Eradication of Carriage

Jan Kluytmans
Vu University Medical Center Amsterdam
Amphia Hospital Breda

Complicating factors

- Carriage is not a disease
- Carriage of specific pathogens increases the risk for development of disease (e.g. S. aureus)
- Carriage is transmittable (patient dependency > possible herd effect)

- Consequences for study design
  - Problems with individual randomization, blinding, meaningfull endpoints etc.

Two examples

- S. aureus and SSI
- Selective Decontamination of the Digestive Tract (SDD)

S. aureus and SSI

- Carriers of S. aureus have an increased risk for the development of SSI after surgery (RR≈10)

  Kluytmans et al. Clin Microbiol Rev 1997;10:505-520

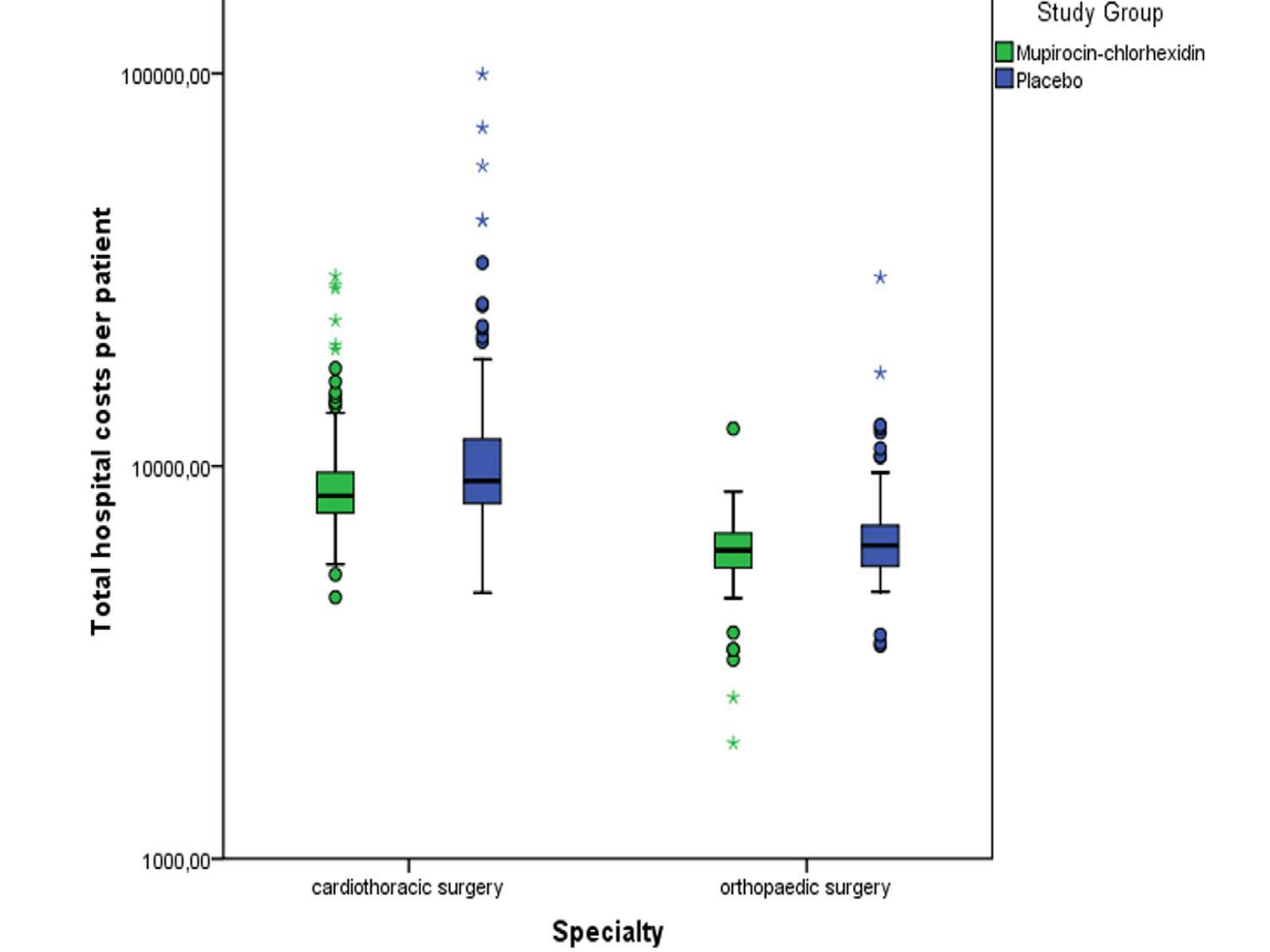
- Peri-operative treatment with mupirocin reduces this risk (Risk Reduction≈60%)

