Improving the understanding of the micro and macro epidemiology of bacterial pathogens using genetic typing approaches part 1

Hajo Grundmann

National Institute for Public Health and the Environment, Bilthoven
Rijksuniversiteit Groningen, NL

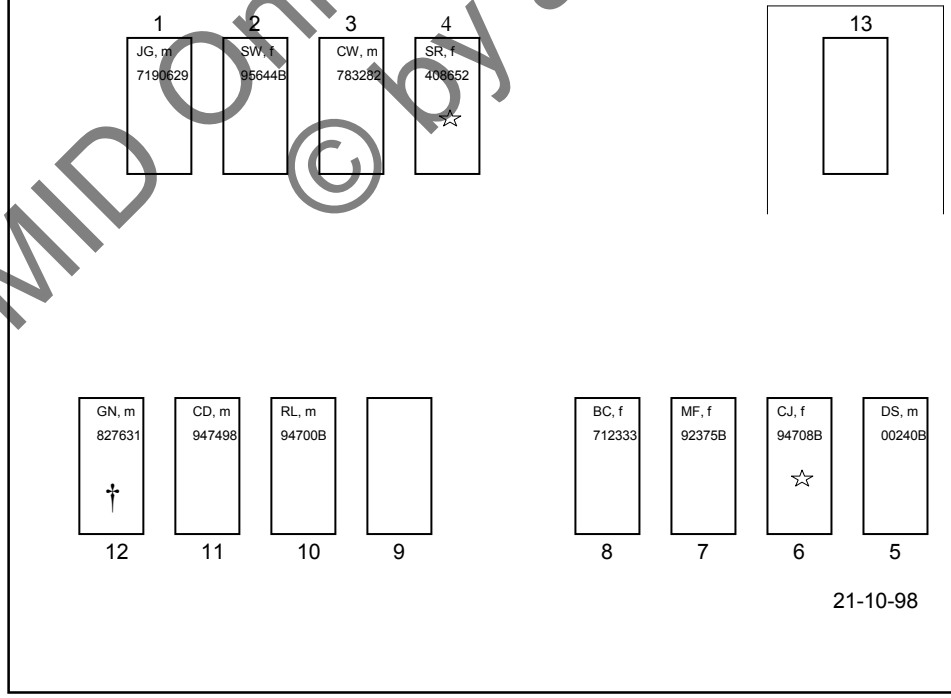
Topics

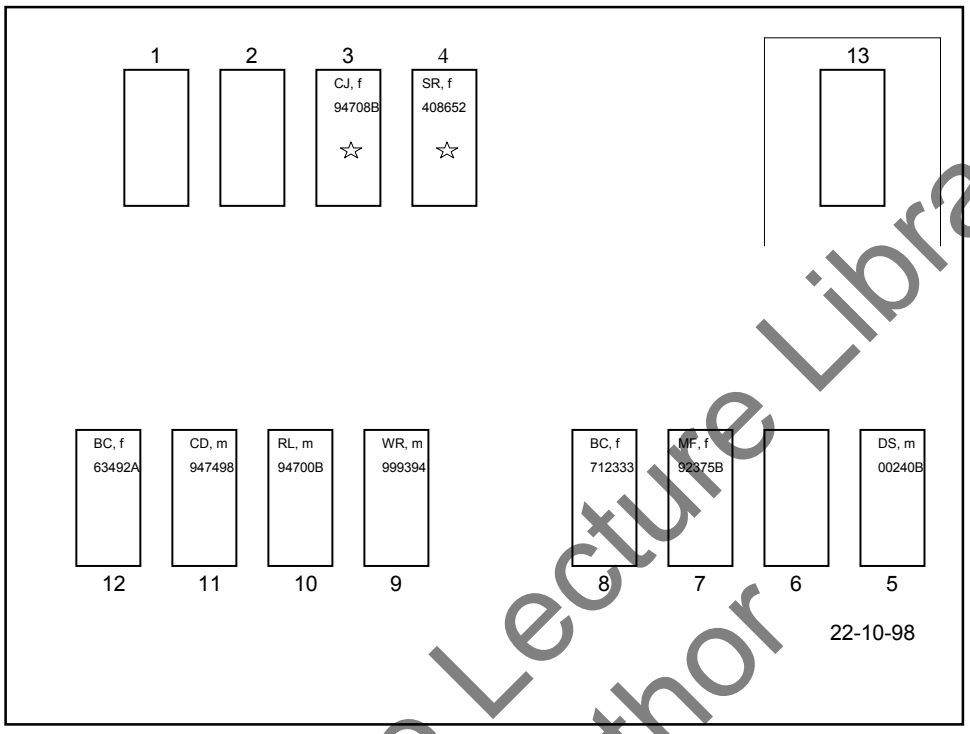
- Objectives for molecular typing of pathogens
- Threats to validity of typing results
- Opportunities of clonality
- Macro and micro- epidemiology and the way forward

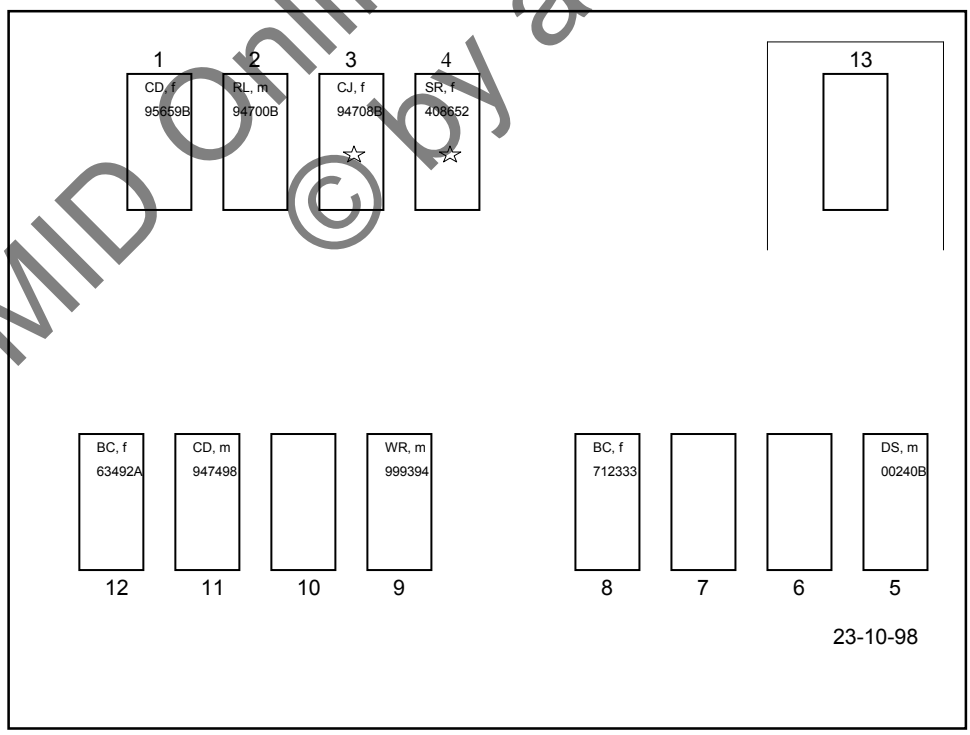
Objectives for molecular typing of pathogens

