Molecular Epidemiology of MRSA in Europe

Alex W. Friedrich, University of Muenster, Germany

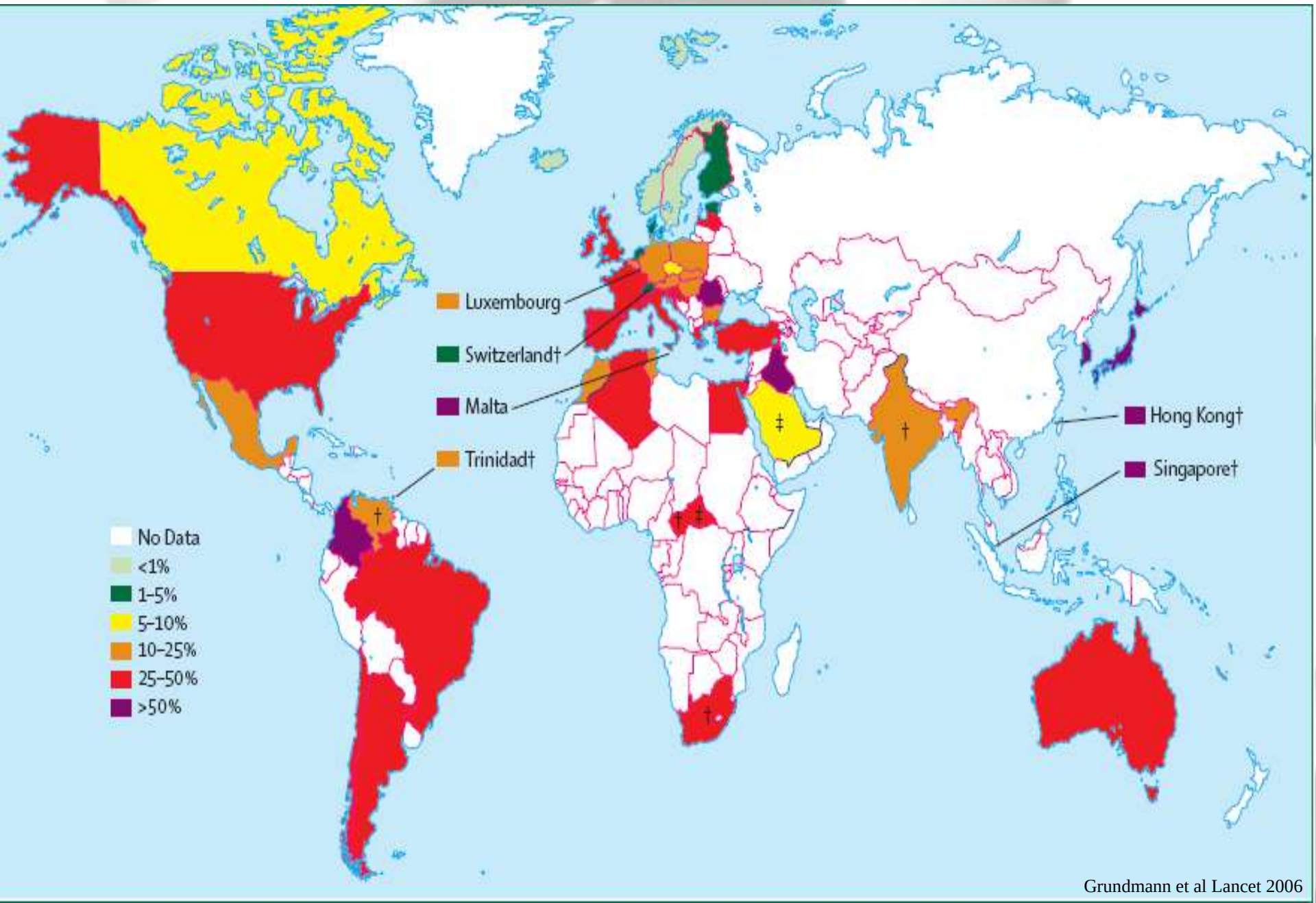
INTERREG - Grenzregionen gestalten Europa
Europäischer Fonds für Regionale Entwicklung der Europäischen Union
INTERREG - Grensregio's bouwen aan Europa
Europees Fonds voor Regionale Ontwikkeling van de Europese Unie

State of **North Rhein-Westfalia**
18 Mio inhabitants
2nd largest university in Germany

Townhall of the Westfalian Peace Treaty
City of Münster

Münsterland

MRSA prevalence in *S. aureus* bacteriaemia worldwide



Grundmann et al Lancet 2006

MRSA in Europe

- Affects **150.000 patients** per year in Europe
- **MRSA-infection**:
  Up to 2,4 times significantly higher Mortality
- Issue of **patient safety**
- **Reason for emerging MRSA**
  - insufficient hygiene in hospitals
  - to many antibiotics given
  - lack of trans-mural case management
- **Nasal carriage** origin of infection
  -> Finding and treating carriers avoids infection !

- **MRSA additional costs**: Per patient: 5.000 € to 20.000 €
  EU healthcare system: 380 Mio € per year
- **Differences in MRSA-Prevalence** between countries

Koeck et al. 2010. Eurosurveillance

Methicillin-resistant *Staphylococcus aureus* (MRSA): burden of disease and control challenges in Europe

R Köck[1,2], K Becker[2], B Cookson[3], J E van Gemert-Pijnen[4], S Harbarth[5,6], J Kluytmans[7,8], M Mielke[9], G Peters[2], R L Skov[10], M J Struelens[11,12], E Tacconelli[13], A Navarro Torné[12], W Witte[14], A W Friedrich (alexander.friedrich@ukmuenster.de)[1]

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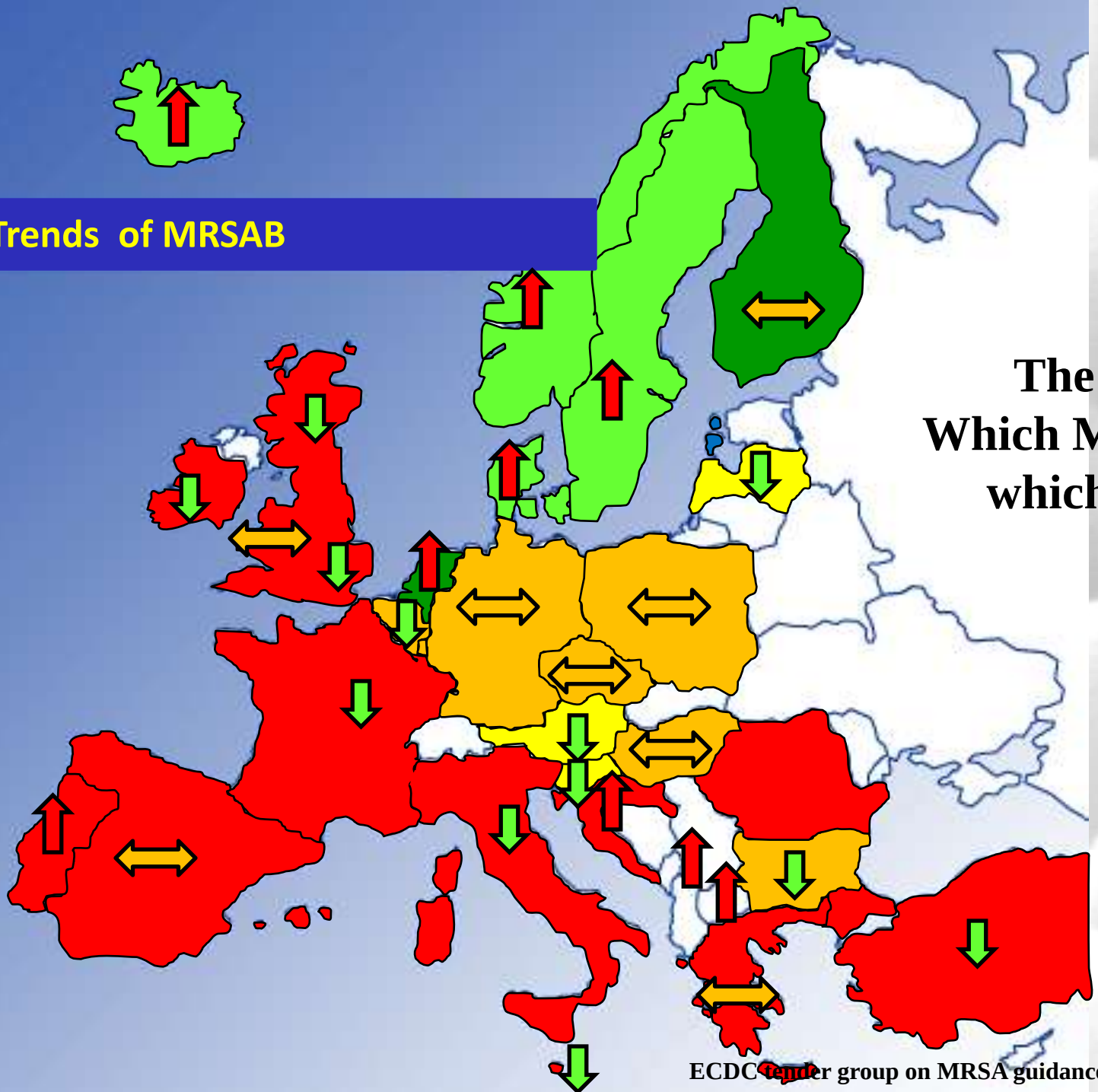
4. Faculty of Behavioural Sciences, University of Twente, Enschede, the Netherlands
5. Infection Control Program, University Hospitals of Geneva, Geneva, Switzerland
6. University of Geneva Medical School, Geneva, Switzerland
7. VU University Medical Centre, Amsterdam
8. Amphia Hospital,
9. Robert Koch Instit
10. Statens Serum Ins
11. Department of Mic started)
12. Scientific Advice U
13. Department of Infe
14. National Reference

Type, place and period of study	Odds ratio/hazard ratio for MRSA-associated mortality (95% CI)	Percentage mortality in MRSA patients
Single-centre, university hospital, Taiwan, 1990–2004	1.78 (1.3–2.44)	50%[a]
Single-centre, university hospital, Belgium, 1992–1998	1.93 (1.18–3.18)	64%[b]
Single-centre, teaching hospital, UK, 1995–2000	1.72 (0.92–3.20)	12%[c]
Veterans affairs healthcare system, USA, 1995–2003	1.8 (1.2–3.0)	34%[d]
Single-centre, university hospital, USA, 1996–2001	5.4 (1.5–18.7)	35%[d]
Single-centre, university hospital, France, 1997–1998	2.97 (1.12–7.88)	43%[e]
Single-centre, tertiary-care teaching hospital, USA, 1997–2000	1.2 (0.68–2.12)	23%[f]
Multi-centre, Germany, 1997–2002	3.84 (1.51–10.2)	17%[c]
Two centres, teaching hospital UK, 1997–2004	1.49 (0.99–2.26)	34%[a]
Single-centre, teaching hospital, USA, 1999–2001	1.4 (0.7–3.0)	31%[a]
Single-centre, teaching hospital, Brazil, 2000–2001	2.52 (0.96–6.6)	55%[a]
Single-centre, university hospital, Taiwan, 2001–2006	0.73 (0.21–2.60)	10%[a]
Single-centre, university hospital, Belgium, 2002–2004	3.04 (1.15–8.04)	42%[g]
Single-centre, university hospital, Germany, 2002–2007	2.6 (1.4–4.9)	42%[d]
Single-centre, tertiary care, USA, 2004–2005	5.1 (1.1–22.9)i	47%[h]

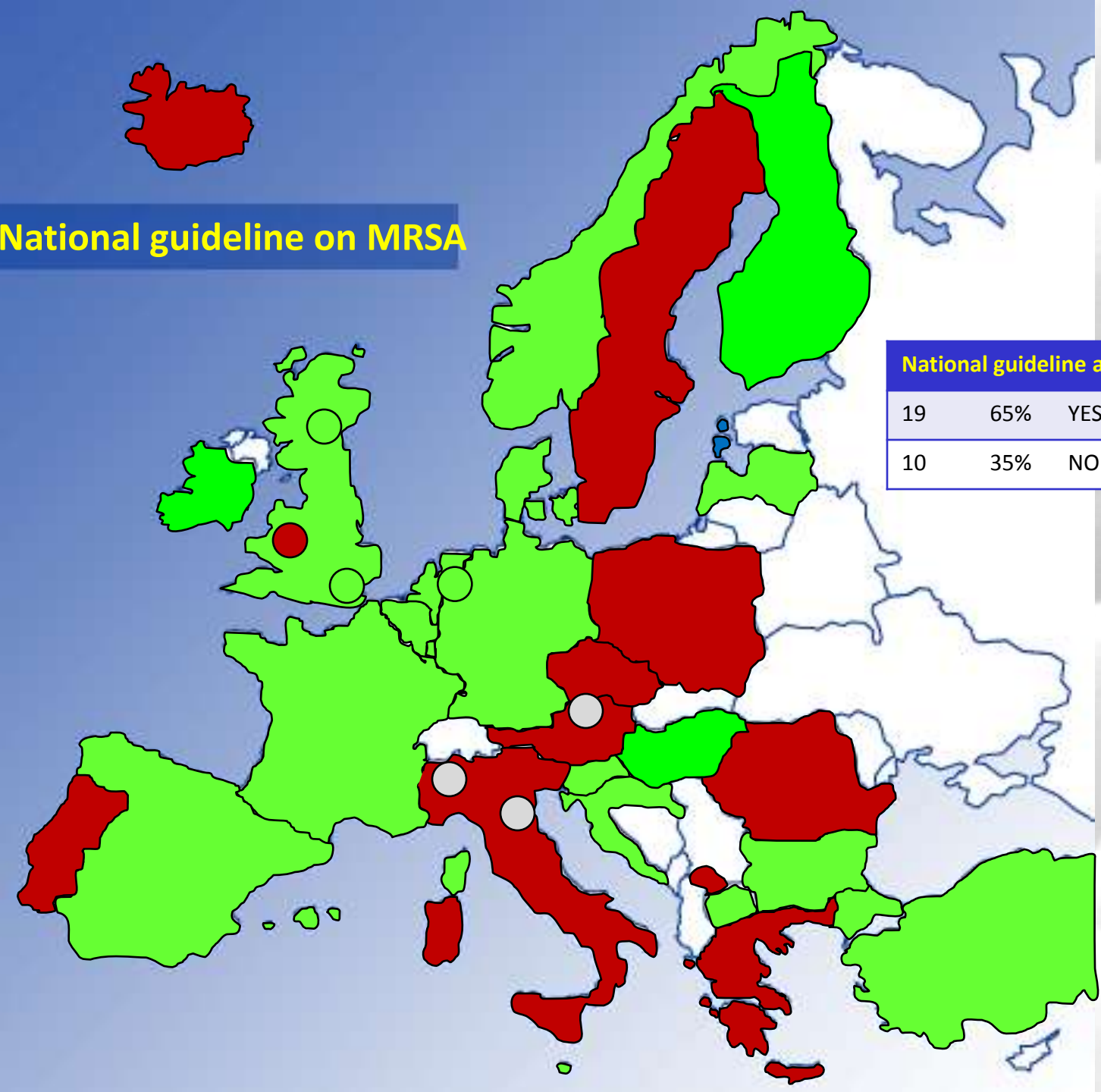
Trends of MRSAB



The question is:
Which MRSA are rising, which are falling ?