  Bode et al. NEJM 2010;263:9-17

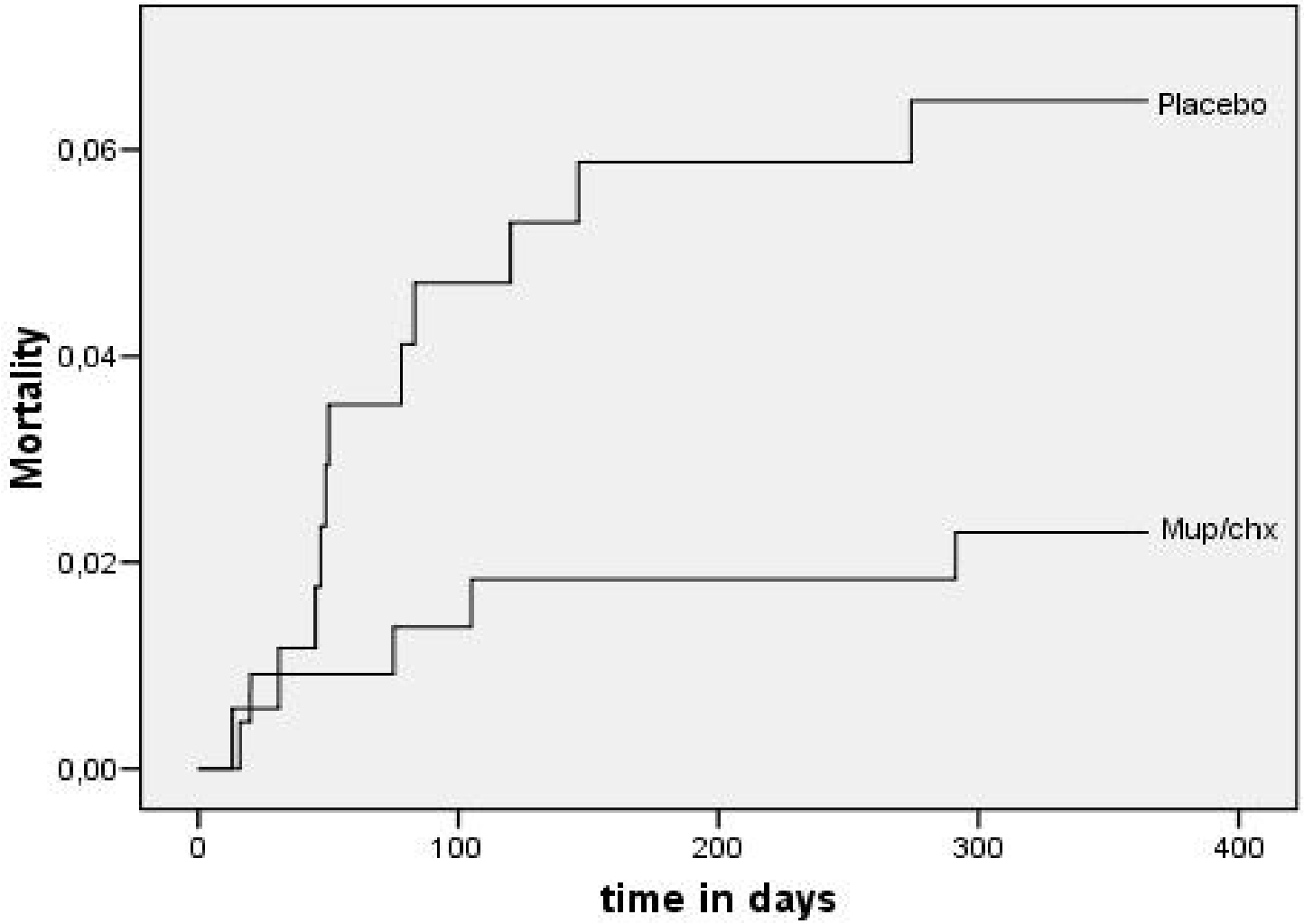
Cost-effectiveness

- Cost reduction per treated carrier was
  - €2841 in cardio-thoracic surgery
  - €955 in orthopedic surgery

Van Rijen et al. Plos One 2012;7:e43065


Study Group
Mupirocin-chlorhexidin
Placebo
100000,00
10000,00
1000,00
Total hospital costs per patient
cardiothoracic surgery
orthopaedic surgery
Specialty

Mortality in cardiothoracic surgery



11/170 (6.5%)

P=0.040

5/218 (2.3%)

Discussion

- Mupirocin is cost-effective and reduces mortality

- For which procedures should it be used?
- Why not use povidone iodine, octinidine, or what else you can think of?

SDD

- Patients in ICU
- Topical antibiotics in oro-pharynx and GI tract (tobramycin, colistin and amphotericin B)
- 4 days of systemic cefotaxim

- Patient dependency
- Blinding impossible
  - Multicenter cluster-randomized study

De Smet et al. NEJM 2009;360:20-31

Adjusted outcomes			
	Standard Care N=1990 OR	SDD N=2045 OR(CI)	SOD N=1904 OR(CI)
Mortality at day 28	1	0.83 (0.72-0.97)	0.86 (0.74-0.99)
ICU Mortality	1	0.81 (0.69-0.94)	0.87 (0.74-1.02)
Hospital Mortality	1	0.88 (0.76-1.01)	0.85 (0.74-0.98)
