</u>, but not only in the ICU setting!**

Hospital Policy for Decolonisation of MRSA Carriers by Region



MacKenzie *Clin Microbiol Infect* 2007;13:269

Decolonisation Methods for MRSA by Region



MacKenzie *Clin Microbiol Infect* 2007;13:269

Drawbacks

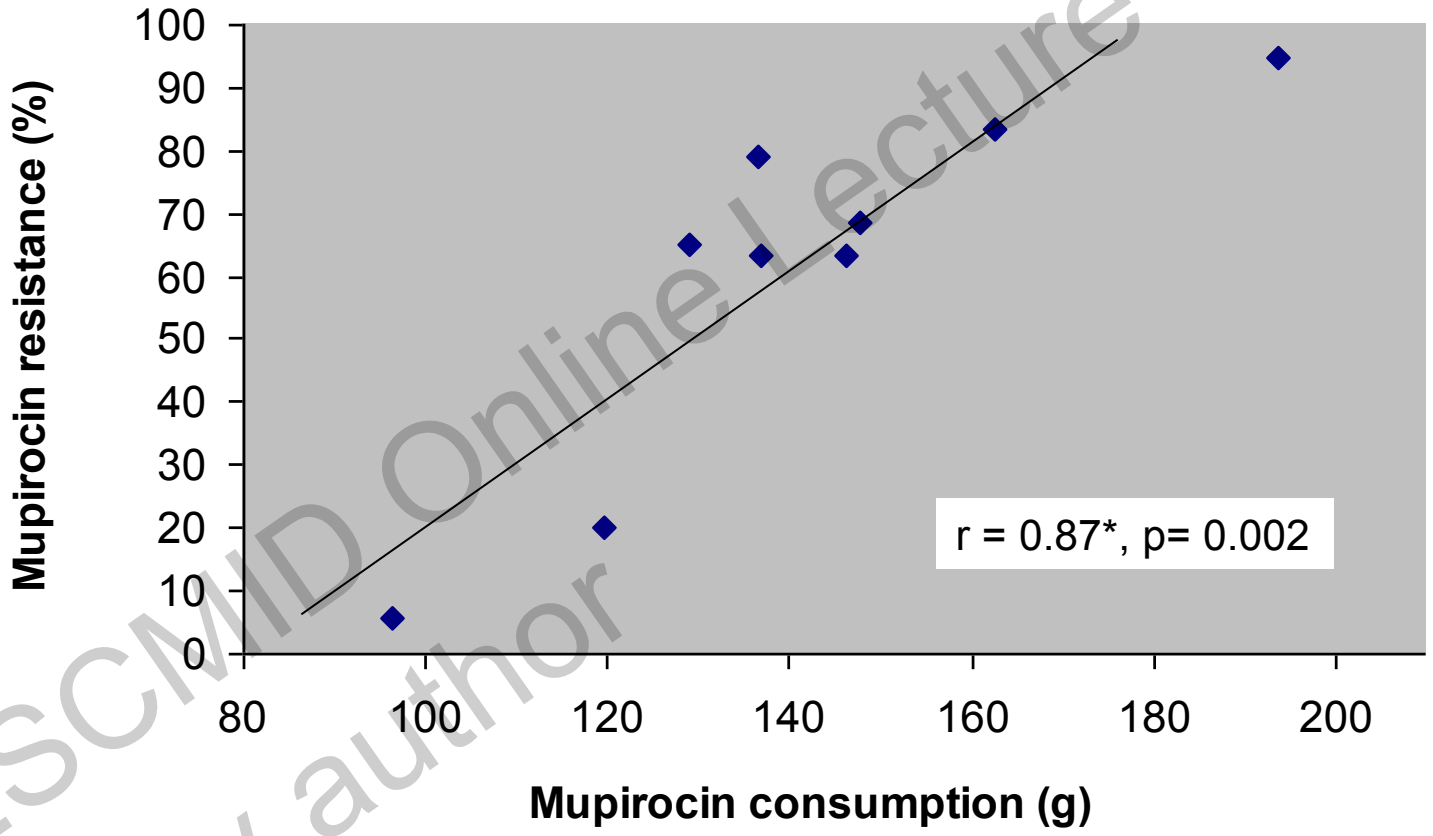
- Only a limited number of effective agents approved for topical decolonization
- Widespread use of mupirocin and chlorhexidine promotes the emergence of resistance against these agents

Efficacy and Limitation of a Chlorhexidine-Based Decolonization Strategy in Preventing Transmission of MRSA in an ICU

- Retrospective interrupted time-series study
- Reduced acquisition of endemic MRSA strain (IRR 0.3; 95% CI 0.19-0.47)
- 4-fold increased acquisition of epidemic MRSA strain
  - chlorhexidine MBCs increased 3-fold
  - Plasmid-borne gene: qacA/B

