

How to Prevent the Spread of Multiresistant Bacteria
Prof. Stephan Harbarth, Geneva University Hospitals
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How to Prevent the Spread of Multiresistant Bacteria

Prof. Stephan Harbarth
Geneva University Hospitals, Switzerland

Hosted by Dr. Sergey Eremin, MD, PhD
Pandemic and Epidemic Diseases
World Health Organization

Sponsored by
WHO Patient Safety Challenge
Clean Care is Safer Care

www.webbertraining.com March 7, 2014

Disclosures

- Advisory board: Destiny Pharma, DaVolterra, bioMérieux
- Financial support for MDRO research activities: B.Braun, Pfizer, UniGe/HUG, **European Commission**

2

Objectives

- Describe different control measures to control the transmission of MDRO
- Discuss the role of hand hygiene compared to other preventive measures
- Present recent research findings of high-quality studies
- To highlight strengths and weaknesses of the current evidence base

3

-- Control of endemic MDRO --

Identify carriers
=> Screening
=> Isolation

4

-- Control of endemic MDRO --

Identify carriers
=> Screening
=> Isolation

Eliminate carriage
=> Decolonization

5

-- Control of endemic MDRO --

Identify carriers
=> Screening
=> Isolation

Eliminate carriage
=> Decolonization

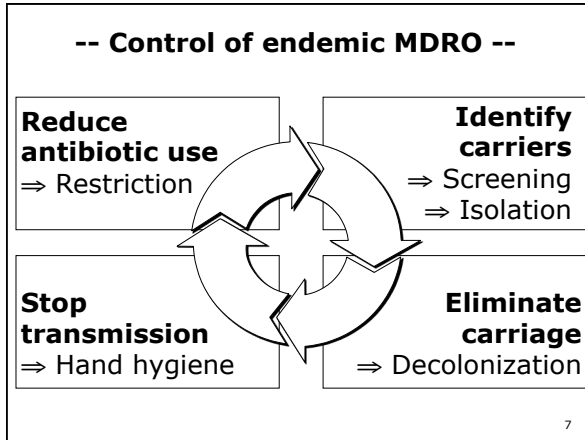
Stop transmission
=> Hand hygiene

6

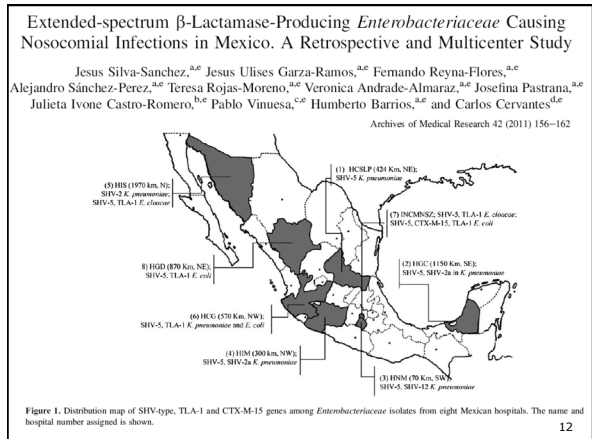
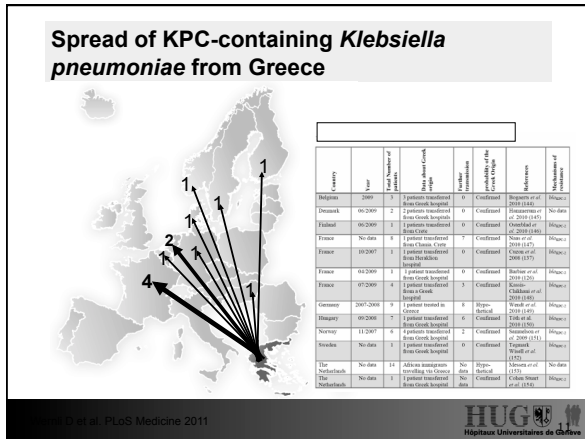
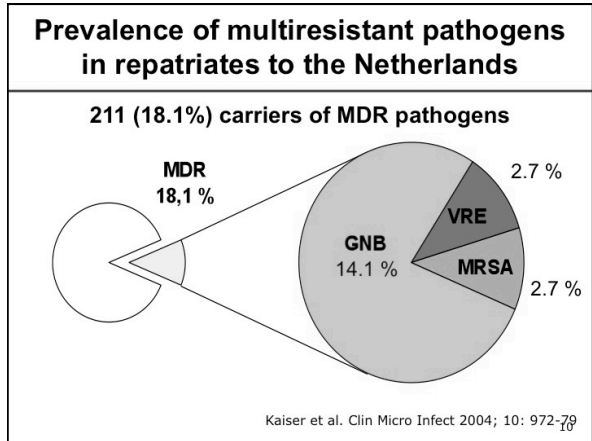
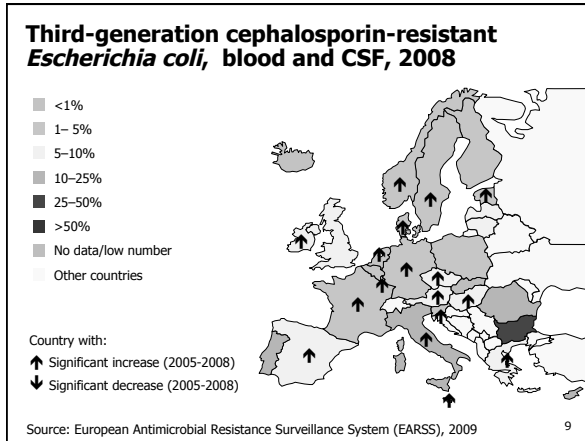
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- ## Improve infection control
- Surveillance of multi-R bacteria
 - Passive: Clinical cultures
 - Active: Surveillance swabs
 - Optional: Genotyping
- 8



