Bacterial fingerprints across Europe

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CHAPTER 10

The dynamic changes of dominant clones of *Staphylococcus aureus* causing bloodstream infections in the European region: Results of a second structured survey

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ABSTRACT

Staphylococcus aureus is one of the most important human pathogens, and methicillin-resistant _S. aureus_ (MRSA) presents a major cause of healthcare- and community-acquired infections. This study aimed to investigate the spatial and temporal changes of _S. aureus_ causing bacteraemia in Europe over a five-year interval and explored the possibility of integrating pathogen-based typing data with epidemiological and clinical information at a European level. Between January and July 2011, 350 laboratories serving over 453 hospitals in 25 countries collected 3,753 isolates (MSSA and MRSA) from patients with _S. aureus_ bloodstream infection. All isolates were sent to the national staphylococcal reference laboratories and characterised by quality-controlled _spa_-typing. Data were uploaded to an interactive web-based mapping tool. A wide geographical distribution of _spa_-types was found with some prevalent in all European countries. MSSA was more diverse than MRSA, which differed considerably between countries with major international clones expanding or receding when compared to a 2006 survey. We provide evidence that a network approach consisting of decentralised typing and visualisation of aggregated data using an interactive mapping tool can provide important information on the dynamics of _S. aureus_ populations such as early signalling of emerging strains, cross-border spread and importation by travel.

INTRODUCTION

Staphylococcus aureus is one of the major causes of bacterial infection in humans [1]. Infections occur in the community or in healthcare settings, predominantly following acquisition from mainly human sources. In Europe, methicillin-resistant *S. aureus* (MRSA) is predominantly acquired in healthcare settings and represents a major challenge to the control of antibiotic resistance in hospitals. MRSA has therefore become the currency with which the success of infection control initiatives is measured at health system levels [2]. *S. aureus* can also acquire particular virulence traits and has been responsible for major outbreaks of toxin-mediated disease in the community [3]. At the same time, *S. aureus* evolves rather gradually by successive acquisition of syntenic changes of largely unaltered core genomes. It is therefore possible to describe transmission and the consecutive spread of bacteria by genetic characterisation of highly polymorphic sites within the core genes of all isolates [4]. The importance of *S. aureus* as a human pathogen, i.e. its potential to cause large scale outbreaks in healthcare settings and in the community, and its predominantly clonal population structure calls for a monitoring tool that scans the distribution and spread of clones of particular public health importance over larger temporal and spatial intervals through repeated surveys. Such a tool is suited to inform the public health and infection control personnel about impeding health threats.

We therefore continued with a Europe-wide initiative to explore and define any dynamic changes in the distribution and spread of clones of *S. aureus* in European hospitals, five years after an initial survey was carried out in 2006 [5]. We also addressed a request from the European Centre for Disease Prevention and Control (ECDC) to explore the usefulness of integration of molecular typing data with epidemiological and clinical data at a European level.

METHODS

spa-typing

Molecular typing for epidemiological purposes utilises highly discriminatory genetic markers that characterise human pathogens allowing the identification of isolates that are distinct versus those that are closely related due to recent common ancestry. The *spa* locus of *S. aureus* codes for protein A, a species-specific gene product known for its IgG binding capacity. This locus is highly polymorphic due to an internal variable region of short tandem repeats which vary not only in numbers but also due to nucleotide substitutions within individual repeat units [6]. DNA sequences of the *spa* gene therefore provide portable and biologically meaningful molecular typing data that have demonstrated their utility for macro- and micro-epidemiological purposes from surveillance through to outbreak investigations at various geographical levels [7,8].

Capacity building

During annually repeated workshops organised for technical personnel from European staphylococcal reference laboratories (SRLs), participants receive hands-on training in *spa*-typing and data analysis according to a standard protocol using a purpose-designed software tool StaphType™ developed by Ridom™, GmbH, Würzburg, Germany [8]. Proficiency testing was carried out by mailing each SRL five well-characterized *S. aureus* isolates and five sequence chromatograms (trace files) of known *spa*-types as described previously [9]. All laboratories participating in the structured survey described here fulfilled quantifiable quality criteria which consisted of an unambiguous base-calling for all sequenced nucleotides for both forward and reverse sequencing runs of the test panel.