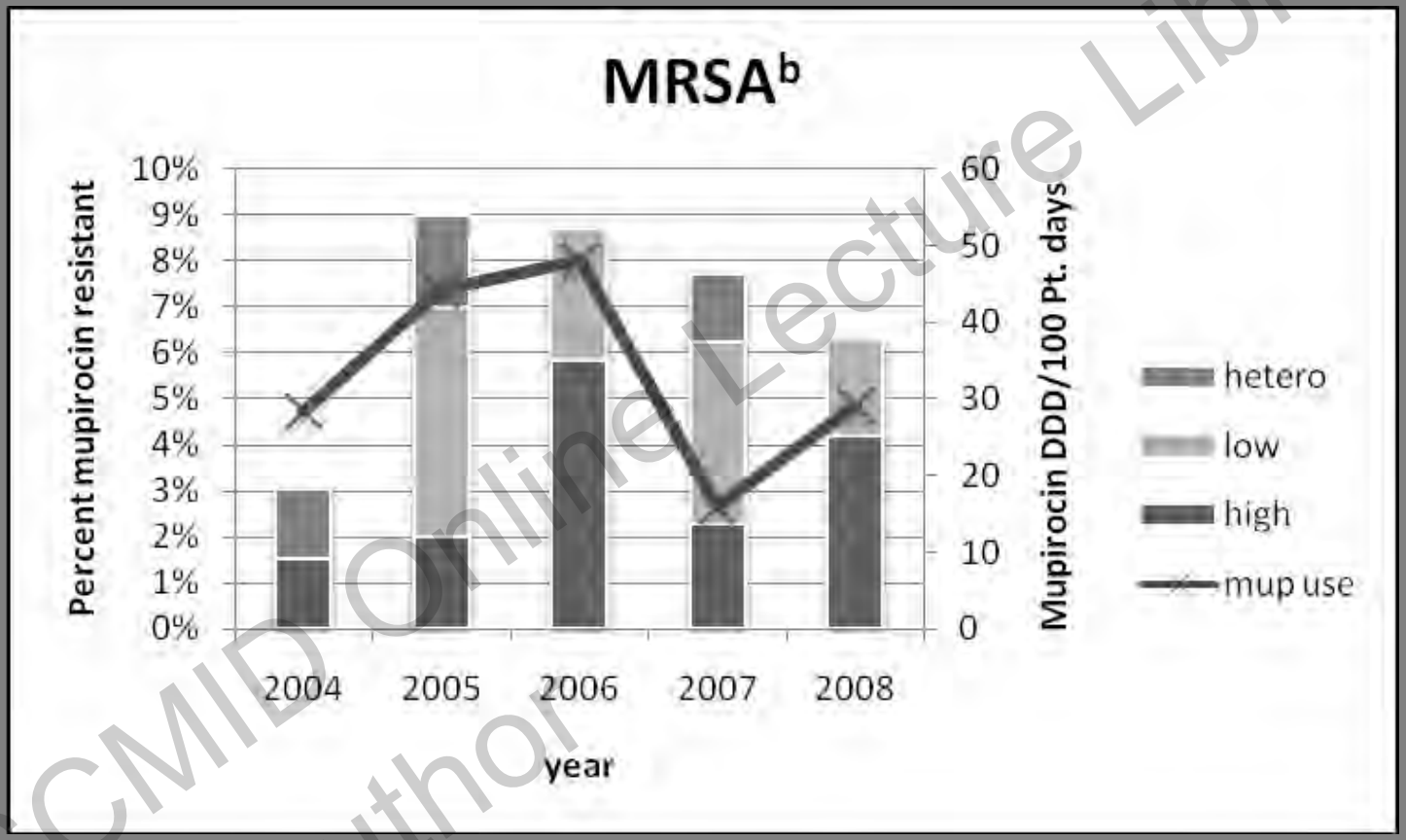
Batra R, Cooper BS, Whiteley C, et al. Clin Infect Dis 2010; 50: 210-217

Relationship between mupirocin consumption and mupirocin resistance



Lee A, et al. J Hosp Infect 2011; 77: 360-2

Mupirocin Resistance at the Providence VAMC



Increasing mupirocin use rate is not associated with significant increases in mupirocin resistance among or MRSA[b] over a 5-year period.

LaPlante KL, Gupta K, ICAAC/IDSA 2009

Study Question

Are low-level mupirocin and chlorhexidine resistance associated with decolonisation failure ?

Lee & Harbarth. Clinical Infectious Diseases 2011;52(12):1422–1430

Methods

Study design

- Retrospective case-control study

Setting

- The University of Geneva Hospitals
- Targeted MRSA screening & decolonization of carriers

Lee & Harbarth. Clin Infect Dis 2011;52(12):1422–1430

Definitions

CASES:

Patients who failed decolonization

- Persistent carriage or relapse
- ≥ 1 positive MRSA culture
  1-12 months after decolonization

CONTROLS:

Patients successfully decolonized

Lee & Harbarth. Clin Infect Dis 2011;52(12):1422–1430

Results - Resistance to Mupirocin and Chlorhexidine

Exposure	Cases n (%)	Controls n (%)	Univariate analysis OR (95% CI)	p value
Resistance combinations				
Fully sensitive	6 (8)	24 (32)	0.1 (0.007-0.37)	**<0.0001**
Mupirocin R only	1 (1)	0 (0)	…	0.32
Chlorhexidine R only	21 (28)	25 (33)	0.7 (0.3-1.6)	0.44
Resistant to both	47 (63)	26 (35)	3.2 (1.6-6.5)	**0.001**

Lee & Harbarth. Clin Infect Dis 2011;52(12):1422–1430

Independent risk factors associated with persistent MRSA colonization

	Multivariate analysis	
Risk factor	**OR (95% CI)**	**p value**
Mupirocin/chlorhexidine resistance	3.4 (1.5-7.8)	0.004
Age (per 1 year increment)	1.04 (1.02-1.1)	0.001
Prior hospitalisation (2 years)	2.4 (1.1-5.7)	0.04
Wound/pressure sore	5.7 (1.8-17.6)	0.003
MRSA-inactive antibiotics	3.1 (1.3-7.2)	0.01
Central venous catheter	5.7 (1.4-23.9)	0.02

Lee & Harbarth. Clin Infect Dis 2011;52(12):1422–1430

RCT of CHG for washing, intranasal mupirocin, and rifampin and doxycycline vs. no treatment for the eradication of MRSA colonization

- 111 patients randomized to treatment vs. 35 to no treatment
- Excellent compliance (92%: >5 d therapy)
- 74% vs. 32% eradication at 3 months

Simor et al. Clin Infect Dis 2007, 44: 178-85

Variables associated with MRSA recolonization (< 3 m)