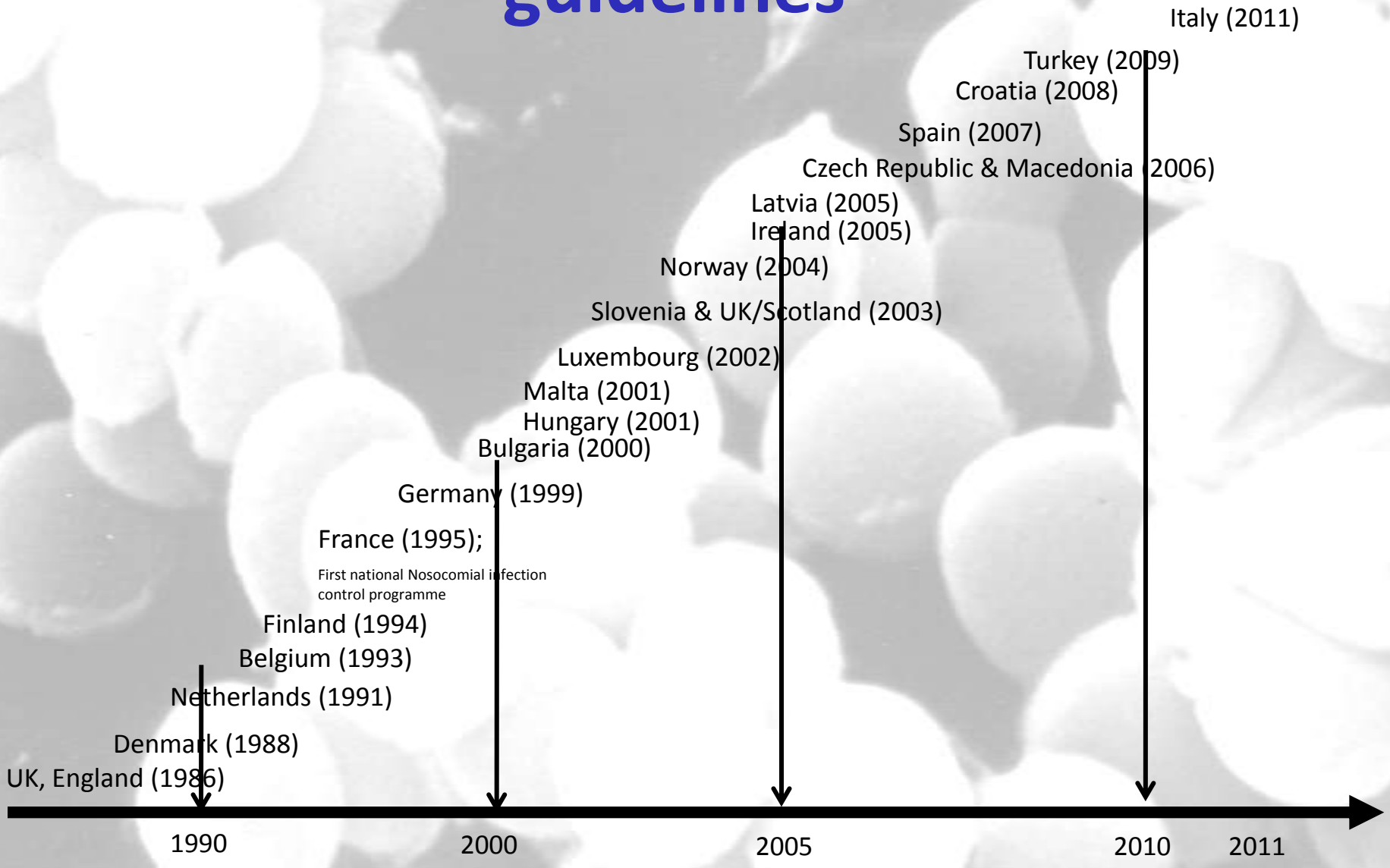
ECDC tender group on MRSA guidance, London, 22 of October 2009

National guideline on MRSA



National guideline available (n=25)			
19	65%	YES	
10	35%	NO	

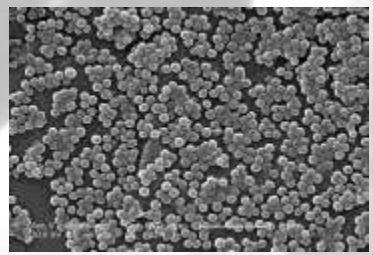
First edition of national MRSA guidelines



Preventive Microbiology
=
infection control

Robert Koch,
founder of modern bacteriology

Vibrio cholerae,



MRSA,

Cholera-infection control measures (1908):

„Everything depends on the fact that we have valid detection methods for the microorganisms.

This counts especially for the human carrries who contribute most for the spread of the disease“

Speech of Robert Koch on 11.2.1908 in front of the Medical order of Berlin
Deutsche Medizinische Wochenschrift, 1908, Nr. 8

MRSA „search&follow-Strategy“ (2010)

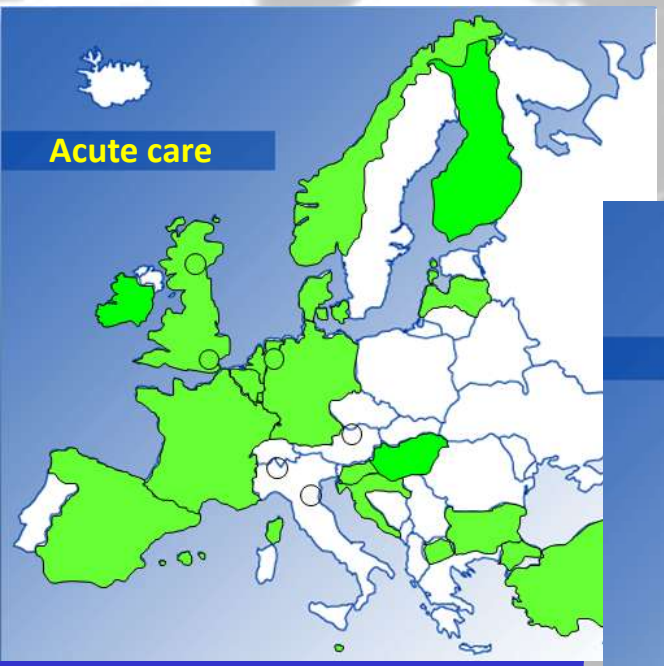
Colonisation comes before infection

A: Rapid identification of MRSA-carriers
B: Decolonization of MRSA-carriers,

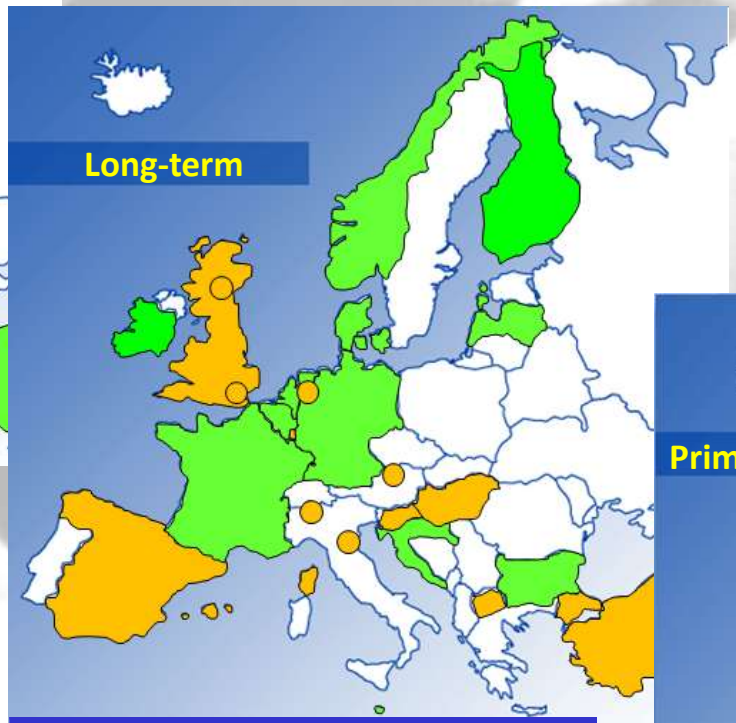
In order to:
a.) prevent infection in the patient
b.) prevent spread to other patients

c.) start early an optimal antibiotic therapy

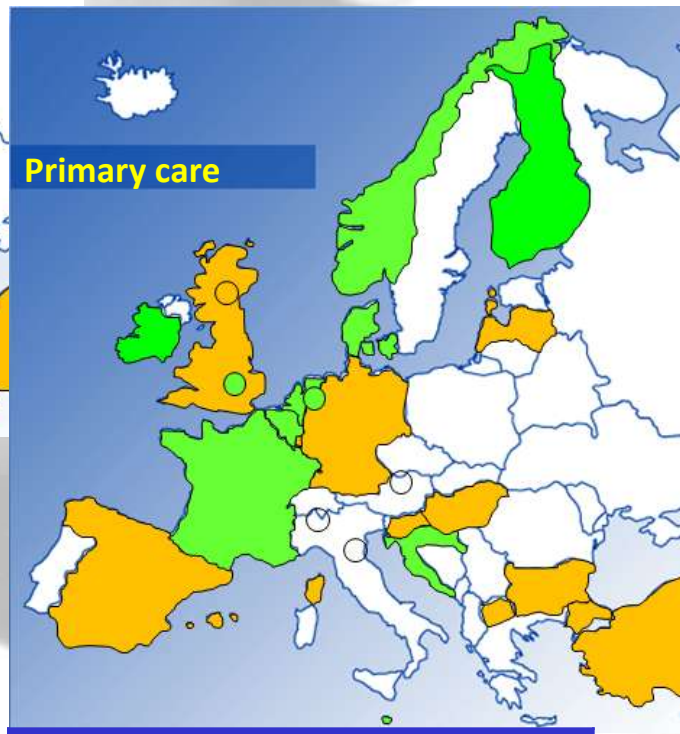
Health-care settings covered by MRSA national guideline



Guideline available (n=19) ?		
19	100%	YES
0	0%	NO



Guideline available ?		
12	63%	YES
7	37%	NO



Guideline available ?		
6	32%	YES
13	68%	NO

SeqNet.org does…

A. Capacity building for sequence based typing in European laboratories

- International workshops since 2004, next 5-8 of October 2010 Münster, Zagreb, Sophia

B. Internal quality control

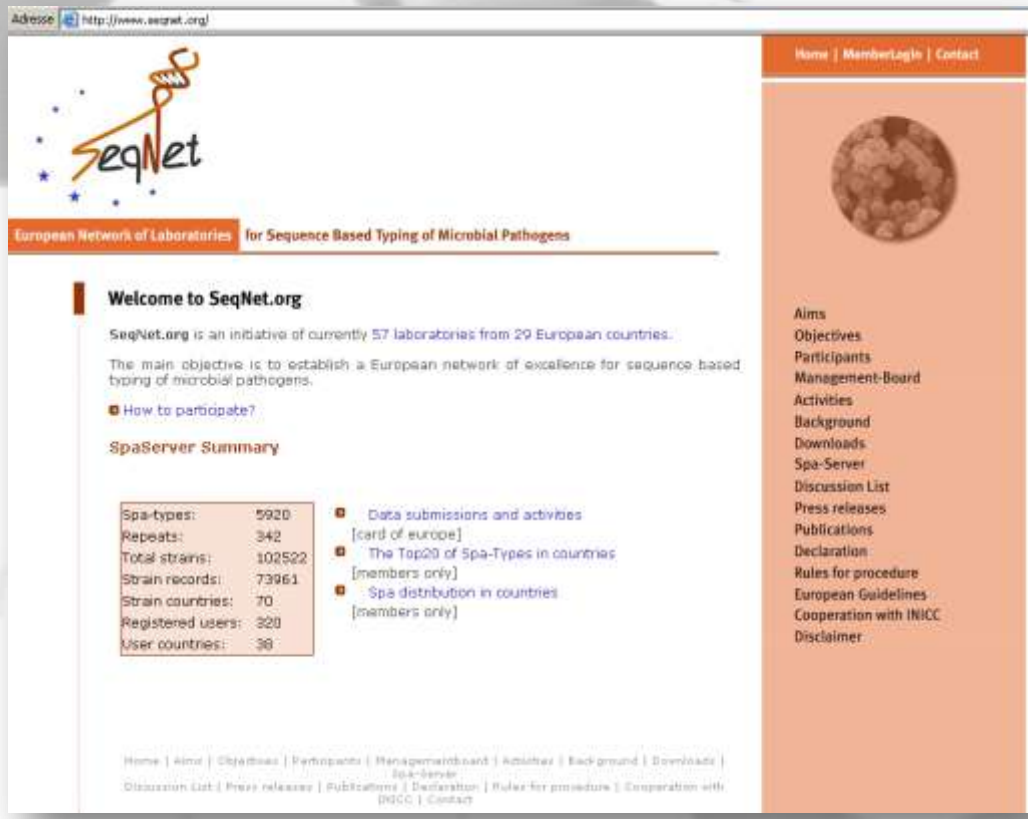
- SOP for internal quality control

C. External quality control

- SeqNet.org certification
- Annual proficiency testing
- Continuous quality control

D. Curatorship for spa server

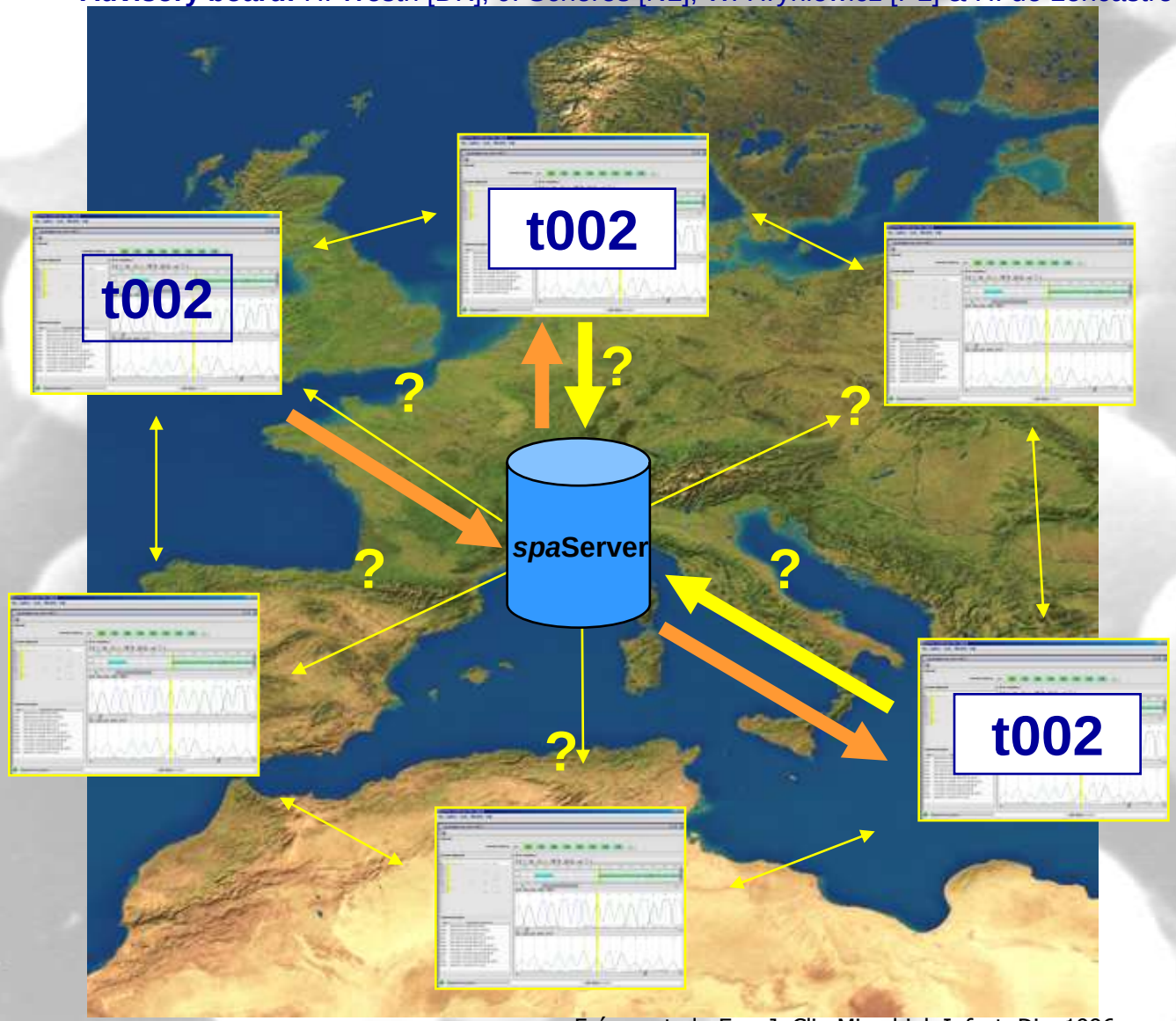
- Synchronization of typing data
- Access via StaphType and Bionumerics
- Study groups within spa server (Euregio study area, SRL-study group)



