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

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Citation style for this article:
Köck R, Becker K, Cookson B, van Gemert-Pijnen JE, Harbarth S, Kluytmans J, Mielke M, Peters G, Skov RL, Struelens MJ, Tacconelli E, Navarro Torné A, Witte W, Friedrich AW. Methicillin-resistant Staphylococcus aureus (MRSA): burden of disease and control challenges in Europe. Euro Surveill. 2010;15(41):pii=19688. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19688

Article published on 14 October 2010

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of healthcare- and community-associated infections worldwide. Within the healthcare setting alone, MRSA infections are estimated to affect more than 150,000 patients annually in the European Union (EU), resulting in attributable extra in-hospital costs of EUR 380 million for EU healthcare systems. Pan-European surveillance data on bloodstream infections show marked variability among EU Member States in the proportion of *S. aureus* that are methicillin-resistant, ranging from less than 1% to more than 50%. In the past five years, the MRSA bacteraemia rates have decreased significantly in 10 EU countries with higher endemic rates of MRSA infections. In addition to healthcare-associated infections, new MRSA strains have recently emerged as community- and livestock-associated human pathogens in most EU Member States. The prevention and control of MRSA have therefore been identified as public health priorities in the EU. In this review, we describe the current burden of MRSA infections in healthcare and community settings across Europe and outline the main threats caused by recent changes in the epidemiology of MRSA. Thereby, we aim at identifying unmet needs of surveillance, prevention and control of MRSA in Europe.

Introduction

Concern about the burden of healthcare-associated infections (HAIs) has a significant European dimension. It has been estimated that 8–12% of patients admitted to hospitals in European countries suffer from adverse events while receiving healthcare, with HAIs being the most prominent of them [1]. The European Centre for Disease Prevention and Control (ECDC) has calculated that HAIs involve 4.1 million patients annually in the European Union (EU) Member States and that such infections directly result in approximately 37,000 deaths [1]. This worrisome incidence of HAIs is rightly considered a major patient safety issue. Another cause for concern is the continuous emergence of various multidrug-resistant bacteria in many healthcare institutions, which narrows the spectrum of effective antibiotics to a clinically challenging extent. Against this background, the Council of the EU has recently launched a recommendation to Member States and the Commission to prevent HAIs and promote patient safety by community, national and institutional action plans [1].

Among the multiresistant bacteria, methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of HAIs in the EU. In 2008, over 380,000 HAIs due to selected antibiotic-resistant bacteria, including those of the bloodstream, lower respiratory tract, skin or soft tissues and urinary tract, were estimated to be acquired annually in hospitals of the EU Member States, Iceland and Norway [2]. Overall, MRSA accounts for 44% (n=171,200) of these HAIs, 22% (n=5,400) of attributable extra deaths and 41% (n=1,050,000) of extra days of hospitalisation associated with these infections [2]. The attributable extra in-hospital costs caused by MRSA are estimated to reach approximately EUR 380 million annually [2]. Moreover, the vast extent of MRSA infections has both evoked fear and fuelled public distrust about healthcare. For many healthcare

consumers, this has made MRSA bloodstream infection rates an indicator of both quality of care and outcome.

In addition to the healthcare settings (healthcare-associated methicillin-resistant *Staphylococcus aureus*, HA-MRSA) [3], the burden of MRSA colonisation and infection has recently expanded to further ecological niches. Since the 1990s, an increasing incidence of MRSA infections arising in the community (community-associated methicillin-resistant *Staphylococcus aureus*, CA-MRSA) has been reported from many countries worldwide [3]. More recently, MRSA have been found to colonise or infect livestock and humans exposed to those animals in several countries. Such MRSA have been dubbed livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) [4]. Interactions between these different reservoirs for MRSA have been reported, including nosocomial infections by CA-MRSA [5,6] and importation of LA-MRSA into hospitals [7].

MRSA is amongst the most challenging infection control issues. In this review, we delineate the burden of MRSA disease in Europe across healthcare sectors and review the economic impact of MRSA infections. Finally, we outline threats due to recent changes in the epidemiology of MRSA and identify unmet needs regarding surveillance, prevention and control of MRSA in Europe.