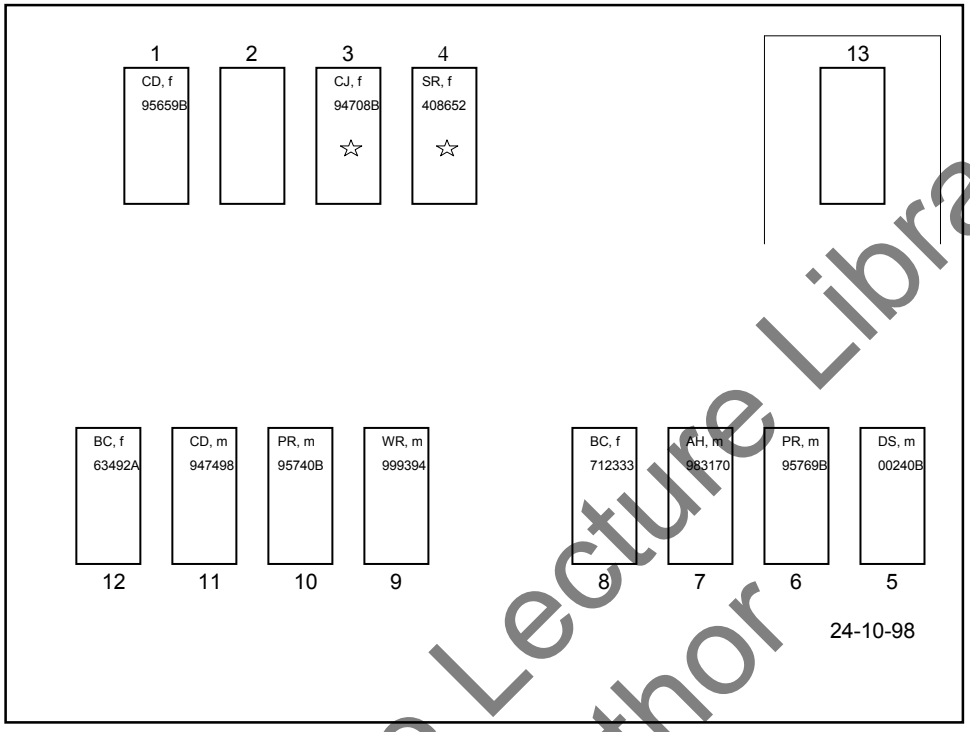
To identify:

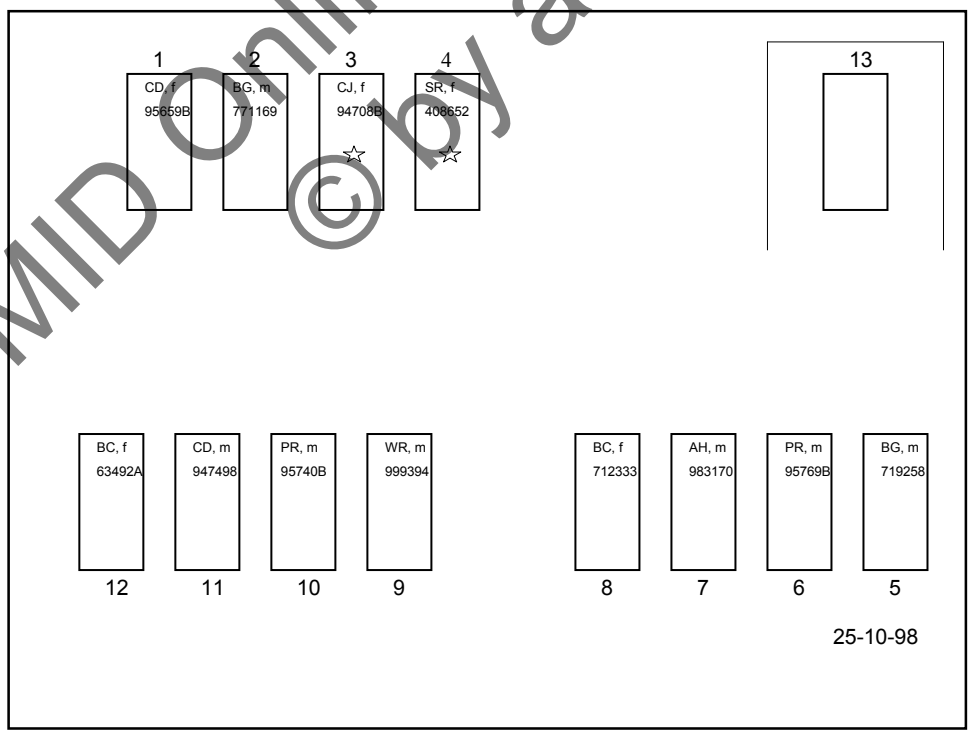
- transmissions
- major clones (genetic population structure)
- geographical dissemination
- secular trends
- evolutionary trajectories
- epidemiological success (founder effects)