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Universal Screening for Methicillin-Resistant *Staphylococcus aureus* at Hospital Admission and Nosocomial Infection in Surgical Patients

MRSA screening

Impact of rapid screening tests on acquisition of methicillin resistant *Staphylococcus aureus*: cluster randomised crossover trial

MRSA screening on admission

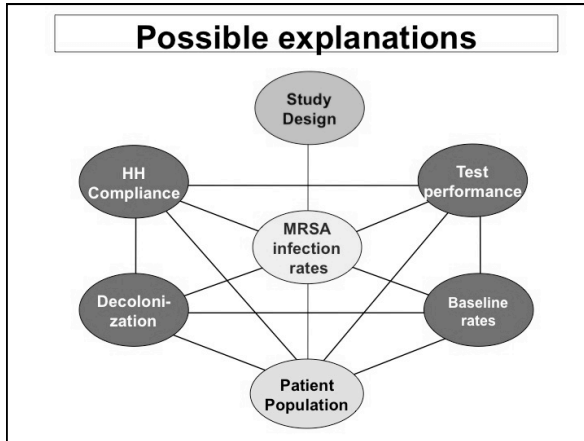
Original article
Impact of rapid screening tests on acquisition of methicillin resistant *Staphylococcus aureus*: cluster randomised crossover trial

Katherine Hardy¹, Charlotte Price², Ala Szczepura³, Savita Govaini¹, Ruth Davies⁴, Nigel Skellern⁵, Sabita Shukla⁶, Claire McHenry⁷, Andrew Bradbury⁸ and Peter W Hawkey⁹*

¹ West Midlands Public Health Laboratory, Heart of England NHS Foundation Trust; ² School of Infection and Immunity, University of Birmingham, Birmingham; ³ Warwick Medical School, University of Warwick, Coventry; ⁴ Warwick Business School, University of Warwick, Coventry; ⁵ Research & Development, Heart of England NHS Foundation Trust; and ⁶ Department of Vascular Surgery, Heart of England NHS Foundation Trust, Birmingham, UK

Authors	HUG, JAMA 2008	Robicsek, Annals 2008	Jeyaratnam, BMJ 2008	Keshtgar, Br J Surg 2008
Country	Switzerland	USA	UK	UK
Setting	Surgery	Hospital-wide	Geriatrics, oncology, surgery	Surgery
Design	Cross-over	Before-after	Cross-over	Before-after
Control group	Yes	No	Yes	No
Admission MRSA prevalence	5.1%	6.3%	6.7%	4.5%
CONCLUSION	Screening did not reduce MRSA infections	Admission screening reduced MRSA disease	Universal MRSA screening is not recommended	MRSA screening reduced MRSA BSI

Harbarth S et al. J Am Coll Surg 2008



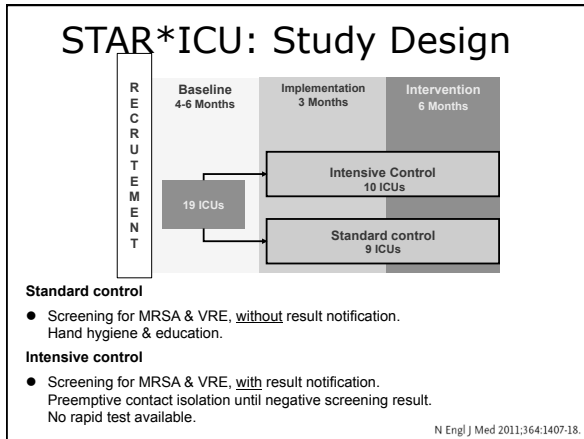
Results of the STAR*ICU Trial

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

W. Charles Huskins, MD, MSc
Mayo Clinic College of Medicine, Rochester, MN

conducted by the
Bacteriology and Mycology Study Group (BAMSG)
19 US academic medical centers

N Engl J Med 2011;364:1407-18.