Methods

We searched PubMed and supplemented this with articles from our personal archives to retrieve the literature for this review. For the PubMed search, a restriction to articles published between 2001 and 2009 and written in English was applied. Our review is structured in two sections: (i). Epidemiology and burden of MRSA infections, in which we outline the main determinants of MRSA disease burden, compared to infections by methicillin-susceptible *S. aureus* (MSSA), and summarise recent trends in the epidemiology of MRSA in Europe in healthcare facilities, the community and livestock; and (ii). Discussion on new reservoirs and control challenges, where, against the background of data described in the first section, we identify potential threats from the current epidemiology of MRSA in Europe and discuss perspectives for the prevention and control of MRSA in European countries.

Epidemiology and burden of MRSA infections

Burden of disease

Monitoring the epidemiology and the burden of MRSA infections in European countries is crucial. This has been underlined by the finding that MRSA does not just replace MSSA as a causative agent for infections, but frequently adds to the latter's disease burden, leading to a net increase in the incidence of *S. aureus* infections (Table 1) [8,9].

Moreover, it has been debated whether MRSA bacteraemia causes higher mortality than MSSA bacteraemia, e.g. due to vancomycin's inferiority in the treatment of deep-seated *S. aureus* infections, compared with semi-synthetic penicillins, compared with semi-synthetic penicillins used for MSSA [10]. Two meta-analyses have found an increased mortality risk of 1.93 (95% CI: 1.54 to 2.42) [10] and 2.03 (95% CI: 1.55 to 2.65) [11] associated with MRSA bacteraemia compared with MSSA. However, there is an ongoing discussion about methodological flaws of the studies included in these meta-analyses, e.g. with respect to whether they fully adjusted for appropriateness of therapy and severity of underlying diseases. Table 2 contains an update of additional (published between 2001 and 2009) regarding this issue: their results still do not clearly answer the initial question.

Besides effects on mortality, several studies mainly from the USA have indicated that MRSA infections cause a significant additional financial burden over

Table 1

Key elements in the recent epidemiology of MRSA infections in Europe

Characteristic	Summary
MRSA vs MSSA infections	Recent investigations indicate that: • MRSA adds to the total burden of *S. aureus* disease; • Invasive MRSA infections are associated with a higher mortality compared with MSSA; • MRSA infections generate extra costs of care mainly due to prolonged length of hospital stay.
Epidemiological reservoirs	In European countries, MRSA is associated with three main reservoirs: healthcare institutions (HA-MRSA), the community (CA-MRSA), and livestock (LA-MRSA).
HA-MRSA	According to the pan-European surveillance systems, EARSS and HELICS, the prevalence of HA-MRSA infection markedly varies between countries but has been decreasing in several over the past five years.
CA-MRSA	CA-MRSA infections have emerged in most European countries but are still less frequent overall than HA-MRSA infections.
LA-MRSA	In the majority of European countries, livestock is colonised with MRSA. The impact of this reservoir on public health is unclear.

CA-MRSA: community-associated methicillin-resistant *Staphylococcus aureus*; EARSS: European Antimicrobial Resistance Surveillance System; HA-MRSA: healthcare-associated methicillin-resistant *Staphylococcus aureus*; HELICS: Hospital in Europe Link for Infection Control through Surveillance; LA-MRSA: livestock-associated methicillin-resistant *Staphylococcus aureus*; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-susceptible *Staphylococcus aureus*.

Table 2

Estimates of mortality of MRSA bacteraemia compared with MSSA bacteraemia from studies published between 2001 and 2009

