



Epidemiology of human MRSA in Europe and public health importance of animal strains

Carl Suetens, ECDC, 08/04/2008

Why was ECDC established?



- Emerging and re-emerging communicable diseases revitalised through globalisation, bio-terrorism, interconnectivity, and EU without internal borders
- Health implications of enlarging EU
- Strengthen EU public health capacity to help meet EU citizen's concerns

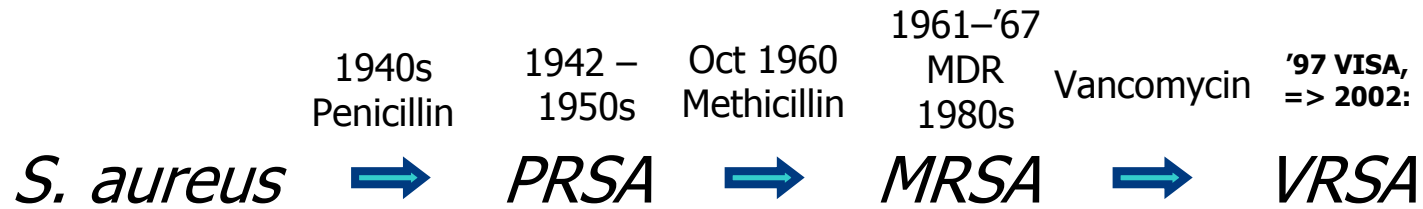
What is the role of ECDC?



Identify, assess & communicate current & emerging health threats to human health from communicable diseases
(ECDC Founding Regulation (851/2004), Article 1)

- EU level disease surveillance
- Scientific opinions and studies
- Early Warning System and response
- Technical assistance and training
- Epidemic intelligence
- Communication to scientific community
- Communication to the public