Friedrich A.W. et al. 2006. Euro Surveill;
Friedrich A. W. et al. 2008. Euro Surveill

Ensuring a common typing language…

Coordinators: A.W. Friedrich [Münster] & W. Witte [Robert Koch Institute]
Advisory board: H. Westh [DK], J. Scheres [NL], W. Hryniewicz [PL] & H. de Lencastre [USA]



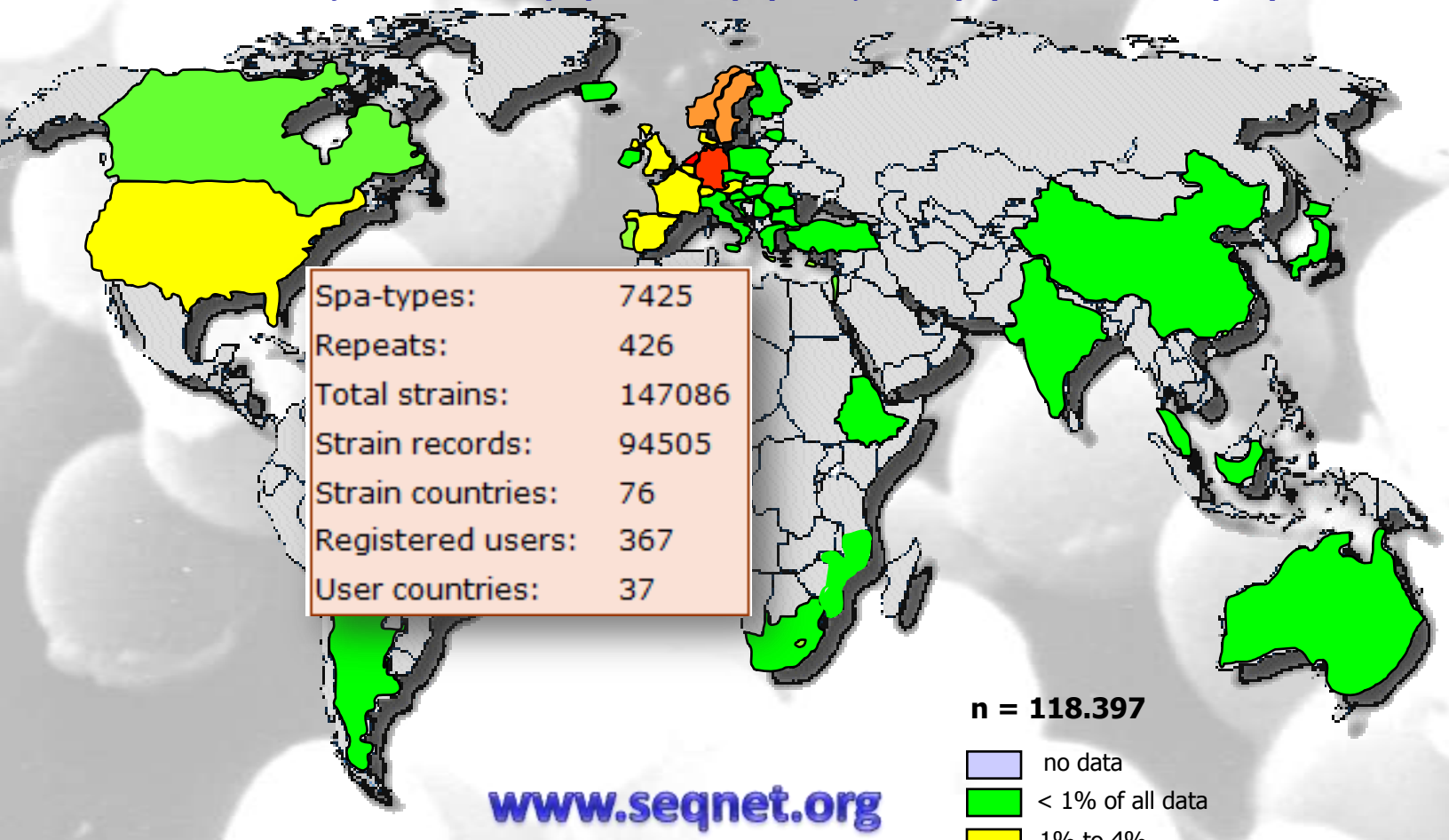
Friedrich A.W. et al. 2006. Euro Surveill; 11
de Sousa et al. 2006. J Clin Microbiol; 44
Friedrich A. W. et al. 2008 Euro Surveill; 13

Frénay et al., Eur. J. Clin Microbiol. Infect. Dis. 1996
Harmsen et al., J Clin Microbiol 2003
Strommenger et al J Clin Microbiol 2006

Austria
Belgium
Bulgaria
Canada
China
Croatia
Czech Republic
Denmark
Finland
France
Germany
Greece
Hungary
India
Italy
Island
Latvia
Lebanon, Jordania
Norway
Malaysia
Netherlands
Poland
Portugal
Romania
Slovenia
Sweden
Switzerland
Thailand
Turkey
UK
USA

SeqNet.org Network
Laboratory-Esperanto for *S. aureus*

Coordinators: A.W. Friedrich [Münster] & W. Witte [Robert Koch Institut]
Advisory board: H. Westh [DK], J. Scheres [NL], W. Hryniewicz [PL] & H. de Lencastre [USA]

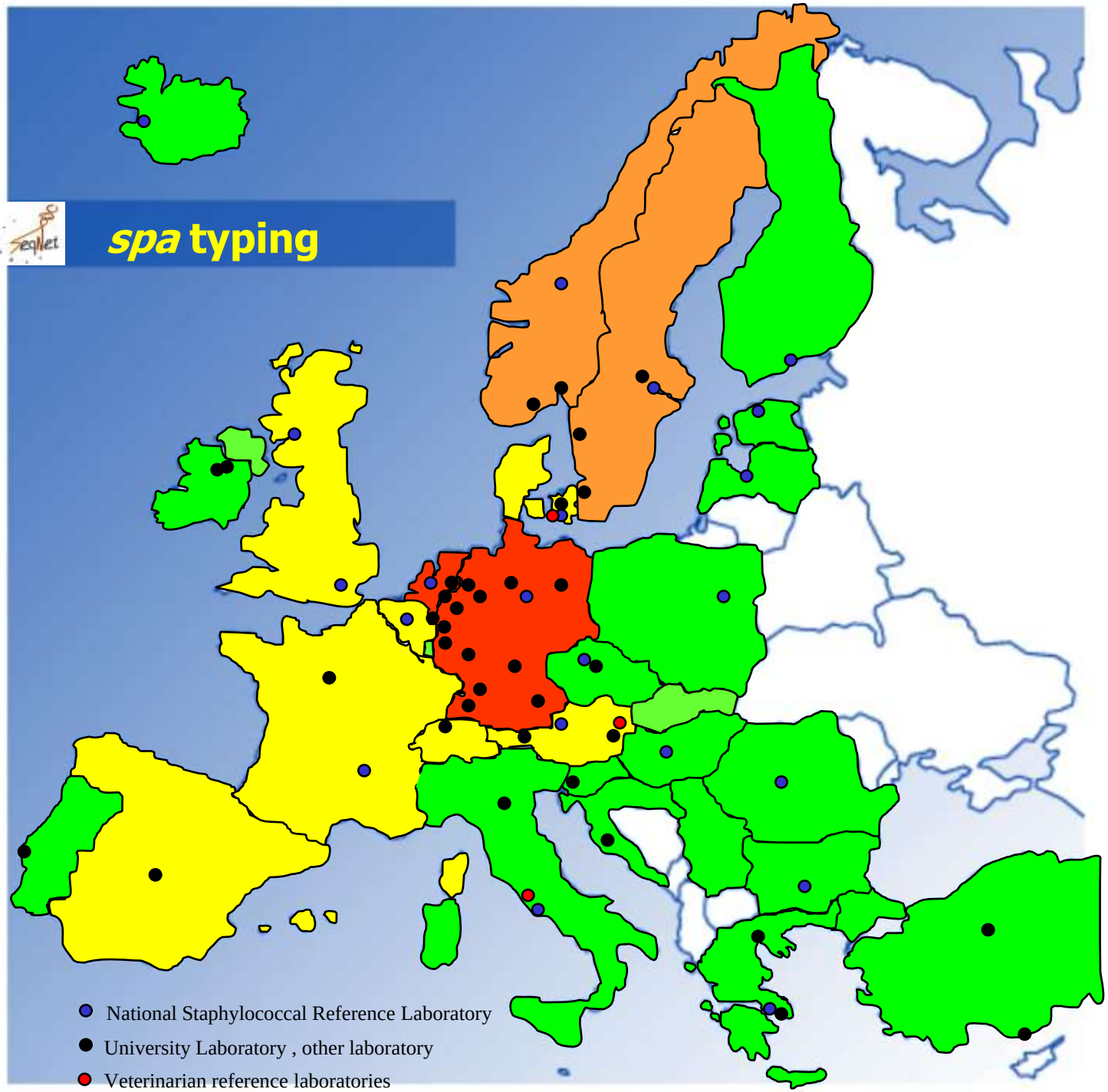


Friedrich A.W. et al. Euro Surveill 2006
de Sousa et al. J Clin Microbiol 2006
Friedrich A. W. et al. Euro Surveill; 2008

Harmsen et al., J Clin Microbiol 2003
Strommenger et al J Clin Microbiol 2006
Grundmann et al. PloS Med. 2010

12.10.2010

spa typing



n = 105443

- no data
- < 1%
- 1% to 4%
- 5% to 10%
- > 10%

Friedrich et al. 2006 Eurosurveillance
Friedrich et.al. 2009 Eurosurveillance

OPEN ACCESS Freely available online PLOS MEDICINE

Geographic Distribution of *Staphylococcus aureus* Causing Invasive Infections in Europe: A Molecular-Epidemiological Analysis

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Abstract

Background: *Staphylococcus aureus* is one of the most important hum
(MRSAs) are a major cause of hospital and community-acquired infection
the dominant clones that cause invasive infections in Europe.

Methods and Findings: In each country, staphylococcal reference labo
number of hospital laboratories to achieve national geo-demographic re
successive methicillin-susceptible (MSSA) and MRSA isolates from patients
protocol. All isolates were sent to the respective national reference labo
sequence typing of the variable region of the staphylococcal *spa* gene (*sp*
database. Relevant genetic and phenotypic information was assembled f
Web-based mapping application. Between September 2006 and February 2
countries collected 2,890 MSSA and MRSA isolates from patients with inv
distribution of *spa* types was found with some prevalent in all European c
Genetic diversity of MRSA differed considerably between countries with
geographical clusters. We provide evidence that a network approach consist
aggregated data using an interactive mapping tool can provide import
populations such as early signalling of emerging strains, cross border spread

Conclusions: In contrast to MSSA, MRSA *spa* types have a predominantly re
indicative of the selection and spread of a limited number of clones within h
efforts aimed at interrupting the spread within and between health care institu
successful and should therefore be strongly encouraged.

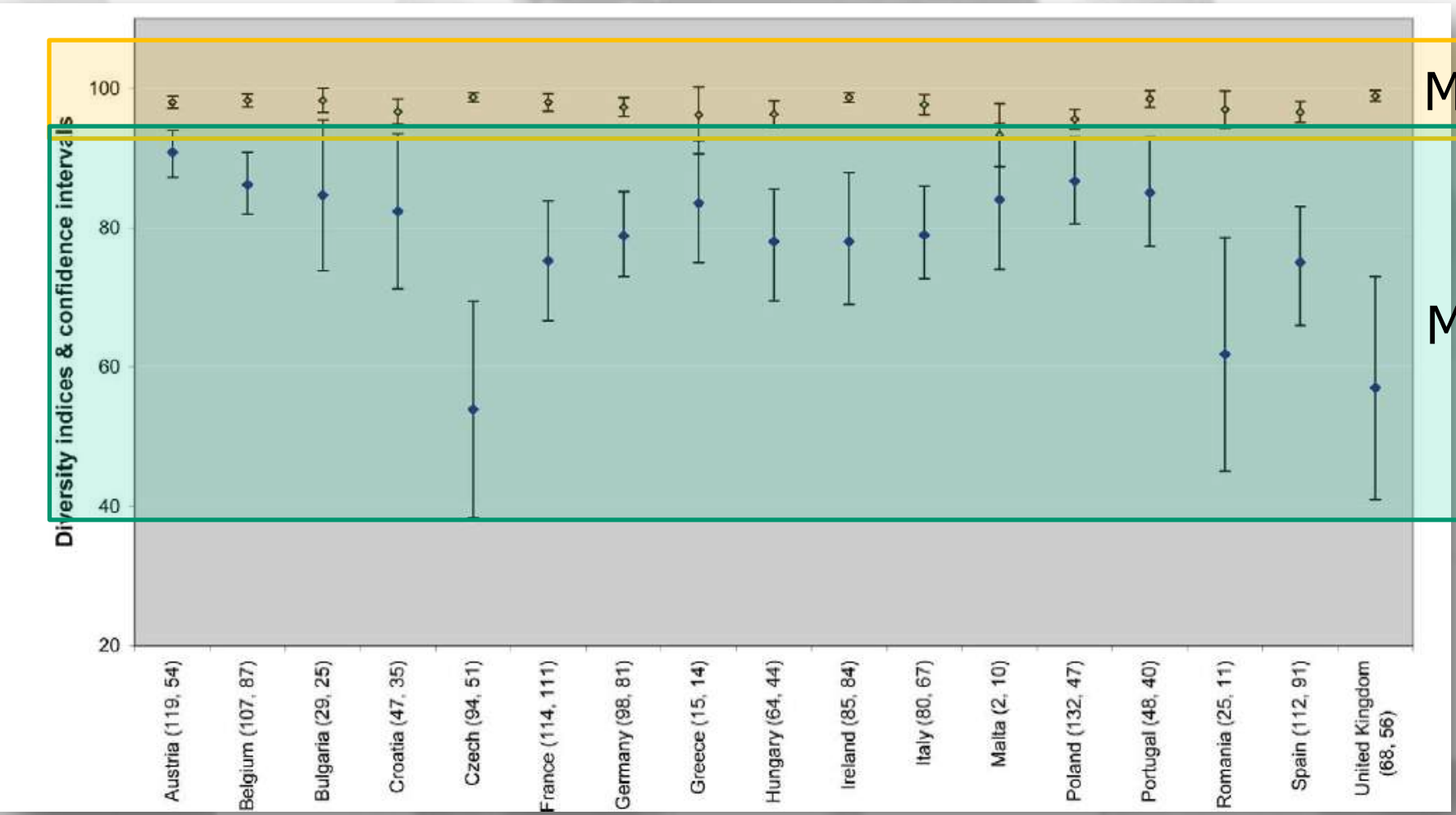
Staphylococcal Reference Laboratory (SRL) Initiative

General results

Statistics	n[a]	MSSA	MRSA	Total/Overall	p-Value*
Frequency (%)	2,890	1,923 (66.5)	967 (33.5)	2,890 (100%)	—
Median age (IQR)	2,836	63 (46–75)	69 (55–78)	66 (49–76)	<0.0001
Male gender (%)	2,862	1,159 (60.8)	606 (63.3)	1,765 (61.7)	0.2
All-cause mortality after 14 d (%)	1,838	153 (13.2)	141(20.8)	294 (16.0)	<0.0001
Hospital acquisition (%)	2,322	777 (51.6)	585 (71.7)	1,362 (58.7)	<0.0001
N spa types	2,850	565	155	660[b]	—
N not typeable	2,850	27 (1.4)	13 (1.3)	40 (1.4)	0.9
Index of diversity (95% CI)	2,850	0.985 (0.983–0.987)	0.940 (0.933–0.947)	0.983 (0.982–0.984)	<0.05[c]
Mean distance in kilometres between laboratories that isolated identical *spa* types (95% CI)	1,614[d]	1,046.2 (1109.5–983.0)	786.8 (975.7–597.9)	—	0.03[d]