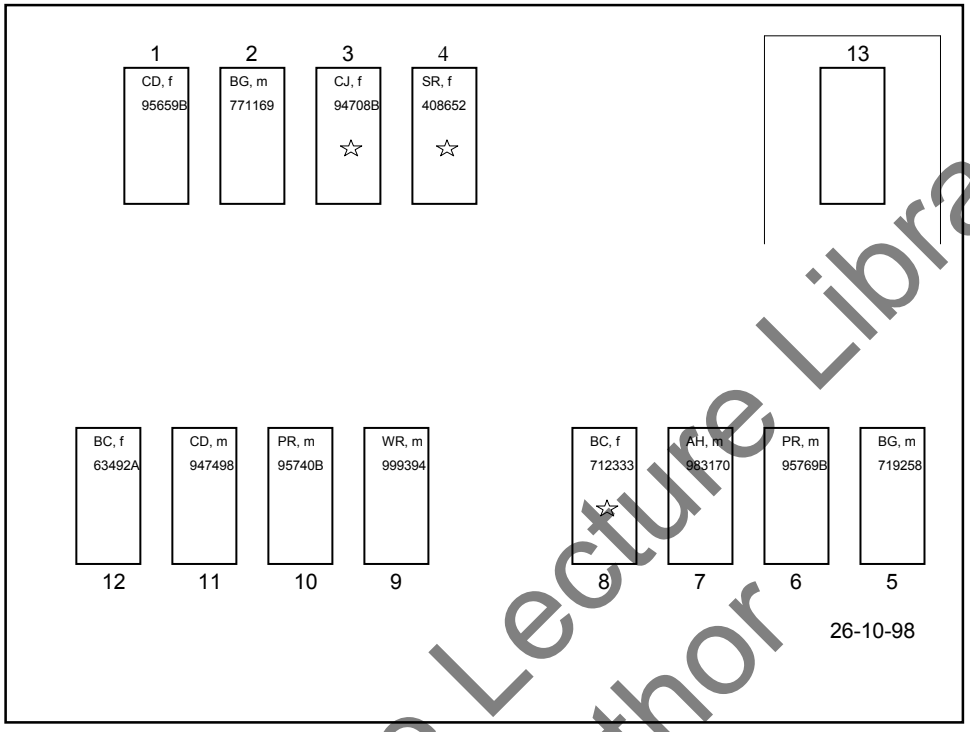


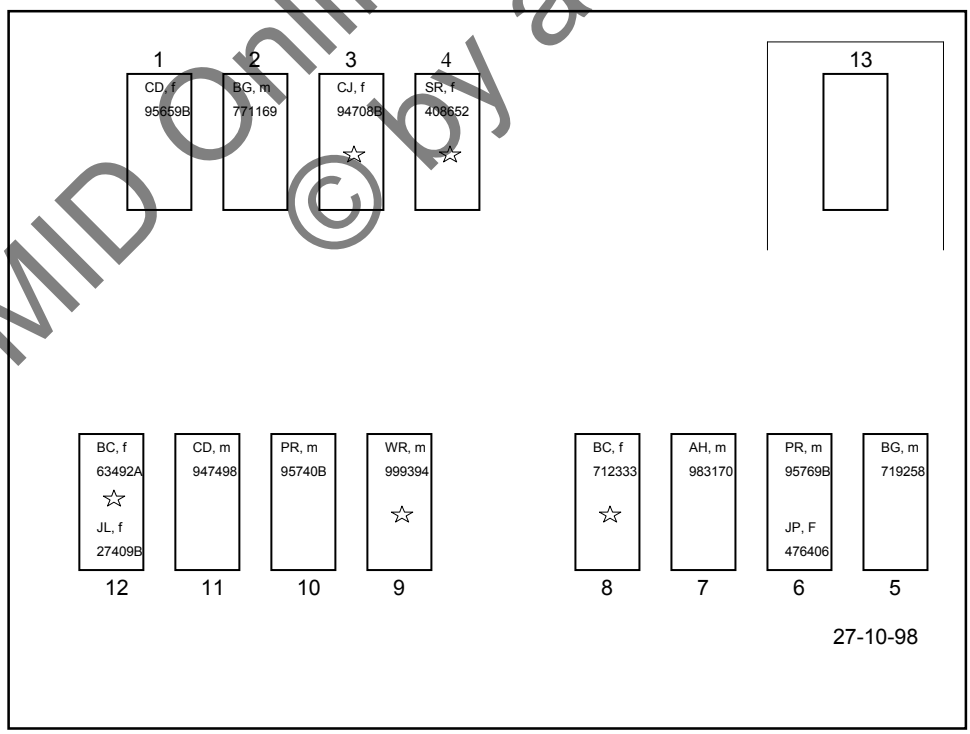


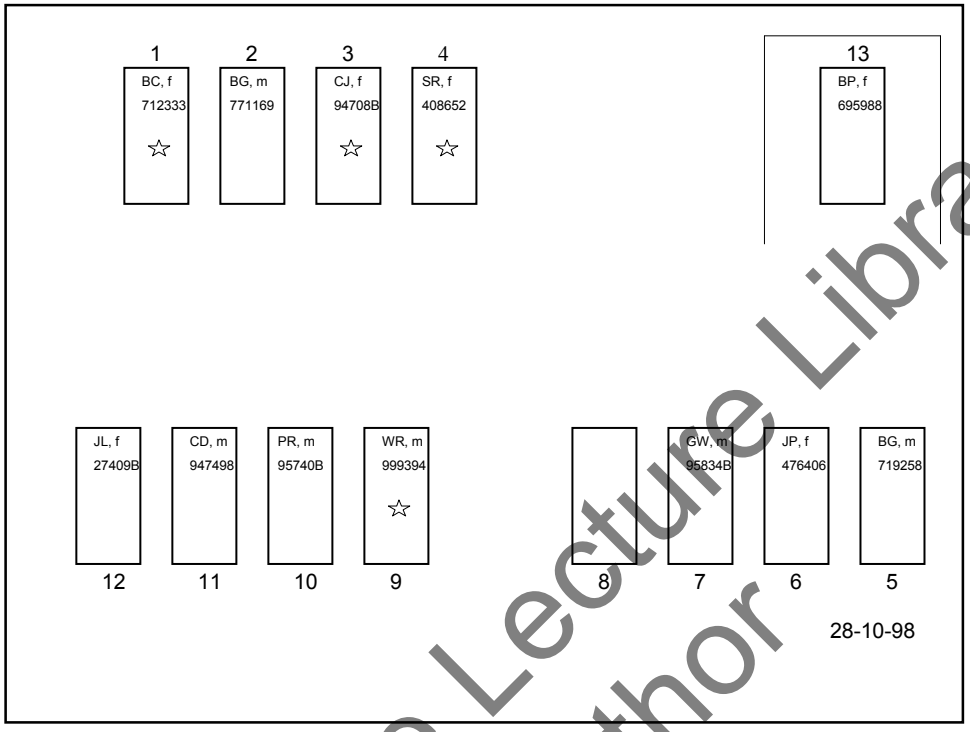