Variable	Relative risk (95% CI)	*P*
Katz index of activities of daily living score[a]	0.45 (0.16–1.31)	.14
Presence of skin lesions	0.71 (0.27–1.87)	.48
Presence of a medical device[b]	1.56 (0.62–3.94)	.35
MRSA recovered from >1 body site	1.39 (0.53–3.70)	.50
Mupirocin-resistant MRSA at baseline	9.37 (2.76–31.87)	.0003
Randomized to received decolonization therapy[c]	0.12 (0.04–0.36)	.0002

Simor et al. Clin Infect Dis 2007, 44: 178-85

Agenda

- Microbiological determinants: Resistance
- **Clinical challenges**

Important questions…

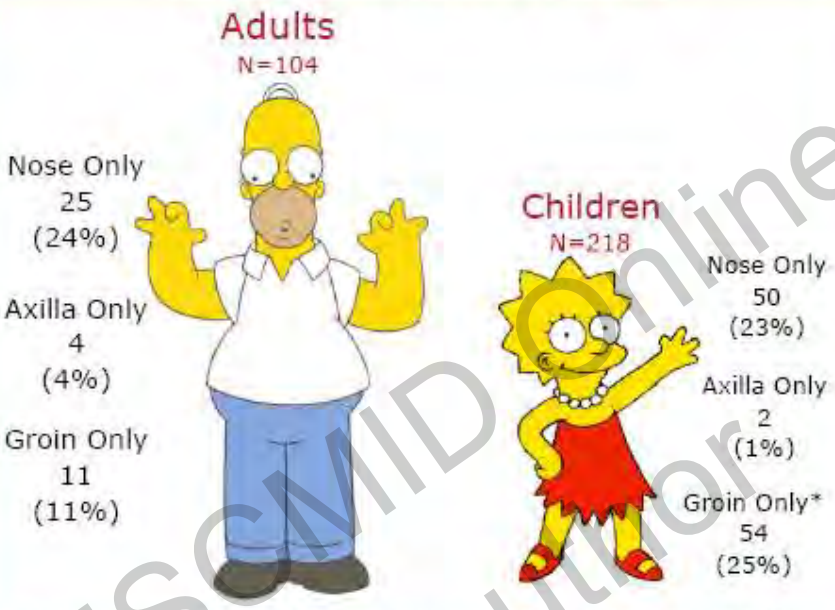
- Who should be decolonized?
  - Patient profile
- When should patients be decolonized?
- How many times?
- How should they be decolonized?
  - Regimens?
  - Duration?
  - Supervision & compliance?
  - Body sites?

Sites of Community-Acquired *Staphylococcus aureus* Colonization in Patients Presenting with Skin and Soft Tissue Infections

Stephanie A. Fritz, MD[1], Joseph M. Fritz, MD[2], Kimberly Mitchell[2], Gregory A. Storch, MD[1,2], Rachel C. Orscheln, MD[1], Brian Wessman, MD[3], Michael Mullins, MD[3], and Bernard C. Camins, MD[2]

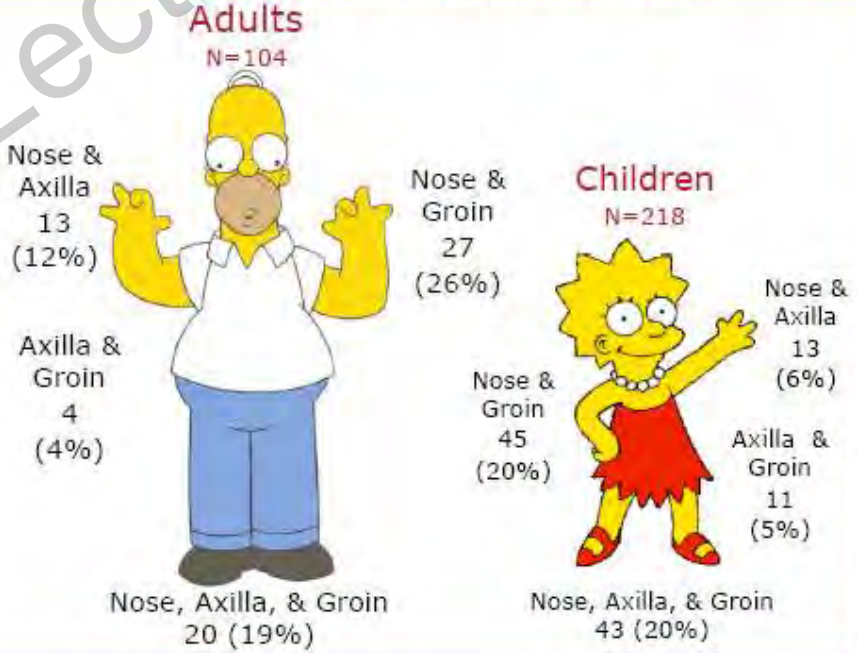
Departments of [1]Pediatrics, [2]Medicine, and [3]Emergency Medicine, Washington University School of Medicine, St. Louis, MO

Single Colonization Sites



*Children were more frequently colonized exclusively in the groin than adults (p=0.003).