*p-Value for the comparison of MSSA versus MRSA.
[a]Number of isolates for which data were available.
[b]Total number of *spa* types includes 60 *spa* types that contain both MSSA and MRSA.
[c]Deduced from non-overlapping 95% confidence intervals.
[d]Includes only MRSA and MSSA with more than ten isolates per *spa* type.
IQR, interquartile range.
doi:10.1371/journal.pmed.1000215.t002

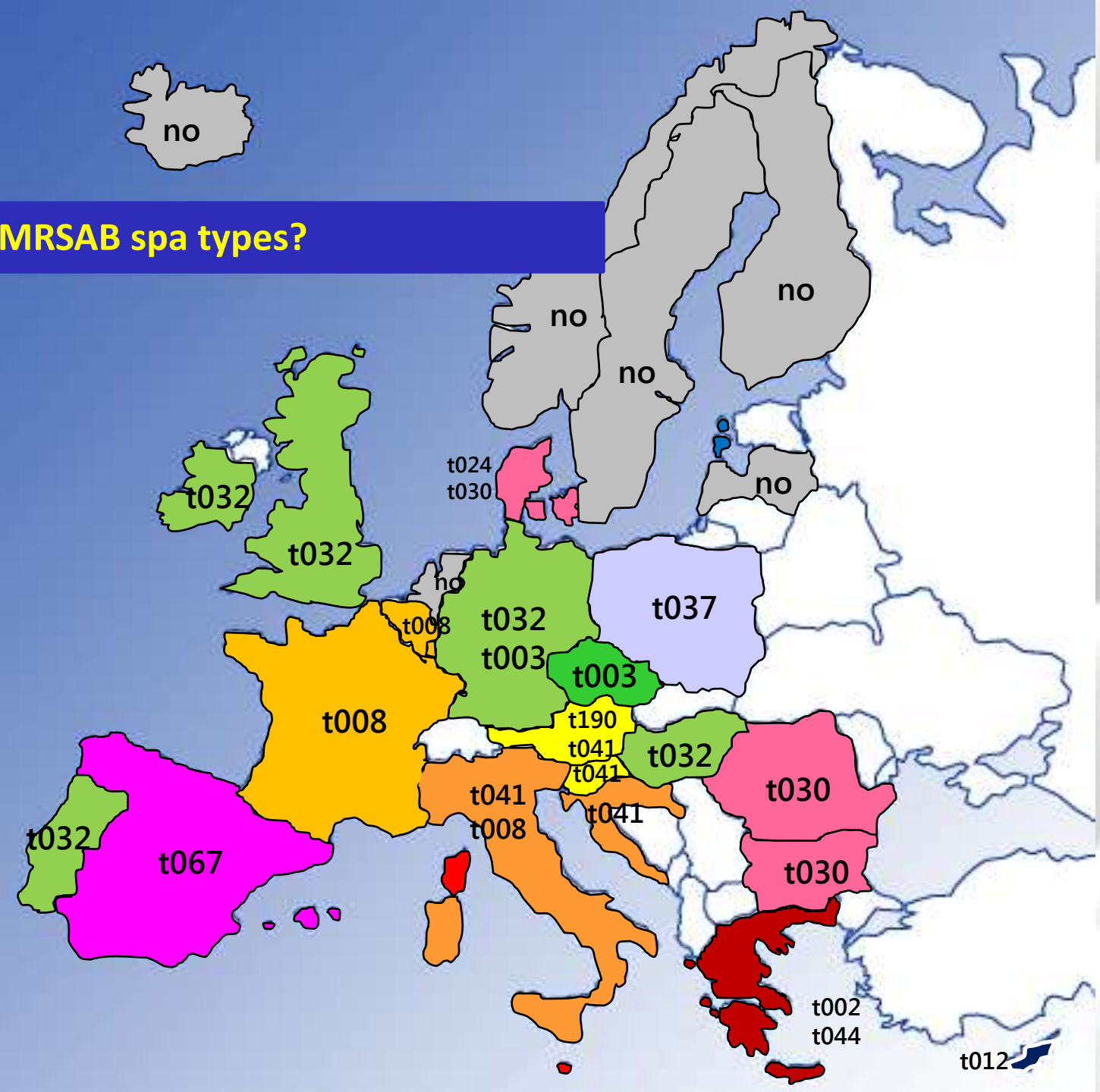
MRSA vs. MSSA

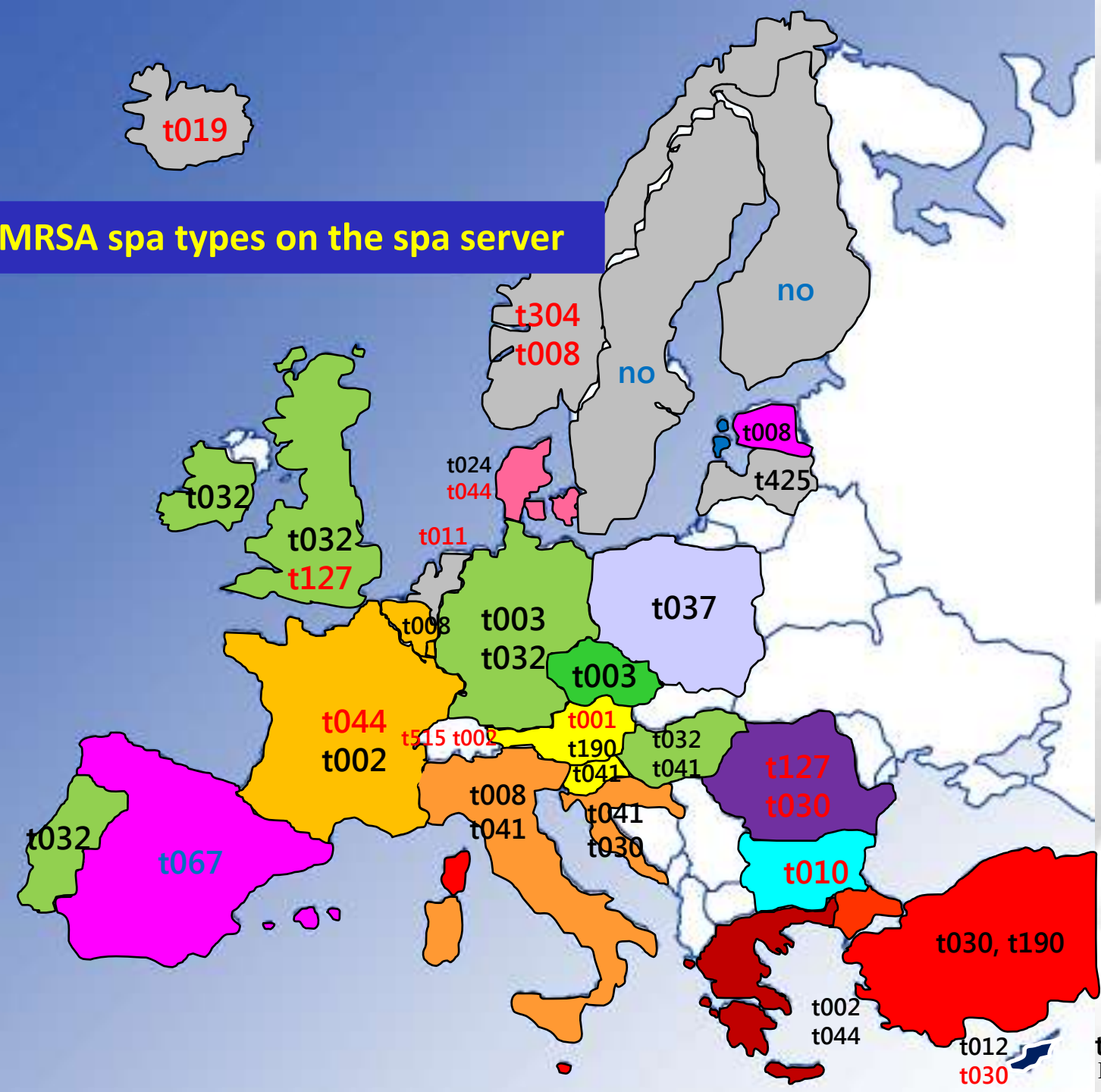

MRSA
MSSA
Diversity indices & confidence intervals
100
80
60
40
20
Austria (119, 54)
Belgium (107, 87)
Bulgaria (29, 25)
Croatia (47, 35)
Czech (94, 51)
France (114, 111)
Germany (98, 81)
Greece (15, 14)
Hungary (64, 44)
Ireland (85, 84)
Italy (80, 67)
Malta (2, 10)
Poland (132, 47)
Portugal (48, 40)
Romania (25, 11)
Spain (112, 91)
United Kingdom (68, 56)

S. aureus blood culture isolates in Europe

Rank	MSSA		Frequency	Percent	Cumulative Percent	Rank	MRSA		Frequency	Percent	Cumulative Percent
	spa Type	MLST					*spa* Type	MLST			
1	t002	ST-5[a], S-231[a]	93	4.8	4.8	1	t032	ST-22[a]	140	14.5	14.4
2	t084	ST-15[a] (ST-18)	89	4.6	9.5	2	t008	ST-8[a] (ST-247, ST-250, ST-254)	120	12.4	26.8
3	t015	ST-45[a]	84	4.4	13.8	3	t041	ST-111[a], ST-228[a]	72	7.4	34.2
4	t091	ST-7[a]	82	4.3	18.1	4	t003	(ST-5) ST-225[a]	71	7.3	41.6
5	t012	ST-30[a]	77	4.0	22.1	5	t002	ST-5[a], ST-231[a]	62	6.4	48.1
6	t127	ST-1[a]	57	3.0	25.1	6	t067	ST-5[a], ST-125[a]	50	5.2	53.3
7	t008	ST-8[a] (ST-247, ST-250, ST-254)	55	2.9	27.9	7	t001	(ST-5, ST-222) ST-228[a]	30	3.1	56.4
8	t021	ST-30[a] (ST-33, ST-55)	49	2.5	30.5	8	t037	ST-239[a] (ST-240), ST-241[a]	27	2.8	59.2
9	t005	ST-22[a] (ST-23, ST-60)	42	2.2	32.7	9	t030	ST-239[a] (ST-246)	20	2.1	61.2
10	t026	(ST-45, ST-47)	27	1.4	34.1	10	t024	ST-8[a]	14	1.4	62.7
11	t065	(ST-45, ST-46)	26	1.4	35.4	11	t190	ST-8[a]	14	1.4	64.1
12	t160	(ST-12, ST-13)	26	1.4	36.8	12	t515	ST-22[a]	12	1.3	65.5
13	t056	(ST-101)	25	1.3	38.1	13	t038	ST-45[a]	12	1.2	66.7
14	t050	ST-45[a]	21	1.1	39.2	14	t022	ST-22[a]	11	1.1	67.8
15	t078	(ST-26)	21	1.1	40.2	15	t740	ST-45[a]	11	1.1	69.0
16	t164	(ST-20)	19	1.0	41.2	16	t012	ST-30[a]	9	0.9	69.9
17	t346	(ST-15, ST-620)	18	0.9	42.2	17	t015	ST-45[a]	9	0.9	70.8
18	t024	ST-8[a]	17	0.9	43.1	18	t044	ST-80[a]	9	0.9	71.8
19	t230	ST-45[a]	17	0.9	43.9	19	t045	ST-5[a] (ST-225)	8	0.8	72.6
20	t166	(ST-34)	16	0.8	44.8	20	t127	ST-1[a]	8	0.8	73.4
—	Other	—	1,062	55.2	100.0	—	Other	—	258	26.6	100.0
Total	—	—	1,923	100	—	—	—	—	967	100	—

STs in parentheses are those associated with the spa type in the SeqNet.org Spa typing data base.
[a]MLST as determined by SRLs.
doi:10.1371/journal.pmed.1000215.t003


MRSAB spa types?
no
no
no
no
no
t024
t030
t032
t032
no
t008
t032
t003
t037
t003
t008
t190
t041
t041
t032
t030
t041
t008
t041
t032
t067
t030
t002
t044
t012