Structured survey

A protocol was agreed by all participating SRLs in June 2010. Utilising the same network of sentinel laboratories, this by and large followed the sampling frame deployed of the first structured survey carried out in 2006 [5]. Briefly, European SRLs were asked to approach sentinel hospital laboratories

which already participated in the previous survey and which provide microbiological diagnostic services for a geo-demographically representative sample for their national patient population. Between January and July 2011, these laboratories were asked to submit, for each hospital they serve, the first five consecutive MSSA and MRSA from individual patients with bloodstream infection. If, due to low incidence, the number of MRSA could not be obtained during these six months, laboratories were entitled to fill-up their quota with MSSA. For small countries, which had only one laboratory such as Cyprus and Malta, larger quota were accepted. Isolates were dispatched by the participating laboratories to the SRLs and, whenever possible, accompanied by additional information, including the sample number, the date of isolation, demographic detail (such as age and gender), epidemiological context (hospital-acquired when disease onset was more than 48h after admission or community-onset otherwise), antibiotic resistance against isoxazolylpenicillin (i.e. oxacillin) or cefoxitin. SRLs confirmed MRSA by *mec*A PCR or determination of minimum inhibitory concentration for oxacillin together with PBP2a agglutination. Discrepancies between genotype or agglutination assay and susceptibility test were scored as inconclusive phenotypes. Additional information could be uploaded to the database and web application if available. This consisted of all cause mortality 14 days after isolation of the initial bloodstream isolate. All SRLs preserved the isolates in strain collections and performed *spa*-typing according to the standard protocol, uploaded the sequence information and made this available by synchronisation with the central Ridom SpaServer (http://www.spaserver.ridom.de) curated by SeqNet.org at the University Medical Center Groningen, Netherlands [10,11]. Currently there are more than 13,000 *spa*-types and 630 repeat units stored on the SpaServer.

Epidemiological and typing data were communicated in parallel to a central purposely designed structured query language (SQL) database at the National Institute for Public Health and the Environment (RIVM) of the Netherlands. For each local laboratory, SRLs also provided the postal address and decimal Cartesian coordinates for automatic geolocation. All data were anonymous and collected in accordance with the European Parliament and Council decision for the epidemiological surveillance and control of communicable disease in the European community [12,13]. Ethical approval and informed consent were thus not required.

Data analysis and geographical illustration

All data were inspected for inconsistencies and analysed on a country-by-country basis and returned to SRLs for feedback, clarification of inconsistencies and final approval in July 2012. After final approval, data were analysed using Stata™ version 11.0 (College Station, Texas, USA) using Pearson chi-square test and Fischer's exact test for proportions and Student t-test for continuous variables. Quantitative differences between the 2006 survey were reported as results. The index of diversity *ID* is an unbiased measure of the probability of drawing two different *spa*-types given the distribution of *spa*-types in the sample. The 95% confidence intervals were calculated as described previously [14]. Multilocus sequence typing (MLST) sequence types were extrapolated from the *spa*-type as per the Ridom SpaServer. Cartesian coordinates where used for geolocation and plotting on Google Maps using the geocoding facility at http://www.spatialepidemiology.net [15]. The web application 'SRL-Maps' (http://www.spatialepidemiology.net/SRL-Maps2) was developed to interrogate the data based on mapping of laboratory locations.

RESULTS

Summary statistics

Between January and July 2011, laboratories from 25 European countries participated in this survey. These included 22 European Union (EU) Member States (Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Malta, the Netherlands, Poland, Portugal, Romania, Slovenia, Spain, Sweden, United Kingdom), two European Economic Area (EEA) countries (Iceland and Norway) and Switzerland. For the United Kingdom, Scotland

participated on its own behalf, whereas England, Northern Ireland and Wales all referred isolates to the same reference centre in England. Two countries (Cyprus and Malta) took the deliberate decision to carry out the necessary investigations in partner (twinning) laboratories as the sample volume would not have justified the necessary investment for sequencing equipment. Since they were also allowed to submit a larger quota, they submitted 34 and 20 isolates, respectively.