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Possible reasons for failure

- **Central laboratory facility**
 - No rapid testing available
- **No intensive search & destroy**
 - No uniform decontamination approach
 - No environmental control
 - No HCW screening

N Engl J Med 2011;364:1407-18.

Possible reasons for failure (2)

- **High rates of MRSA & VRE acquisition in both arms**
 - Antibiotic misuse and overuse?
- **Universal gloving policy:**
 - In intervention ICUs, health care providers used clean gloves, gowns, and hand hygiene less frequently than required for contacts with patients assigned to barrier precautions

N Engl J Med 2011;364:1407-18.

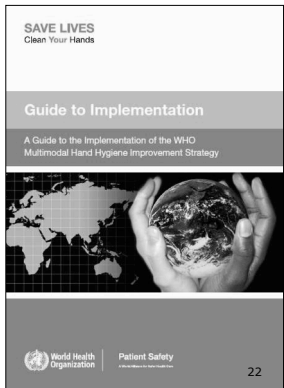
Improve infection control

- Surveillance
- Promote and improve hand hygiene

21

Implementation tools: Key tools

- Guide to Implementation of the WHO Multimodal Hand Hygiene Improvement Strategy
- Template Action Plan



SAVE LIVES
Clean Your Hands

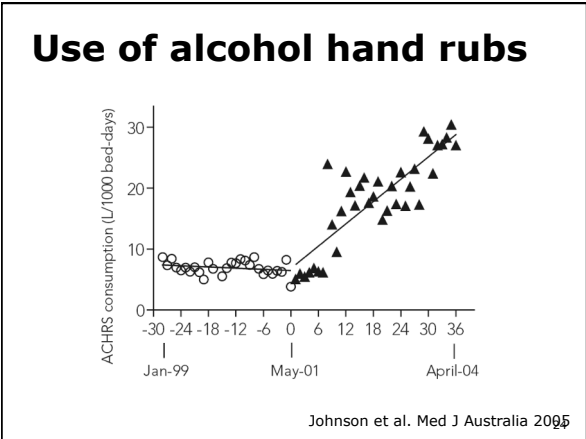
Guide to Implementation
A Guide to the Implementation of the WHO Multimodal Hand Hygiene Improvement Strategy