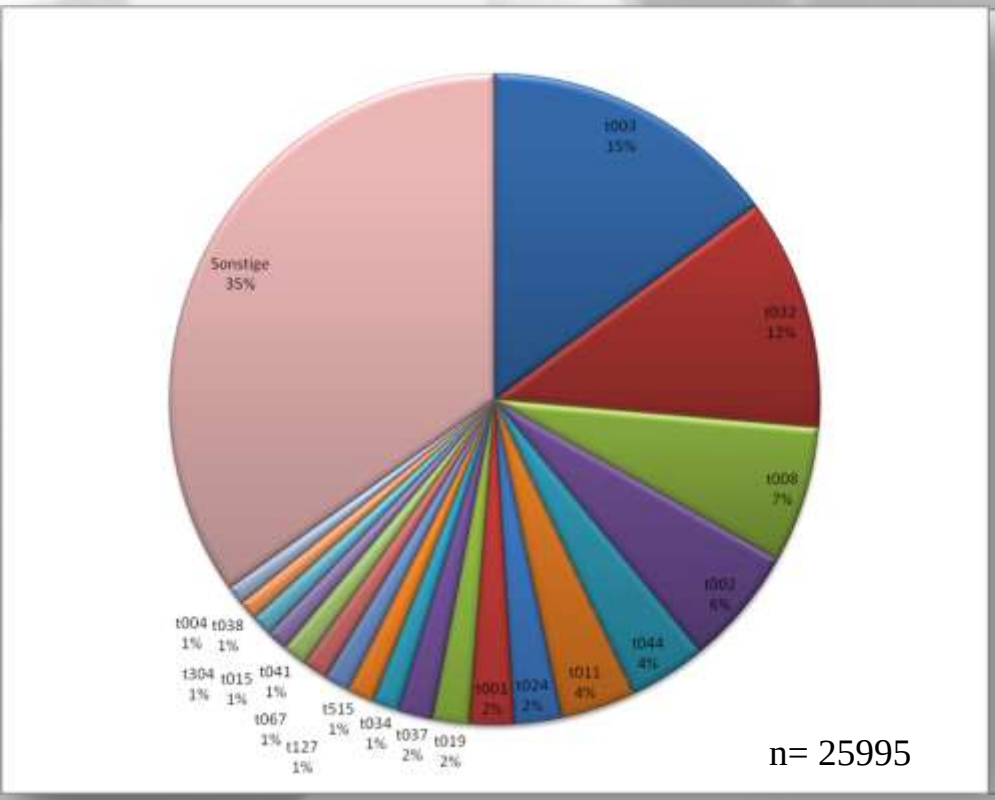


t030 t190
ST239 ST8
CC8 CC8

t030
Lebanon

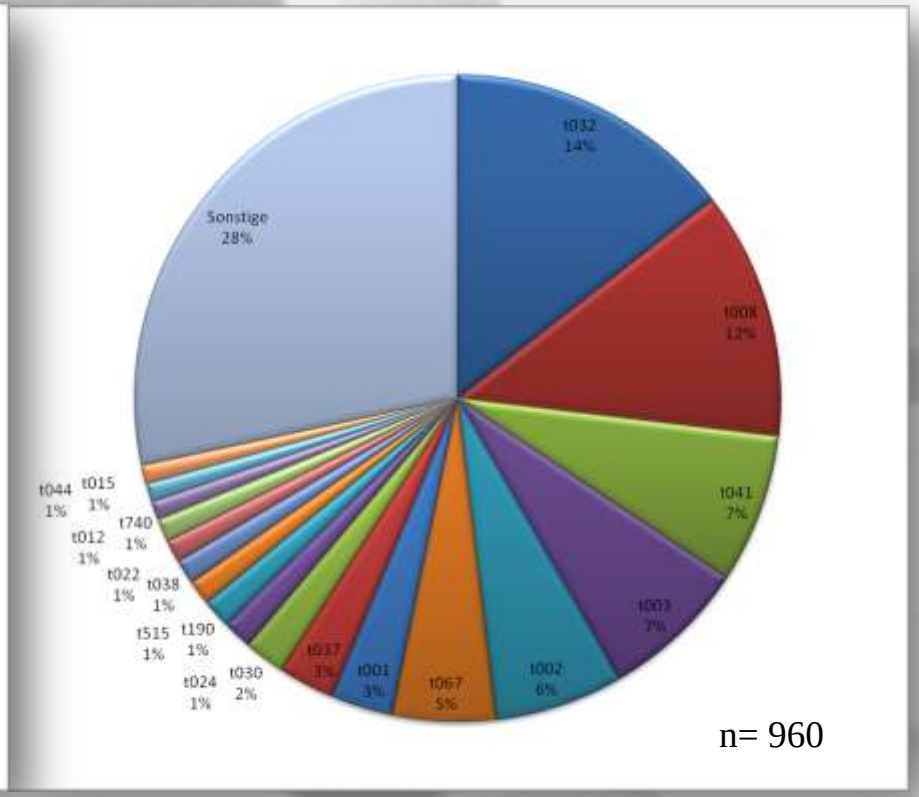
TOP 30 MRSA in Europe

MRSA on the *spa* server



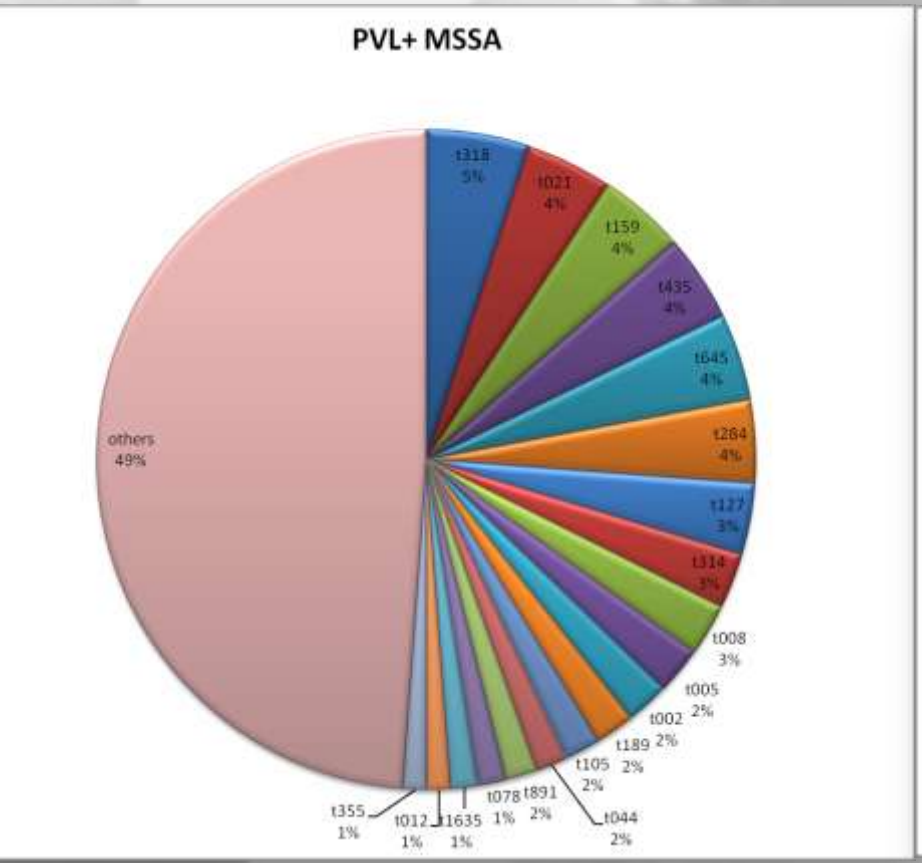
n= 25995

MRSAB from SRL-study

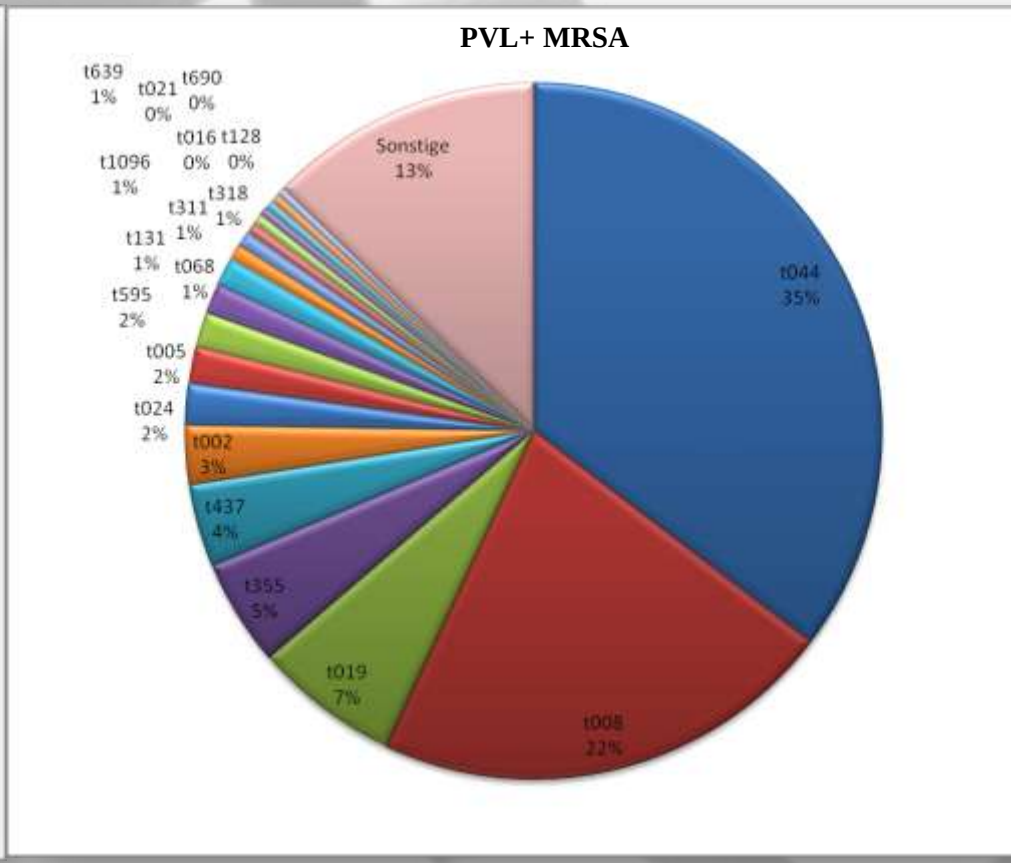


n= 960

PVL-positive CA-MRSA

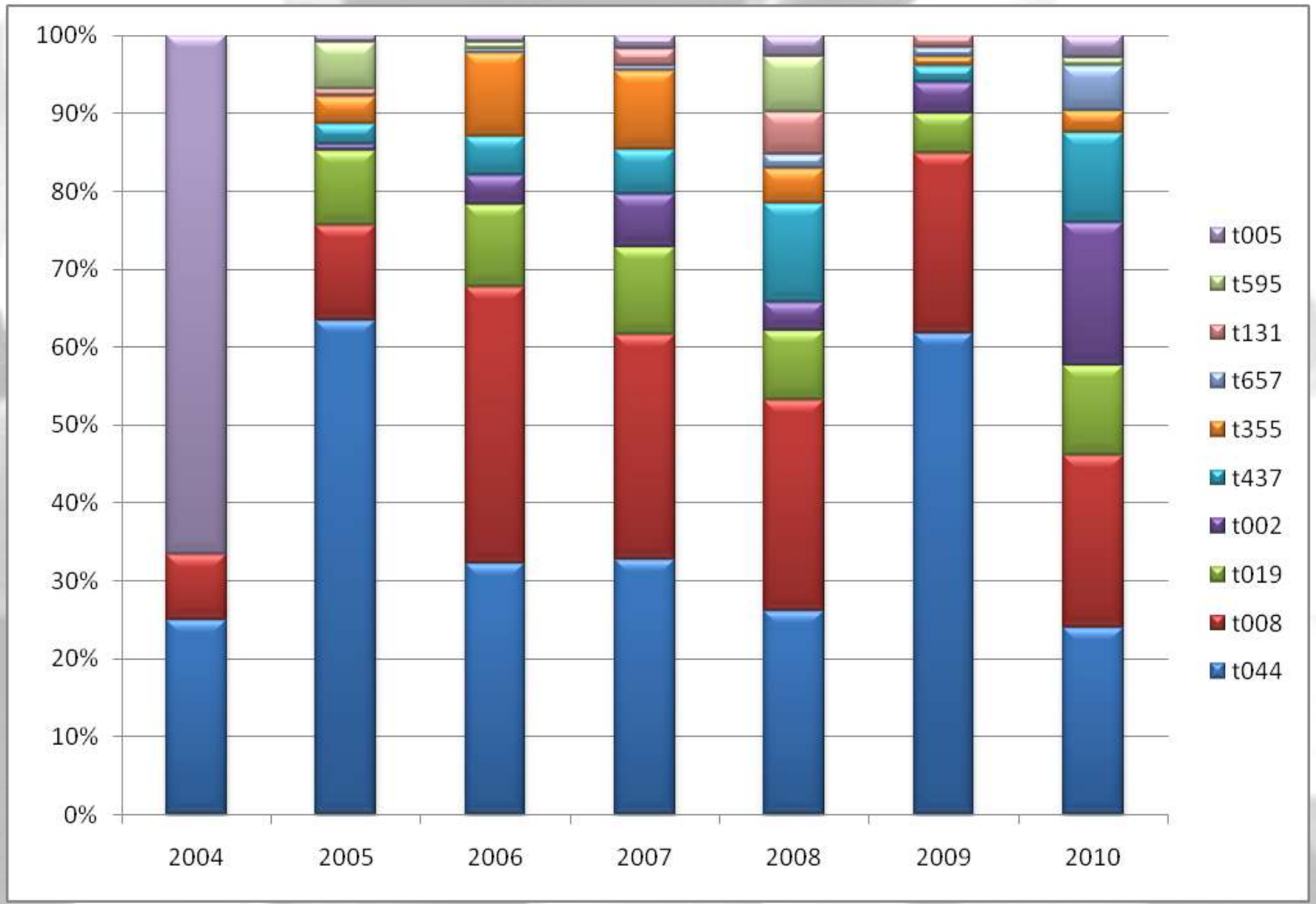


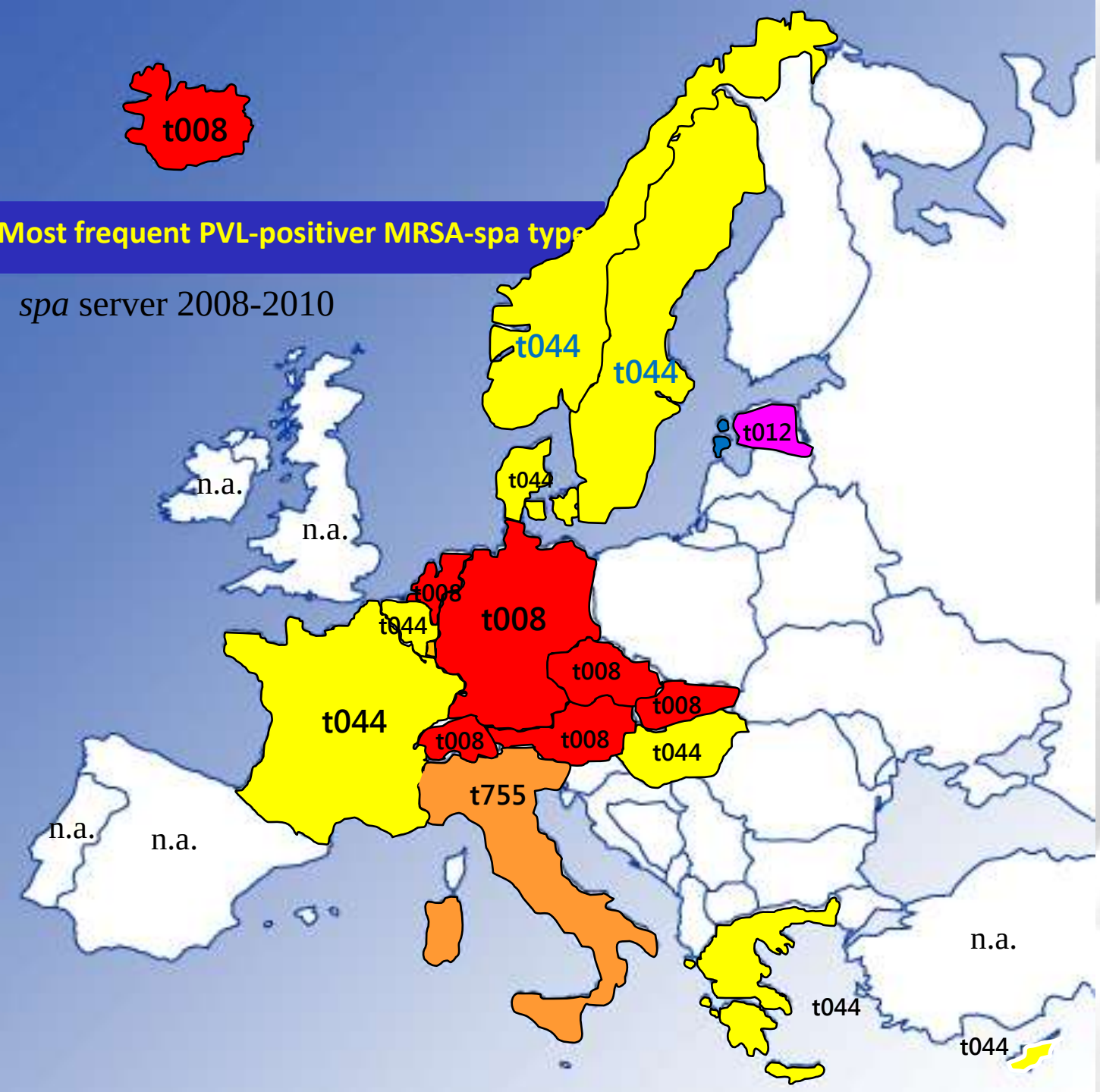
194 different *spa* types



75 different *spa* types

Change over time
PVL+ MRSA (n= 2035)