Type, place and period of study	Number of patients with *S. aureus* infection (% of MRSA cases)	Percentage mortality in MRSA patients	Percentage mortality in MSSA patients	Odds ratio/hazard ratio for MRSA–associated mortality (95% CI)	Reference
Single-centre, university hospital, Taiwan, 1990–2004	1,148 (74)	50%[a]	28%[a]	1.78 (1.3–2.44)	Wang *et al.* [12]
Single-centre, university hospital, Belgium, 1992–1998	85 (44.7)	64%[b]	24%[b]	1.93 (1.18–3.18)	Blot *et al.* [13]
Single-centre, teaching hospital, UK, 1995–2000	815 (46.9)	12%[c]	5%[c]	1.72 (0.92–3.20)	Melzer *et al.* [14]
Veterans affairs healthcare system, USA, 1995–2003	438 (44)	34%[d]	20%[d]	1.8 (1.2–3.0)	Shurland *et al.* [15]
Single-centre, university hospital, USA, 1996–2001	143 (38)	35%[d]	12%[d]	5.4 (1.5–18.7)	Reed SD *et al.* [16]
Single-centre, university hospital, France, 1997–1998	99 (30)	43%[e]	20%[e]	2.97 (1.12–7.88)	Talon *et al.* [17]
Single-centre, tertiary–care teaching hospital, USA, 1997–2000	348 (28)	23%[f]	20%[f]	1.2 (0.68–2.12)	Cosgrove SE *et al.* [18]
Multi-centre, Germany, 1997–2002	378 (25.1)	17%[c]	6%[c]	3.84 (1.51–10.2)	Gastmeier *et al.* [19]
Two centres, teaching hospital UK, 1997–2004	461 (50)	34%[a]	27%[a]	1.49 (0.99–2.26)	Wyllie *et al.* [8]
Single-centre, teaching hospital, USA, 1999–2001	353 (48)	31%[a]	15%[a]	1.4 (0.7–3.0)	Lodise *et al.* [20]
Single-centre, teaching hospital, Brazil, 2000–2001	111 (55)	55%[a]	25%[a]	2.52 (0.96–6.6)	Guilarde *et al.* [21]
Single-centre, university hospital, Taiwan, 2001–2006	215 (14)	10%[a]	13%[a]	0.73 (0.21–2.60)	Wang *et al.* [22]
Single-centre, university hospital, Belgium, 2002–2004	154 (43)	42%[g]	24%[g]	3.04 (1.15–8.04)	Libert *et al.* [23]
Single-centre, university hospital, Germany, 2002–2007	521 (13)	42%[d]	19%[d]	2.6 (1.4–4.9)	Rieg *et al.* [24]
Single-centre, tertiary care, USA, 2004–2005	68 (53)	47%[h]	19%[h]	5.1 (1.1–22.9)i	Malani *et al.* [25]

CI: confidence interval; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-susceptible *Staphylococcus aureus*; UK: United Kingdom; USA: United States of America.

[a] Thirty-day mortality.
[b] Mortality at the end of hospital stay.
[c] Time frame of mortality not provided.
[d] Ninety-day/12-week mortality.
[e] Fourteen-day mortality.
[f] Seven-day mortality.
[g] Bloodstream infection-related mortality.
[h] Six-month mortality.

Table 3

Estimates from recently published (2001–2009) studies of hospital financial burden associated with MRSA infections compared with MSSA infections

Type of infection, setting of study	Number of patients	Effect on hospital length of stay	Effects on costs	Reference
Bacteraemia, one teaching hospital, USA, 1997–2000	96 MRSA vs 252 MSSA	Median LOS: 9 days (MRSA) vs 7 days (MSSA), p=0.045; MRSA independent risk factor for increased LOS (1.3–fold, p=0.016)	Hospital charges after *S. aureus* bacteraemia: USD 26,424 (MRSA) vs USD 19,212 (MSSA), p=0.008	Cosgrove SE *et al.* [18]
Haemodialysis-related infections, one teaching hospital, USA, 1996–2001	54 MRSA vs 89 MSSA	Median LOS: 11d (MRSA) vs 7days (MSSA), p<0.001	Adjusted median costs for initial hospitalisation: USD 21,251 (MRSA) vs USD 13,978 (MSSA), p=0.012 and after 12 weeks: USD 25,518 (MRSA) vs USD 17,354 (MSSA), p=0.015	Reed SD *et al.* [16]
Surgical site infections, one tertiary care and one community hospital, USA, 1994–2000	121 MRSA vs 165 MSSA vs 193 uninfected controls	Median LOS after surgery: 5 days (uninfected) vs 14 days (MSSA) vs 23 days (MRSA), P<0.001. Median LOS after infection: 15 days (MRSA) vs 10 days (MSSA), P<0.001	Median costs for uninfected patients: USD 29,455 vs USD 92,363 (MRSA) vs USD 52,791 (MSSA), p<0.001	Engemann JJ *et al.* [26]
BSIs, one tertiary care hospital, USA, 2000–2003	95 MRSA vs 87 MSSA	LOS after infection: 10.5 days (MSSA) vs 20.5 days (MRSA), p=0.003; adjusted mean excess LOS ratio: 1.1 (95% CI, 0.8–1.4, not significant)	Median total hospital costs: USD 42,137 (MSSA) vs USD 113,852 (MRSA); adjusted mean excess cost ratio: 1.2 (95%CI, 0.9–1.6, not significant)	Ben–David D *et al.* [27]
Ventilator-associated pneumonia, 16 teaching and 43 nonteaching hospitals, USA, 2002–2003	95 MSSA vs 59 MRSA	Total inpatient LOS: 20 days (MRSA) vs 15d (MSSA), p=0.04. MRSA patients consumed excess resources of 3.8 inpatient days, p=0.08	Patients with MRSA–VAP consumed excess resources of USD 7731 (p=0.035) in total costs	Shorr AF *et al.* [28]