World Health Organization Patient Safety

22

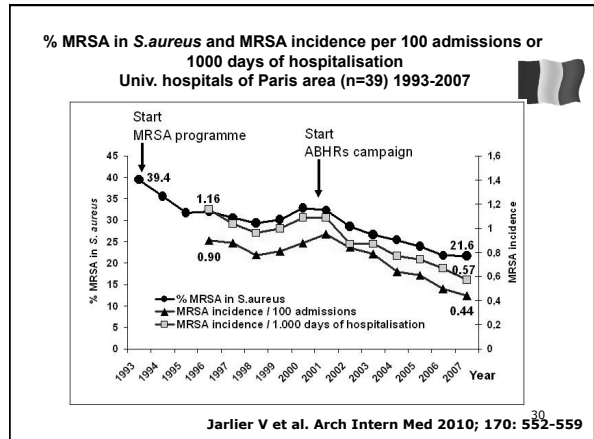
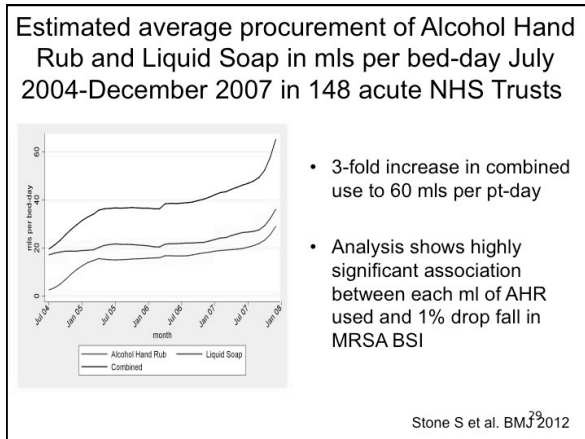
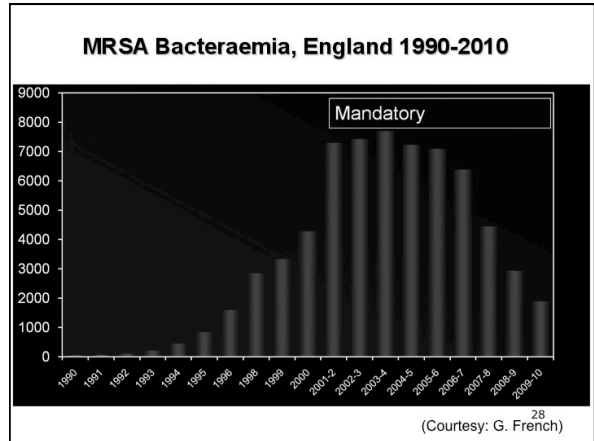
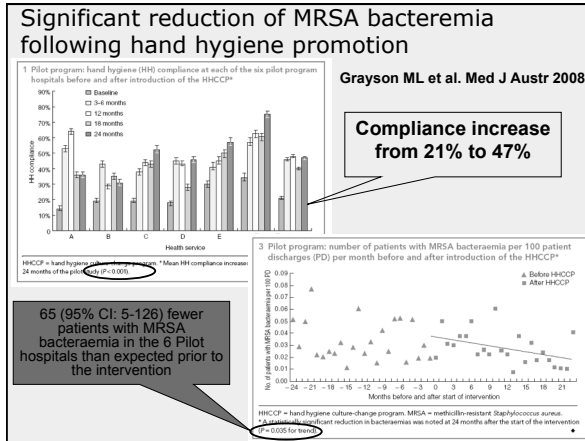
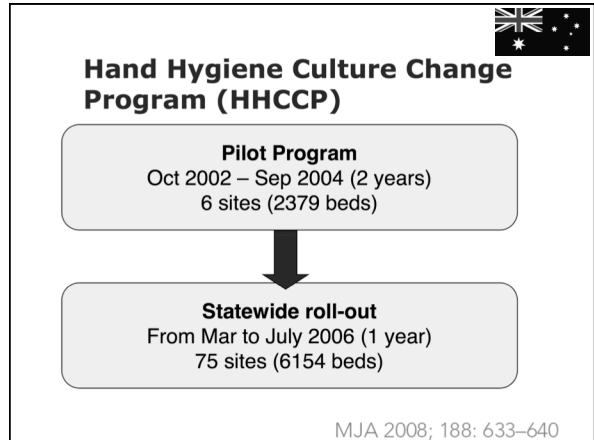
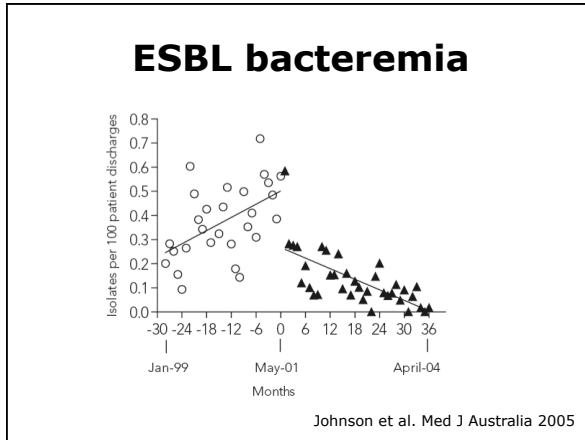
The 5 core components of the WHO Multimodal Hand Hygiene Improvement Strategy

1. System change
 - Alcohol-based handrub at point of care
 - Access to safe, continuous water supply, soap and towels
2. Training and Education
3. Observation and feedback
4. Reminders in the hospital
5. Hospital safety climate



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ARPAC
Antibiotic Resistance Prevention and Control

Alcohol-Handrub Policy Predicts Low Hospital MRSA Rate

- Linear regression modelling of general infection control policies to predict local MRSA rate
- adjusted for antibiotic consumption, case-mix, hospital size and teaching status:

- Alcohol-based hand rubs (mean difference -10.3 % MRSA rate; $p=0.005$)

MacKenzie *Clin Microbiol Infect* 2007;13:269

Downloaded from bmjopen.bmj.com on September 20, 2013 - Published by group.bmj.com

Open Access Research

BMJ **open**

Comparison of strategies to reduce meticillin-resistant *Staphylococcus aureus* rates in surgical patients: a controlled multicentre intervention trial

Andie S Lee,^{1,2} Ben S Cooper,^{3,4} Sutbhi Malhotra-Kumar,⁵ Annie Chalfine,⁶ George L Daikos,⁷ Carolina Fankhauser,⁸ Biljana Carevic,⁹ Sebastian Lemmen,⁹ José Antonio Martínez,¹⁰ Cristina Masuet-Aumatell,¹¹ Angelo Pan,¹² Gabby Phillips,¹³ Bina Rubnovitch,¹⁴ Herman Goossens,⁵ Christian Brun-Buisson,¹⁵ Stephan Harbarth,¹ for the MOSAR WP4 Study Group