Altogether, 350 laboratories serving 453 hospitals submitted data for 3,753 *S. aureus* isolates from patients with bloodstream infections, isolated during the six months investigation period. Table 1 gives a summary overview of the number of participating laboratories and hospitals, isolates and *spa*-types submitted by country. The combined collection consisted of 2,621 (69%) MSSA and 1,130 (31%) MRSA. Two isolates had an inconclusive resistance phenotype. One was *spa*-type t127 and the other *spa* non-typable. Eight-hundred and sixty-one different *spa*-types were discerned of which 720 were MSSA and 228 MRSA. Eighty-five *spa*-types were shared between MSSA and MRSA. When compared to results obtained during 2006, the *spa*-type per isolate ratio had remained at 0.23, indicating a similar sample diversity in both surveys. Fifty-one (1.4%) isolates were *spa* non-typable. Typability of isolates ranged from 93.3 to 100% depending on the country.

Bloodstream infections with *S. aureus* occurred at an older age (median: 68 years, Table 2) and predominantly among men, which is in accordance with previous findings [5,16]. The proportion of males was even higher among MRSA than MSSA bloodstream infections ($p=0.03$). The median age at infection with MRSA was three years older than that with MSSA. Compared with 2006 data, the age distribution for both MSSA and MRSA in 2011 had shifted slightly to older age groups ($p<0.001$).

In 2011, data on all-cause mortality 14 days after index blood culture were available for 65.5% of all cases. Overall all-cause mortality was 19.4%. There was a difference between MRSA and MSSA in terms of all-cause mortality whereby 17.1% of patients with MSSA infections died compared to 24.4% of patients with MRSA ($p<0.001$). This difference was also identified in 2006 and is explained by various confounders that put MRSA patients at a higher risk of dying than those with MSSA infections [17]. Overall, there were more patient deaths in 2011 compared with the 2006 survey (16%, $p=0.004$). Although observed for both, MSSA and MRSA infections, this trend was only significant for MRSA infection ($p=0.004$). Whether this difference indicates an evolution towards more virulence or changes in host factors such as the increase in age cannot be determined from this dataset.

Fifty-six percent of MSSA and 33.4% of MRSA infections had the onset of disease in the community, indicating that MRSA remains predominantly hospital-acquired. But there was a significant increase in the proportion of cases with community onset compared with the previous survey, (MSSA 2006, 48.4%, $p<0.001$; MRSA 2006: 28.3%, $p=0.02$). A comparison of the most prevalent *spa*-types among hospital-associated MRSA (HA-MRSA) and community-onset isolates (CO-MRSA) revealed little difference (not shown). In the 2011 sample, the five top ranking *spa*-types comprised 52% and 45% of all HA-MRSA and CO-MRSA, respectively.

The high overall diversity (*ID*=0.985) is indicative of the good discriminatory ability of *spa*-typing but, as with the 2006 sample, there has been a significant difference between MSSA and MRSA as a result of the oligo-clonal nature of MRSA spreading through European countries.

Table 1. Summary overview of the 2011 participating laboratories, hospitals, number of invasive isolates MSSA and MRSA and *spa*-types by country.