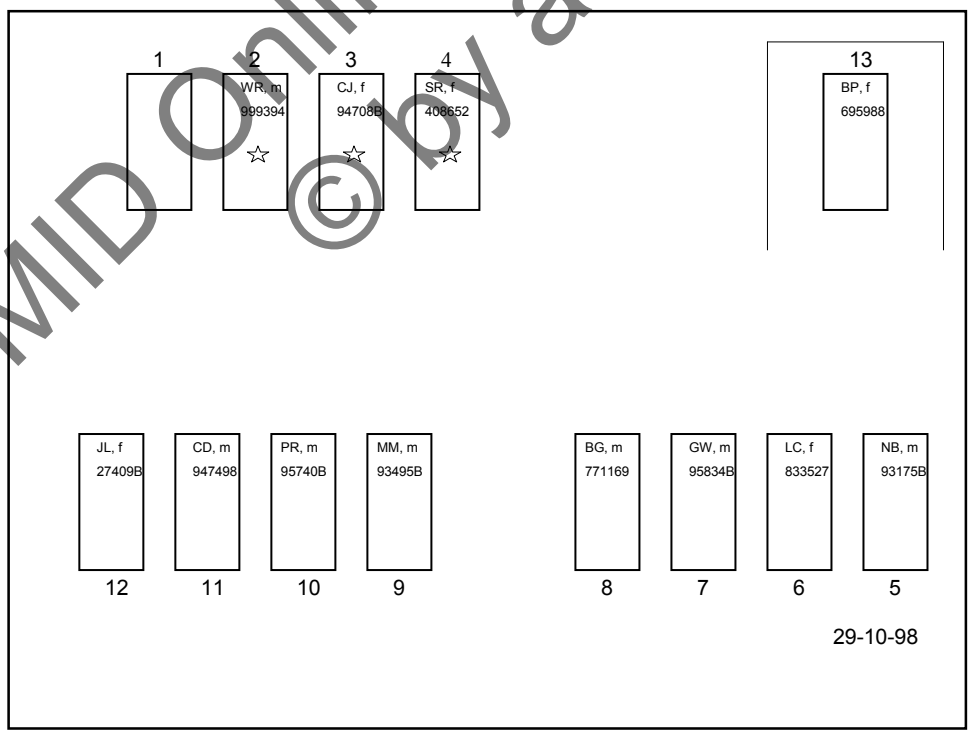


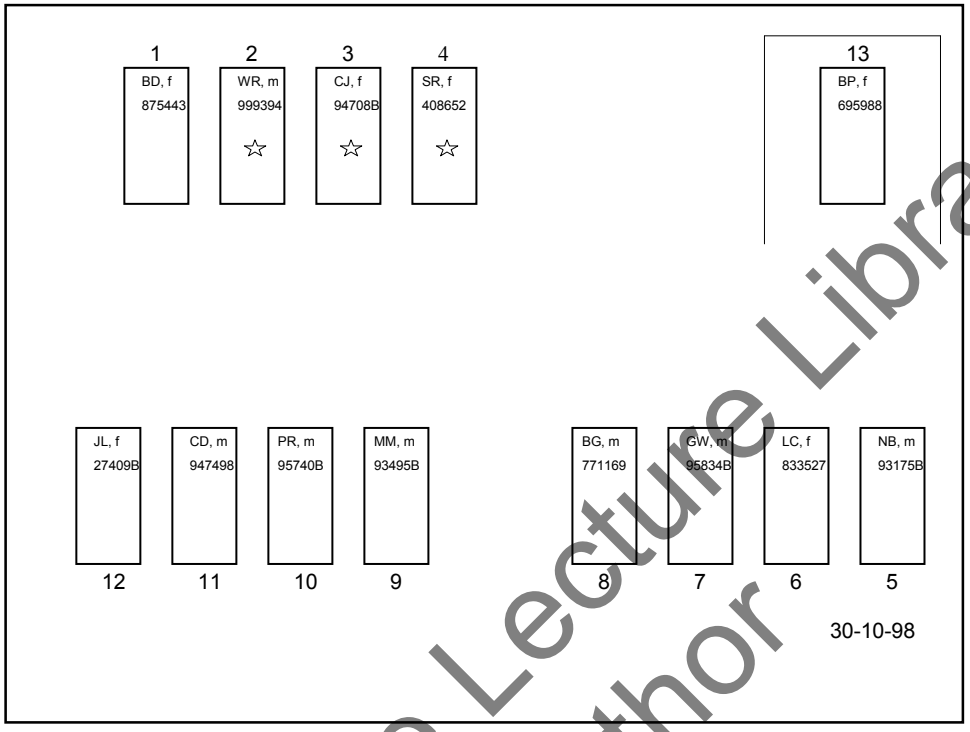


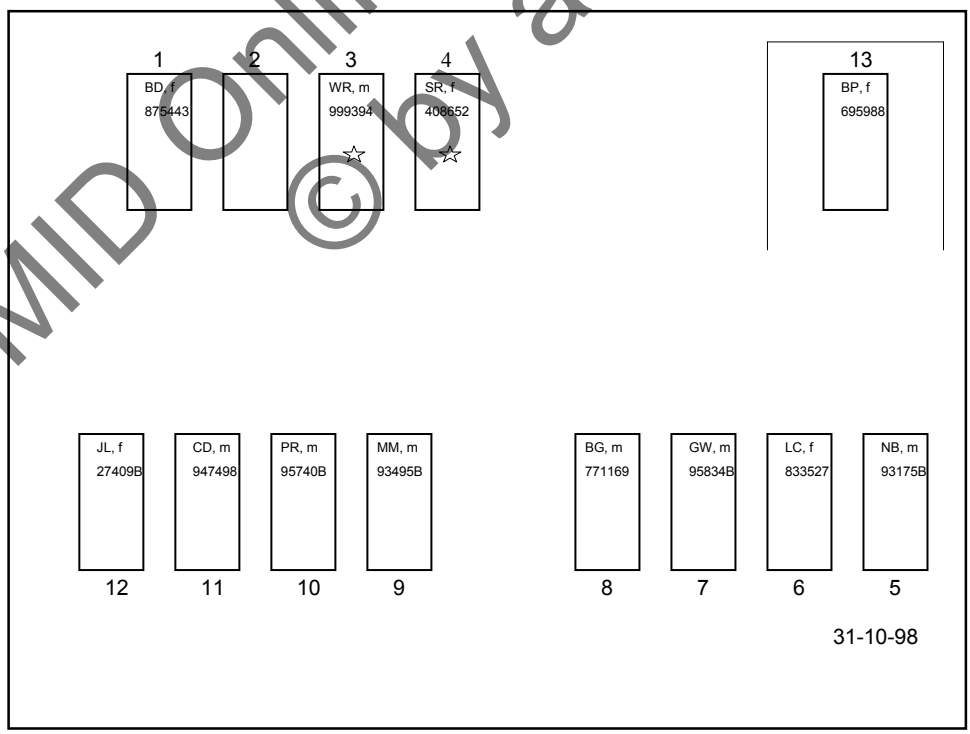