Evolution of resistance in *S. aureus*



whyfiles.org/shorties/085fast_evolution



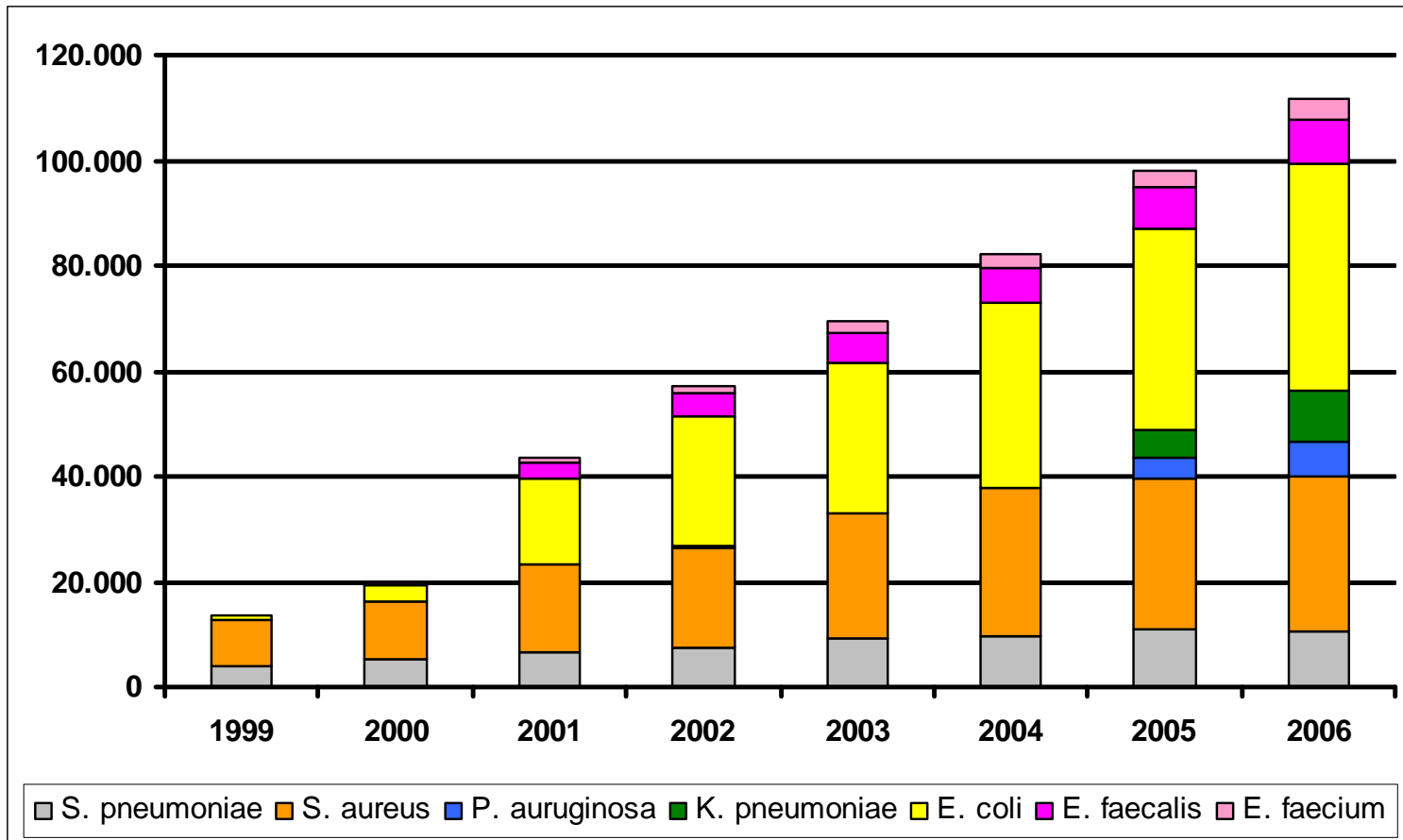
Impact of MRSA infections

- *S. aureus* bacteremia before 1940: 80% associated mortality => 20-30% after introduction of penicillin
- Mortality MRSA bacteremia vs MSSA bacteremia
 - Cosgrove et al., *Clin Infect Dis*, 2003, 36, 53-59 (metaanalysis): Pooled OR 1.9 (95% CI 1.5-2.4)
- Morbidity & mortality MRSA vs MSSA in pneumonia
 - Shorr. Morbidity and cost burden of MRSA in early onset VAP. *Critical care* 2006, 10:R97
 - Most mortality studies negative, eg Combes et al. Impact of Methicillin Resistance on Outcome of *S. aureus* VAP. *Am J Respir Crit Care Med*, 2004, 170, 786-792

European Surveillance of MRSA: EARSS 1999-2007



- Number of samples per species per year



EARSS

EUROPEAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM

rivm

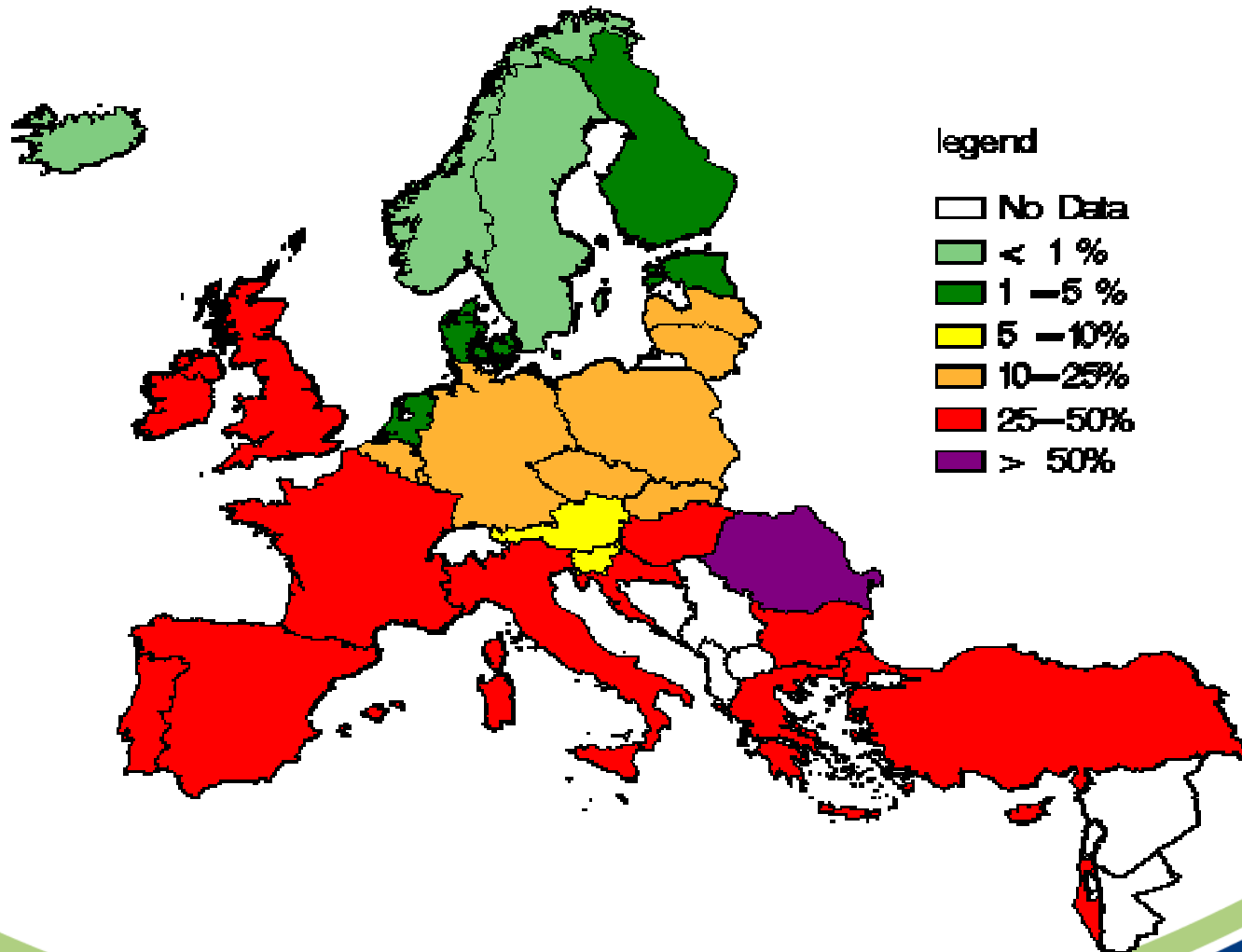
National Institute
for Public Health and
the Environment

Evolution of MRSA resistance rates in blood isolates in Europe, 2001-2006 (EARSS)

