

Perspectives

EUREGIO MRSA-NET TWENTE/MÜNSTERLAND – A DUTCH-GERMAN CROSS-BORDER NETWORK FOR THE PREVENTION AND CONTROL OF INFECTIONS CAUSED BY METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is associated with increased mortality and morbidity and a leading cause of hospital-acquired infections. Community-acquired (CA)-MRSA are a growing concern worldwide. In the last 10 years, an increase in the MRSA rate from 2% to approximately 23% has been observed in Germany, while a rate under 5% has been recorded for many years in the Netherlands and Scandinavia. In the Netherlands in particular, MRSA rates have become very low in stationary care due to a consistent 'search and destroy' policy. The main focus in Germany lies on hospital-acquired MRSA, whereas the Netherlands focus on the control of the importation of MRSA cases from abroad and on CA-MRSA. As MRSA in hospitals and in the community can be a problem in cross-border health care, the European Union-funded EUREGIO MRSA-net project was established in the bordering regions Twente/Achterhoek, the Netherlands and Münsterland, Germany. The main aim of the project is the creation of a network of the major health care providers in the EUREGIO and the surveillance and prevention of MRSA infections. A spotyping network was established in order to understand the regional and cross-border dissemination of epidemic and potentially highly virulent MRSA genotypes. As the reduction of differences in health care quality is an important prerequisite for cross-border health care, a transborder quality group comprising hospitals, general practitioners, public health authorities, laboratories, and insurance companies has been established since 2005 equalising the quality criteria for the control of MRSA on both sides of the border.

Introduction

Staphylococcus aureus is responsible for the majority of healthcare-associated infections worldwide. These infections include skin and mucosa infections, pneumonia and septicæmia. Infections caused by methicillin-resistant *S. aureus* (MRSA) are particularly critical because the therapeutic options are limited. Consequently, infections with MRSA are associated with a higher morbidity and lethality compared to other staphylococci. In the past ten years, an increase in the prevalence of MRSA infections has been observed in Germany. Although it has been assumed

that the rate of MRSA isolations from blood cultures in Germany has stabilised at a level around 20-30%, this is still significantly higher than in neighbouring countries such as The Netherlands and Denmark, where the rates have been around 1% for many years [1]. This is a clear signal that the MRSA rates in hospitals can be minimised by adopting a consistent and co-ordinated "search and destroy" approach [2].

The EUREGIO MRSA-net project is a regional network designed to protect the population in the Dutch-German border region Twente/Münsterland (Figure 1) against MRSA infections [3,4]. It was launched to improve the implementation of MRSA prevention and control strategies within the EUREGIO by exchanging knowledge and technology. It represents a regional network for the control of

FIGURE 1
EUREGIO* MRSA-net project area



* The name EUREGIO stands for European region. It is used to refer geographically to a section of the Dutch-German border area covering parts of the Dutch provinces Gelderland, Overijssel, and Drenthe as well as parts of the German federal states Nordrhein-Westfalen and Niedersachsen. The MRSA-net project does not cover the whole of the EUREGIO.

MRSA involving local healthcare providers as recommended by the conference of the Germany's state health ministers in Dessau in June 2006. In Germany, the project is being co-ordinated by the Institute for Hygiene at the University Hospital Münster and the State Institute for Health and Work in North Rhine-Westphalia. In the Netherlands, it is co-ordinated by the laboratory Twente-Achterhoek and the University of Twente in Enschede.

Methods

The major objective of the EUREGIO MRSA-net project is to improve patient safety and cross-border patient exchange in the EUREGIO. Its main activities are:

1. The creation of a euregional and cross-border network in the EUREGIO: 74 coordinator meetings, 21 round table discussions and four general meetings of all hospitals in the area have been organised to date;
2. Prevalence screening on admission of the patient to hospital and evaluation of regional risk factors: Over a four week period in November 2006, all patients in all participating hospitals in the region were screened at admission and asked for MRSA-associated risk factors;
3. Development of an MRSA prevention and control concept: Comparison and matching of recommended hygiene standards in the region [4,5];
4. Establishment of an international web-based communication portal for handling MRSA problems (24-hour help desks) for healthcare workers, patients and the public [5];
5. Training and professional development of healthcare personnel: 146 seminars and presentations for staff have been arranged to date;
6. Creating public awareness for MRSA and infections in general: The project was presented in 16 reports on national and regional television, seven radio reports and 45 contributions to local and national press;
7. Construction of an online *spa*-typing network for an early warning system.