Lee AS et al. (2013). *BMJ Open*

32 mosar

Study Design

MOSAR surgery study

Prospective, controlled, multicentre, intervention
March 2008 to July 2010

33 Collection of data regarding MRSA rates and secondary outcomes

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Methods

Setting and Participants

33 surgical wards
10 hospitals
9 countries

- Serbia
- France
- Spain
- Italy
- Greece
- Scotland
- Israel
- Germany
- Switzerland

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Results

Overall Hand Hygiene Compliance

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Results

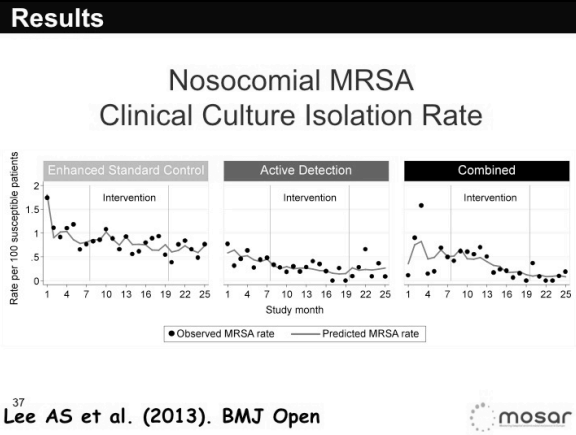
MRSA Screening on Admission

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MRSA Clinical Culture Isolation Rate

Variable	aIRR*	95% CI	P Value
Baseline Phase			
Trend	0.97	0.89-1.06	0.55
Intervention Phase			
Change in level			
Enhanced Standard Control	1.44	0.96-2.15	0.076
Comparing study arms			
Enhanced Standard Control	1.00	-	-
MRSA screening	0.61	0.37-1.00	0.048
Combined	1.13	0.71-1.79	0.60
Change in trend			
Enhanced Standard Control	0.99	0.91-1.09	0.88
Comparing study arms			
Enhanced Standard Control	1.00	-	-
MRSA screening	0.95	0.90-1.01	0.076
Combined	0.88	0.82-0.95	0.001
Washout Phase			
Change in level	1.90	0.91-3.95	0.087
Change in trend	1.02	0.91-1.15	0.74

38
*aIRR = Adjusted incidence rate ratio

MRSA Clinical Culture Isolation Rate Clean Surgery Wards

- Change in trend in MRSA rates
 - Screening and decolonisation arm
aIRR 0.85, 95% CI 0.74-0.97, p=0.02
 - Combined arm
aIRR 0.82, 95% CI 0.71-0.95, p=0.01

39
Lee AS et al. (2013). BMJ Open

mosar

Discussion

Conclusions

1. Compared to enhanced standard control measures with hand hygiene promotion, MRSA screening was more effective at initially reducing MRSA clinical culture isolation rates in surgical units
2. Combining both strategies resulted in more marked reduction in MRSA rates over time
3. The effect of screening and decolonisation on MRSA rates was more pronounced in clean surgery wards
4. These findings are generalisable to a variety of healthcare settings

40
Lee AS et al. (2013). BMJ Open

mosar

Improve infection control

- Surveillance
- Promote and improve hand hygiene
- Use cohorting and isolation precautions (gowns, gloves, signs)

41

ISOLATION & COHORTING FOR MRSA

Systematic review with 6 high-quality studies

- **Isolation wards**
 - 1 effective, 1 ineffective, 1 transient
- **Single room isolation**
 - 1 transient hospital wide
- **Cohorting**
 - 1 effective hospital wide
- **Cohorting & Single Room**
 - 1 effective in paediatric ICU

Cooper BS, Stone SP, Kibbler CC, et al. Systematic review of isolation policies in the management of MRSA. Health Technol Assess 2003;7:1-484

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Control of ESBL-*Klebsiella* spp

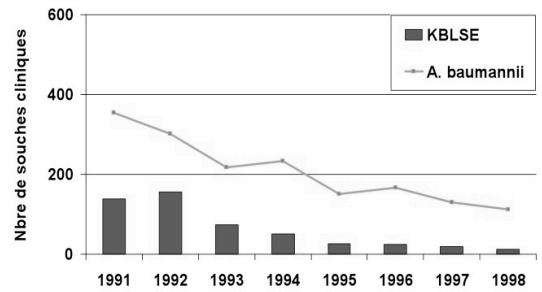
- Modes of patient-to-patient transmission include transmission via colonisation of the inanimate environment, the hands of healthcare personnel, and of medical equipment¹
- **ALL THESE MODES CAN BE DECREASED BY ISOLATION**