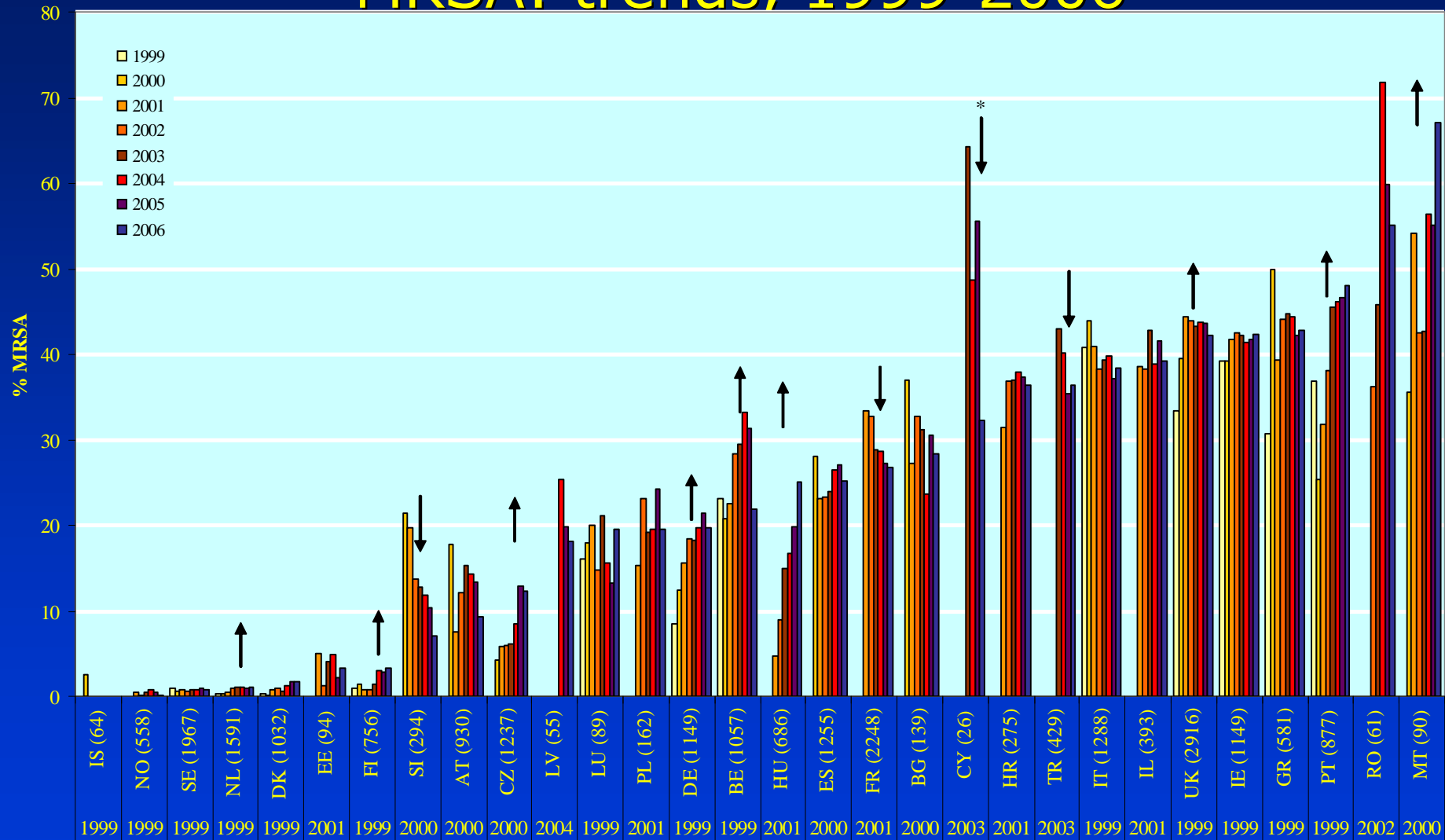


Proportion of MRSA isolates in participating countries in 2008

(c) EARSS



MRSA: trends, 1999-2006



Country code (average number of isolates reported per year) & year of surveillance start