Altogether, 40 hospitals in a region covering 8,000 km² and comprising 2.7 million inhabitants (950,000 inhabitants in the Dutch area) have participated in the project so far (Table 1). The healthcare structures in the EUREGIO vary strongly between the

Dutch and the German side of the border: While on the German side there are six patient beds per 1,000 inhabitants, there are two patient beds per 1,000 inhabitants on the Dutch side. The same applies to doctors working outside hospitals. 163 doctors per 100,000 inhabitants (50% general practitioners (GPs) and 50% specialists) work in the Münsterland area compared to about 43 GPs per 100,000 inhabitants in the project area in Twente/Achterhoek.

The EUREGIO project involves 40 hospitals (four in the Dutch part), eight regional microbiological laboratories (one in the Dutch part), six public health offices (one in the Dutch part), and five professional institutions (e.g. Medical Order, Medical Association, health insurances such as the AOK Westphalia-Lippe). Patient interests regarding the quality of cross-border health were taken into account through collaboration with EPECS (European Patient Empowerment for Customised Solutions). In addition, nursing homes, ambulatory nursing services, and patient transportation services were included. The validation of special microbiological diagnostic procedures to detect MRSA was carried out by the Institute of Medical Microbiology at the University Hospital of Münster.

Results and discussion

Creating a crossborder network

The different actors involved in healthcare in the area were invited to round table discussions and informed about the project on several occasions. The motto for these round table discussions was "MRSA: One border, one problem, two results". The discussions showed that post-discharge case management of MRSA patients was not done regularly on the German side. Therefore, a 12-month-long case management system was established that required GPs to

FIGURE 2

MRSA decolonisation planning tool for planning the 12-month-long case management period in hospitals and ambulatory care on the German side of the EUREGIO MRSA-net



TABLE 1

Comparison of healthcare structures between the Dutch and the German bordering regions in the EUREGIO MRSA-net Twente/Münsterland, 2006

| | EUREGIO MRSA-net Dutch part (Twente) | EUREGIO MRSA-net German part (Münsterland) |
|---|--------------------------------------|--|
| No. of inhabitants | 950,000 | 1,700,000 |
| No. of acute care hospitals | 4 | 33 |
| No. of patient beds | 2,200 | 10,139 |
| Hospital patient beds/1,000 inhabitants | 2 | 6 |
| No. general practices (and specialists only in the German part) | 358 | 3,128 |
| General practices/1,000 inhabitants | 0.4 | 1.8 |
| No. of public health service offices | 1 | 5 |

recall a patient twice to control their colonisation status, first three to six months and again 12 months after discharge from hospital. Only after 12 months of negative screening results was a patient to be considered MRSA-negative. Patients admitted to a hospital during that period need to be screened before admission or isolated until they are excluded as persistent carriers of MRSA.

In order to improve the communication between hospitals and GPs, an MRSA patient management checklist was developed as well as a decolonisation planning tool (Figure 2) that facilitates the planning of the 12-month case management. The checklist informs the GP about the MRSA patient's condition at the time of hospital discharge and the treatment steps needed for his decolonisation. As consistent protocols for infection control outside the hospitals did not exist on the German side, such protocols were developed for patient transport services, nursing homes, ambulatory care.

Following the Dutch example of controlled decolonisation also after stationary care, an agreement was achieved between the Association Of Statutory Health Insurance for physicians (Kassenärztliche Vereinigung Westfalen-Lippe (KVWL)) and the primary health insurances (especially the AOK Westfalen-Lippe) regarding payment for GP services. According to this agreement, preventive decolonisation and control screening are now possible in ambulatory care after discharge from hospital and thus before next hospitalisation of the patient.

Finally, the public health offices were involved in the development of the network from the beginning. Acting within the scope of national legislation, the five German public health offices participated in the project as external quality controllers for all health institutions in the region. In order to make the regional MRSA epidemiology comparable, the hospitals were provided with the EpiMRSA software (Ridom GmbH, Würzburg) which enabled them to collect relevant data for standardised and cross-border analysis of MRSA-associated data (e.g. MRSA incidence, swabbing frequency and infection rates, *spa* types). These comparable data were regularly collected from all hospitals by the German public health offices, which allows for a better comparability and sustainability [5].

Prevalence screening and risk factor analysis

In November 2006, the MRSA-net project screened, during a four-week period, 86% of all inpatient admissions to German hospitals in the EUREGIO and interviewed all patients with regard to risk factors. This four-week prevalence screening was established in order to validate the already established screening recommendations. Preliminary analysis of the data indicates that the prevalence of MRSA varies between different districts and between different hospitals within the region.

