

# Community-associated MRSA as a cause of HAI

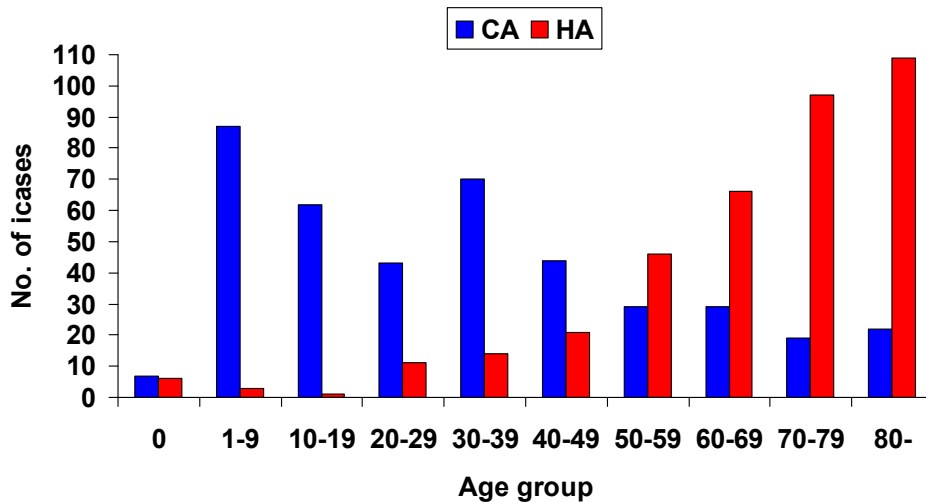
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# CA-MRSA

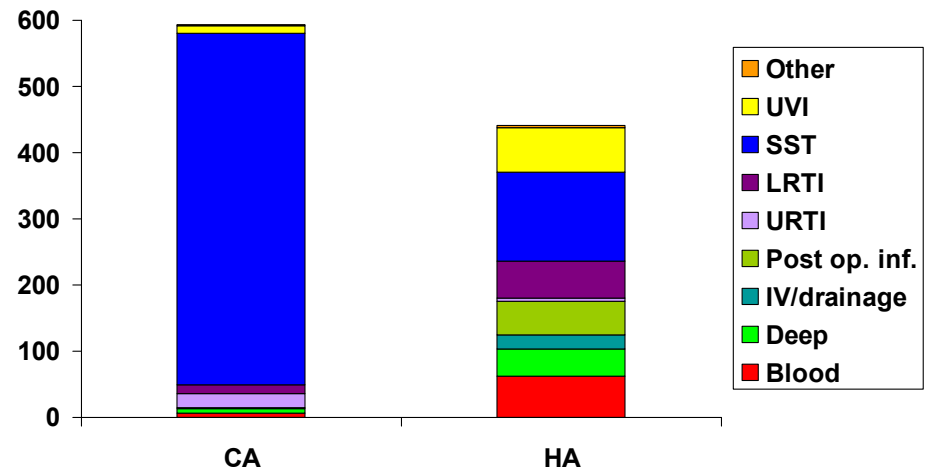
- In the late 1990s, the epidemiology of MRSA infections began to change
  - **from** being almost exclusively a health care associated infection
  - **to** also cause infection in otherwise healthy persons without any connection to health care
- Specific strain types, different from those typically found in HA-MRSA

# Epidemiology of MRSA illustrated by Danish national data

Age distribution



Type of infection



# Microbiology of CA-MRSA

- Large diversity of strains, distinct lineages – not just feral descendants of HA-MRSA strains,
  - at present 5 lineages are found worldwide
    - ST1-IV (USA400); ST8-IV (USA300); ST30-IV (Pacific); ST59-IV and V (USA1000, Taiwan); ST80-IV (European)
  - CC398 from production animals
- SCC *mec* type IV
  - type V, new variants
- Often less multiresistant
  - At least used to be
- Most of the dominant CA-MRSA strains produce the Panton–Valentine leukocidin (PVL)

# Risk factors for MRSA

## Traditional risk factors for nosocomial MRSA infection

- Previous hospital stay
- Prolonged length of stay prior to infection
- Surgical procedure(s)
- Enteral feeding
- Previous antibiotic use
- Central venous catheter insertion