Country	No. Laboratories	No. Hospitals	No. isolates	MSSA	MRSA*	No. *spa*-types MSSA	No. *spa*-types MRSA	No. non-typable	% non-typable
Belgium	17	17	133	76	57	53	25	3	2.2
Bulgaria	11	11	46	33	13	25	8	0	0.0
Cyprus	1	1	34	20	14	17	10	1	2.9
Czech Republic	20	20	144	95	49	63	9	0	0.0
Denmark	16	58	288	276	10	150	7	2	0.7
Finland	17	43	173	163	10	89	5	2	1.2
France	34	34	286	166	120	98	31	3	1.0
Germany	10	26	161	100	61	62	22	0	0.0
Greece	1	13	85	47	38	33	15	0	0
Hungary	13	13	125	74	51	39	13	1	0.8
Iceland	1	1	9	7	2	6	2	0	0.0
Ireland	21	27	193	117	76	68	21	13	6.7
Italy	23	23	200	103	97	61	36	0	0.0
Latvia	8	8	36	33	3	17	2	1	2.8
Malta	1	1	20	10	10	10	7	0	0
the Netherlands	2	16	138	130	8	77	5	7	5.1
Norway	22	n.d.**	84	80	4	61	3	0	0.0
Poland	49	52	391	312	79	136	25	0	0.0
Portugal	1	19	195	99	96	52	23	0	0.0
Romania	5	5	37	15	22	13	7	0	0.0
Slovenia	10	13	164	142	22	40	3	9	5.5
Spain	1	30	129	35	94	30	27	0	0.0
Sweden	23	n.d.	225	215	10	114	10	1	0.4
Switzerland	6	6	60	46	14	39	9	1	1.7
UK-England, Northern Ireland and Wales	16	16	164	108	56	63	25	7	4.3
UK-Scotland	21	n.d.	233	119	114	69	35	0	0.0
Total	350	453	3753	2621	1130	720	228	51	1.4

* Note that the number of MRSA does not reflect a prevalence or occurrence in particular countries as the protocol asked for submission of the first five isolates of each phenotype.
** n.d. = not determined

Table 2. Comparison of *S. aureus* isolated from patients with bloodstream infections in 25 European countries in 2011 with 2006.

	2011					2006					p-values comparing 2011 vs 2006[d]		
	n[a]	MSSA	MRSA	Total/ Overall[b]	p-value[c]	n[a]	MSSA	MRSA	Total/ Overall[b]	p-value[c]	MSSA	MRSA	overall
Frequency (%)	3753	2621 (69.9)	1130 (30.1)	3751 (100%)	-	2890	1923 (66.5)	967 (33.5)	2890 (100%)	-	0.004	0.004	-
Median age (IQR)	3753	67 (52 – 78)	70 (57 – 80)	68 (54 – 79)	<0.001	2836	63 (46 – 75)	69 (55 – 78)	66 (49 – 76)	<0.001	<0.001	0.190	<0.001
Male gender (%)	3702	1572 (60.9)	723 (64.7)	2295 (62.0)	0.029	2862	1159 (60.8)	606 (63.3)	1765 (61.7)	0.2	0.994	0.504	0.768
All-cause mortality after 14 days (%)	2458	289 (17.1)	188 (24.4)	477 (19.4)	<0.001	1838	153 (13.2)	141 (20.8)	294 (16.0)	<0.001	0.004	0.107	0.004
Hospital acquisition (%)	2863	831 (44.0)	649 (66.6)	1480 (51.7)	<0.001	2322	777 (51.6)	585 (71.7)	1362 (58.7)	<0.001	<0.001	0.020	<0.001
No. *spa*-types[e]	3702	720	228	862*	-	2850	565	155	660*	-	-	-	-
No. non-typable	3753	41 (1.6)	9 (0.8)	51 (1.4)	0.060	2890	27 (1.4)	13 (1.3)	40 (1.4)	0.9	0.660	0.220	0.930
Index of diversity (CI_{95})	3688	0.986 (0.983 – 0.987)	0.942 (0.933 – 0.947)	0.985 (0.982 – 0.984)	<0.05**	2850	0.985 (0.983 – 0.987)	0.940 (0.933 – 0.947)	0.983 (0.982 – 0.984)	<0.05**	-	-	-

[a] Number of isolates for which information was available for each variable. In 2011, two isolates had an undetermined MRSA status. [b] Total number of isolates with an MSSA/MRSA status and data from the considered variable. [c] p-value for the comparison of MSSA vs MRSA. [d] p-value comparing each of the three variables from 2011 with its counterpart from 2006 (e.g. MSSA 2011 vs MSSA 2006). [e] Number of typable isolates: MSSA= 2580 and MRSA=1121. *Total number of *spa*-types includes 85 *spa*-types that contain both MSSA and MRSA in 2011 and 60 *spa*-types in 2006. **Deduced from non-overlapping 95% confidence intervals. IQR= interquartile range.