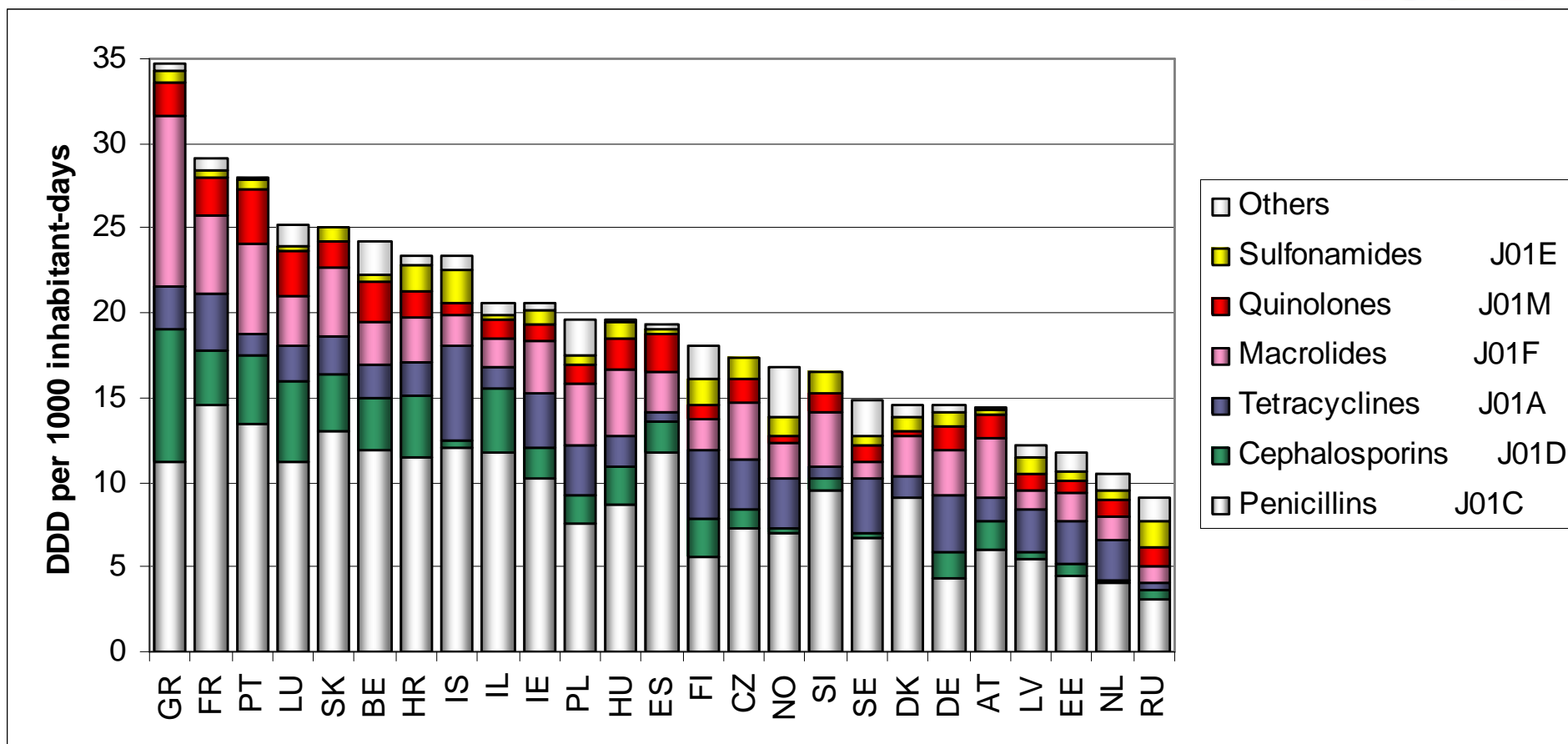
EARSS

EUROPEAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM

rivm

National Institute
for Public Health and
the Environment

Antibiotic use in humans (ESAC), 2005



MRSA : 3 epidemiological patterns



Healthcare-associated MRSA



Community-associated MRSA

Animal MRSA



Healthcare-associated MRSA

- First described in UK, 1961 – clonal waves, MDR in '80s
- Infections: Bloodstream infections, Hospital-acquired Pneumonia, Surgical site infections, Urinary tract infections, ...
- Risk factors: hospitalisation, invasive devices, underlying illness, AB use => later also LTCF (nursing homes...)
- \pm 4% of all nosocomial infections in the EU (*S. aureus* 15% (prevalence surveys), 24% mean %MRSA (EARSS))
=> \pm 1-200 000 nosocomial MRSA infections per year in EU27
- Major clones < 4 MRSA lineages (CC5, CC8, CC22, CC45), e.g. UK E-MRSA-15&16, Iberian... (SCC*mec* types I,II, III + IV)



Community-associated MRSA



- First described in Australia, 1993 (indigenous population)
- Frequent Panton-Valentine Leukocidin (PVL) positive, less MDR
- Infections: Skin and soft tissue infections, septic arthritis, TSS, necrotising pneumonia
- Main risk factor: high intensity physical contact (jailed inmates, MSM, military recruits, sportsmen, children in day care centres), younger patients
- Major clones: USA300 (ST8-SCC mec IV) , ST30 (Australia, Europe), ST80 (Mediterranean clone), ST-8 (French clone), ...
- Emergence in hospitals, mainly US (e.g. King MD et al. Emergence of community-associated methicillin-resistant *Staphylococcus aureus* USA300 genotype as a major cause of health care-associated blood stream infections. Clin Infect Dis. 2006 Mar 1;42(5):647-56)
- Ratio colonisation:infection 4:1 (Harbarth S. et al. Community-associated methicillin-resistant *Staphylococcus aureus*, Switzerland. Emerg Infect Dis, 2005 Jun)
- More sensitive to antibiotics (fluoroquinolones, tetra, ctmx)