## Risk factors for community-acquired (CA) MRSA

- History of colonization/infection with CA-MRSA
- Close contact with a person colonized/infected with CA-MRSA
- children <10 years
- Indigenous people
- Especially identified in USA
  - Participation in contact sports
  - Injection drug use
  - Living in correctional facilities or shelters
  - Military personnel
  - Men who have sex with men

# Common risk factors in populations at highest risk

- One or more of the following are characteristic of the populations at highest risk
  - frequent Antibiotic use and overuse
  - Poor hygiene / **C**leanliness
  - **C**ompromised skin
  - Frequent skin **c**ontact
  - **C**ontaminated surfaces and shared items
  - **C**rowding (up to 7.5 persons per bedroom)
- **These groups amplify MRSA!**
  - MRSA is likely to disseminate from these communities to the population in general

# Definition of CA MRSA

- However no single definition exists for CA-MRSA
  - Clindamycin/ciprofloxacin susceptibility
  - Non-multidrug resistant (only resistant to 1-2 classes of antibiotics)
  - *SCCmec* IV (V)
  - PVL positive
  - Epidemiological
    - Community onset and lack of health care-associated risk factors
      - Previous MRSA positive

# Definition of CA MRSA

- The definition is further complicated by
  - *S. aureus*/MRSA can be carried for prolonged time without/before causing infections
  - 80% of bacteraemias are endogenous i.e. caused by the same strain as the person carries
- Acquisition
  - Time and place where the infection starts?
  - Time and place where the MRSA strain is acquired ?
- Differentiation between hospital-acquired and CA is thus difficult
  - Hospital onset vs community onset

# Evidence of CA-MRSA as cause of HAI

- In UK the situation is dominated by ST22 (EMRSA 15) and ST36 (EMRSA 16)
  - Single reports on nosocomial transmission of CA-MRSA strains

Community-associated meticillin-resistant *Staphylococcus aureus*: nosocomial transmission in a neonatal unit

M.D. David <sup>a</sup>, A.M. Kearns <sup>b,\*</sup>, S. Gossain <sup>a</sup>, M. Ganner <sup>b</sup>, A. Holmes <sup>b</sup>

Journal of Hospital Infection, 2006, 64, 244

Outbreak of ciprofloxacin-susceptible community-associated meticillin-resistant *Staphylococcus aureus* in a neonatal unit

Seetulsingha P et al, J Hosp Infect. 2008; 68:374-5.

Hospital-associated transmission of Panton-Valentine Leukocidin (PVL) positive community associated MRSA in the West Midlands

CDR Weekly, HPA, 2006; 16 No. 50, 14 December

- In Greece, ST80 caused 25% of hospital-acquired infections in 2004

Chini V et al. Scand J Infect Dis 2008;40:368–372

# Displacement of HA-MRSA strains by CA-MRSA strains

**Table 2. Rates of hospital-onset bloodstream infections caused by inferred community genotype (CG) and hospital genotype (HG), 2000–2006.**

Patient location and genotype	Incidence density rates		Risk ratio (95% CI)	P
	Period 1	Period 2		
<b>Hospital<sup>a</sup></b>				
Total	0.215	0.207	0.96 (0.73–1.27)	.79
CG	0.05	0.1	1.93 (1.2–3.1)	.01
HG	0.16	0.11	0.66 (0.46–0.93)	.02
<b>Intensive care unit<sup>b</sup></b>				
Total	0.29	0.31	1.08 (0.67–1.74)	.86
CG	0.05	0.17	3.12 (1.25–7.81)	.02
HG	0.23	0.14	0.61 (0.33–1.13)	.15
<b>Non-intensive care unit<sup>c</sup></b>				
Total	0.19	0.18	0.91 (0.65–1.27)	.63
CG	0.05	0.08	1.55 (0.88–2.73)	.16
HG	0.14	0.1	0.68 (0.44–1.03)	.08

**NOTE.** The study period was divided into 2 study periods: period 1 (January 2000–June 2003) and period 2 (July 2003–December 2006). The bacteremia rates are shown with a risk ratio with period 1 as reference.