1. Falagas ME, Journal of Hospital Infection 2009;73: 345

43

Effect of Contact Isolation

Paris, GH Bichat - Claude Bernard

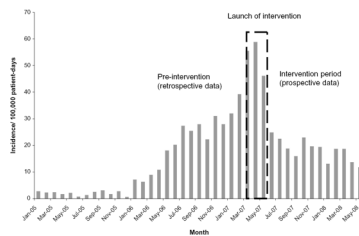


Courtesy: JC Lucet

Containment of a Country-wide Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* in Israeli Hospitals via a Nationally Implemented Intervention

Clinical Infectious Diseases 2011;52(7):1-8

Mitchell J. Schwaber,¹ Boaz Lev,² Avi Israeli,² Ester Solter,¹ Gill Smolian,¹ Bina Rubinovitch,¹ Itamar Shalit,¹ Yehuda Carmeli,¹ and the Israel Carbapenem-Resistant Enterobacteriaceae Working Group³



45

CDC recommendation

- **In acute care settings, implement contact precautions for all patients known to be colonized/infected with MDROs including ESBL-producing bacteria**
- This was a grade 1B recommendation: Strongly recommended for implementation and supported by some experimental, clinical, or epidemiologic studies and a strong theoretical rationale

46

Gloves and gowns block 90% of resistant bacteria

Organism	HCW Room Entries	Hand + Before (%)	Gown and/or Glove + After %	Hands + After Removal	Effectiveness of PPE
<i>A. baumannii</i> ¹	202	1.5%	38.7%	4.5%	88%
<i>P. aeruginosa</i> ¹	133	0%	8.2%	0.7%	90%
VRE ²	94	0%	9%	0%	100%
MRSA ²	81	2%	19%	2.6%	85%

1. Morgan D, et al, Infect Control Hosp Epidemiol July 2010; 31: 716-21
2. Snyder G, et al, Infect Control Hosp Epidemiol July 2008; 29: 584-89

47

Improve infection control

- Surveillance
- Promote and improve hand hygiene
- Use cohorting and isolation precautions (gowns, gloves, signs)
- Environmental control

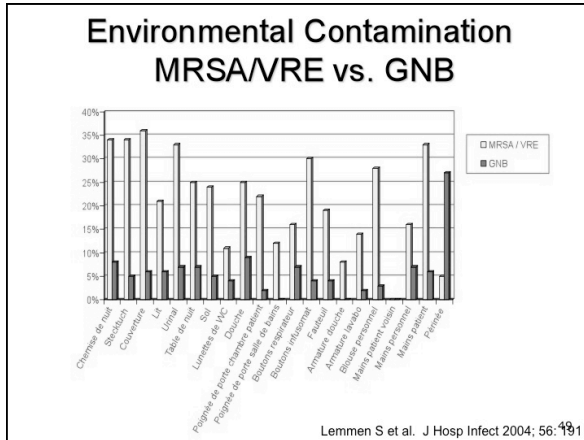
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Acinetobacter Outbreak

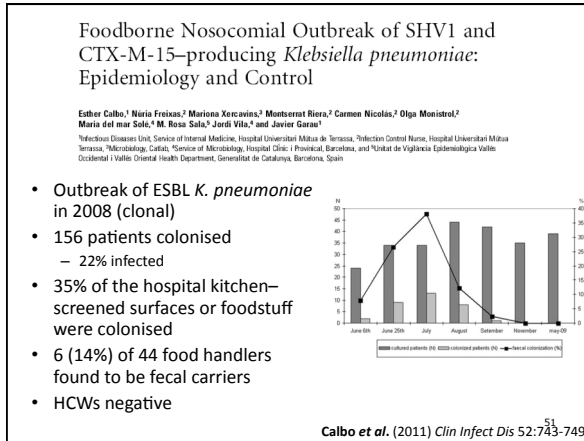
- Index patient**
 - Severe burn injuries, transfer from Bali (Oct 2002)
 - Multi-R *Acinetobacter* at admission
- Outbreak**
 - Spread to 2 patients
 - 6 months later: 6 new cases
 - Closure of the burn unit
- Environment**
 - Widespread contamination: 16/161 (10%) positive swabs

Patients *Environment*

► Environmental cleaning & disinfection

► Complete replacement of all disposable material

Zanetti G et al. Infect Control Hosp Epidemiol 2007; 28: 723-25



The New York Times

DOCTORS | FEBRUARY 27, 2014, 1:00 PM

Stethoscopes as Germ Carriers

By NICHOLAS BAKALAR

Doctors' stethoscopes are contaminated with bacteria that can easily be transferred from one patient to another, a new study has found.

Researchers cultured bacteria from the fingertips, palms and stethoscopes of three doctors who had done standard physical examinations on 83 patients at a Swiss hospital. They tested for the presence of viable bacterial cells, looking specifically for the potentially deadly methicillin-resistant *Staphylococcus aureus*, or MRSA. The study appears in the March issue of the Mayo Clinic Proceedings.