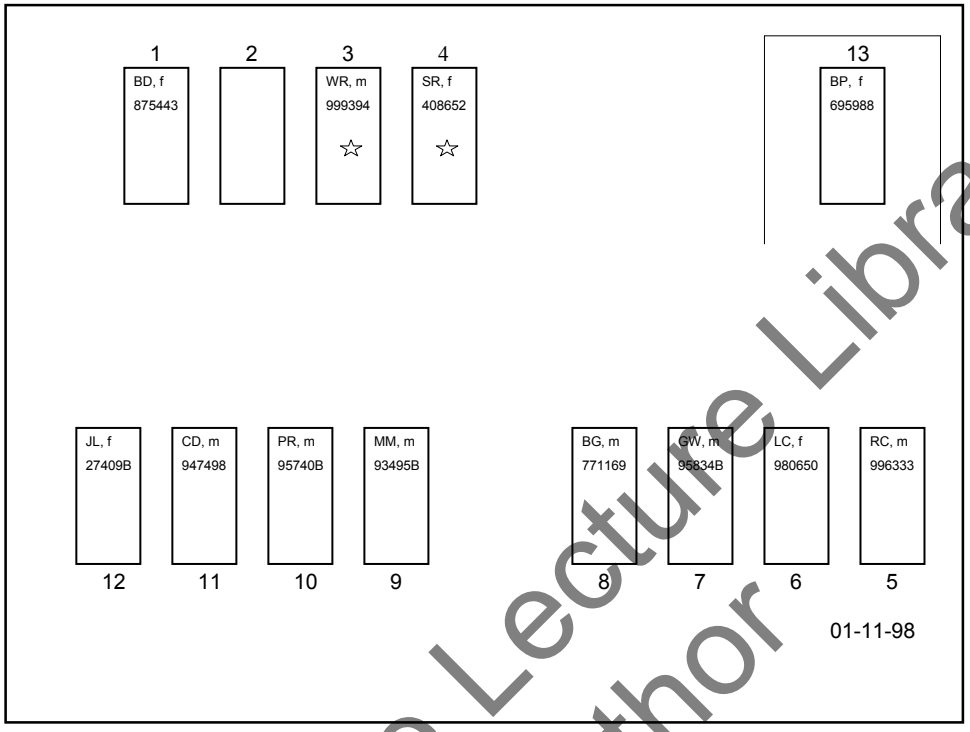


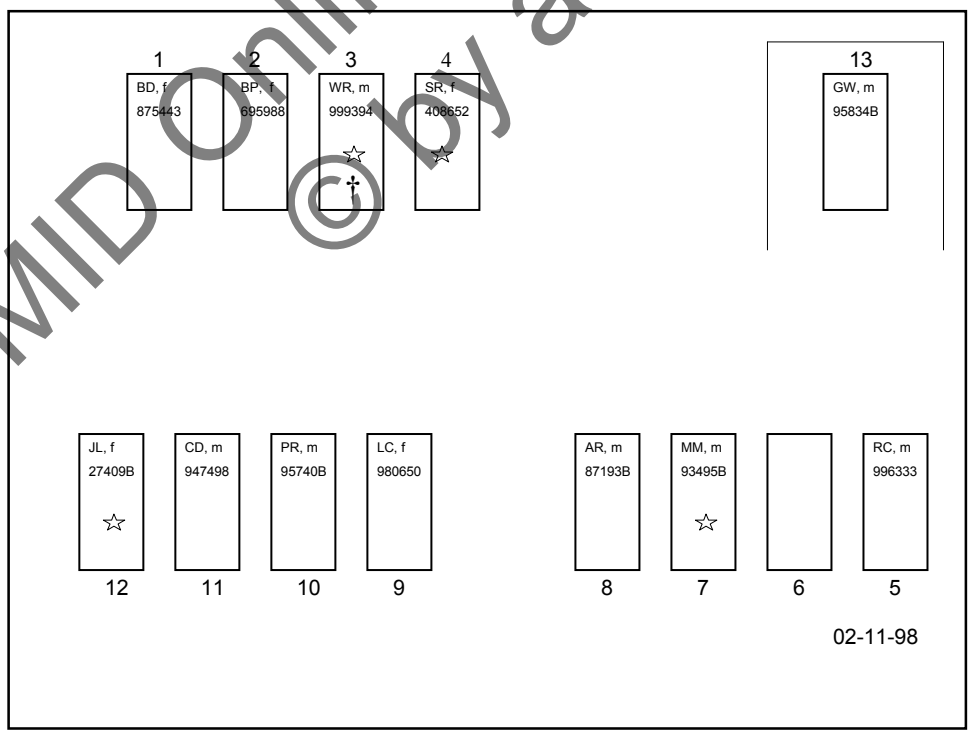


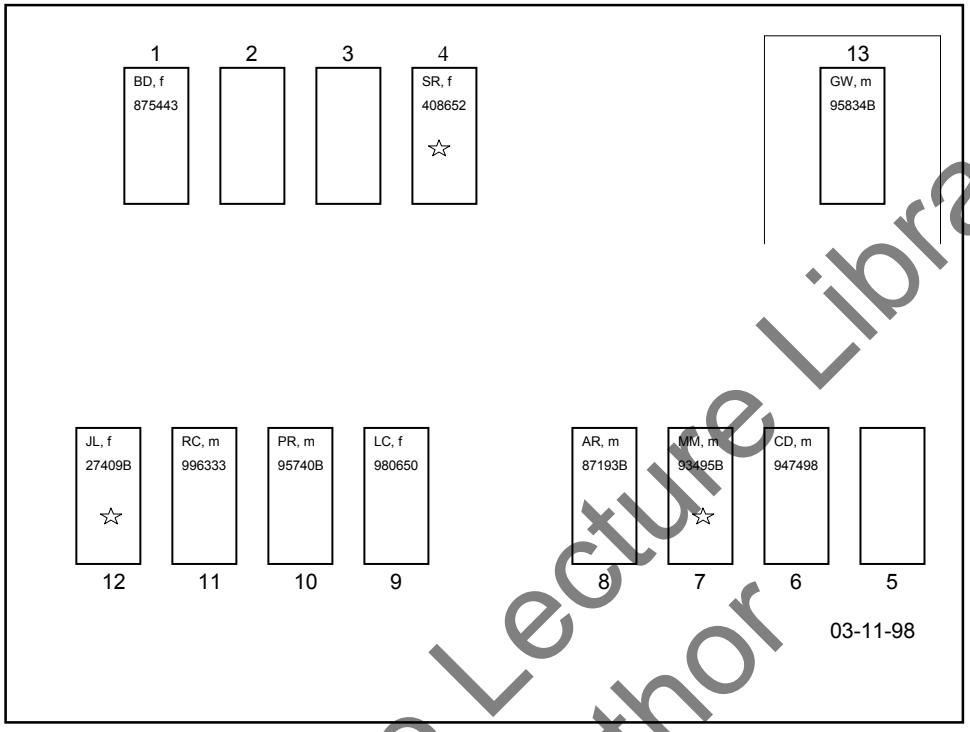


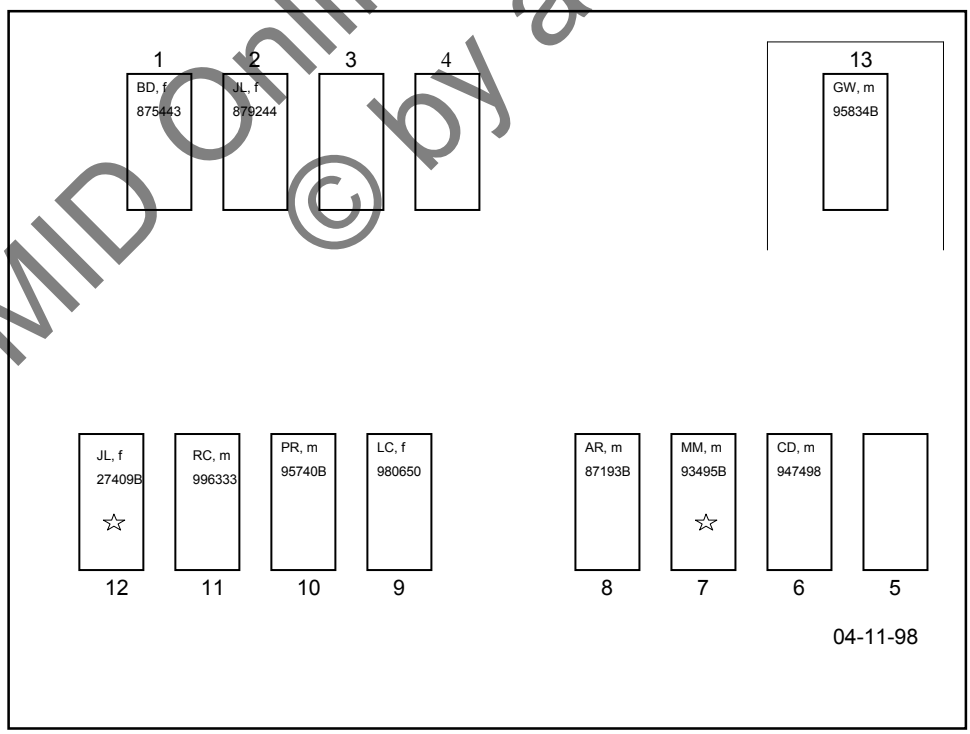