Multiple Colonization Sites



ICAAC 2008
K-4075

Highly Effective Regimen for Decolonization of Methicillin-Resistant *Staphylococcus aureus* Carriers

M. Buehlmann, MD; R. Frei, MD; L. Fenner, MD; M. Dangel, MPH; U. Fluckiger, MD; A. F. Widmer, MD, MS

- Basel Univ. Hospital, period 2002-2007
- 62 patients, 2.1± 1.8 decolonization cycles
- 65% ultimately required systemic AB
- Decolonization successful:
  - 54 (87%) in the intent-to-treat analysis
  - 51 (98%) in the on-treatment analysis

➲ Buehlmann M et al. ICHE 2008; 29: 510-16

MRSA decolonization: success rate, risk factors for failure and optimal duration of follow-up

P. Kohler · A. Bregenzer-Witteck · G. Rettenmund · S. Otterbech · M. Schlegel

St. Gallen Hospital, period 2007-2009

51 patients, median follow-up: 13 months

65% decolonized without routine AB use

Decolonization unsuccessful:

- Isolation of MRSA spa-type 002 (OR 5.8)
- Colonization of the respiratory tract (OR 9.1)

➲ Kohler P et al. Infection 2013; 41: 33-40

A Holistic Approach to MRSA Eradication in Critically Ill Patients with MRSA Pneumonia

C. Wenisch, H. Laferl, M. Szell, K.H. Smolle, A. Grisold, G. Bertha, R. Krause

Table 1
MRSA-eradication protocol.

	Dosage	Duration (days)
A. Measures		
Body washing (incl. hair, groins, etc.):	Twice daily	7
Chlorhexidine Gluconate 4% w/v		
Microbiological swab cultures from nose, enoral, catheter exit site, tracheostoma exit site and culture of tracheal secretions	After end of eradication measures	4 (2, 3, 4, and 7 days after end of treatment)

Hibiscrub® (Tubifoam Limited, Knutsford, Cheshire, UK); Bactropan® (Glaxo-Smith-Kline, Vienna, Austria); Chlorhexamed® (Glaxo-Smith-Kline, Innsbruck, Austria); Zyvoxid® (Pfizer, Puurs, Belgium); Rifoldin® (Aventis, Vienna, Austria); Sterillium® (Bode Chemie, Germany)

CONCLUSION:

We conclude that in patients with MRSA pneumonia an approach using a 7-day course of intravenous linezolid plus rifampicin, intratracheal vancomycin, nasal mupirocin, cutaneous and oropharyngeal chlorhexidin plus povidone-iodine cures pneumonia and is effective for MRSA eradication.

➲ Wenisch et al. Infection 2006; 34: 148-154

J Antimicrob Chemother 2011; **66**: 2409–2417
doi:10.1093/jac/dkr243 Advance Access publication 30 June 2011

Journal of Antimicrobial Chemotherapy

Eradication of carriage with methicillin-resistant *Staphylococcus aureus*: effectiveness of a national guideline

Heidi S. M. Ammerlaan[1]*, Jan A. J. W. Kluytmans[2,3], Hanneke Berkhout[4], Anton Buiting[5], Els I. G. B. de Brauwer[6], Peterhans J. van den Broek[7], Paula van Gelderen[2], Sander (A.) C. A. P. Leenders[8], Alewijn Ott[9], Clemens Richter[10], Lodewijk Spanjaard[11], Ingrid J. B. Spijkerman[2], Frank H. van Tiel[12], G. Paul Voorn[13], Mireille W. H. Wulf[14], Jan van Zeijl[15], Annet Troelstra[1] and Marc J. M. Bonten[1,16] on behalf of the MRSA Eradication Study Group†

J Antimicrob Chemother 2011; **66**: 2418–2424
doi:10.1093/jac/dkr250 Advance Access publication 30 June 2011

Journal of Antimicrobial Chemotherapy

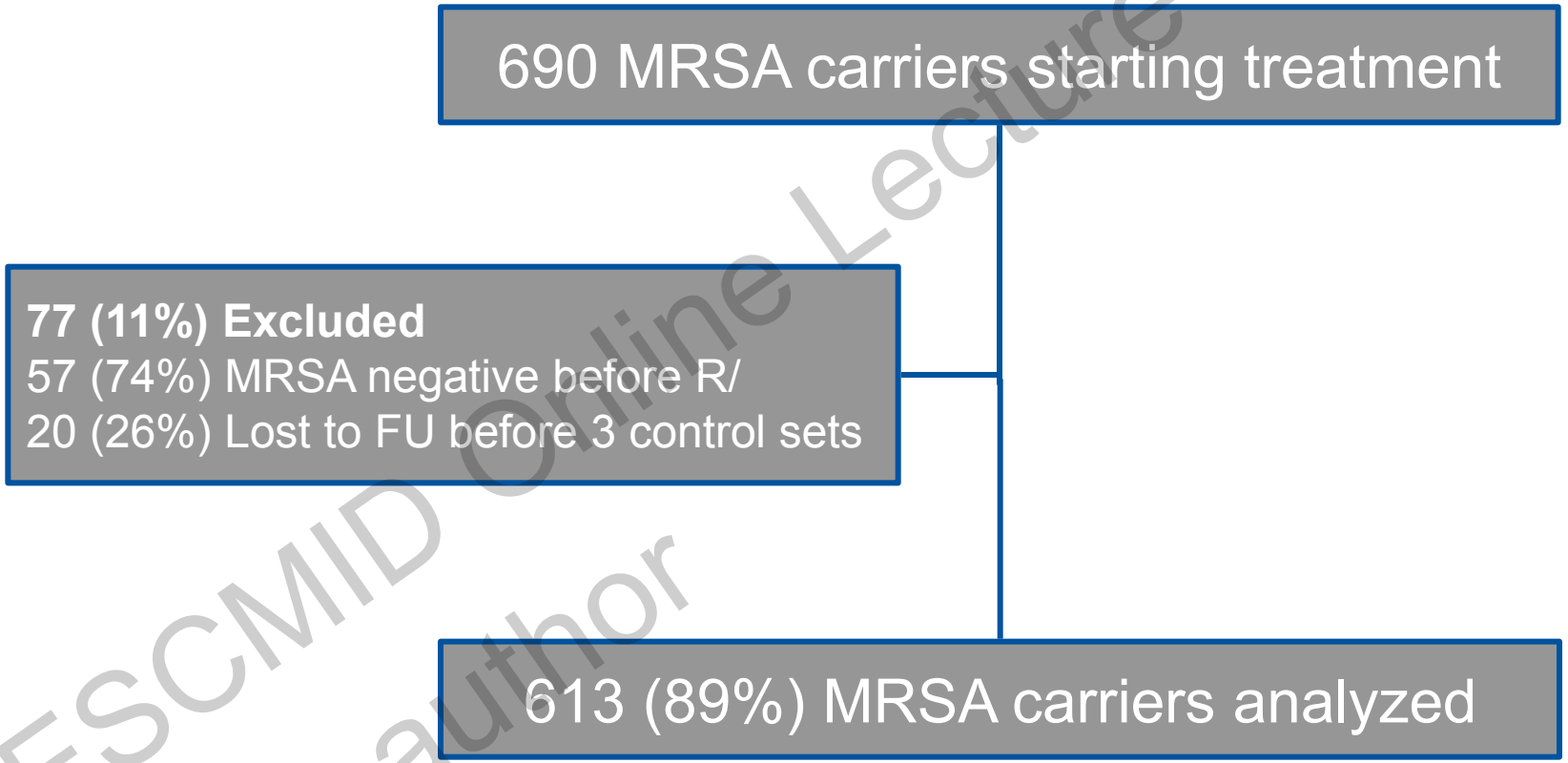
Eradication of carriage with methicillin-resistant *Staphylococcus aureus*: determinants of treatment failure