BSI: bloodstream infection; ICU: intensive care unit; LOS: length of stay; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-susceptible *Staphylococcus aureus*; SSI: surgical site infection; USA: United States of America; USD: United States dollars; VAP: ventilator-associated pneumonia.

MSSA infections after adjustment for co-morbidities, which is largely the result of prolonged hospital stay and occupation of isolation rooms (Table 3).

Moreover, a Dutch study has recently estimated that the implementation of a MRSA 'search and destroy' policy was highly cost–effective in one hospital under investigation [29]. During the study period, no MRSA bacteraemia was observed in this hospital. Assuming that 50% of all nosocomial *S. aureus* would be MRSA, if no search and destroy strategy had been implemented the authors estimated 36 MRSA bacteraemia cases per year were thus avoided [29].

Furthermore, it has been found that MRSA carriers are at risk for MRSA infection, since up to 29% of persons colonised with MRSA subsequently develop MRSA morbidity [30,31]. For example, MRSA carriers in long-term care facilities have a 1.4-fold increased risk for mortality within 36 months [32] and 5% of long-term carriers have been shown to die because of an MRSA infection within four years of carriage [30].

Epidemiology of healthcare-associated MRSA

Nosocomial infections acquired by patients receiving institutional healthcare have long been the classical presentation of MRSA infections. Risk factors for MRSA acquisition include hospital care, care in chronic care facilities and nursing homes for elderly people, presence of indwelling devices or chronic wounds and previous antibiotic treatment.

The majority of HA-MRSA strains isolated in European countries have emerged from the introduction of the staphylococcal cassette chromosome *mec* (SCC*mec*) harbouring the methicillin-resistance gene *mec*A, into five *S. aureus* clonal complexes (CC), as defined by multi–locus sequence typing (MLST): CC5, CC8, CC22, CC30 and CC45 [3].

Recent data on the burden of HA-MRSA disease on a European scale are available from two surveillance systems supported by ECDC (EARSS, HELICS). The European Antimicrobial Resistance Surveillance System (EARSS) is used in most European countries to record the incidence of bloodstream and cerebrospinal MRSA infections, representing severe clinical courses of (mostly HA-) MRSA morbidity. As shown recently, hospitals contributing to EARSS provide care for about 20% of the EU population, accession countries and Israel [33]. However, EARSS coverage ranges between 5% and 100%, depending on the country, and therefore representative data from all countries are not available [33]. In 2008, the proportion of MRSA in *S. aureus* blood culture isolates was less than 5% in Denmark, Estonia, Finland, Iceland, the Netherlands, Norway and Sweden. In three countries (Austria, Luxembourg, Slovenia), a proportion of less than 10% was found, while in eight countries the proportion was between 10%-24% (Belgium, Czech Republic, France, Germany, Hungary, Latvia, Poland, Switzerland) In total, 13 countries reported a proportion equal to or above 25% (Bulgaria, Croatia, Cyprus, Greece, Israel, Italy, Malta, Portugal, Republic of Ireland, Romania, Spain, Turkey, United Kingdom) including two countries (Malta, Portugal) with proportions above 50% [33].