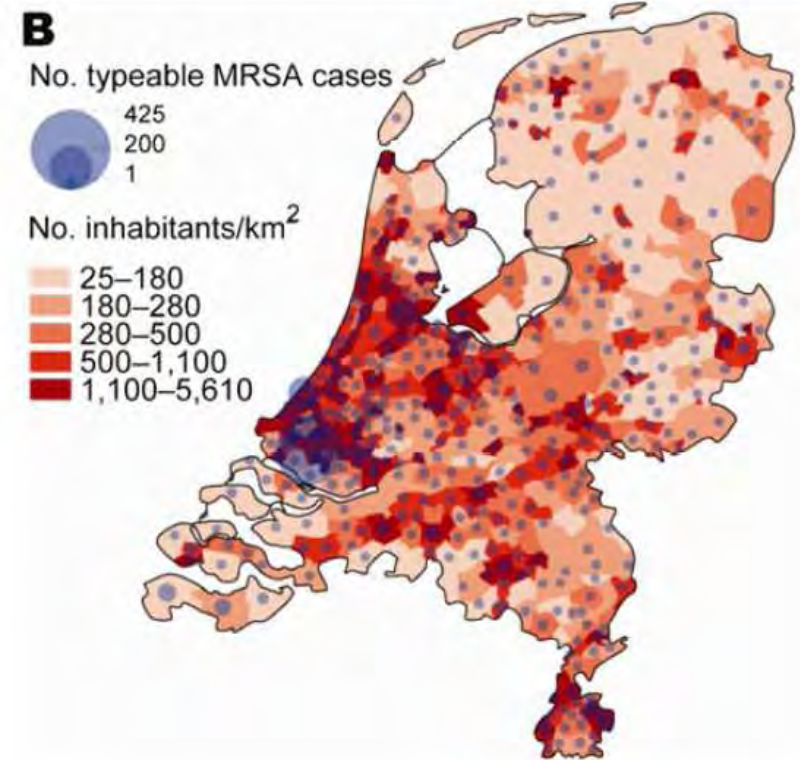
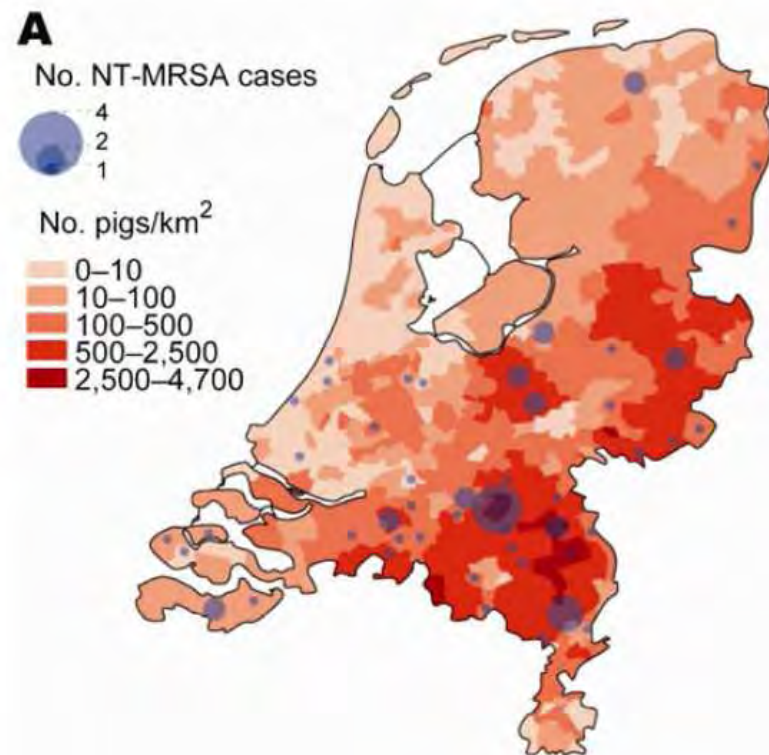
Animal MRSA in humans: occurrence



- Non-typable by PFGE with *Sma*I restriction digest (NT-MRSA)
- MLST type ST398, major *spa* types: t011, t108, t034, t567
- Mostly PVL negative, 1 PVL+ ST398 report from China
- Netherlands, France, Denmark, Germany, Austria, Italia, Spain, Hong-Kong, Thailand, Canada, Belgium
- MRSA carriage in pigs and pig farmers:
 - NL: 11 to 39% MRSA+ pigs in farms and slaughterhouses
 - Canada (20 farms, Khanna et al, 2007): farmers 20%, pigs 25%
 - BE: representative national survey in 50 pig farms, 2007 (BAPCOC report; O. Denis et al., 2008): farmers 37.8% (95% CI 25.6-50.0%), pigs 44%
- High prevalence in veterinarians:
 - 34/272 (12.5%) from 9 countries at international conference in Denmark, 31/34 ST398 (Wulf MW et al., CMI 2008, 14, 29-34)