Fingerprints on the doctors' dominant hands were the most contaminated, but the part of the stethoscope that touches the patients' skin held more than twice as much bacteria as the physicians' palms. The stethoscopes were more contaminated with MRSA than some parts of the palms, but not others.

The authors acknowledge that the study was small and may not be applicable to other health care sites. Except for MRSA, they did not distinguish harmful from harmless bacteria.

That bacteria are found on stethoscopes is "not a surprise," said the senior author, Dr. Didier Pittet, a professor of medicine at the University of Geneva Hospitals. He cleans his own stethoscope with alcohol swabs after each examination, but "most physicians do not," he said, adding, "We don't have any easy solutions. It may be time to have one stethoscope per patient, at least in I.C.U.s, but this is impractical in a large hospital with many patients. It's embarrassing because we don't have any guidelines."

Longtin Y et al (2014). Mayo Clin Proc

- ### Improve infection control
- Surveillance
 - Promote and improve hand hygiene
 - Use cohorting and isolation precautions (gowns, gloves, signs)
 - Environmental control
 - Decolonization
- 53

J Antimicrob Chemother 2013; 68: 2375–2382
doi:10.1093/jac/dkt174 Advance Access publication 29 May 2013

Decolonization of intestinal carriage of extended-spectrum β -lactamase-producing Enterobacteriaceae with oral colistin and neomycin: a randomized, double-blind, placebo-controlled trial

Benedikt Huttner^{1*}, Thomas Haustein¹, Ilker Uçkay¹, Gesuele Renzi², Andrew Stewardson¹, Danièle Schorrer³, Americo Agostinho³, Antoine Andremonet³, Jacques Schrenzel³, Didier Pittet¹ and Stephan Harbarth¹

¹Infection Control Program, Geneva University Hospital and Faculty of Medicine, Rue Gabrielle-Perret-Gentil 4, 1211 Geneva 4, Switzerland; ²Clinical Microbiology Laboratory, Service of Infectious Diseases, Geneva University Hospital, Rue Gabrielle-Perret-Gentil 4, 1211 Geneva 4, Switzerland; ³Pharmacy, Geneva University Hospital, Rue Gabrielle-Perret-Gentil 4, 1211 Geneva 4, Switzerland; *Assistance publique—Hôpitaux de Paris (AP-HP) and University Paris-Diderot Medical School, Paris, France

Huttner et al. (2013). J Antimicrob Chemother.

54

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Need for a randomized, controlled study*

Colistin sulfate
(50mg 4x/d)
+
Neomycine sulfate
(250mg 4x/day)

10
days

PLACEBO

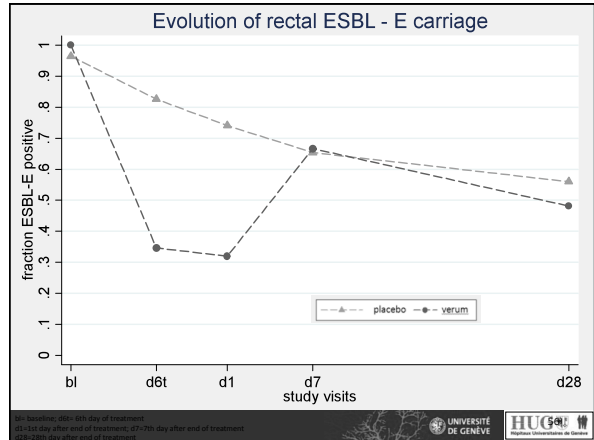
Nitrofurantoin
(100mg 3x/d)

5
days

PLACEBO

Sample size: 27 patients in each group**

* Investigator initiated, financed by HUG (PRD 08-II-6)
** 70% vs 30%, 1-beta 0.8, alpha 0.05 (two-sided)



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 13, 2013 VOL. 368 NO. 24

Targeted versus Universal Decolonization to Prevent ICU Infection

Susan S. Huang, M.D., M.P.H., Edward Septimus, M.D., Ken Kleinman, Sc.D., Julia Moody, M.S.,

Group 1: Screen/Isolate
Group 2: Screen/Decolonize (Mupi/CHX)
Group 3: Universal Decolonization (Mupi/CHX)

A. MRSA Clinical Culture

Hazard Ratio

Group

P=0.01

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A. MRSA Clinical Culture

C. Bloodstream Infection from Any Pathogen

Hazard Ratio

Group

P<0.001

The NEW ENGLAND JOURNAL of MEDICINE

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Targeted versus Universal Decolonization to Prevent ICU Infection

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Group 3: Universal Decolonization (Mupi/CHX)