The attributable fraction of HAI caused by MRSA is documented by the EU-wide surveillance network of infections in intensive care units (ICUs), which was established under the name "HELICS". In 2007, the HELICS network (involving 13 European countries) reported that, of 54,574 patients staying in an ICU for more than two days, 6.2% acquired pneumonia. Overall, 17% of all cases of ICU-acquired pneumonia [34] were caused by *S. aureus*, 33% of which were MRSA. Moreover, ICU-acquired BSIs were caused by *S. aureus* in 11% of all 4,812 cases included in the report with an MRSA proportion of 42% [34].

According to EARSS 2008 data, a significant declining trend of invasive MRSA infections has been observed in Austria, Poland, Latvia, Romania, Italy, France, Belgium and the United Kingdom over the last four years of surveillance [33]. Likewise, there was a significant decrease in the mean incidence of ICU-acquired MRSA infection reported via HELICS between 2004 and 2007 [34]. These trends illustrate that many European countries have experienced successes in the prevention and control of MRSA in the healthcare setting as indicated by either continuously low incidence rates or recently decreasing rates of MRSA infections.

Epidemiology of community-associated MRSA

Until the 1990s, infections due to MRSA were rarely observed in the community. Since then, a rapid emergence of CA-MRSA was first reported from Australia and the USA, where outbreaks were described amongst underprivileged aboriginal communities, schoolchildren, prison inmates, soldiers, athletes and men who have sex with men [35]. These communities have not been reported so far as major reservoirs for CA-MRSA in Europe. Risk factors for the development of CA-MRSA infection include close contact with other people with CA-MRSA, e.g. having a family member from a country with a high prevalence of CA-MRSA, living in crowded facilities, poor hygiene, sharing of personal items and performing contact sports [36,37]. These observations help to elucidate the spread of MRSA outside healthcare settings. So far, the most important risk factor for CA-MRSA infections in many European countries is travel to countries with a higher prevalence of CA-MRSA [38-40].

CA-MRSA causes mainly skin- and soft-tissue infections ranging in severity from furuncles to necrotising fasciitis [37]. Moreover, the description of serious invasive CA-MRSA infections, such as necrotising pneumonia, is cause for concern, because these infections are associated with a lethality of up to 75% [41].

The epidemic rise in CA-MRSA infections in the USA was mainly due to the successful spread of an MRSA strain associated with the pulsed-field gel electrophoresis (PFGE) profile USA300 within the MLST ST8/SCC*mec* IV clone and harbouring the *lukS-lukF* genes, encoding the Panton-Valentine leukocidin (PVL) [35]. Other clones have contributed to this epidemic to a lesser extent [3].

In several European countries, infections due to the predominant USA clone (USA300/ST8) have also been reported [39,42-44]. However, the spread of this clone seems hitherto limited in Europe where other PVL-positive CA-MRSA clones, especially ST80/to44/SCC*mec* IV, are also prevalent [3,46].

Defining the overall burden of CA-MRSA in European countries and comparing proportions of CA-MRSA among all MRSA isolates between different studies is hindered by differences in the definitions used [37]. However, the proportion of CA-MRSA with respect to total MRSA is reported to range between 1% and 2% in Spain and Germany [42,43] and 29–56% in Denmark and Sweden, partly reflecting the low prevalence of HA-MRSA in these Scandinavian countries [47,48]. Among outpatients with *S. aureus* infections, MRSA accounted for 6% in the Ligurian region in Italy [49], 14% in Germany [50], 18% in France [51] and 30% in Greece [52].

Epidemiology of livestock-associated MRSA

Recently, it has been found that the burden of MRSA colonisation and infection also involves animals, particularly livestock. In Europe, a recent survey published by the European Food Safety Authority (EFSA) identified MRSA in pig holdings of 17 EU Member States [53]. The MRSA clone, which was isolated from the vast majority of pigs, was non-typeable by PFGE after *Sma*I digestion – due to DNA methylation not, however, affecting the *Sma*I isoschizomer *Cfr*9I [54] – was tetracycline-resistant, and belonged to MLST CC398 [53].Besides swine, MRSA CC398 strains have also been detected in other animals such as cattle [55] and poultry [4]. Although the animals are mostly colonised by MRSA, infections have been described in pigs [56] and horses [57].