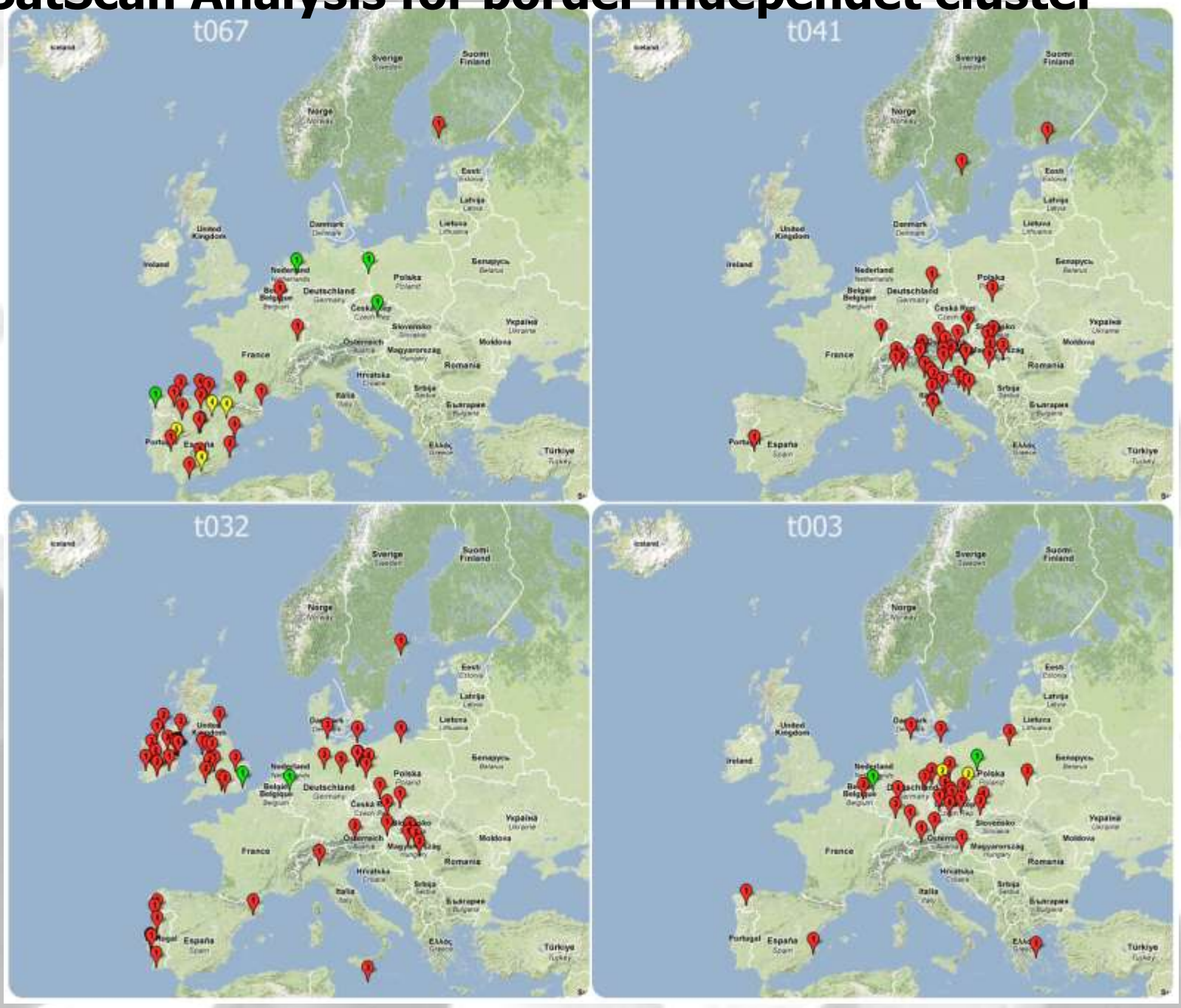


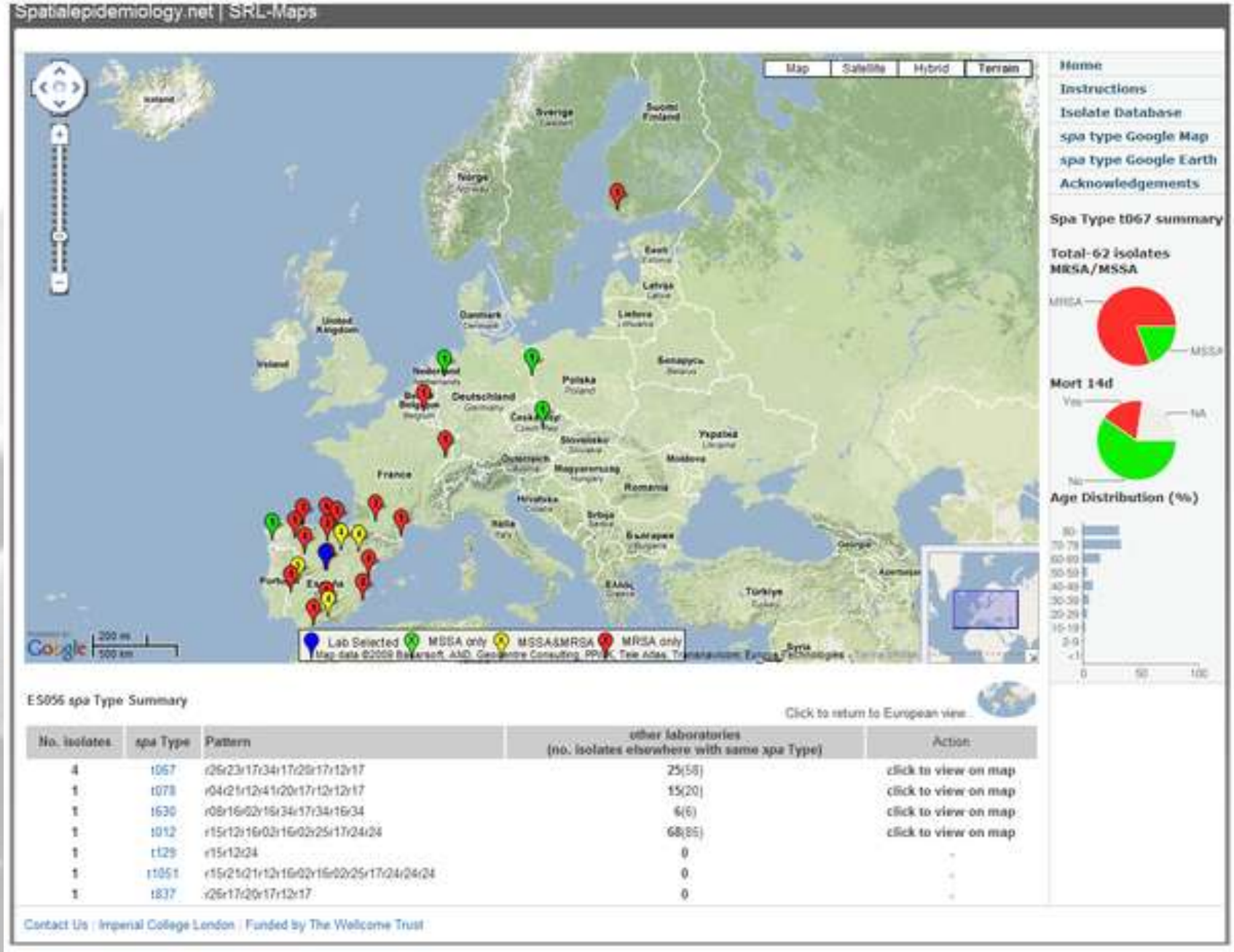

t008
Most frequent PVL-positiver MRSA-spa type
spa server 2008-2010
t044
t044
t012
t044
n.a.
n.a.
t008
t008
t044
t008
t008
t008
t044
t008
t008
t044
t755
n.a.
n.a.
n.a.
t044
t044

Regional Cluster

Regional Cluster Number	*spa* Type	*spa* Complex[a]	ST[b]	Window Centre	Window Radius (km)	Countries reporting Clustered *spa* Type within Window	*n* Isolates Observed	*n* Isolates Expected[c]	Log Likelihood Ratio	*n* MRSA among Observed Isolates	Percent MRSA among Observed Isolates
1	**t067**	2	5 & 125	Alicante, Spain	716	ES, FR	55	4.7	126.9	46	84
2	**t041**	1	228	Split, Croatia	522	AT, HR, HU, SI, IT	59	10.6	84.76	59	100
3	**t032**	32	22	Belfast, Northern Ireland (UK)	596	IE, UK	77	15.9	84.74	75	97
4	**t003**	45	225	Leipzig, Germany	386	CZ, DE, PL	58	10.0	82.26	54	93
5	**t008**	8	8	Perpignan, France	931	AT, BE, DE, ES, FR, HR, PT, SI	119	45.5	72.96	105	88
6	**t740**	740	45	Goes, Netherlands	81	BE, NL	15	0.6	50.36	11	73
7	**t030**	12	239	Pleven, Bulgaria	331	BG, RO	16	0.7	45.24	15	94
8	**t037**	12	239	Plock, Poland	330	PL	21	2.2	36.02	18	86
9	**t038**	740	45	Wilrijk, Belgium	92	BE	12	0.8	32.71	12	100
10	**t190**	190	8	St Pölten, Austria	56	AT	10	0.3	29.63	9	90
11	**t001**	1	228	Sibenik, Croatia	885	AT, DE, HU, IT, MT	29	10.2	27.55	29	100
12	**t435**	435	427	Daugavpils, Latvia	189	LV	8	0.2	25.82	0	0
13	**t425**	239	368	Riga, Latvia	0	LV	5	0.1	22.76	5	100
14	**t127**	127	1	Inowroclaw, Poland	131	PL	12	0.9	22.65	0	0
15	**t032**	32	22	Berlin, Germany	128	DE	19	3.2	22.2	19	100
16	**t015**	15	45	Lomza, Poland	581	CZ, LV, PL	35	11	20.72	7	20
17	**t091**	91	7	Ried, Austria	771	AT, BE, CZ, DE, FR, HR, HU, IT, NL, PL, SI	71	42.8	20.68	4	6
18	**t777**	777	5	Laval, France	277	FR	7	0.3	20.61	7	100
19	**t081**	78	25	Maków Mazowiecki, Poland	0	PL	4	0.0	19.37	3	75
20	**t515**	32	22	Mullingar, Ireland	196	IE, Northern Ireland (UK)	9	0.7	18.94	9	100
21	**t002**	2	5, 231	Coimbra, Portugal	484	ES, PT	33	10.6	18.37	20	61
22	**t230**	728	45	Hilleroed, Denmark	235	DE, DK, SE	11	1.4	17.19	0	0
23	**t044**	44	80	Nicosia, Cyprus	916	GR, CY	6	0.2	17.09	6	100
24	**t2054**	8	8	St Mande, France	226	BE, FR4	5	0.2	16.64	3	60
25	**t062**	singleton	5	Szolnok, Hungary	145	HU	6	0.3	15.24	6	100
Total	—	—	—	—	368 (mean)	339	702	173.1	—	522	74

SatScan Analysis for border independet cluster





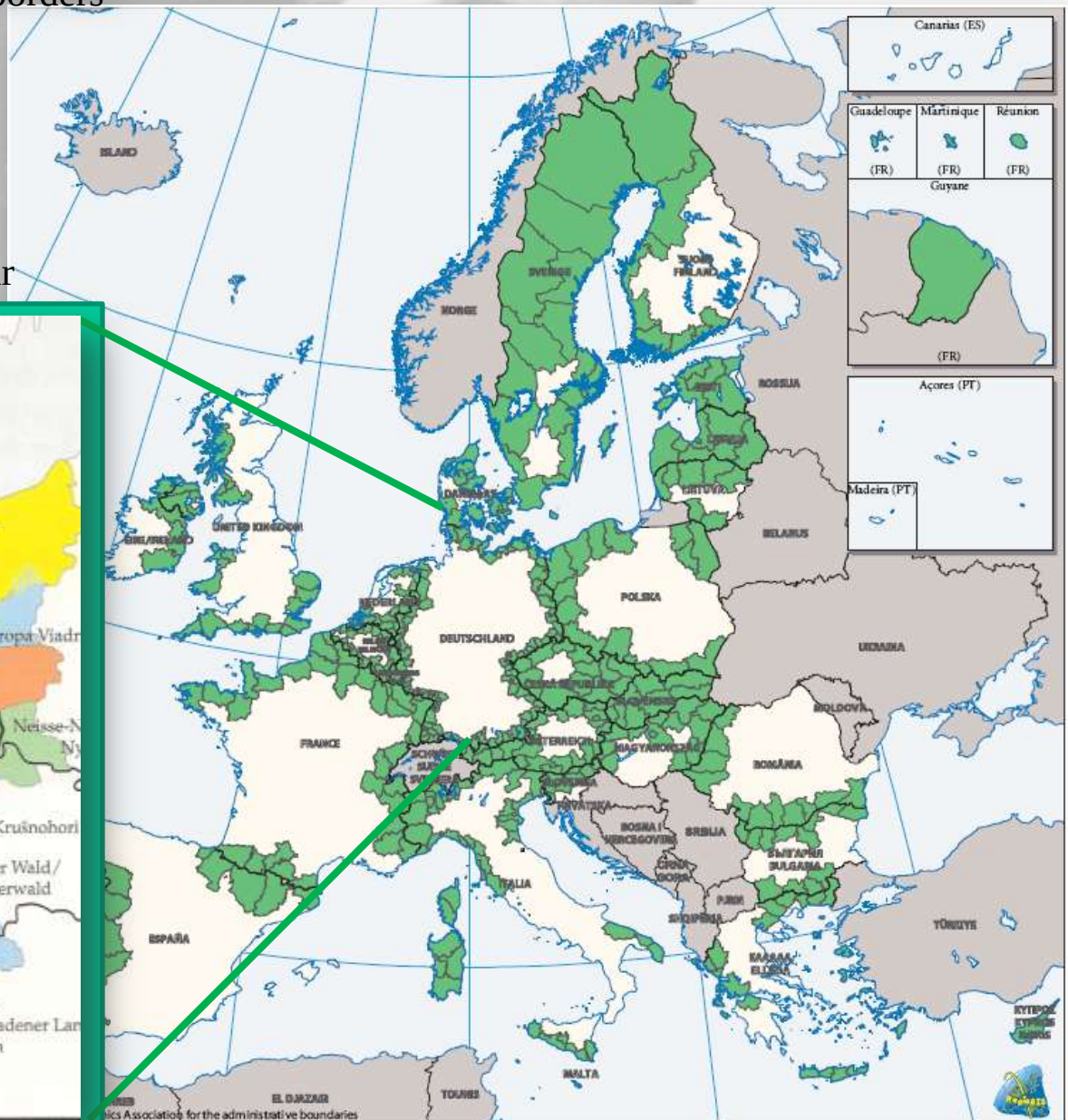
http://www.spatialepidemiology.net/srl-maps/

INTERREG - Grenzregionen gestalten Europa
Europäischer Fonds für Regionale Entwicklung der Europäischen Union

INTERREG - Grensregio's bouwen aan Europa
Europees Fonds voor Regionale Ontwikkeling van de Europese Unie

22% of European population lives close borders

<u>Dutch-German Euregios</u>
Since 1958
12,4 Mio inhabitants
12.000 crossborder commuters/day
500 to 30.000 crossborder patient per year



INTERREG Deutschland Nederland

INTERREG - Grenzregionen gestalten Europa
Europäischer Fonds für Regionale Entwicklung der Europäischen Union

INTERREG - Grensregio's bouwen aan Europa
Europees Fonds voor Regionale Ontwikkeling van de Europese Unie

Euregio-Projekte:

EURSAFETY HEALTH-NET

Euregionales Netzwerk
für Patientensicherheit
und Infektionsprävention

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KlinikumOldenburg

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Niedersächsisches Landesgesundheitsamt

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www.eursafety.eu
www.mrsa-net.eu

EUREGIO MRSA-net (2009)

- Crossborder network of 44 German and Dutch hospitals
- Integrated network with GPs
- Common quality standards (search&follow)

- Prevalence screening of 23566 (D) and 3544 (NL) patients
- Each new MRSA isolate from all patients is *spa* typed by hospitals
- Hospital and laboratory data collected on EUREGIO server

Twente/Achterhoek

Inhab. 990.000

2,5 beds/ 1000 inhab

36 GPs/100.000 inhab

Microbiologists: 2,9 per 1000 patients

MRSA : 78 (7,8/100.000 inhab)

0,1 per 100 admissions

MRSA/ *S. aureus*: 1%

MRSAB: 1 (0,1/100.000)

Münsterland

Inhab: 1.566.000

6,9 beds/1000 Einw.