Duration of intubation	1	1.10 (0.99-1.22)	1.03 (0.90-1.17)
Duration of ICU-stay	1	1.09 (0.99-1.21)	1.06 (0.94-1.19)
Duration of hospital stay	1	1.13 (1.01-1.25)	1.13 (0.96-1.32)

Random effects logistic regression model with adjustment for age, gender, APACHE II score, ventilation, surgical/non-surgical and study center.

Infections and resistance

Articles

Selective digestive tract decontamination and selective oropharyngeal decontamination and antibiotic resistance in patients in intensive-care units: an open-label, clustered group-randomised, crossover study

Anne Marie G A de Smet, Jan A J W Kluytmans, Hetty E M Blok, Ellen M Mascini, Robin F J Benus, Alexandra T Bernards, Ed J Kuijper, Maurine A Leverstein-van Hall, Arjan R Jansz, Bartelt M de Jongh, Gerard J van Asselt, Ine H M E Frenay, Steven F T Thijsen, Simon N M Conijn, Jan A Kaan, Jan P Arends, Patrick D J Sturm, Martin C J Bootsma, Marc J M Bonten

ICU-acquired bacteremia and candidemia

	Crude odds ratio (95% CI)
	SDD *vs* standard care
Any microorganism, apart from coagulase-negative staphylococci	0·48 (0·38–0·60); ARR 6·4%; NNT 16
Candida spp and other yeasts*	0·33 (0·13–0·82); ARR 0·7%; NNT 152
HRMO†	0·41 (0·18–0·94); ARR 0·6%; NNT 170