The impact of a livestock reservoir for humans is currently under investigation. Whereas 23–38% of persons having contact with MRSA-positive pigs or veal calves were colonised with MRSA [7,58,59], only 4% of their family members, who had no direct exposure to the animals, were colonised in one study [60]. In areas with a high density of MRSA CC398-positive swine, this clone can influence the MRSA epidemiology markedly in healthcare settings. For instance, it has led to a three-fold increase in MRSA incidence over a few years in a Dutch hospital located in a pig-dense area [7], and, in a German hospital situated in a region with intense livestock farming, 22% of MRSA patients colonised with MRSA at hospital admission carried it [61].

This continuous import of MRSA CC398 from an animal reservoir into hospitals can result in nosocomial spread of MRSA to patient groups susceptible to the development of MRSA infections [44]. Nosocomial transmission of MRSA CC398 has indeed been reported [62]. Moreover, this strain has caused severe human infections such as endocarditis, soft-tissue infections and ventilator-associated pneumonia [63-65].

Nevertheless, the burden of human infections caused by MRSA CC398 in Europe remains poorly understood. The proportion of MRSA CC398 among all MRSA ranges from 0.3% in Germany [65] to 41% in the Netherlands [66]. Matters of further concern include the facts that PVL-encoding genes have been detected in a few MRSA CC398 isolates [67] and a *cfr* plasmid conferring resistance against oxazolidinones was found in an MRSA CC398 background [68].

Another potential human health threat is related to food contamination with MRSA, which was documented by a Dutch study in 11.9% of retail meat products from several animal species, including beef (10.6%), pork (10.7%) and chicken (16%) [69]; detection by use of enrichment cultures only suggests low quantity contamination. The majority of these isolates belonged to the CC398 lineage, with only 15% to other clonal lineages [69]. To date, two outbreaks of human disease have been related to the consumption of MRSA-contaminated meat, one as a classical food intoxication [70] and the other with contaminated food as the source of nosocomial transmission [71]. Both were caused by non-CC398 MRSA strains. Thus, presently, food does not seem to be an important source for MRSA transmission or infection.

New reservoirs and control challenges

The recently decreasing or maintained low-level incidence of HA-MRSA in BSIs in many European countries [33] is encouraging. In a majority of countries, these successes can be linked to the implementation of multi–faceted preventive interventions (including measures focussing on screening, contact precautions, decolonisation, antibiotic stewardship, or bundles of preventive measures and care). In France, a national hospital infection control programme has been initiated and developed over 16 years, resulting in a 30% reduction of surgical site infections and a 20% decrease in MRSA rates from blood cultures [72]. In Belgium, a sustained decrease in the incidence of HA-MRSA infections was recorded between 2004 and 2008, measureable as a decrease in the mean proportion of MRSA of *S. aureus* (30–25%) and a decrease in the median incidence of nosocomial MRSA (3.2 to 1.6 per 100 admissions) [73]. This success has been achieved by a multi–faceted approach, including the update and strengthening of national MRSA guidelines, the extension of prospective surveillance and screening activities [74], and activities to promote the prudent use of antibiotics [75]. In England, a governmental reduction target in MRSA bacteraemia was set in 2004, demanding halving the

number of MRSA isolated from blood cultures by 2008, against the baseline of 2003–2004. In order to achieve this aim, a bundle of measures was consecutively implemented in English hospitals, including the mandatory reporting of all MRSA bacteraemia by the hospital chief executive officers, public benchmarking of MRSA incidence rates, the production of guidance on preventing HAIs, the establishment of a national hand hygiene campaign, prudent use of antibiotics, and the implementation of so called 'high impact interventions', i.e. care bundles focussing on key clinical procedures that can increase the risk of infection if not performed appropriately (e.g. central venous catheter care) [76]. After five years, data confirm a 62% reduction in the incidence of MRSA from blood cultures in England [77].