# Evidence of CA-MRSA as cause of HAI

- In USA the epidemiology both in the community but also increasingly in hospitals is dominated by ST8-IV, spatype t008 (USA300)

## MAJOR ARTICLE

Emergence of Community-Associated Methicillin-Resistant *Staphylococcus aureus* USA300 Genotype as a Major Cause of Health Care–Associated Blood Stream Infections

**Seybold U *et al* Clin Infect Dis 2006; 42:647–56.**

Changes in the Epidemiology of Methicillin-Resistant *Staphylococcus aureus* in Intensive Care Units in US Hospitals, 1992–2003

**Klevens RM *et al* Clin Infect Dis 2006; 42:389–91.**

**Miller LG, Emerg Inf Dis 2007;13,236-42**

**Community-associated Methicillin-resistant *Staphylococcus aureus* Isolates Causing Healthcare-associated Infections<sup>1</sup>**

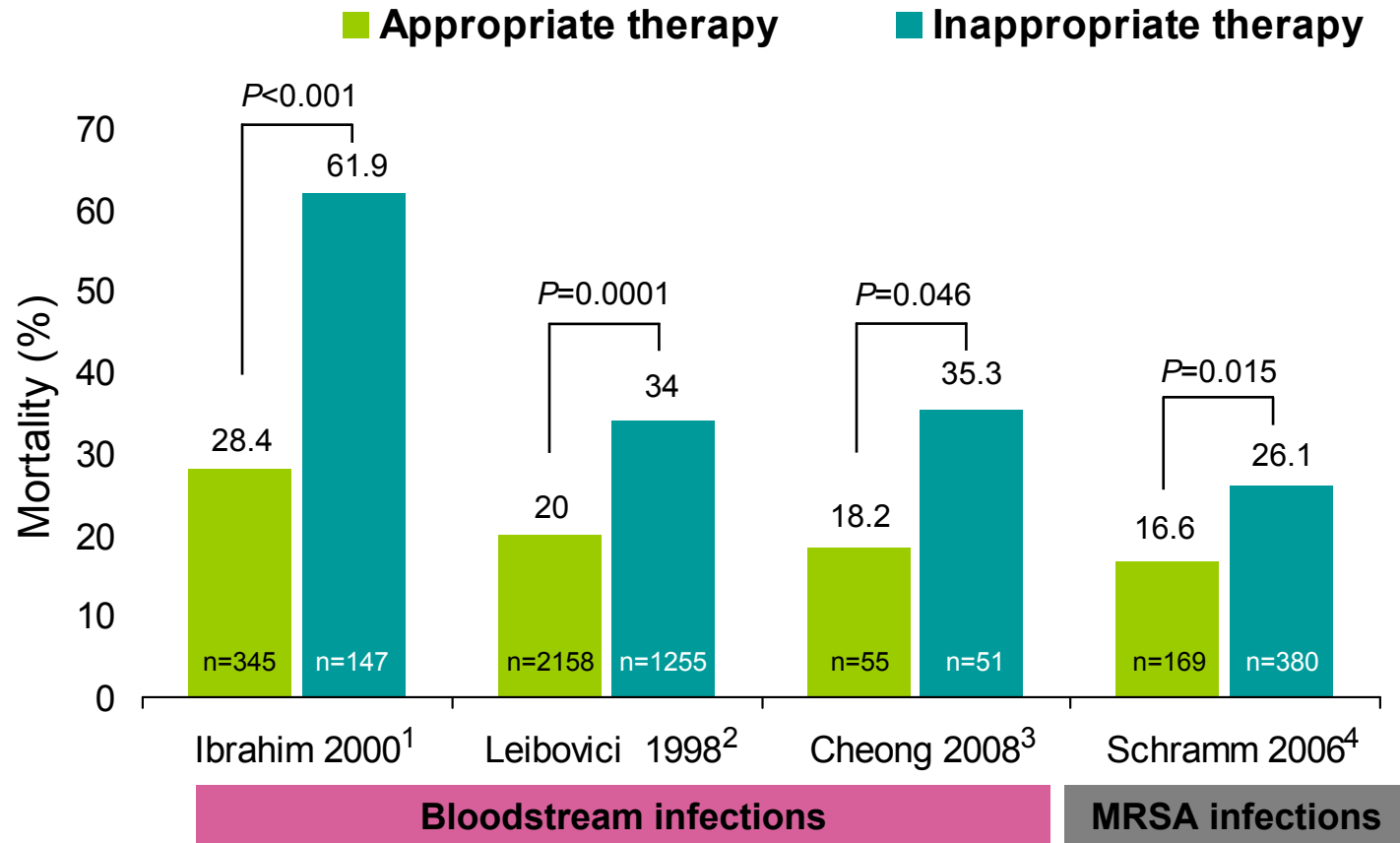
# CO-MRSA bacteraemia

- CO-MRSA bacteraemia\* is frequent
  - 61% of SAB cases were community onset in a recent large multicentre investigation from Australia and New Zealand<sup>1</sup>
    - 18% were MRSA
    - 27% of all MRSA cases had a typical CA-MRSA susceptibility profile
  - 39.7% in a multicentre study of invasive MRSA clones in France in 2006–2007
  - 24% of MRSA bacteraemia patients consulting a Taiwanese emergency department did not have health care associated risk factors

\*Community-onset infection:  
present on admission or  
diagnosed within the first 72 hours  