Heidi S. M. Ammerlaan[1]*, Jan A. J. W. Kluytmans[2,3], Hanneke Berkhout[4], Anton Buiting[5], Els I. G. B. de Brauwer[6], Peterhans J. van den Broek[7], Paula van Gelderen[2], Sander (A.) C. A. P. Leenders[8], Alewijn Ott[9], Clemens Richter[10], Lodewijk Spanjaard[11], Ingrid J. B. Spijkerman[2], Frank H. van Tiel[12], G. Paul Voorn[13], Mireille W. H. Wulf[14], Jan van Zeijl[15], Annet Troelstra[1] and Marc J. M. Bonten[1,16] on behalf of the MRSA Eradication Study Group†

MRSA eradication study

Patient flow diagram

Universitair Medisch Centrum Utrecht



Courtesy: H Ammerlaan & M. Bonten

MRSA eradication study

Patient flow diagram

Universitair Medisch Centrum Utrecht

613 MRSA carriers

3 months after the last treatment

26% not successfully decolonized / re-colonized

74% successfully decolonized

NA = 114

114 (24%) lost to FU

368 (97%) Decolonized ≤ 3 mnt

11 (3%) Re-colonized

Courtesy: H Ammerlaan & M. Bonten

MRSA eradication study

Multivariate analysis: treatment failure

Universitair Medisch Centrum Utrecht

	All carriers starting R1
	n = 613
	OR (95% CI)
Chronic pulmonary disease	5.00 (1.71 to 14.60)
ADL (daily life activities) dependency	2.70 (1.38 to 5.31)
Devices	1.96 (1.05 to 3.66)
Throat carriage	3.65 (2.33 to 5.72)
Perineal carriage	2.00 (1.30 to 3.09)
First decolonization treatment	
- Nasal ointment & body wash	.
- Doxycycline & rifampicin & NO & BW	0.14 (0.06 to 0.33)
- Co-trimoxazole & rifampicin & NO & BW	0.20 (0.09 to 0.46)
R1 according to the guideline	0.54 (0.36 to 0.82)