Prevalence screening was also performed in one of the four Dutch hospitals in the EUREGIO. MRSA admission prevalence was shown to be about three-fold lower than on the German side of the border. Panton-Valentine leukocidin-producing community-acquired (CA)-MRSA infections only rarely contribute to the MRSA admission burden of regional hospitals (Netherlands: 8%, Germany: <1%). On the German side, the screening programme following the current national guidelines would have detected less than 50% of the MRSA carriers that were identified in our prevalence screening exercise. Screening of patients with a history of previous hospitalisation (not only in foreign "high-prevalence" countries,

but also in German facilities) is therefore of great importance for successful MRSA detection for the hospitals in the EUREGIO.

Following this period of prevalence screening, MRSA prevention strategies and screening indications were adapted to a common euregional standard in all participating hospitals.

Prevention via the development of a web-based communication system for MRSA

The most important instruments needed to successfully implement prevention strategies and control measures are application plans and target group-specific infection control protocols.

We carried out 28 application tests with different target groups (doctors, nursing staff, and ward assistants) and examined infection control protocols of different hospitals on both sides of the border. The tests showed that information in the protocols was too difficult to understand or incomplete, or was not provided at all [6,7]. The tests also brought up over 160 practical questions about MRSA, to which the established infection control protocols and national guidelines did not provide answers.

We have developed a target group-oriented, user-friendly web-based portal and practical questions and answers about MRSA. The national guidelines of the German Robert Koch Institute (RKI) and of the Dutch Working Group for Infection Prevention (WIP) provide the basis for the bi-lingual portal [8]. It can be accessed via www.mrsa-net.nl.

Further education and professional development

In order to create sustainable structures, more than 140 training courses have been organised to date for healthcare professionals in the EUREGIO. The medical association, the KVWL, the local doctors' association, and quality circles worked together to provide and carry out a series of professional educational courses for GPs and regional pharmacotherapy consultants. Regular analysis of the antibiotic prescriptions from all doctors in ambulatory care was established on the German side, following the Dutch experience.

Public Awareness

All information about the project is arranged according to target group and can be called up on the MRSA-net homepage. An around the clock "MRSA-net helpdesk" has been established in 2005. On average, more than 200 phone calls are registered per month by the helpdesk (80% of them on the German side). Two thirds of the phone calls come from health professionals seeking information about how to handle MRSA patients, and one third of the calls from patients or their relatives asking for general information about MRSA, its transmission in home settings, and the possible health risks for household contacts.

Leaflets and posters on the subject are available for patients and their relatives in printed or electronic form. The project has also been presented in a number of media reports (for details visit www.mrsa-net.eu). High priority is given to a systematic publicity campaign, because, especially in Germany, people feel they are not adequately informed about the MRSA problem.

EUREGIO MRSA-net *spa*-typing network

The Institute of Hygiene in Münster has developed a sequence-based typing strategy [9-11] that enables the online and real-time comparison of laboratory typing data on a region-wide and cross-border level for the first time. This method, which is based on *spa* typing, is used as a 'common laboratory language', elucidates epidemiologic correlations and helps to construct a molecular surveillance system [12].

Thirty-two hospitals in the EUREGIO (including four Dutch hospitals) agreed to *spa*-type the first MRSA-isolate from every patient. Five others *spa*-type MRSA from blood culture and in case of clusters. Furthermore, *spa*-typing data is collected and exchanged via the common server. On the German side, 20 sentinel GPs for CA-MRSA were encouraged to collect swabs from patients with soft tissue infections and send them to the euregional laboratories to be *spa*-typed. The typing data (i.e. regional distribution of *spa* types and occurrence of new types) have been analysed regionally and on both sides of the border since the project began. Table 2 shows the most prevalent *spa* types found in the EUREGIO.

On the one hand, it has been shown that certain *spa* types occur on both sides of the border. A comparison with data from the international typing initiative SeqNet.org (<http://www.seqnet.org>) has demonstrated that these types can also be found in other European countries and that they belong to 'epidemic' clonal lineages (e.g. t032, t003, t001). These types are also found all over the EUREGIO.

On the other hand, however, significant differences in the molecular epidemiology of MRSA have been found on both sides

of the border (e.g. t026). These differences are illustrated in an online geographic analysis tool (Figure 3).

An early warning system based on a Z-Score analysis of current and historical *spa*-typing data [13] was designed to identify an unusual accumulation of specific MRSA *spa* types, which are considered to be particularly epidemic or virulent (Figure 4).