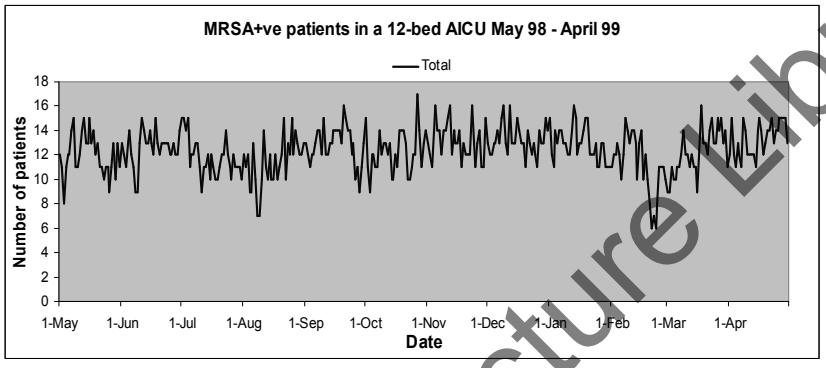


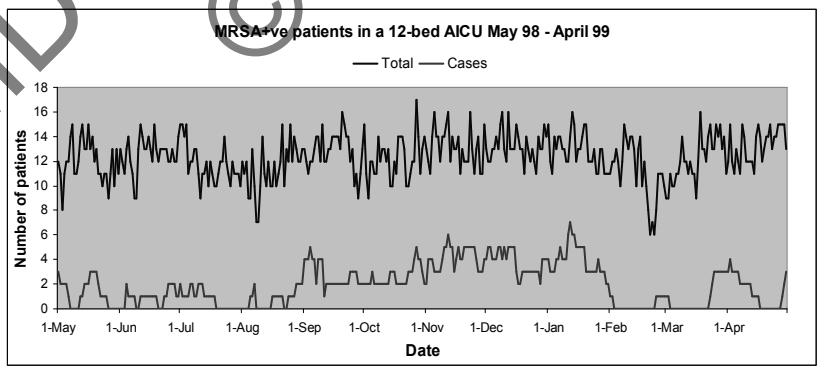
What the …. is going on ?