Overall distribution of *spa*-types

For MSSA, the top 20 ranking *spa*-types contained 43.2% of all MSSA isolates (Table 3). Importantly, there was very little difference among the first 11 ranking *spa*-types between the 2011 and 2006 datasets. Only changes in rank order were observed. Ranks 12 to 20 contained four new *spa*-types in 2011 (Table 3, Supplementary Table 1 for comparison with 2006, available upon request).

For MRSA, the top 20 ranking MRSA *spa*-types represent 68.1% of all MRSA isolates (73.4% in 2006). There were no differences in the top six *spa*-types (albeit in relative ranking). t032/ST22 now comprises 17.9% of all MRSA sampled in 2011 (up from 14.5% in 2006, p=0.036, Figure 1, Table 3, see also Supplementary Table 1 for comparison with 2006, available upon request). Except for t515, all ST22 related *spa*-types (t032, t022, t747, t2357, t6057) have significantly increased in frequency and this lineage made up 36% of the top 20 ranking isolates in 2011, whereas in 2006 this figure was still lower at 23%. Three *spa*-types have significantly decreased compared to the 2006 collection. t008/ST8 mainly found in France decreased from 12.4% to 8.4% (p=0.003). t041/ST228 decreased from 7.4 % in 2006 to 2.1% in 2011 (p<0.001). Finally international clone t030/ST239 decreased from 2.1% to 0.8% (p=0.013).

Table 3. Twenty most frequent *spa*-types and MLST types among isolates collected in 25 European countries in 2011.

MSSA						MRSA					
Rank	*spa*-type	Multilocus sequence type	Freq.	%	cum. %	Rank	*spa*-type	Multilocus sequence type	Freq.	%	cum. %
1	t091	ST7	138	5.3	5.3	1	t032	ST22	202	17.9	17.9
2	t084	ST15	124	4.7	10.0	2	t003	ST225	99	8.8	26.6
3	t002	ST5	121	4.6	14.6	3	t008	ST8	95	8.4	35.0
4	t015	ST45	98	3.7	18.4	4	t002	ST5	87	7.7	42.7
5	t008	ST8	97	3.7	22.1	5	t067	ST125	50	4.4	47.2
6	t012	ST30	90	3.4	25.5	6	t041	ST228	24	2.1	49.3
7	t127	ST1	83	3.2	28.7	7	t777*	ST5	21	1.9	51.2
8	t021	ST30	50	1.9	30.6	8	t018*	ST36	20	1.8	52.9
9	t065	ST45	38	1.4	32.1	9	t022	ST22	20	1.8	54.7
10	t026	ST45	34	1.3	33.4	10	t037	ST239	19	1.7	56.4
11	t005	ST22	33	1.3	34.6	11	t127	ST1	18	1.6	58.0
12	t230	ST45	32	1.2	35.9	12	t747*	ST22	17	1.5	59.5
13	t216*	ST59	28	1.1	36.9	13	t044	ST80	15	1.3	60.8
14	t056	ST101	27	1.0	38.0	14	t2357*	ST22	15	1.3	62.1
15	t148	ST72	25	1.0	38.9	15	t024	ST8	14	1.2	63.4
16	t024	ST8	23	0.9	39.8	16	t740	ST45	12	1.1	64.4
17	t346	ST15	23	0.9	40.7	17	t515	ST22	12	1.1	65.5
18	t571*	ST398	23	0.9	41.5	18	t6057*	ST22	11	1.0	66.5
19	t701*	ST8	23	0.9	42.4	19	t030	ST239	9	0.8	67.3
20	t189*	ST188	21	0.8	43.2	20	t014*	ST225	9	0.8	68.1
other	-	-	1489	56.8	100.0	other	-	-	361	31.9	100.0
	Total		**2621**	**100**			**Total**		**1130**	**100**	

* New among the top 20 in 2011.