Conclusion

Because of the success of the EUREGIO MRSA-net in establishing regional and local measures against MRSA (see Box), the Robert Koch Institute considers this project as a prototype for regional networks dealing with infectious disease issues [4,5]. The differences in the prevalence of MRSA between Germany and

TABLE 2
MRSA prevalence and *spa* types in the EUREGIO Twente/Münsterland* between July 2005 and June 2006

| | EUREGIO MRSA-net Dutch part | EUREGIO MRSA-net German part |
|---|---|---|
| Number of MRSA | 54 | 1,034 |
| Predominant <i>spa</i> types | t002, t012, t019, t026, t044, t065 (accounting for 87% of all MRSA) | t003, t032, t004, t011, t008 (accounting for 78% of all MRSA) |
| No. of PVL-positive MRSA (% of all MRSA), (associated <i>spa</i> types) | 5 (8.3%), (t044, t016) | 5 (0.6%), (t044, t019, t437) |

MRSA: methicillin-resistant *Staphylococcus aureus*; PVL: Panton-Valentine Leukocidin.

* isolates obtained in 33 regional German acute care hospitals and four regional Dutch acute care hospitals

FIGURE 3
Online geographic illustration database showing the incidence rates (per 100,000 inhabitants) of MRSA *spa* types (here t032) isolated from patients in the hospitals of the EUREGIO MRSA-net Twente/Münsterland

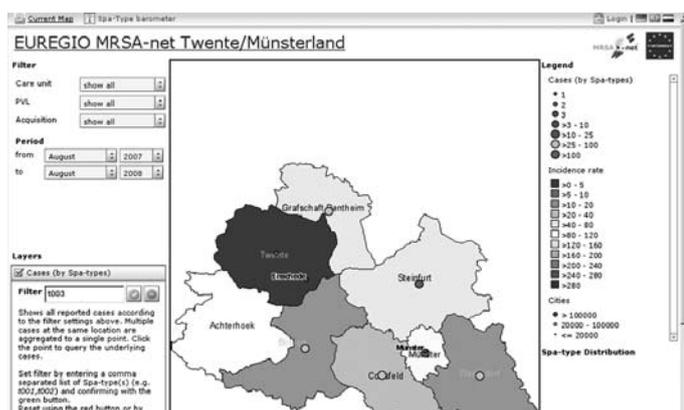
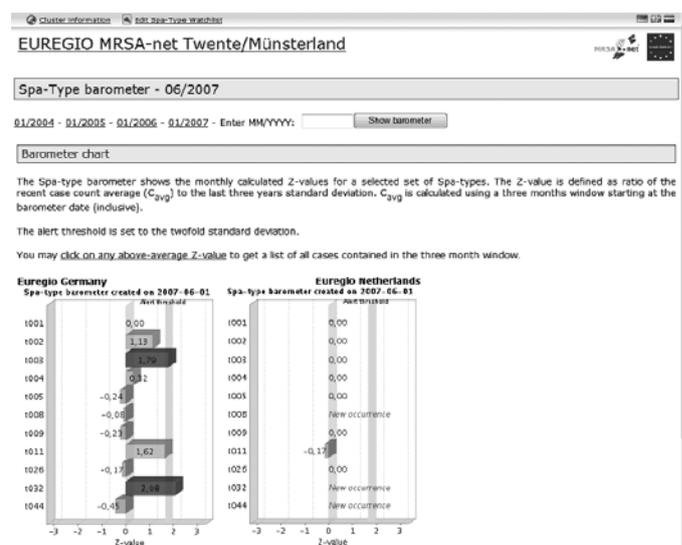


FIGURE 4
spa type-based barometer for the identification of newly imported or emerging *spa* types as surrogate markers for highly epidemic or virulent clones in the EUREGIO



Box

Milestones achieved of the EUREGIO MRSA-net Twente/Münsterland

1. Creation of a cross-border MRSA network of all institutions involved in healthcare in the Münsterland/Twente region;
2. Comparison of national guidelines and creation of workable and user-friendly MRSA infection control protocols;
3. Further education and professional development of healthcare staff;
4. Enhancement of public awareness towards MRSA and prevention of infectious diseases in general by (regional) media reports;
5. Establishment of a *spa*-typing network for comparable molecular surveillance of MRSA and CA-MRSA in the EUREGIO;
6. Close co-operation with public health offices (Öffentlicher Gesundheitsdienst in Germany and Geneeskundige en Gezondheidsdienst in The Netherlands);
7. Creation of a quality euregional health net (with quality seal) and the creation of structures necessary to achieve a long-term decrease in the MRSA rate in the EUREGIO.

the Netherlands are considerable and have led to problems in cross-border healthcare activities and treatment of patients in the German-Dutch border region. However, the exchange of know-how and experience in MRSA management will improve the quality of patient treatment on both sides of the border and can provide an advantage for the people living in the border regions.

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