Geographical distribution of ST398 MRSA versus other genotypes



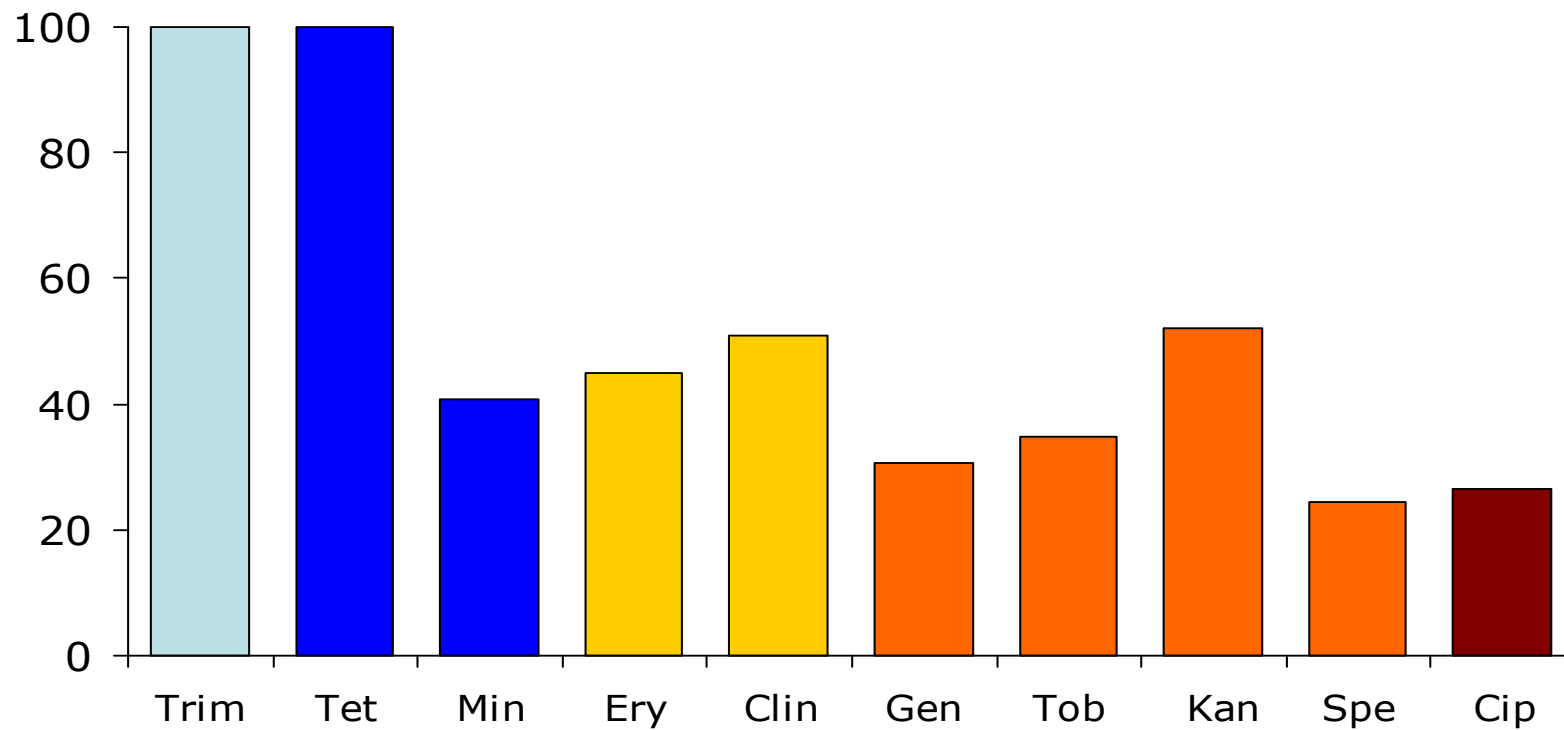
van Loo I, Huijsdens X, Tiemersma E, de Neeling A, van de Sande-Bruinsma N, Beaujean D, Voss A, Kluytmans J. Emergence of methicillin-resistant *Staphylococcus aureus* of animal origin in humans. *Emerg Infect Dis.* 2007 Dec;13(12):1834-9.

Animal MRSA in humans: risk factors



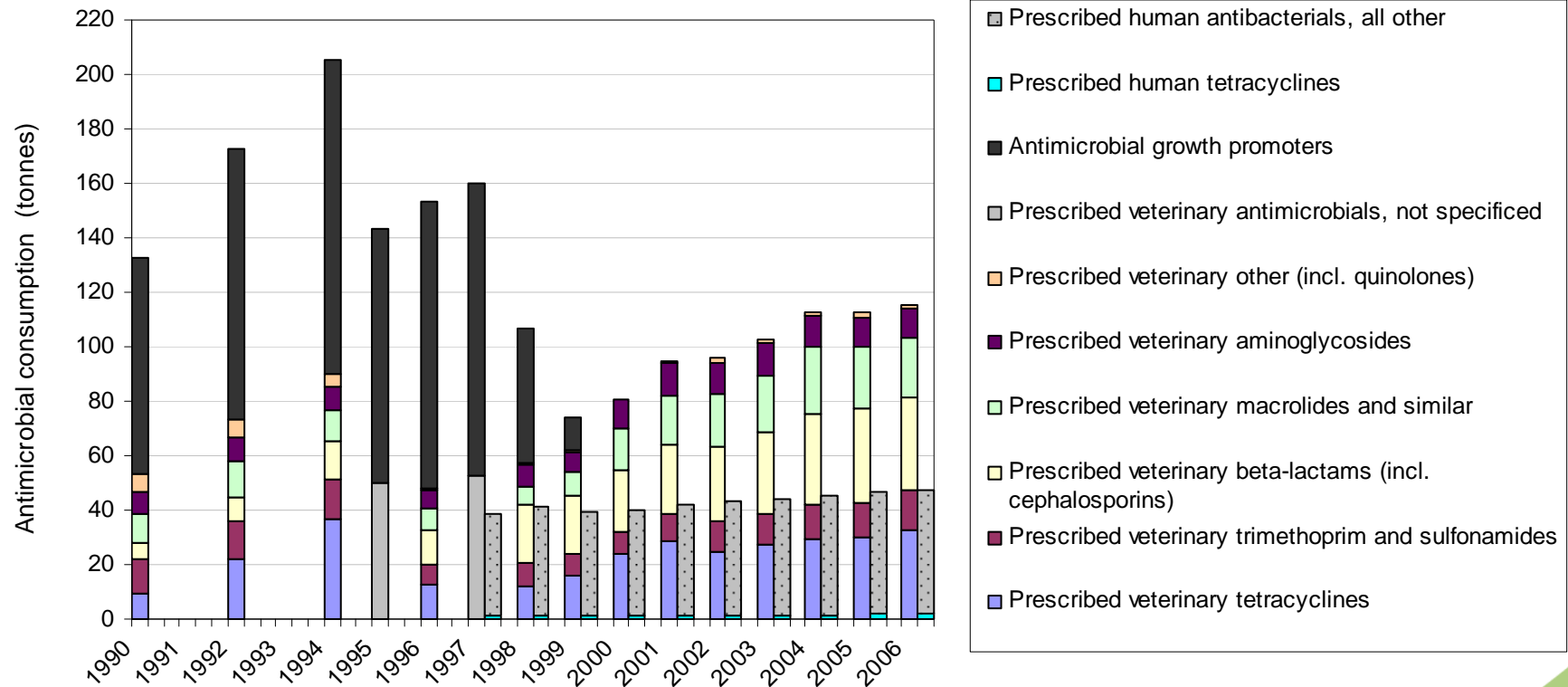
- NL (case-control study national MRSA database, Van Loo et al. EID 2007): contact with pigs (OR 12) and cattle (OR 20)
- BE (national prevalence survey in pig farms, cross-sectional): frequency of pig contact (OR 10), reported contact with dogs (OR 16) and horses (OR 5)
- Canada (veterinary conference): large-animal practice (OR 2.9)
- Reported protective measures (masks, gowns, gloves) often no effect => needs further research
- Resistance to doxycycline => spread facilitated by abundant use of tetracyclines in farming (De Neeling et al., Vet Microbiol. 2007)