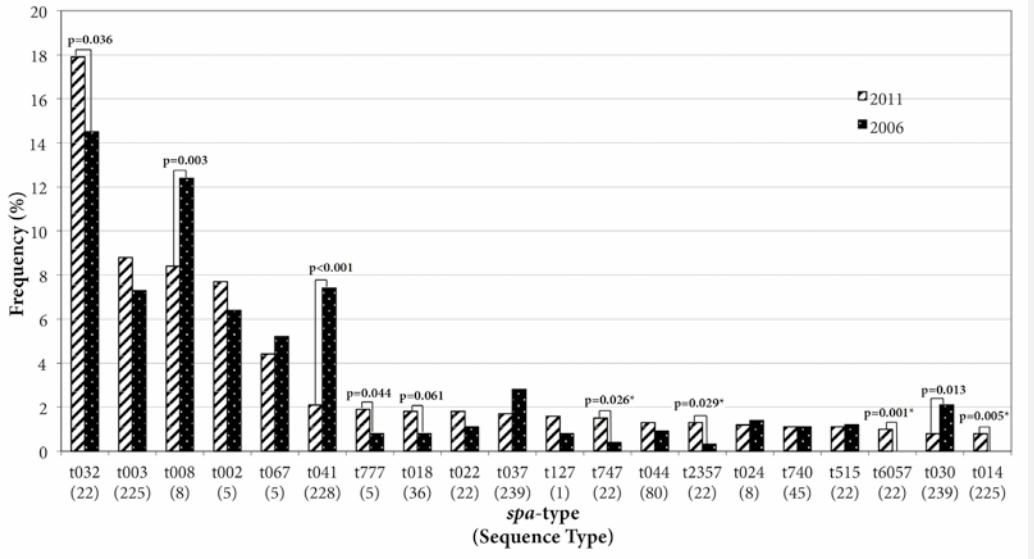

Figure 1. Comparison of *spa*-type frequencies between 2011 and 2006. *Fisher's exact test

DISCUSSION

This survey represents a repetition of a previous study carried out in 2006 and was designed to investigate (i) the temporal and spatial changes of *S. aureus* clones of particular public health importance in Europe, and (ii) the feasibility and utility of integrating molecular typing data with epidemiological and clinical information at a European level.

We previously demonstrated the feasibility of creating a collaborative consortium of SRLs across Europe and alignment of *S. aureus* typing methodology in addition to harmonizing processes and data format at a European level [5]. The continuation of this effort has shown that collaboration between countries can be maintained over extended intervals and provide added value to the understanding of the dynamic spread of *S. aureus* while quality, consistency of molecular typing and communication improves.

The results described herein are testimony to the usefulness of structured surveys to generate information for public health action in a timely and economic fashion. Repeating surveys through previously created networks of sentinel hospital laboratories allows for consistent observations about the changing epidemiology of infections caused by clones of particular public health importance. In case of *S. aureus,* these clones are responsible for community and hospital-associated infections, are often resistant to a range of antibiotic compounds and circulate among patients of extended hospital referral networks in Europe. They typically have a defined geographical distribution and show a steady diffusion along hospital patient referral lines. Moreover, our results suggest that HA-MRSA are filtering into the community at an increasing rate. The proportion of community onset infections caused by international HA-MRSA clones have increased over the last five years from 28.3% to 33.4%. This difference is significant and relevant as it indicates a trend to more export of hospital-associated clones into the community probably as a result of shorter hospital stay.

Among MRSA a dynamic expansion could be demonstrated for several *spa*-types. MRSA isolates with *spa*-types belonging to ST22 increased most markedly making ST22 the most critically expanding MRSA clone in Europe. This lineage (designated EMRSA-15) was first described during hospital outbreaks in England. It caused a nationwide epidemic of healthcare-associated infections in the 1990s and is still the most prevalent HA-MRSA in the UK [18]. This clone has spread from the UK and Ireland and has become abundant in Germany, Hungary, Portugal and Northern Italy. MRSA belonging to *spa*-type t018/ST36 has attained a foothold in Poland and t067/ST125, abundant in Spain during the 2006 survey [19], has been causing an outbreak in hospitals in a single health district in Finland in 2011 [20]. Among MSSA, *spa*-type t571/ST398 appears to be spreading in France and Belgium [21]. Our observations indicate that infections with this clone are more frequent among men of younger age and may be associated with higher mortality. Its MRSA counterpart has been described as an ancestral human variant of the livestock-associated MRSA clone ST398, which caused outbreaks of community-acquired infections in Northern Manhattan that were linked to immigrants from the Dominican Republic [22,23]. Conversely, a reduction of the international clone ST239 consisting of the *spa*-types t030 and t037 and t041/ST228 was observed. It appears that the decline of ST239 is genuine as it mainly occurred in Poland, whereas the reduction of t041/ST228 can be explained by the fact that Austria and Croatia did not participate in the 2011 survey. Both countries contributed a high proportion of this type to the 2006 dataset. This highlights the importance of consistent participation in this type of pathogen-specific surveillance initiatives and the vulnerability of networks that depend on the goodwill and enthusiasm of the participants.