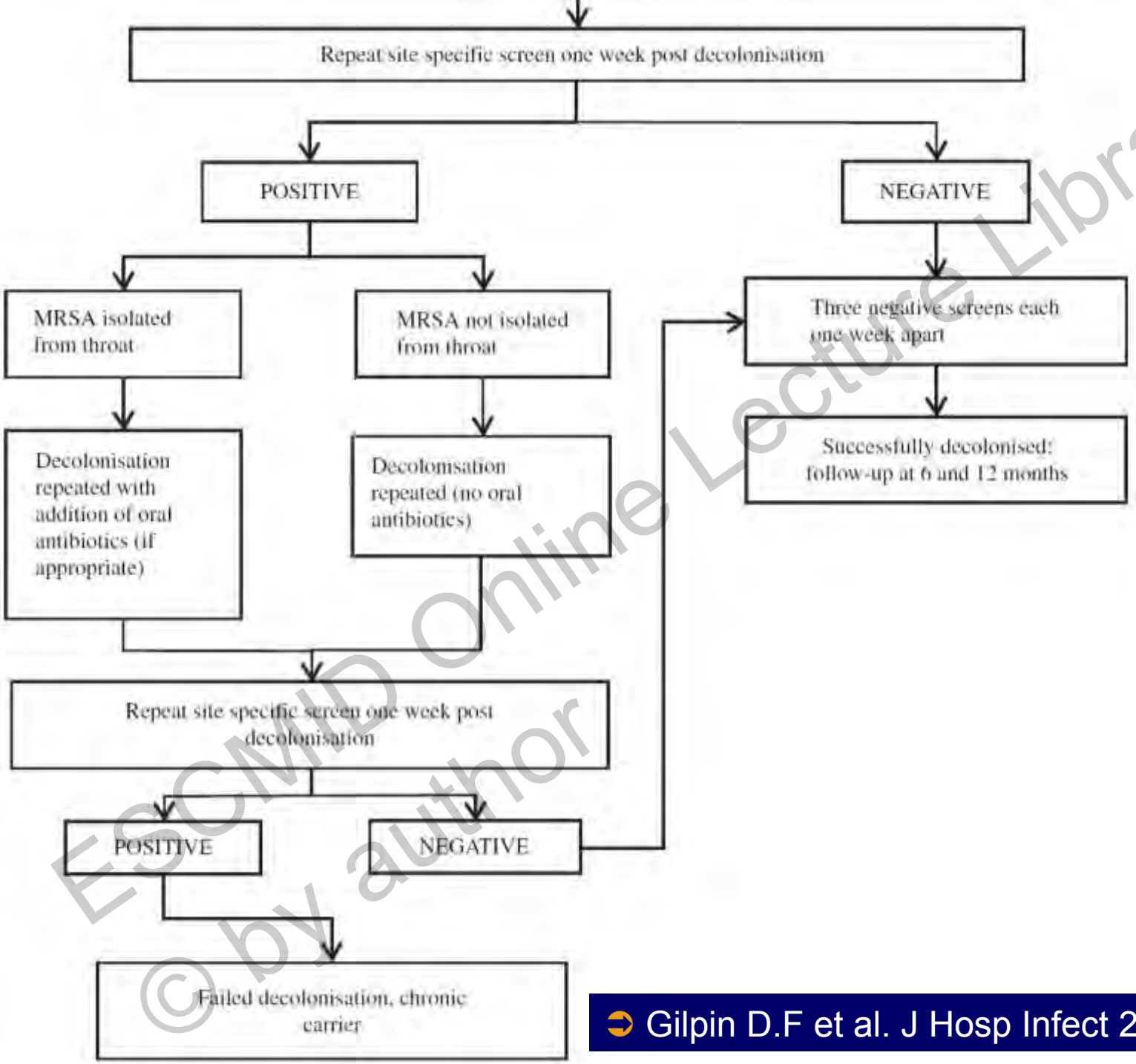
Courtesy: H Ammerlaan & M. Bonten

Efficacy of a standard meticillin-resistant *Staphylococcus aureus* decolonisation protocol in routine clinical practice

D.F. Gilpin [a,*], S. Small [b], S. Bakkshi [a], M.P. Kearney [b], C. Cardwell [c], M.M. Tunney [a]

- Belfast, Northern Ireland, period 2005-08
- 137 patients, multiple decolonization cycles, often with systemic AB
- Decolonization successful:
  - 79 (58%) were successfully decolonised.
  - Only 44/137 (32%) patients were MRSA negative 12 months later

➲ Gilpin D.F et al. J Hosp Infect 2010; 75: 93-98



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D.F. Gilpin [a,*], S. Small [b], S. Bakkshi [a], M.P. Kearney [b], C. Cardwell [c], M.M. Tunney [a]

- Decolonization less successful in patients:
  - Colonised with a mupirocin-resistant isolate (aOR: 0.08; 95% CI: 0.02–0.30)
  - With throat colonisation (0.22; 0.07–0.68)
  - Aged >80 years (0.30; 0.10–0.93)

➲ Gilpin D.F et al. J Hosp Infect 2010; 75: 93-98

Important reminder

- Success of MRSA decolonization not only depends on the choice of agents used, but also on the **quality and supervision** of the application

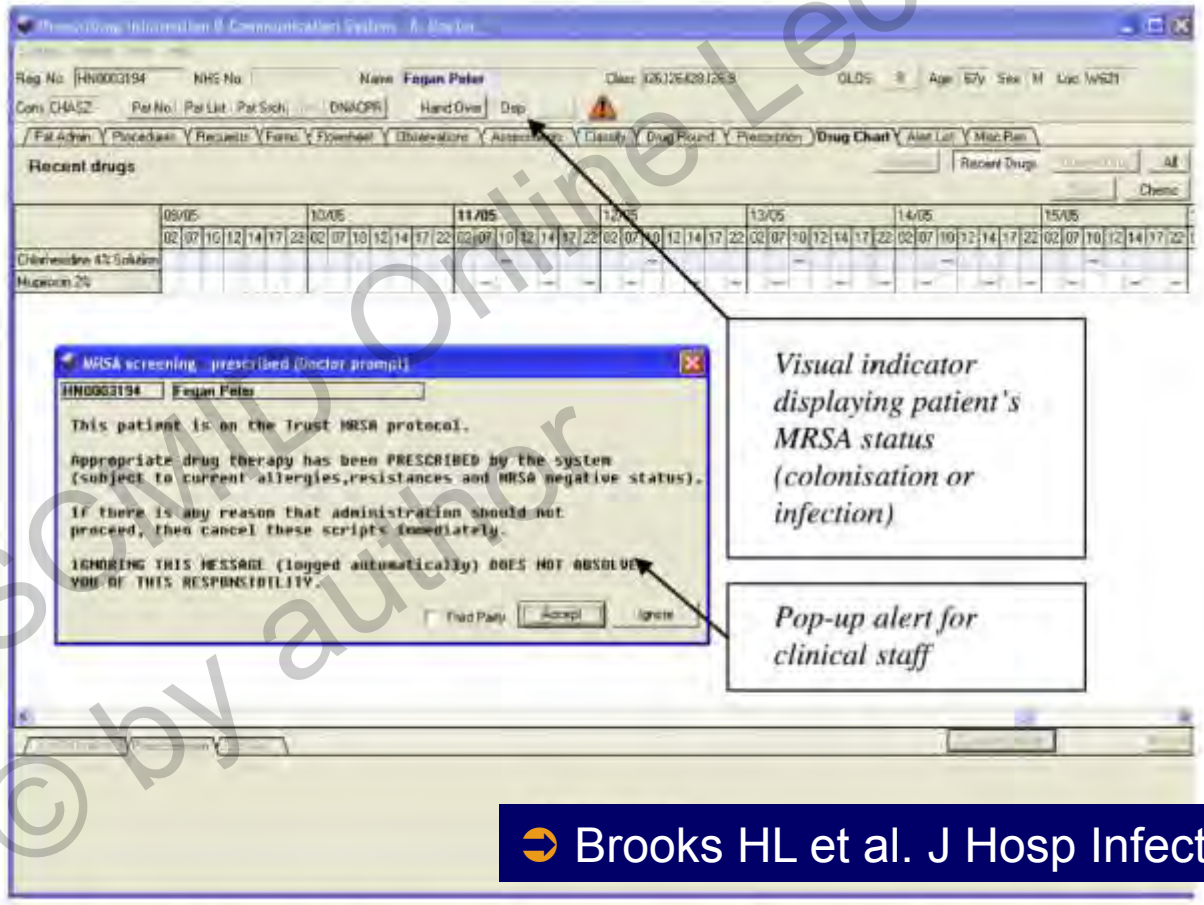
MRSA decolonisation planning tool for planning the 12-month-long case management period in hospitals and ambulatory care on the German side of the EUREGIO MRSA-net