A. MRSA Clinical Culture

C. Bloodstream Infection from Any Pathogen

B. MRSA Bloodstream Infection

Hazard Ratio

Group

P=0.11

Table 3. Frequency and Rates of Outcomes during the Baseline and Intervention Periods, According to Study Group.^a

Outcome	Group 1		Group 2		Group 3	
	Baseline	Intervention	Baseline	Intervention	Baseline	Intervention
MRSA clinical cultures	216 (3.4)	279 (3.2)	245 (4.3)	301 (3.2)	240 (3.4)	217 (2.1)
Bloodstream infection						
MRSA	37 (0.6)	63 (0.7)	31 (0.5)	61 (0.6)	46 (0.6)	48 (0.5)
Any pathogen ^b	265 (4.2)	360 (4.1)	273 (4.8)	341 (3.7)	412 (5.1)	356 (3.6)
Gram-positive organism	165 (2.6)	228 (2.6)	159 (2.8)	201 (2.2)	253 (3.7)	187 (1.9)
Skin commensal organism	50 (0.8)	55 (0.6)	49 (0.9)	46 (0.5)	120 (1.8)	38 (0.4)
Noncommensal organism	115 (1.8)	173 (2.0)	110 (1.9)	157 (1.7)	133 (2.0)	149 (1.5)
Gram-negative organism	62 (1.0)	83 (0.9)	58 (1.0)	75 (0.8)	100 (1.5)	107 (1.1)
Candida species	38 (0.6)	49 (0.6)	56 (1.0)	63 (0.7)	59 (0.9)	62 (0.6)

Table 3B. Bloodstream Pathogens by Study Arm in Baseline and Intervention Periods for 1,000 Attributable ICU Days^a

Pathogen (Ordered by Frequency)	Bloodstream Infections per 1,000 Attributable ICU Days					
	Baseline	Intervention	Baseline	Intervention	Baseline	Intervention
Total Events (N)	265	360	273	341	412	356
Staphylococcus aureus (N)	77	128	70	108	80	92
Methicillin-Resistant (MRSA)	0.46	0.49	0.47	0.58	0.59	0.38
Methicillin-Susceptible (MSSA)	0.77	0.97	0.75	0.59	0.61	0.54
Total	1.23	1.46	1.23	1.15	1.19	0.92
Coagulase-Negative Staphylococcus ^b (N)	43	54	43	42	116	38
Total	0.77	0.62	0.75	0.46	1.72	0.36

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Important issues to consider

- Very high MRSA on-admission prevalence
- High BSI rates in the universal decolonization arm (including 2 BMT units, by chance !)
- Surprisingly low rate of previously unknown MRSA carriers at admission
- Nasal screening only
- Slow screening method (no PCR tests)
- Chlorhex-R and HH issues: not addressed

61

Independent risk factors associated with persistent MRSA colonization

Risk factor	Multivariate analysis	
	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



Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units: an interrupted time series study and cluster randomised trial

Lennie P G Derde, Ben S Cooper, Herman Goossens, Surbhi Malhotra-Kumar, Rob J L Willems, Marek Gniadkowski, Waleria Hymniewicz, Joanna Empel, Mirjam J D Dautzenberg, Djillali Annane, Irene Aragão, Annie Chalfine, Uga Dumpis, Francisco Esteves, Helen Giamarelou, Igor Muzlovic, Giuseppe Nardi, George L Petrikos, Viktorija Tomic, Antonio Torres Marti, Pascal Stammet, Christian Brun-Buisson*, Marc J M Bonten*, on behalf of the MOSAR WP3 Study Team

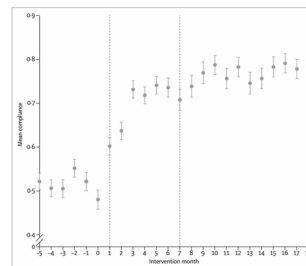
- Reduction in MDRO acquisition by CBW plus hand hygiene program
 - Mainly caused by reduction in MRSA acquisition
- Screening and isolation of identified carriers did not have an incremental effect



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Interventions

- Hand Hygiene compliance improved from 52 % to 69% to 77% from phase 1 to 3



64

Infection Control

- Promote adherence to alcohol-based hand hygiene & basic infection control
- Improve systems to recognize and detect patients colonized with MDROs
- Implement barrier precautions in high-risk situations and during outbreaks
- Don't forget the environment
- Adapt preventive measures to your local setting and epidemiology

65

5 May 2014 Role of hand hygiene to combat antimicrobial resistance

<http://www.who.int/gpsc/5may/en/>



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make sure the WHO 5 Moments are part of
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How to Prevent the Spread of Multiresistant Bacteria

Prof. Stephan Harbarth, Geneva University Hospitals

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