following admission<sup>4</sup>

Turnidge JD *et al. J Med Austr*, submitted for publication  
Dauwalder O *et al. JCM* 2008; 46:3454-3458  
Liao C-H *et al. IJAA* 2008; 32:326-32

# Inappropriate antibiotic therapy increases mortality rates



1. Ibrahim E *et al.* *Chest* 2000;118:146–155
2. Leibovici L *et al.* *J Intern Med* 1998;244:379–386
3. Cheong HS *et al.* *Eur J Clin Microbiol Infect Dis* 2008; Epub ahead of print
4. Schramm GE *et al.* *Crit Care Med* 2006;34:2069–2074

# Optimal empiric therapy

- The empiric regimen for clinically suspected *S. aureus* infection is determined by the likelihood that MRSA is the cause, based on:
  - Local prevalence of MRSA
  - Patient's history of MRSA carriage or infection
  - Other risk factors for MRSA infection

**Can you predict whether your patient is at risk  
of being MRSA positive?**

- Increasing prevalence of MRSA in otherwise healthy persons thus push towards empiric usage of anti-MRSA antimicrobials

# Mathematical modelling

- By mathematical modeling one can examine the possible influence of transmission of MRSA in the community
  - Applied the model by Cooper et al on a large hospital outbreak in Vejle County, Denmark
    - Assumption that transmission in the community is negligible (holds true for the outbreak in Vejle County)
  - Used the model to see “what if” there is transmission in the community