Friedrich AW, et al. Euro Surveill. 2008;13(35): 18965.

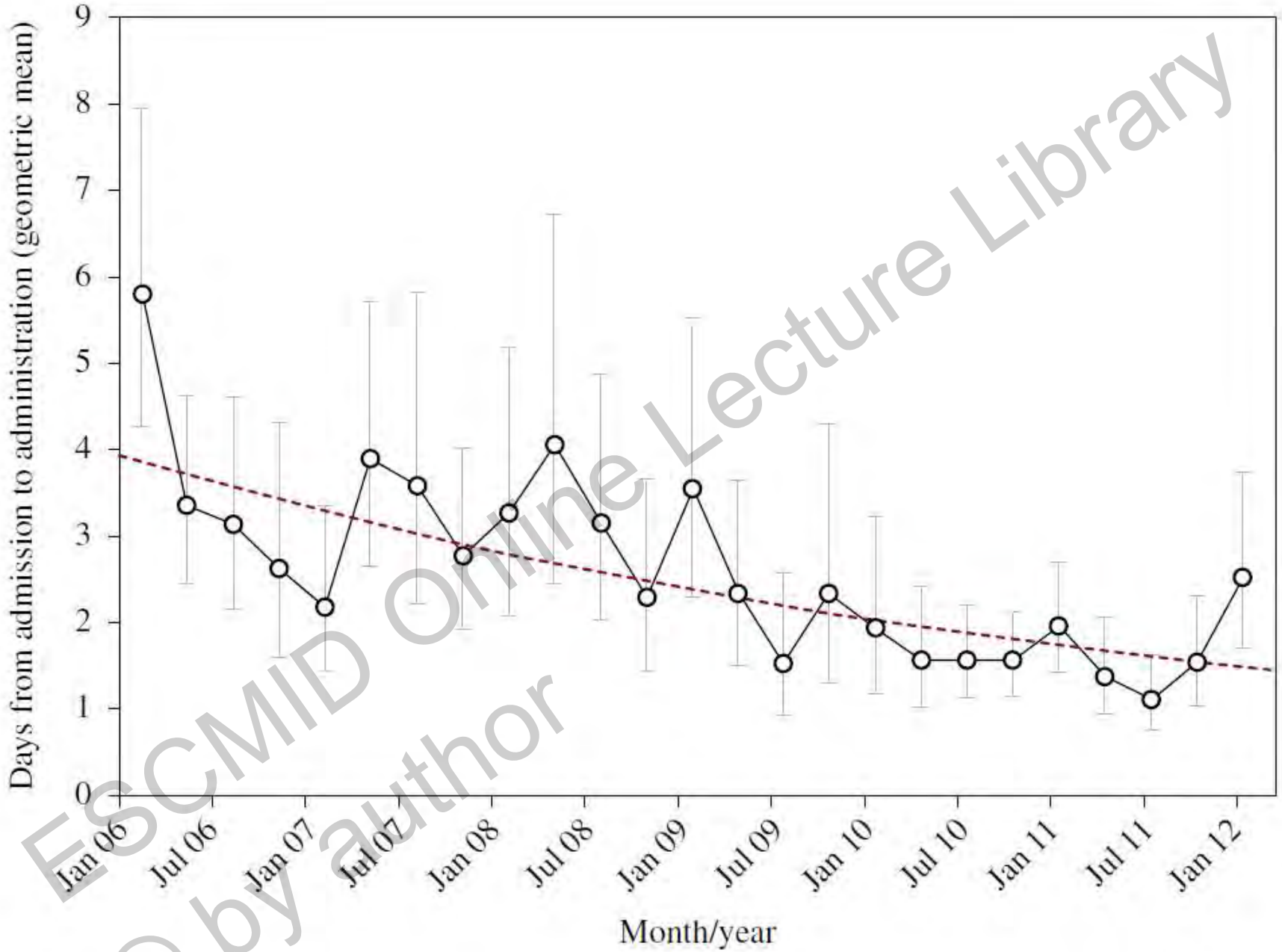
Improving the timeliness of meticillin-resistant *Staphylococcus aureus* antimicrobial decolonization therapy administration: a descriptive account☆

H.L. Brooks[a], J. Hodson[a], S.J. Richardson[a], L. Stezhka[a], M.J. Gill[a], J.J. Coleman[a,b,*]

[a] *University Hospitals Birmingham NHS Foundation Trust, Edgbaston, Birmingham, UK*
[b] *College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK*