To what extent the multi–faceted approaches linked to the decreasing trends in MRSA infections in these countries can serve as examples of good practice for planning and implementing national control interventions in other EU countries with different healthcare structures and resource attribution, remains to be seen.

Nevertheless, the burden of HA-MRSA extends beyond acute care hospitals to long-term care facilities (LCTFs), such as nursing homes. This has been underlined in several studies showing high prevalence rates of MRSA carriage among LTCF residents and marked rate variation between nursing homes and regions in Belgium (2–43%) [78], Germany (1%) [79], Spain (16%) [80], France (38%) [81] and the UK (5–23%) [82,83]. Despite this variation, in the majority of cases, the clonal structure of MRSA isolates from nursing home residents was closely related to that found among patients in neighbouring acute care hospitals [78]. In addition, a recent study has shown that within six weeks after discharge from a hospital, less than 14% of LTCF residents are readmitted [84], which highlights that an appreciable percentage of patients circulates between hospital and LTCF several times per year. Consequently, effective MRSA containment in the healthcare setting cannot be limited to acute care hospitals, but must include LCTFs also. Otherwise, the significant MRSA reservoir that has developed in LTCFs and the transmission dynamics between LTCFs and acute care hospitals due to the transfer of patients is bound to compromise control. That this problem may be underestimated is indeed suggested by an admittedly limited number of published investigations [85].

A second challenge concerns CA-MRSA which has now emerged across Europe. Although its prevalence is still considerably lower than in the USA, the number of CA-MRSA infections appears to be increasing, especially in those European countries where the incidence of HA-MRSA is low and surveillance of MRSA more extensive [30,31]. The problem of CA-MRSA infections is not limited to the community but also affects nosocomial infections due to the introduction of CA-MRSA in healthcare settings [86,87]. In addition, only a limited number of European countries have developed national strategies and no common European strategy has yet been developed for the surveillance or the prevention of CA-MRSA spread.

The final challenge to tackle is the animal MRSA reservoir. Despite the EU-wide spread of MRSA in pigs, its implications for humans directly or indirectly exposed to livestock and for patients attending healthcare institutions located in farming areas remain unclear. Although epidemic spread of LA-MRSA among persons without direct contact to animals is rare, and the burden of human infections caused by LA-MRSA strains is still lower than that observed for CA-MRSA, infection control guidelines in many European countries should address the potential risk of acquiring MRSA via contact with livestock farming.

Conclusions

MRSA infections constitute an important and still evolving public health challenge for European countries. Successful MRSA control in some countries and facilities offers opportunities for identifying effective interventions and reassessment of best practice. In contrast, the rapid emergence of MRSA in the community and in livestock underpins the fact that MRSA transmission can occur in everyday life, in home care, during travel, leisure activities, cross-border commuting,

Table 4

Controlling MRSA: public health challenges and perspectives

Objective	Need for improvement
Strengthening prevention and control of HA-MRSA	Systematic assessment of effectiveness of MRSA control strategies and review of national guidelines for MRSA prevention and control
Control of emerging threats	Guidance on the prevention and control of CA-MRSA, LA-MRSA and HA-MRSA in long-term care facilities
Intersectoral coordination	Coordinated actions to control the spread of MRSA between different healthcare sectors (hospitals, long-term care facilities, ambulatory care) and veterinary care
European healthcare cooperation	European-wide concerted actions to control cross-border MRSA spread

CA-MRSA: community-associated methicillin-resistant *Staphylococcus aureus*; HA-MRSA: healthcare-associated methicillin-resistant *Staphylococcus aureus*; LA-MRSA: livestock-associated methicillin-resistant *Staphylococcus aureus*; MRSA: methicillin-resistant *Staphylococcus aureus*.

exposure to contaminated food samples or livestock transport. For long-term success in controlling MRSA, coordinated actions between different healthcare sectors (acute, long-term, ambulatory) and veterinary care are warranted and concerted efforts at European level will be of increasing importance. These efforts should begin with an agreement upon definitions for CA- and LA-MRSA and continue with the improvement of evidence-based guidance and the implementation of preventive measures to result in better prevention and control of MRSA in Europe (Table 4).

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