146 GPs+Specialists/100.000 inhab

Microbiologists: 1,0 per 1000 patients

MRSA: 2953 (189/100.000 inhab)

1,6/100 admissions

MRSA/ *S. aureus*: 3%-30%

MRSAB: 41 (2,6/100.0000)

EUREGIO mrsa-net
Twente/Münsterland

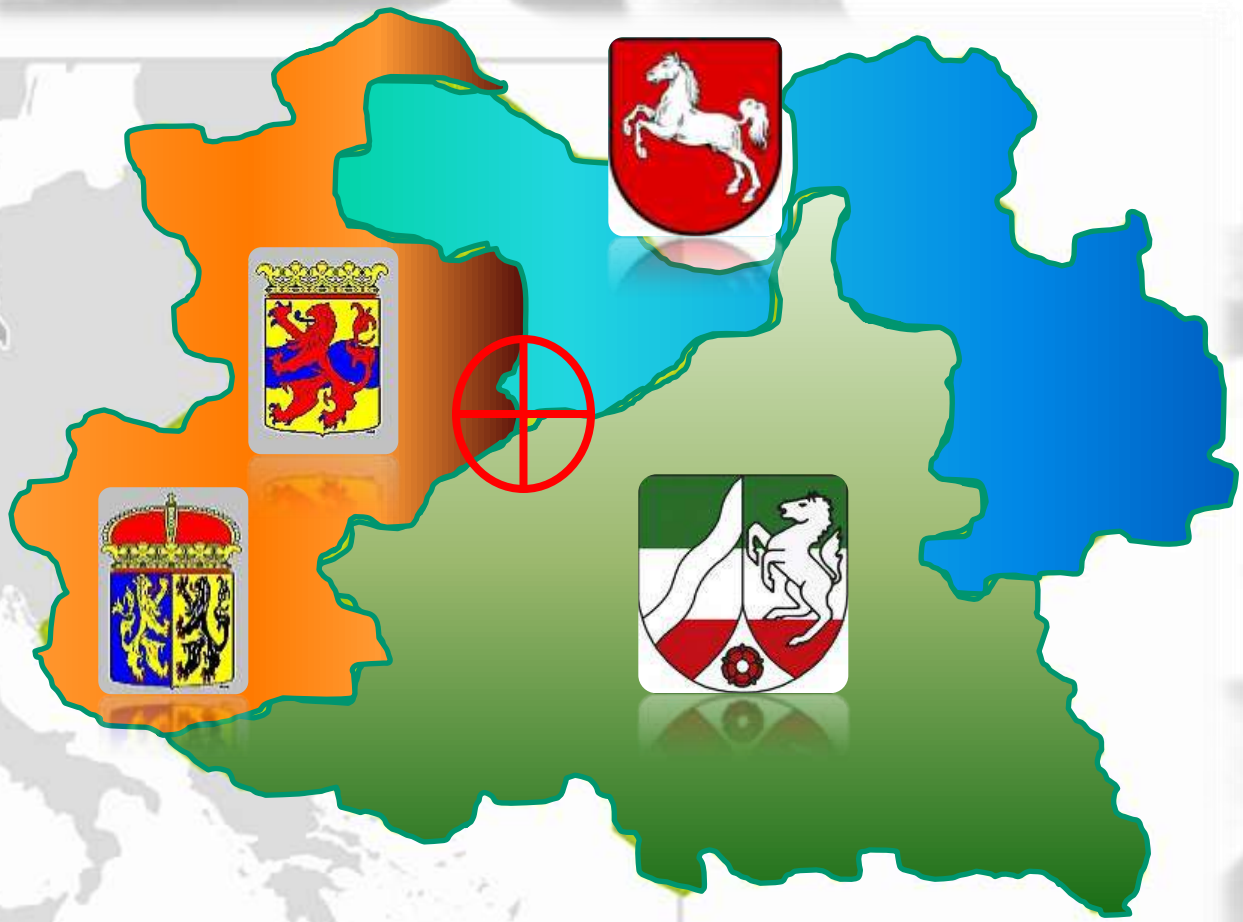
Achterhoek | NL Borken | GER

INTERREG - Grenzregionen gestalten Europa
Europäischer Fonds für Regionale Entwicklung der Europäischen Union
INTERREG - Grensregio's bouwen aan Europa
Europees Fonds voor Regionale Ontwikkeling van de Europese Unie

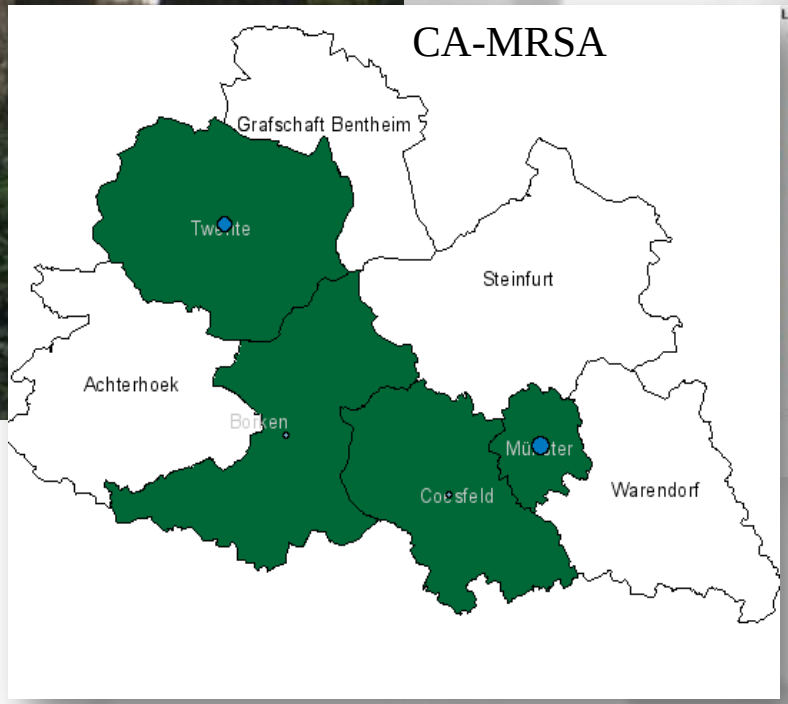
provincie Gelderland
provincie limburg
provincie Overijssel

Friedrich et al. 2008. Eurosurveillance
Köck et al. 2009, JHI
Böcher et al. JAC 2010

EUREGIO mrsa-net Twente/Münsterland



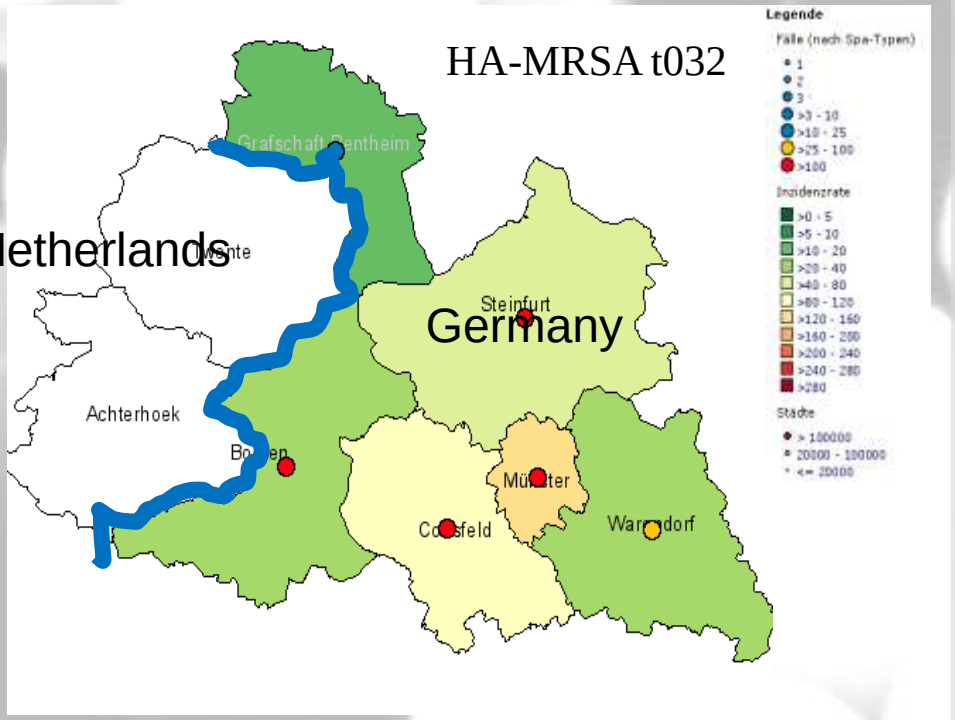
Friedrich et al. 2008. Eurosurveillance



Dreiländereck: NL, NRW, Nds

Real-time Surveillance of human MRSA isolates in the EUREGIO

Healthcare-associated (HA-) MRSA



I

- HA-MRSA respect the borders
- **Patients coming from German hospitals are put into isolation**
- **HA-MRSA not transmitted via social contacts**

Livestock-associated (LA-)MRSA

Incidence of *spa* types indicative for MLST CC398 (**t011, t034, t108, t567, t571, t588, t753, t898, t899, t1184, t125, t1451, t1456, t1457, t2123, t2330, t2383, t2582, t3013**):
Equal incidence of LA-MRSA genotypes on both sides of the border

Friedrich et al. 2008. Eurosurveillance
Data from EUREGIO MRSA-GIS, 2010, date of data retrieval June, 21st 2010

Prevalence screening in the EUREGIO (n= 23,566)

- Admission screening and risk factor analysis of all patients in all 44 hospitals in the EUREGIO
- All MRSA spa typed
- 1,6 / 100 patients colonized at admission
- 33% of all patients with MRSA risk factor
- 89% of patients with MRSA show up with classical HA risk factors

Risk factor	MRSA (n=354)	No MRSA (n=20836)	Beta Coefficient	OR	95% CI		*P*
home							
Antibiotics	89	2742	0.29	1.3	1.0	1.8	0.0776
Haemodialysis	3	179	-§	-§	-§	-	-§
Burning trauma	0	39	-§	-§	-§	-§	-§
Chron. wounds	48	415	4.0	54.5	26.2	113.6	<0.001
Katheter	49	541	2.09	8.1	4.1	15.9	<0.001
Chron. nursing	55	662	1.22	3.4	1.8	6.4	<0.001

22% of MRSA carriers without classical risk factors

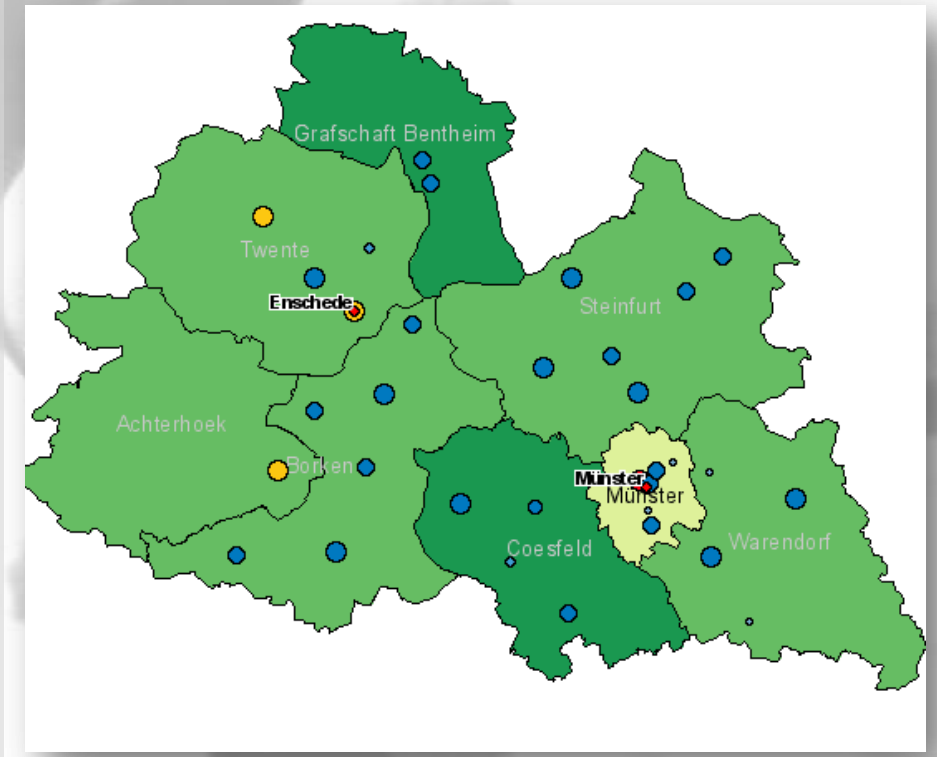
Köck et al. J Hosp Inf 2009 71:320-326

Real-time Surveillance of human MRSA isolates in the EUREGIO

Healthcare-associated (HA-) MRSA

Incidence of all MRSA cases per 100.000 inhabitants:
HA-MRSA respect the borders

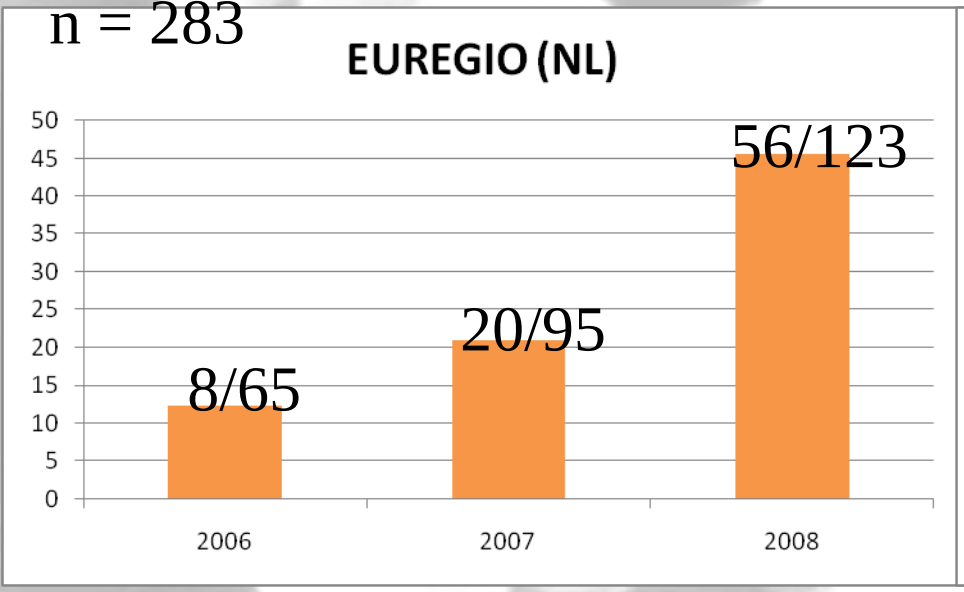
Livestock-associated (LA-)MRSA

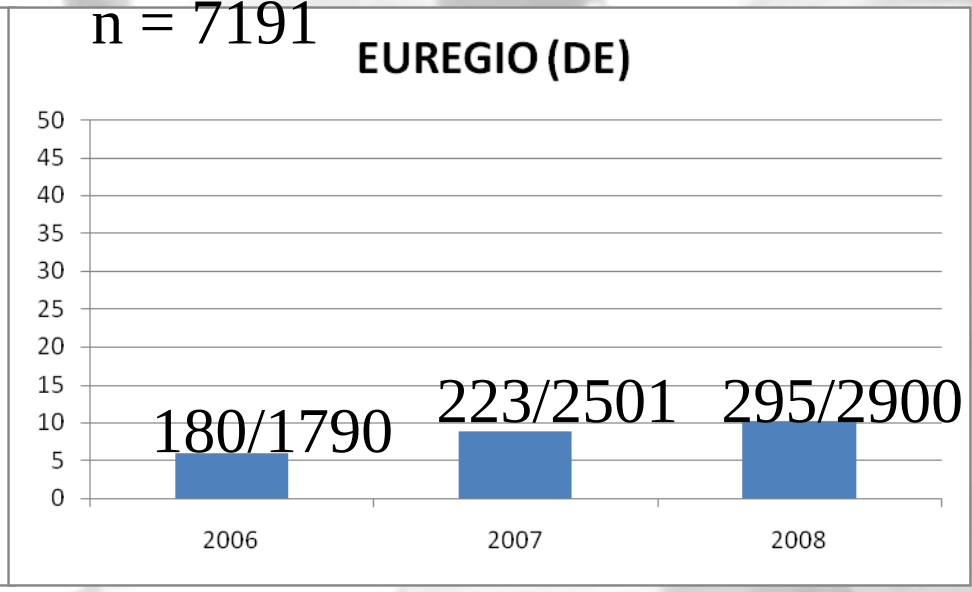


Incidence of *spa* types indicative for MLST CC398 (**t011, t034, t108, t567, t571, t588, t753, t898, t899, t1184, t125, t1451, t1456, t1457, t2123, t2330, t2383, t2582, t3013**):
Equal incidence of LA-MRSA genotypes on both sides of the border

Friedrich et al. 2008. Eurosurveillance
Data from EUREGIO MRSA-GIS, 2010, date of data retrieval June, 21st 2010