➲ Brooks HL et al. J Hosp Infect 2014; 86: 209-15

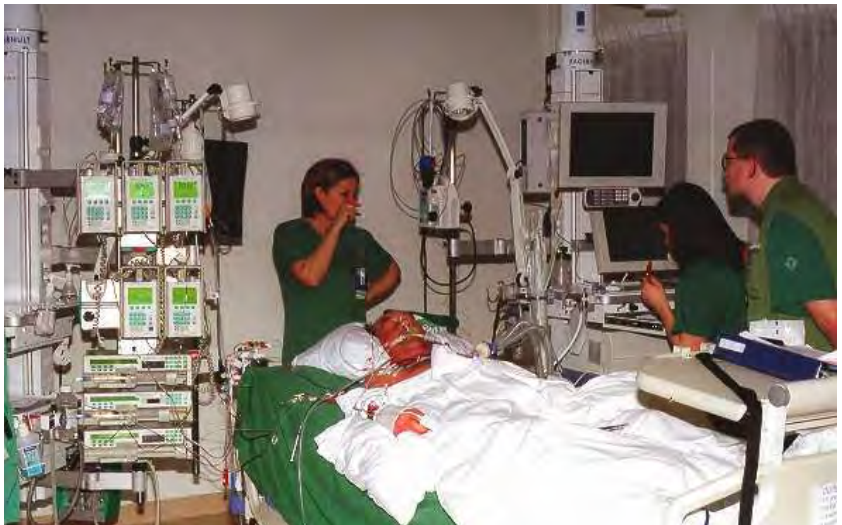


Brooks HL et al. J Hosp Infect 2014; 86: 209-15

Important reminder (II)

- Success of MRSA decolonization not only depends on the choice of agents used, but also on **patient compliance**

- Characteristics of MRSA carriers in the ICU:
  - Wounds
  - Multiple devices
  - Multiple comorbidities



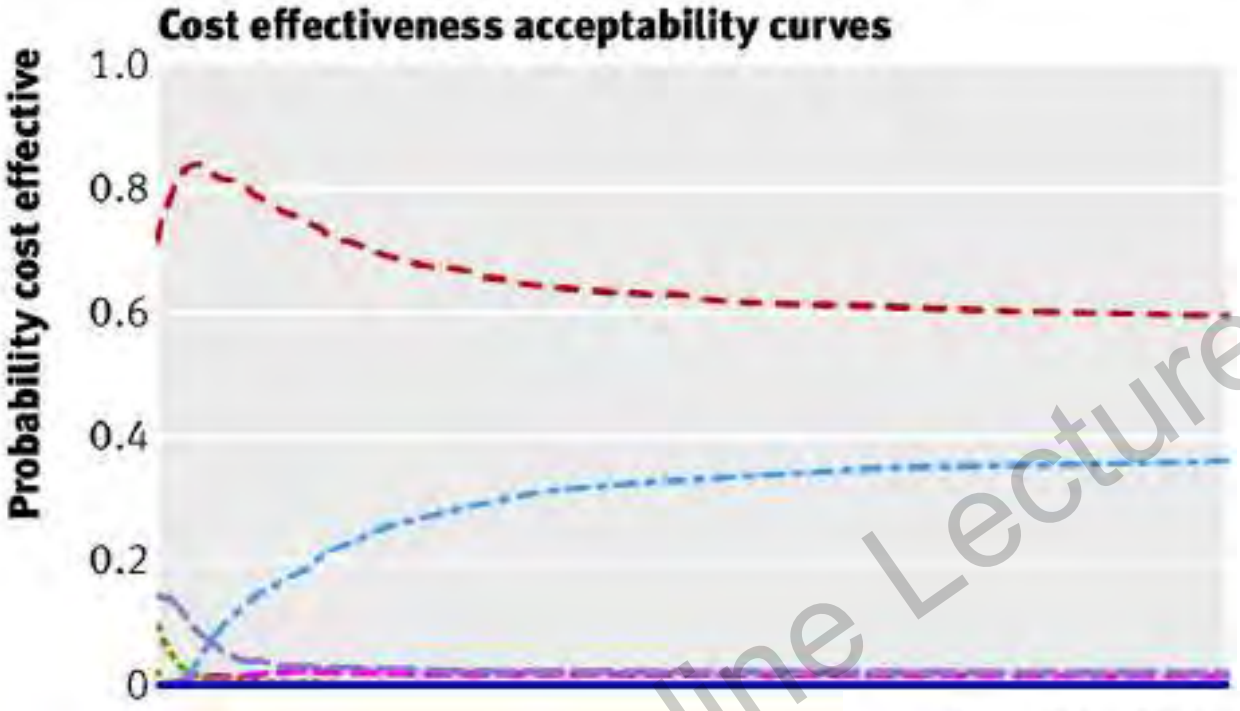
Agenda

- Microbiological determinants: Resistance
- Clinical challenges
- **Health-economic determinants**

Screening, isolation, and decolonisation strategies in the control of meticillin resistant *Staphylococcus aureus* in intensive care units: cost effectiveness evaluation

Julie V Robotham *mathematical modeller*[1], Nicholas Graves *professor of health economics*[2], Barry D Cookson *director*[3], Adrian G Barnett *associate professor*[2], Jennie A Wilson *deputy director*[4], Jonathan D Edgeworth *consultant microbiologist and honorary senior lecturer*[56], Rahul Batra *infection research fellow*[6], Brian H Cuthbertson *chief*[7], Ben S Cooper *senior research fellow*[8 9]

Conclusions MRSA control strategies that use decolonisation are likely to be cost saving in an intensive care unit setting provided resistance is lacking, and combining universal screening using polymerase chain reaction with decolonisation is likely to represent good value for money if untargeted decolonisation is considered unacceptable. In intensive



BMJ 2011;343:d5694

Conclusions (1)

1. MRSA decolonisation may be benefitial, but it is challenging and requires skills & resources
2. Resistance correlates with use of decolonising agents
3. Mupirocin and chlorhexidine resistance in MRSA is increasingly common

   → strongly associated with failure of decolonization therapy

Conclusions (2)

4. Emergence of resistance and its impact should be monitored in institutions with widespread use of these agents

5. Alternative agents may be required to effectively control MRSA in settings with high prevalence of resistance