Acquired Respiratory Tract Colonization

	SC N=881	SOD N=886	SDD N=828
Tobramycin resistance:			
•*Escherichia coli* and Klebsiella spp	31 (3.5)	19 (2.1)	9 (1.1)
•Other Enterobacteriaceae	25 (2.8)	41 (4.6)	15 (1.8)
•Acinetobacter spp and *S. maltophilia*	40 (4.5)	45 (5.1)	49 (5.9)
•Other GNF-GNR¶	18 (2.0)	20 (2.3)	49 (5.9)
•Any Gram-negative rods	104 (11.8)	112 (12.6)	115 (13.9)

Cefotaxim resistance:			
•*Escherichia coli* and Klebsiella spp	13 (1.5)	12 (1.4)	2 (0.2)
•Other Enterobacteriaceae	44 (5.0)	42 (4.7)	18 (2.2)
•With any Enterobacteriaceae	56 (6.4)	56 (6.3)	20 (2.4)

Colistin resistance:			
Proteus spp and Serratia spp	130 (14.8)	112 (12.6)	55 (6.6)

SDD

- Reduces mortality
- Prevents the development of bacteremia
- Is associated with lower resistance rates

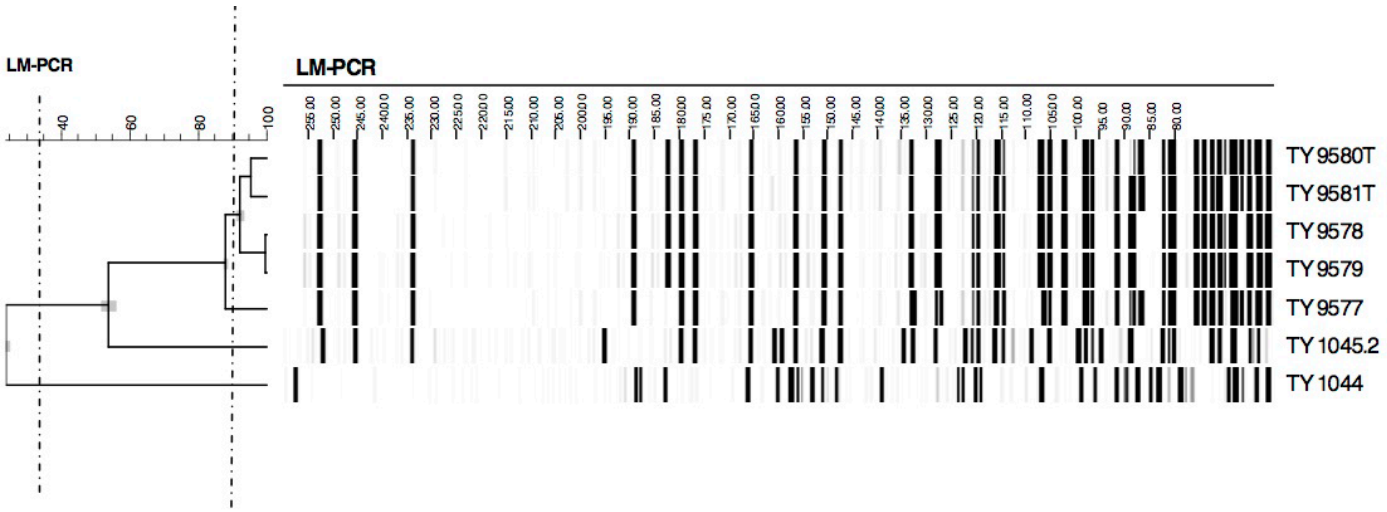
- Limitations
  - Low prevalence of resistance (no MRSA)
  - Long term effects are unknown

Eradication of carriage

- Can have substantial impact on clinical meaningful end-points
- Is a preventive strategy and not a treatment of disease
- Can be used to prevent the occurrence of disease in other persons (transmission)

Example

- Recent outbreak of MRSA in oncology



A Patient 2
B partner medewerker MSSA
C patient 1
D medewerker MRSA
E veronderstelde index
F controle S. aureus
G controle CNS

Example

- Source was a nurse who was colonized persistently with the outbreak strain
  - Is decolonization of the nurse justified?
  - Do we need effective agents for this?
  - Could new agents get a licence for this indication?