Limitations of this study that deserve to be addressed consist of a deliberate decision that was taken by the SRLs to provide only isolates from bloodstream infections. This slight deviation from the sampling frame of the previous survey may have skewed the *spa*-type distribution ever so slightly. Moreover, the fixed number of isolates that were collected from each participating centre was owed to the trade-off between the desire to make the workload of SRLs predictable and manageable and the inability to precisely determine incidence and the absolute increase or decrease of *spa*-types. Thus,

findings generated through these types of structured surveys must be put into context of surveillance data from other European-wide initiatives such as EARS-net and/or HAI-net. The nature of structured surveys does not allow for early warning and response as it merely provides a rather static population snapshot of the *spa*-types i.e. clones that were extant and caused bloodstream infections at the time of sampling. The value of these snapshots should, however, not be underestimated, as they provide an unbiased view, which can be used to identify clones of public health importance and their geographic abundance and can inform *ad hoc* epidemiological investigations about the dignity and geographical origin of organisms isolated during outbreaks.

The exchange of typing results using an illustrative mapping tool such as SRL-maps of the spatialepidemiology.net website provides the means to determine the reach and expansion of clones with proven success simultaneously for different countries. Initiatives such as these could lead to an improved and sustainable effort to control and eradicate emerging high-risk clones at the level of healthcare institutions once international agencies secure the sustainability for these repeated efforts.

A consistent integration of typing data with pre-existing epidemiological and/or clinical data collected through other European surveillance initiatives (such as EARS-net, ESAC-net or HAI-net) will, however, still depend on the successful implementation of further alignment of sampling methodology, diagnostic procedures and of the regulatory framework across Europe. It would require a systematic and internationally accepted identification code for hospitals and diagnostic laboratories, as well as for bacterial isolates which are reported through different surveillance initiatives and for patients from whom these organisms were originally recovered. This would require novel regulatory approaches on the part of European national governments. Moreover, data protection and confidentiality issues would need to be resolved before such regulations could be enacted. The alternative would be a fully decentralised approach. This would require additional efforts from hospitals and laboratories to provide pertinent epidemiological and clinical information in addition to molecular typing and antibiotic susceptibility data and to report this bundled information whilst maintaining full confidentiality. However, as such efforts require a considerable degree of reorganisation they may seem unrealistic under the current climate of austerity and economic streamlining. During the deliberations with the representatives of the SRLs in Europe, the possibility to collect more accurate data about source patients (epidemiology and clinical outcome) was appraised. The prevailing consensus was that this would be unrealistic given the scarcity of information provided to diagnostic laboratories by clinicians on the request forms and the inability of laboratories to fund these additional enquiries from their own budgets. It is important to note that these concerns were not raised by single members of the SRL working group, but appears to represent a common view across Europe as a whole.

In conclusion, collaborative typing initiatives are able to identify the continental spread of high-risk clones across national boundaries and can provide an indication to health care systems about the emergence of threats caused by successful and antibiotic-resistant bacteria. The geographic diffusion of antibiotic-susceptible and -resistant clones of *S. aureus* can be made visible with the help of intuitive information tools such as interactive websites in a timely manner and can improve the coherence of individual laboratory results towards a better understanding of the population dynamic of these important pathogens. A simple integration of typing data with data from other existing surveillance efforts is, however, currently constrained by regulatory hurdles and legitimate concerns about patient data protection.

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PART 3

‘Happiness is not something ready made. It comes from your own actions.’
Dalai Lama