LA-MRSA in human MRSA-isolates of the EUREGIO



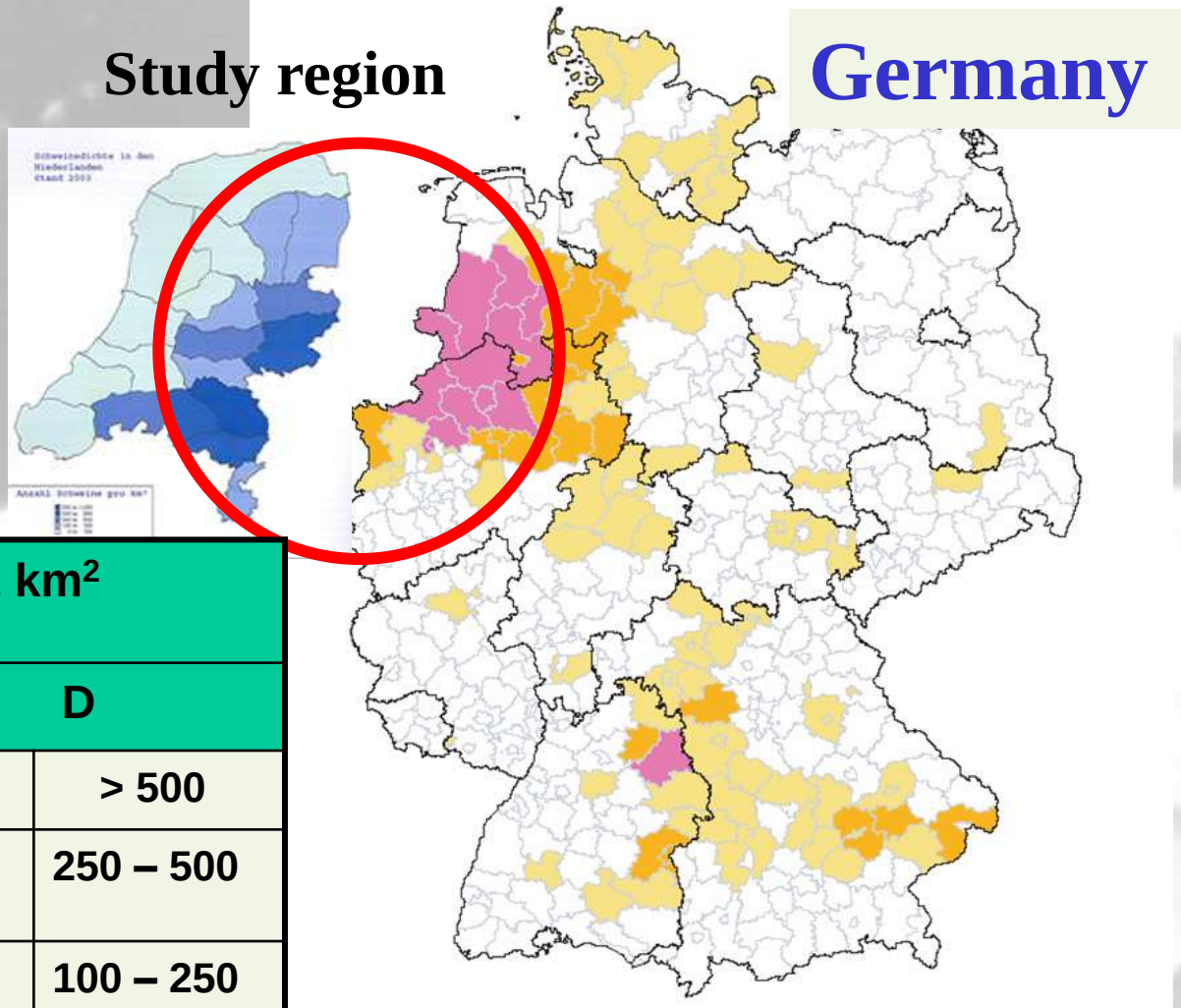


Pig density in the Dutch-German border region

Study region

Germany

Netherlands



Pigs / 100 ha or 1 km²			
NL		D	
> 500			> 500
300 – 500			250 – 500
100 – 300			100 – 250
0 – 100			0 – 100

Trading networks are important for spreading

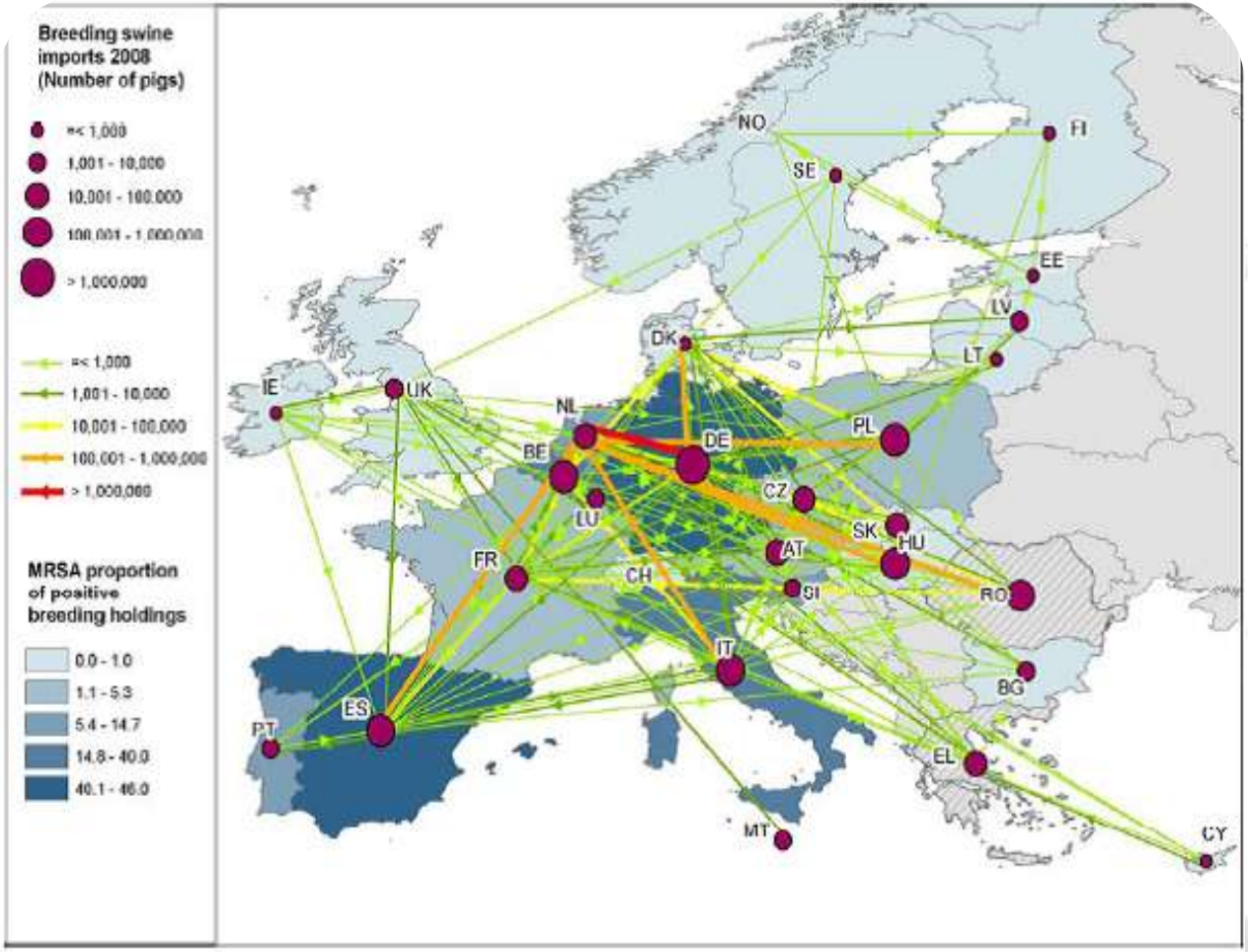


Figure 14: Prevalence of MRSA-positive breeding holdings in 2008 (EFSA, 2009) and within-Community trades of breeding pigs in 2008[a] [15]

Case-control study: Risk factors for the acquisition of LA-MRSA

Risk factor	Number of patients				Univariate analysis	Final logistic regression model	
	Case group		Control group		*P* value[a]	Odds ratio (CI 95%)[b]	*P* value[b]
	Yes	No	Yes	No			
Residence in a nursing home	0	100	2	98	0.497	NA	NA
Prescribing of antibiotics[c]	35	65	39	61	0.7	NA	NA
Haemodialysis	0	100	2	98	0.3	NA	NA
Male gender	77	23	62	38	0.03	NA	NA
Age 0–2 years	3	97	2	98	1.0	NA	NA
Age 3–18 years	9	91	2	98	0.0588	9.629 (1.374–67.476)	0.023
Age 19–65 years	61	39	60	40	0.885	NA	NA
Age 66–80 years	24	76	33	67	0.159	NA	NA
Age>81 years	3	97	3	97	1.0	NA	NA
Indwelling devices	12	88	28	72	0.008	0.327 (0.105–1.024)	0.055
Hospitalization[c]	46	54	70	30	<0.001	NA	NA
Contact with human MRSA carriers	8	92	13	87	0.356	NA	NA
Chronic need for nursing care	3	97	23	77	<0.001	0.065 (0.008–0.524)	0.010
Skin lesions	5	95	23	77	0.001	0.247 (0.060–1.009)	0.052
Contact with pets	78	22	48	52	<0.001	NA	NA
Contact with horses	19	81	5	95	0.005	2.955 (0.834–10.473)	0.093
Contact with cattle	25	75	3	97	<0.001	8.607 (1.729–42.854)	0.009
Contact with pigs	62	38	6	94	<0.001	20.455 (7.831–64.386)	<0.001
Contact with sheep	2	98	2	98	0.689	NA	NA

NA not available

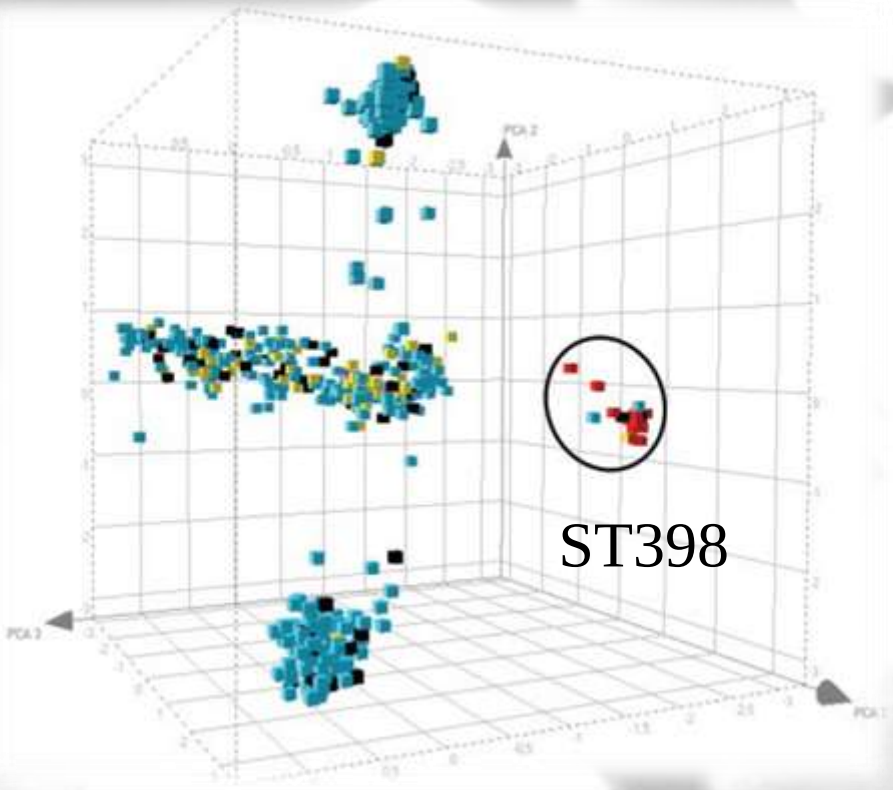
[a] *P* value resulting from univariate (Chi-square or Fisher Exact test) analysis; all factors with $P<0.2$ were included in the initial regression model

[b] Odds ratio (95% confidence interval, CI) and *P* value of variables included in the final logistic regression model

[c] During the previous 6 months

Köck et al. 2009, Eur J Clin Microbiol Infect Dis 28:1375-82

AFLP-analysis of clinical MSSA/MRSA-isolates



Blue, carriage isolates (n = 829);
black, bacteremia isolates (n = 146);
yellow, animal isolates (n =77);
red, ST398 MRSA isolates (n = 46);
pink, reference strains (Mu50/N315).

van Belkum A, et al. 2008. Methicillin-resistant and -susceptible *Staphylococcus aureus* sequence type 398 in pigs and humans. Emerg Infect Dis. 14:479-83.

Other reservoirs for MRSA?

- MRSA in horses, cattle
- MRSA in cats and dogs
- MRSA in rabbits
- MRSA in rats

Walther et al. Berl Munch Tierarztl Wochenschr 2006
Weese et al. J Am Vet Med Assoc 2007
Moodley et al. J Am Vet Med Assoc 2007

MRSA is not the same as MRSA

t011, t034, t108, t567, t571, t588, t753, t898, t899, t1184, t1254, t1255, t1451, t1456, t1457, t2123, t2330, t2383, t2582, t3013, t1197, t1344, t1793, t1939, t2329, t2922, t2346, t2370, t3479, t4659, t4838, t4854, t4872, t6291, t6292, t6293

PVL –negative (2 exceptions in SE, NL)
Livestock-associated (LA)-MRSA

t044, t019, t131, t376, t639, t237, t1199, t1201, t1206, t1200, t008, t437, t216, t005, t310, t1276, t355, t595, t311, t1277, t450, t019, t021, t318, t1273, t914, t202, t128, t125, t558, t175, t1274, t1272

PVL –positive
Community-acquired (CA)-MRSA

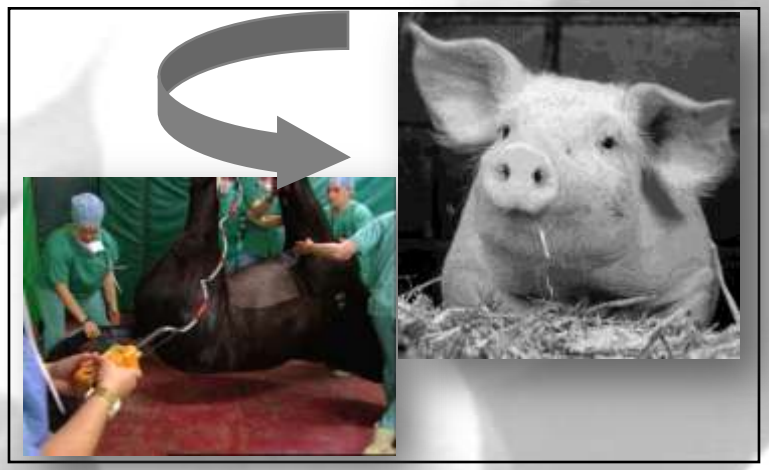
Hospital-acquired (HA)-MRSA

t003, t032, t008, t002, t037, t044, t001, t004, t015, t024, t084, t012, t045,t091, t127, t437, t067, t041, t019, t005, t030, t021, t038, t065, t026, t018, t022, t172

Community-MRSA

Hospital-MRSA

Extended MRSA-Epidemiology



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Conclusions

1. **MRSA** spread **different** from **MSSA**

2. Resistances diffuse locally und regionally across the border
   Transmission of **HA- MRSA** via health care networks
   of **LA-MRSA** via production ways
   of **CA-MRSA** via social networks

3. MRSA-prevention needs to be implemented at the critical points

4. **Preventive Microbiology**, infection control and antibiotic stewardship is the **future**

5. Molecular typing is of **epidemiological** and **clinical** interest

6. Collaboration between human medicine and veterinary medicine necessary (One-health)

Thanks to

- Dag Harmsen
- Alex Mellmann
- Robin Köck
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- Wolfgang Witte
- All SeqNet.org participants and the SRL study group