- How much transmission ?
- What are the risk factors ?
- What interventions ?
  - effective
  - affordable
  - timely

Cohort study

The following variables were recorded for each patient: age, sex, underlying conditions, reason for admission, urgency of admission (binary variable, defined as an "urgent" admission when patients had life-threatening conditions that required medical intervention within 24 h or as "planned" or "medical" otherwise), known MRSA carriage (before admission), previous hospitalization and origin of referral, immediate unit within the hospital before the ICU, time and place of intubation, Acute Physiology and Chronic Health Evaluation (APACHE) II score at 24 h, Glasgow coma score, number of organs that would fail without mechanical or pharmacologic support, duration and type of intubation, duration and type of nutrition (total parenteral or enteral), renal replacement therapy, delivery of nitric oxide, type and urgency of recent surgery, bronchoscopy and device use, radiologic and other diagnostic procedures that required transport to different hospital areas, and location of bed within the unit. Daily bed occupancy and nurse staffing levels on the ICU were also recorded. The previous day's nurse staffing levels were ascertained every morning and were calculated as the average number of qualified nurses per shift, excluding the 1 nurse not engaged in immediate patient care. Understaffing was determined by dividing the nurse staffing level by daily bed occupancy, and ratios <1 were considered to reflect a relative staff deficit.





Grundmann H, Hori S, Winter R, et al.

Risk factors for the transmission of MRSA in intensive care units: fitting a model to the data

J Infect Dis 2002, 185: 481– 488.

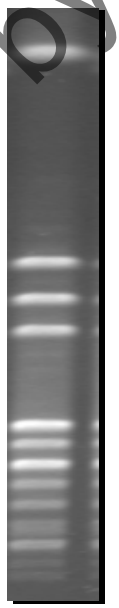
Clone A

Sub type a1

EMRSA 15

Clone B

Sub-type b1

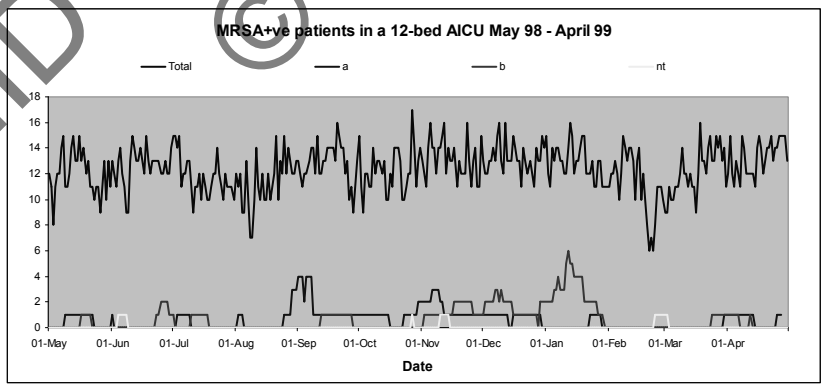


EMRSA 16

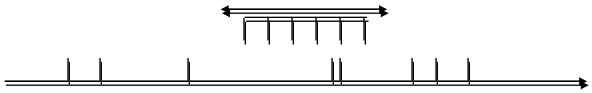
Genetic typing: Results

- 20 isolates belonged to genotype A
- 21 isolates belonged to genotype B
- 4 isolates were unavailable for typing
- genetic diversity was 0.52 (CI_{95} 0.45 - 0.62)

does that help?



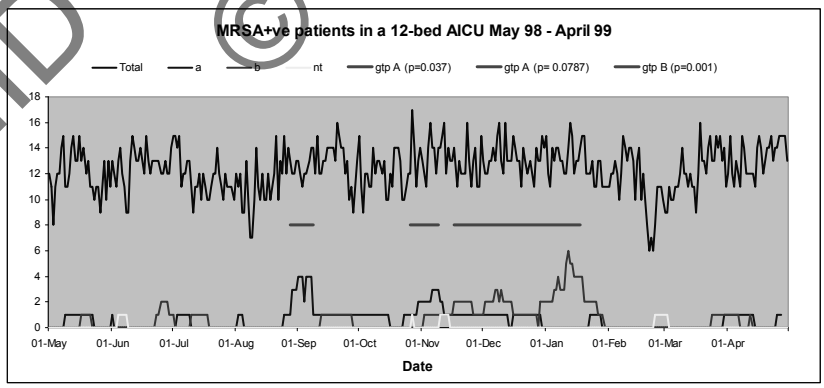
Detection of clustered cases



"sliding window or scan method"

- Test statistic S_w is the maximum number of cases when a predefined window is moved along a time series.
- The p value gives the probability for this number under the assumption of random distribution (null hypothesis)

Knox and Lancashire, 1982



Cohort study: Results 1

Independently associated with sporadic cases:

- Urgency of admission RR 3.2, p=0.018
- Bronchoscopy RR 3.5, p=0.010

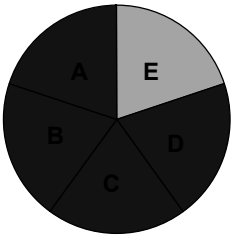
Cohort study: Results 2

Independently associated with clustered cases:

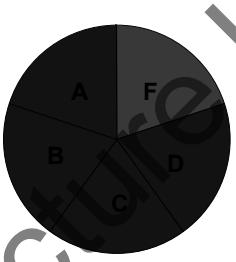
- Days of understaffing RR 1.05, p=0.001