Proportion of human MRSA isolates resistant to antibiotics, pig farmers and relatives, Belgium 2007



Source: Belgian Reference Laboratory for Staphylococci – MRSA (Struelens, Denis)

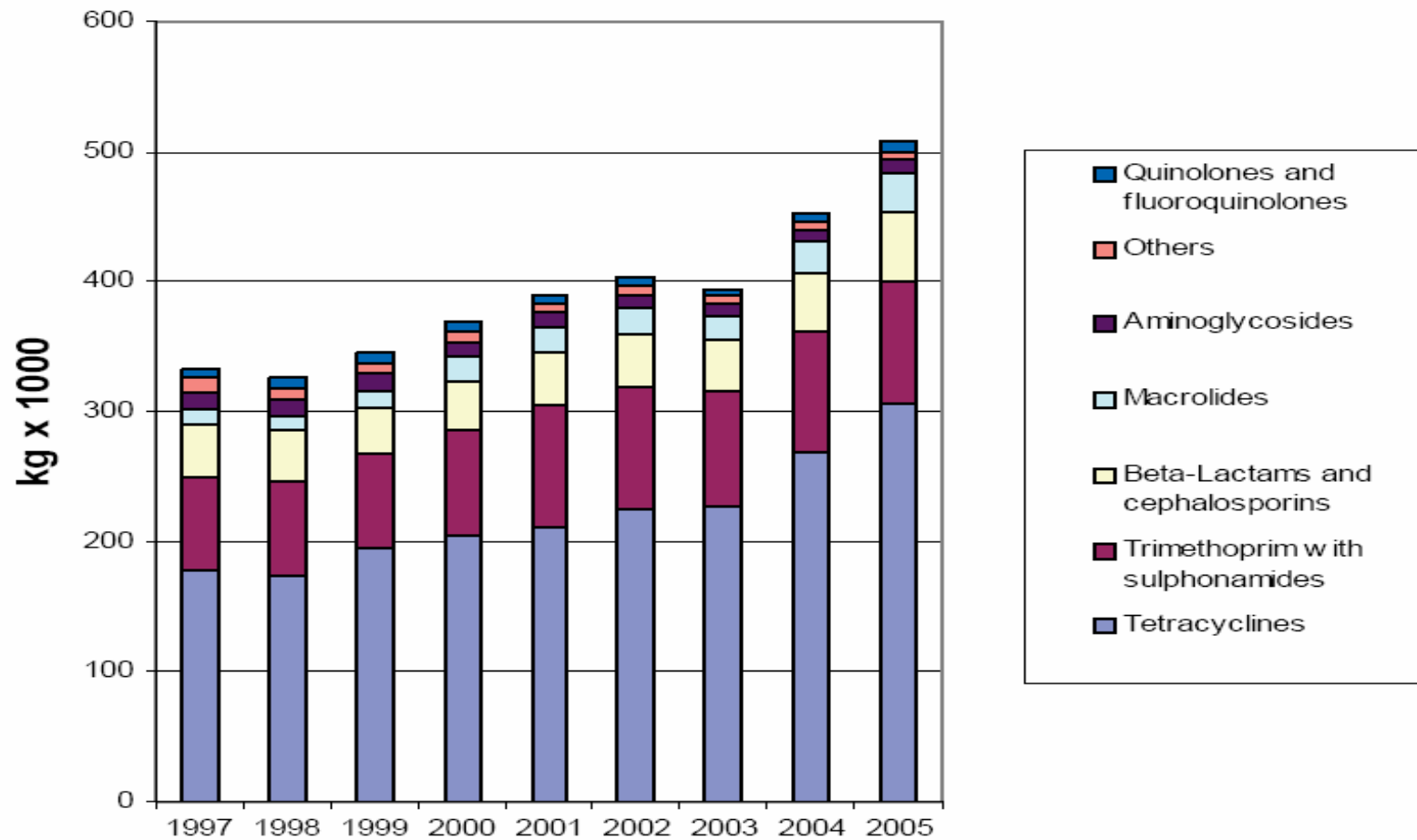
Consumption of Prescribed Antimicrobials and Growth Promoters in Animal Production and Prescribed Antibacterials in Humans, Denmark, 1990-2006



Adapted from: DANMAP2004 report.



Antibacterial Drugs for Therapeutic Use in Food Animals, Netherlands, 1997-2005



Source: MARAN 2005 report.