uncolonized

colonized

isolated

Hospital

$x_1$

$y_1$

$z$

Community

"high risk"  
group

$x_2$

$y_2$

"low risk"  
group

$x_3$

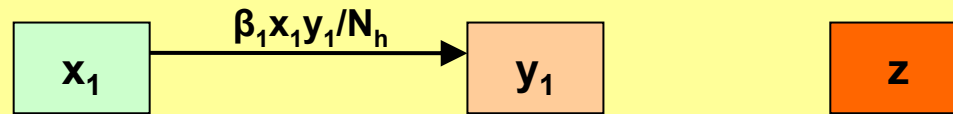
$y_3$

uncolonized

colonized

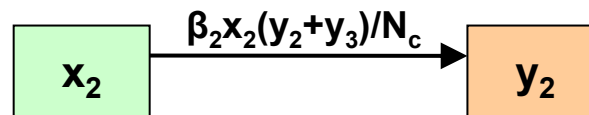
isolated

Hospital

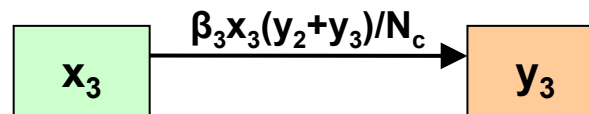


Community

"high risk"  
group