Factors causing MRSA colonisation a case-case study

cases



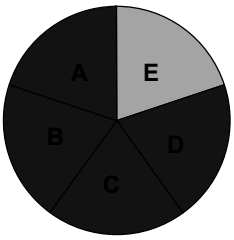
control-cases



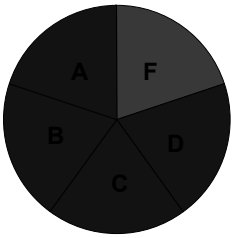
(McCathy & Gieseke 1999)

Factors causing MRSA colonisation a case-case study

clustered cases



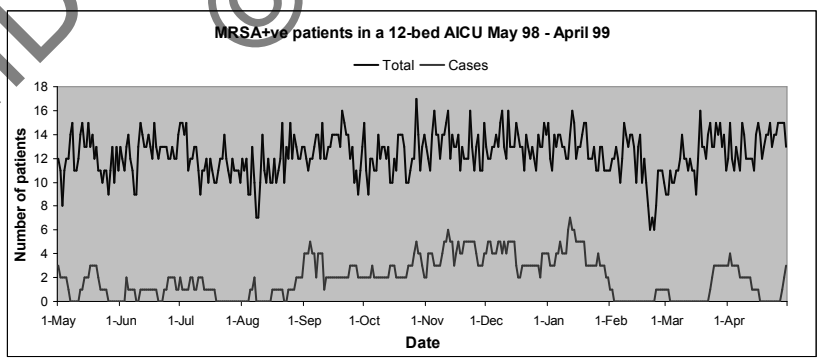
sporadic cases



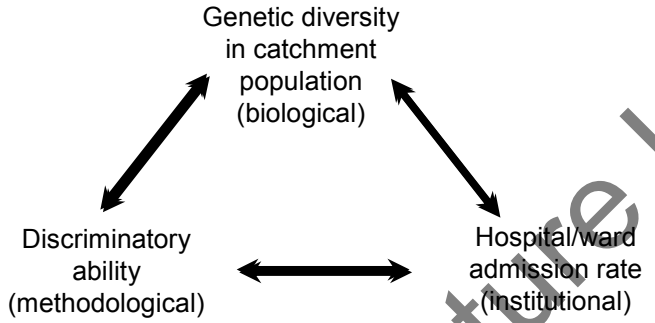
Case-case comparison

Comparing clustered with non-clustered cases:

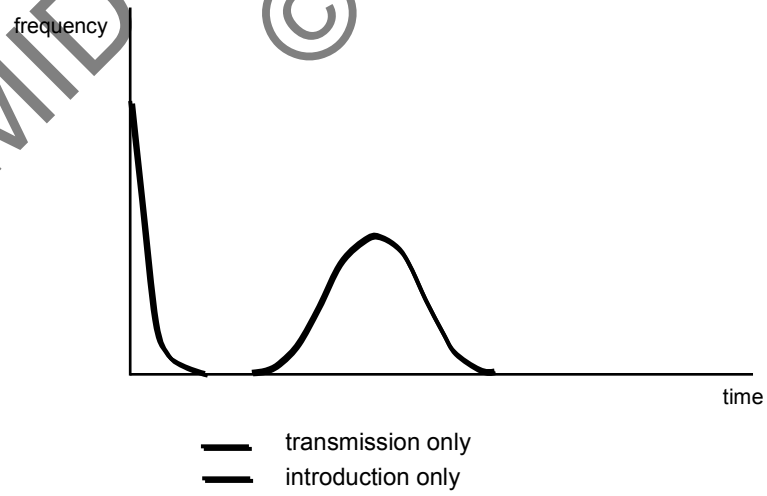
- Understaffing > 10 days OR 5.7, p=0.01
- Admission from a different hospital OR 0.16, p=0.01



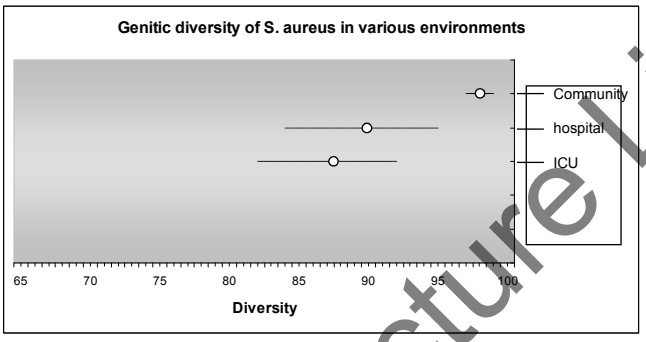
Constraints when identifying episodes of transmissions for hospital infection control



Average waiting times until isolation of identical *S. aureus* strain under different assumptions



Diversity of *Staphylococcus aureus* carriage strains in the UK

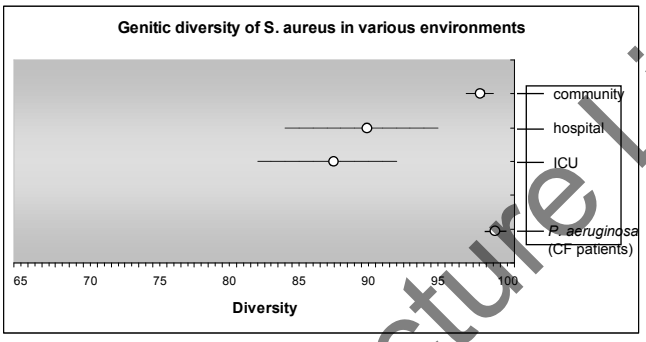


Grundmann H, Hori S, Tanner G.
Determining confidence intervals when measuring genetic diversity.
J Clin Microbiol 2001, 39: 4190 - 4192.

Expected average waiting times
depend strongly on catchment population

community	245 days
hospital	21 days
intensive care unit	9 days
observed	165 days

Diversity of *Staphylococcus aureus* carriage strains and *P. aeruginosa* from CF patients in the UK



Genetic diversity of 950 strains of *P. aeruginosa* from the cystic fibrosis community in the UK

(*Spe* I macrorestriction analysis)