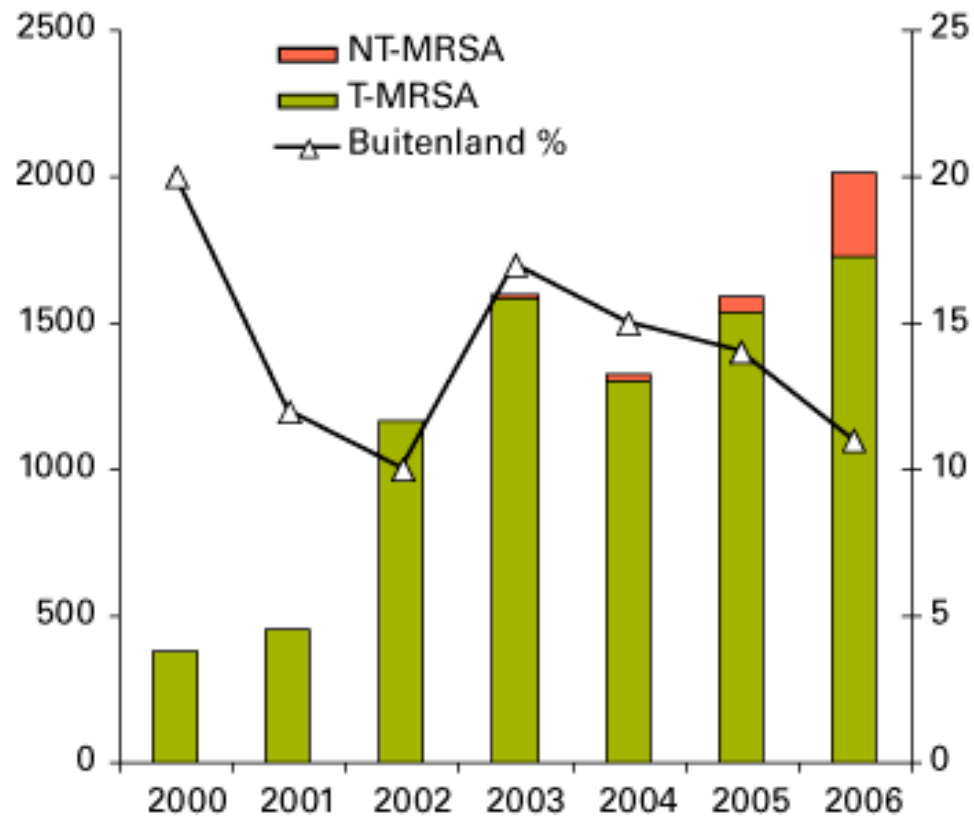


Animal MRSA: impact



- NT-MRSA cases found in national surveillance of MRSA in hospitals (e.g. NL, BE)
- First hospital outbreak described (Wulf et al. First outbreak of MRSA ST398 in a Dutch hospital, June 2007. Euro Surveill 2008;13(9)):
 - 5 patients (2 diabetic foot ulcers) and 5 healthcare workers (238 screened)
 - *Spa* type t567
 - Possible source: HCW living on grounds of pig farm

Proportion of animal MRSA in national surveillance in The Netherlands



Wannet W.J.B. et al. Infectieziekten bulletin 2007, 18 (10), 347-351

Van Rijen MM, van Keulen PH, Kluytmans JA. Increase in a Dutch hospital of methicillin-resistant *Staphylococcus aureus* related to animal farming. Clin Infect Dis. 2008 Jan 15;46(2):261-3.

Human infections with MRSA ST398 in Belgium

Année	Sexe	Age (ans)	Source	Unité d'hospitalisation	Acquisition	Commune
2003	M	67	Respiratoire	Méd. Interne	Communautaire	St-Truiden
2003	F	76	Hémoculture	Autre	Nosocomiale	Brugge
2005	M	70	Dépistage	Autre	Nosocomiale	Brugge
2005	F	67	Urines	Méd. Interne	Nosocomiale	Roeselare
2005	F	76	Respiratoire	Gériatrie	Communautaire	Roeselare
2005	F	?	NP	NP	NP	Roeselare
2006	M	6	Hémoculture	Pédiatrie	Communautaire	Ieper
2006	F	64	Pus	Chir.	NP	Roeselaere

Source: Belgian Reference Laboratory for Staphylococci – MRSA (Struelens, O. Denis)

Ph. Declercq et al. CA-MRSA Infection of Porcine Origin

Figure 1. (a) Fore arm after initial debridement (2 March 2006). (b) Fore arm after final treatment (22 March 2006).



Public health importance

- Farmers, veterinarians and family:
 - *S. aureus* carriage in hospitals => risk of infection vs non-carriage x 4 (Safdar and Bradley, Am J Med, 2008, 121, 310-5)
 - ⇒ increased risk of MRSA infection if hospitalized =
 $.05_{NI} * .15_{SA} * .6_{MRSA\%} * 4 = 1.8\%$
 - ⇒ First line treatment of infections (e.g. skin) in this population may be ineffective
- Potential for inter-human transmission & hospital epidemics
 - ⇒ New challenge for MRSA control, particularly low-prevalence countries
 - ⇒ Need for adapted guidelines: MRSA screening in hospital e.g. at admission, impact on infection control procedures in hospitals (isolation, decolonization etc)
- Food hygiene (van Loo IH et al. Methicillin-resistant Staphylococcus aureus in meat products, the Netherlands. Emerg Infect Dis. 2007 Nov;13(11):1753-5)