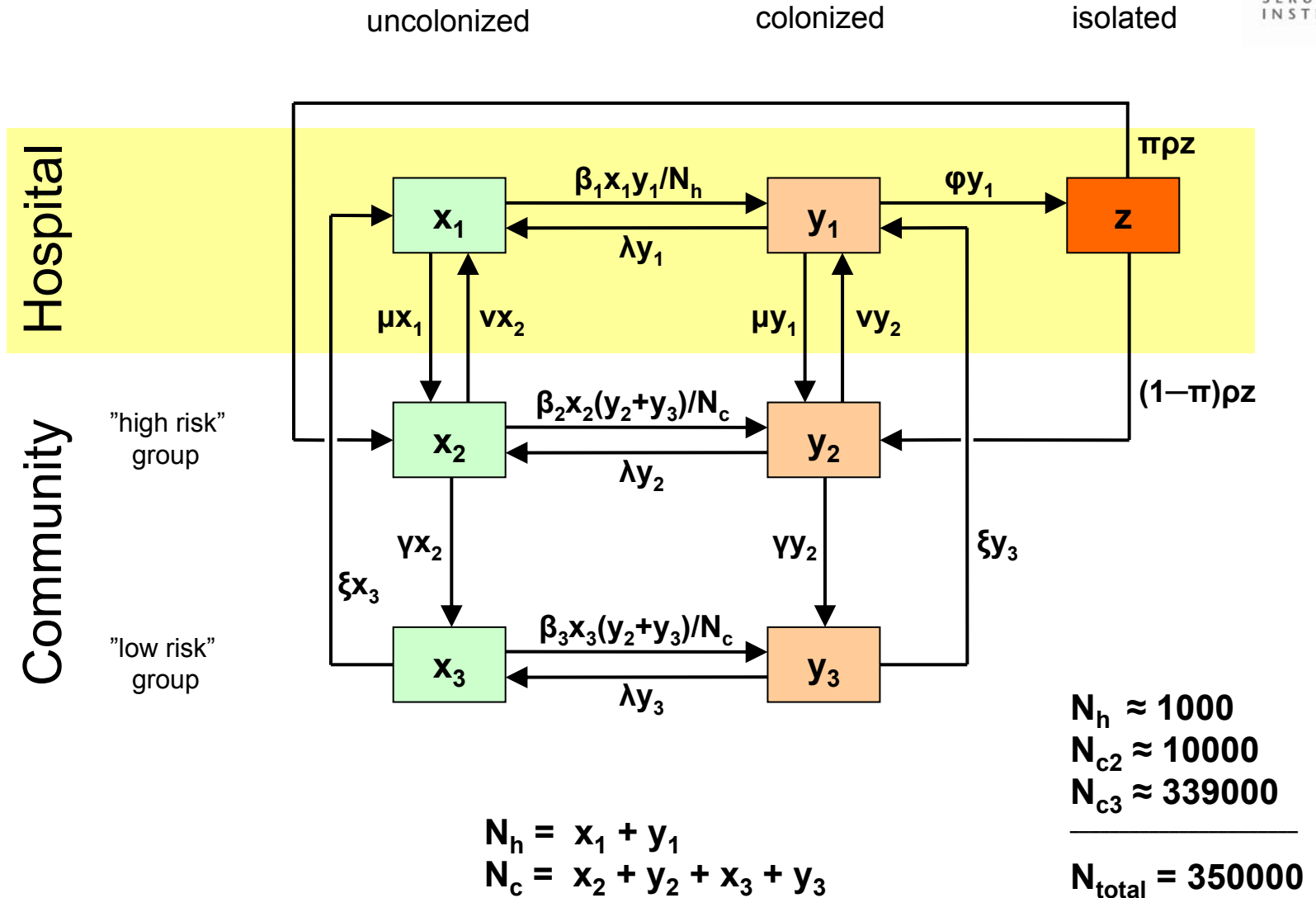


"low risk"  
group



$$N_h = x_1 + y_1$$

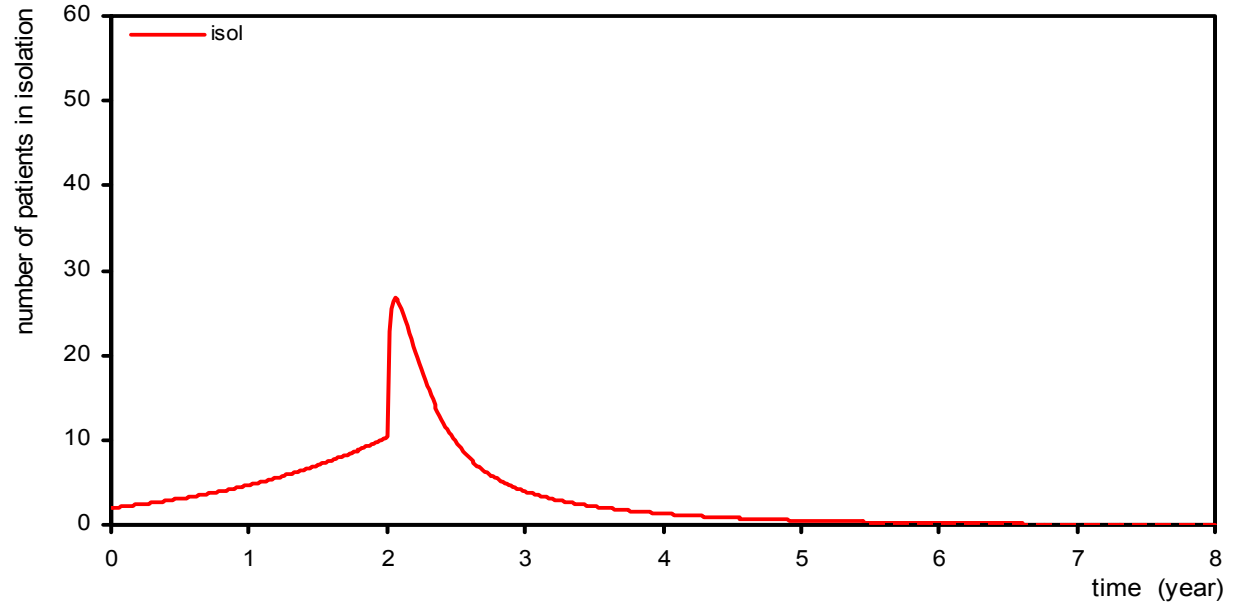
$$N_c = x_2 + y_2 + x_3 + y_3$$



## Case 0 deterministic

Transmission in hospitals only.

Increased isolation rate after  $T_{iso} = 2$  years.



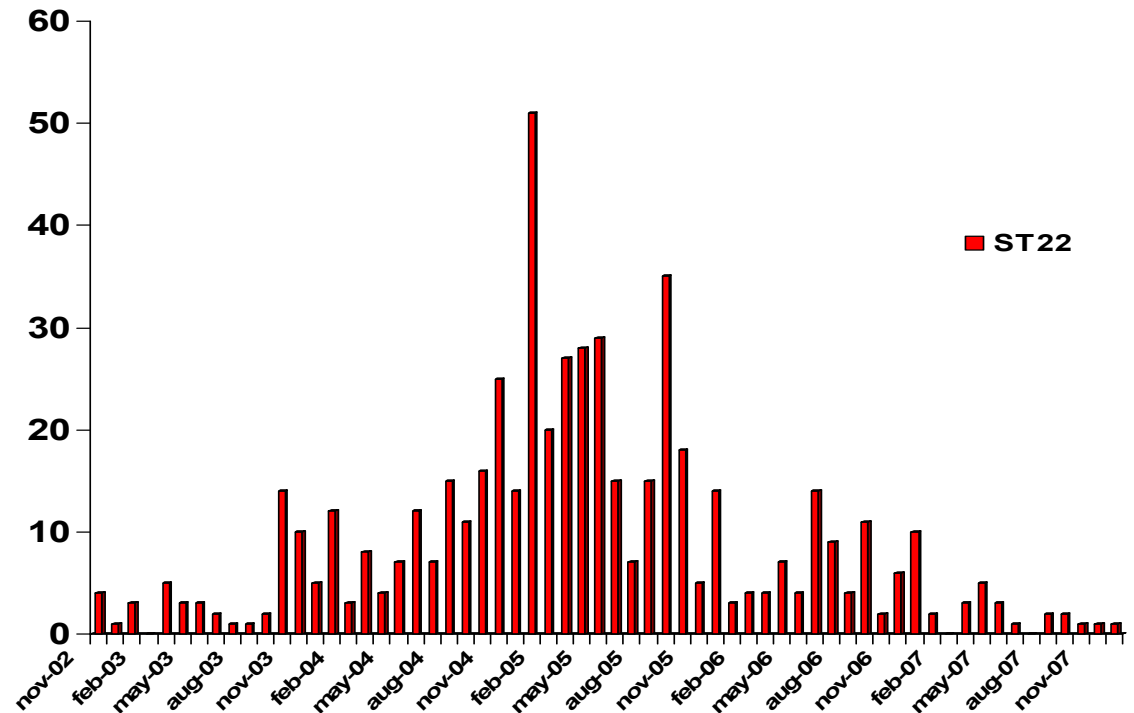
## Parameter values:

### Transmission

$\beta_1 = 0.1515$  (hospital)  
 $\beta_2 = 0$  (comm. "high")  
 $\beta_3 = 0$  (comm. "low")

### Isolation rate

$\varphi = 0.0259$  /day (before  $T_{iso}$ )  
 $\varphi = 0.3333$  /day (after  $T_{iso}$ )



## Case 0 *stochastic*

Transmission in  
hospitals only.

Increased isolation rate  
after  $T_{\text{iso}} = 2$  years.

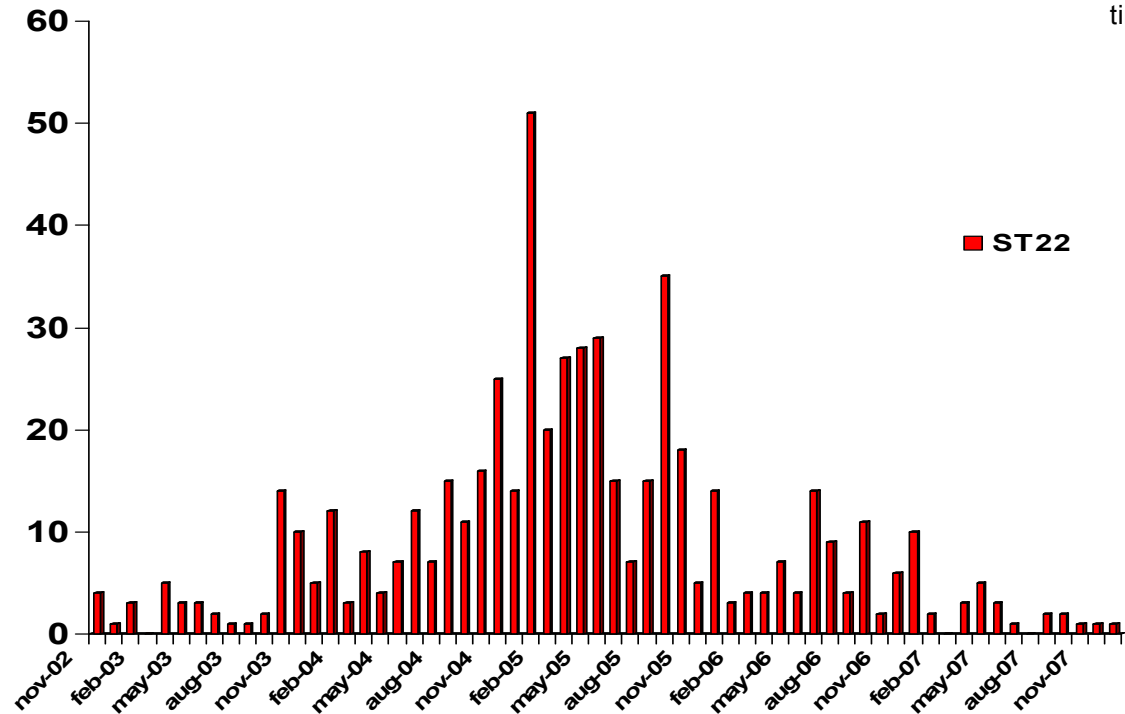
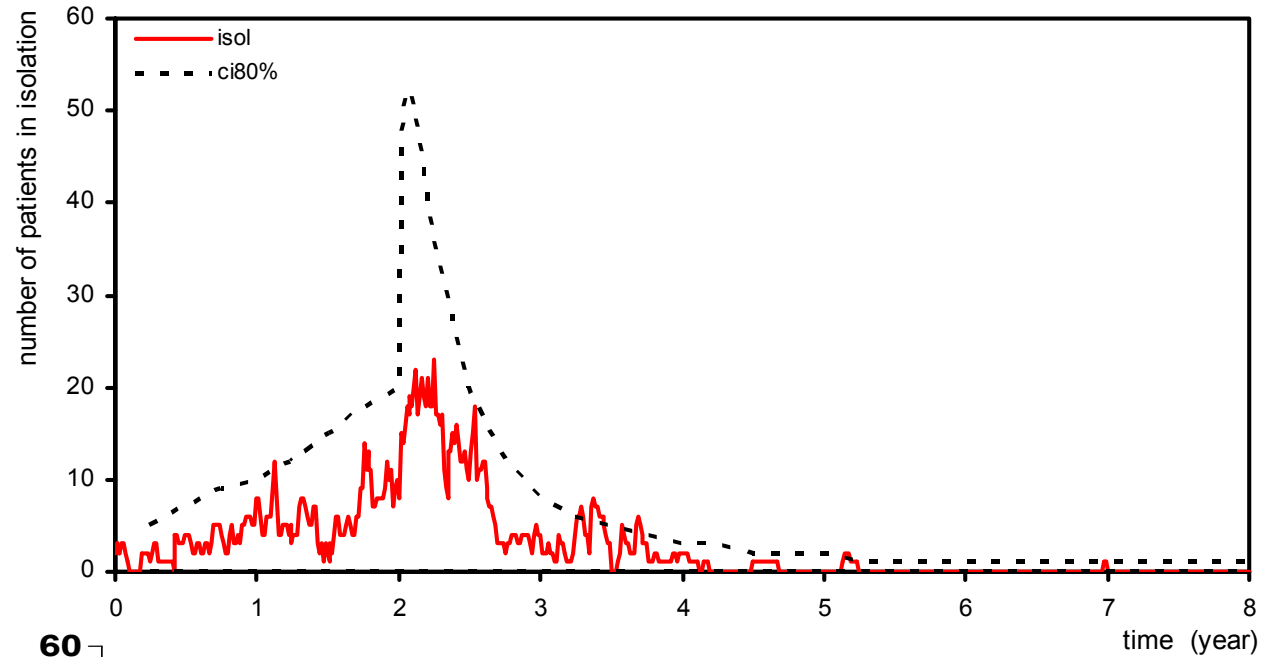
### Parameter values:

#### Transmission

$\beta_1 = 0.1515$  (hospital)  
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 $\beta_3 = 0$  (comm."low")

#### Isolation rate

$\phi = 0.0259$  /day (before  $T_{\text{iso}}$ )  
 $\phi = 0.3333$  /day (after  $T_{\text{iso}}$ )



# Eradication treatment

- **Treatment principles:**
  - Eradication treatment was not commenced until infection was cleared and risk factors removed (if possible)
  - For community associated cases the whole household was treated simultaneously.
  - Topical treatment was first line treatment
    - mupirocin x3/day in the nares and chlorhexidine body and hair wash x1 daily for 5 days
  - Cleaning: Changing of towels and underwear daily, changing of linen and cleaning of the environment was recommended on day 2 and 5
  - In case of failure, topical treatment was repeated with or without systemic antibiotics (two antibiotics, based on resistance pattern).
- Full follow up
  - $\geq 3$  set of swabs; one at minimum 6 months after end of eradication treatment
- Success was defined as full follow up and continued negative at the 6 months control.

# Long term outcome of treatment

	Total (%)	Throat neg (%)	Throat pos (%)
Success	143 (83)	105 (96)	38 (62)
Failure	3 (2)	1 (<1)	2 (3)
Still in treatment	5 (3)	0 (-)	5 (8)
Await 3rd control	21 (12)	5(4)	16 (27)
Total	172 (100)	111 (100)	61 (100)

# Conclusions

- In UK, HA-MRSA still dominates. However, in USA and low level countries like Denmark, CA-MRSA causes a significant portion of HAI
  - The boundary between HA-MRSA and CA-MRSA is getting increasingly blurred
  - CA-MRSA is moving from being a problem in closed risk communities to disseminate into the general population

# Conclusions

- Mathematical modelling supports that transmission of MRSA in the community significantly influence the occurrence of MRSA in hospitals and thereby HAI
- Therefore, CA-MRSA must be taken seriously and should be suppressed
- Data from Denmark show that it is possible successfully to eradicate carriage of MRSA also in the community

# Aknowlegdements

Staphylococcus Laboratory

Marit Sørum

Lone Ryste Hansen

Stine Freese Madsen

Jette Mondrup

Mathematical simulation

Klaus Skovbo Jensen