

HIC@RE ... and its relevance for a company like RIEMSER

HIC@RE ... und seine Bedeutung für ein Unternehmen wie RIEMSER

Abstract

The increased incidence of infections caused by methicillin-resistant strains of *Staphylococcus aureus* (MRSA) burdens the healthcare systems with significant additional costs. Simple measures such as active MRSA screening can lead to a reduction of infectious events and massive savings. To establish an effective and comprehensive strategy for prevention and eradication of MRSA, the cooperation and networking of all stakeholders in the health care system is necessary. Pharmaceutical companies are part of the health care system; they therefore have a vital and ethical interest that care within the health system will be further optimized and thus continue to remain affordable. The targets of the HIC@RE project demonstrate the interests of the pharmaceutical and health-care research company RIEMSER Arzneimittel AG, so that a sufficient rationale is given for cooperation in this project.

Keywords: multi-resistance, MRSA, *S. aureus*, prevention, screening, cost, economical burden

Zusammenfassung

Das gehäufte Auftreten von Infektionen, die durch Methicillin-resistente Stämme von *Staphylococcus aureus* (MRSA) verursacht werden, belastet die Gesundheitssysteme mit erheblichen Zusatzkosten. Einfache Maßnahmen wie das aktive MRSA-Screening können bereits zu einer Reduktion der Infektionsereignisse und damit zu massiven Einsparungen führen. Zur Etablierung einer effektiven und flächendeckenden Präventions- und Eradikations-Strategie ist jedoch die Kooperation und Vernetzung aller Akteure in der Gesundheitsversorgung erforderlich. Pharmazeutische Unternehmen haben ein vitales und ethisches Interesse daran, dass die Versorgung im Gesundheitssystem weiterhin optimiert wird und damit auch bezahlbar bleibt, weil sie Bestandteil dieses Systems sind. In den Zielen des HIC@RE-Projektes werden die Interessen des in der Versorgungsforschung aktiven Pharmaunternehmens RIEMSER Arzneimittel AG abgebildet, so dass die Rationale für eine Projektkooperation gegeben ist.

Schlüsselwörter: Multiresistenz, MRSA, *S. aureus*, Prävention, Screening, Kosten, wirtschaftlicher Schaden

Introduction

Infections by multi-resistant bacteria (MRB) are a growing problem. This applies especially to infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) strains.

In the past, the prevalence of MRSA in Germany has also increased dramatically. In the year 1990 the frequency of MRSA in all bacterial isolates of *S. aureus* was just 1.7%, but rose to 15% in 1998 and to around 21% in 2001, respectively [1]. MRSA surveillance-data of recent years reported a near doubling of MRSA cases for every

1,000 patient days from 0.63 in 2004 to 1.14 in 2009 [2].

According to the data from the European Antimicrobial Resistance Surveillance System (EARSS) for 2006, the incidence of MRSA bacteremia had risen to 25–50% of all *S. aureus*-bacteremia in most southern European countries as well as in France, Belgium and Great Britain. In Germany at that time, the frequency of MRSA bacteremia was between 10 and 25% of all bacteremia with by *S. aureus* [3]. Local studies have shown that the total rate of new nosocomial infections with *S. aureus* correlates with the increase of MRSA-infections [4] indi-

Berno Müller¹
Jürgen Becker¹

1. RIEMSER Arzneimittel AG,
Medical Science &
Operations, Greifswald –
Insel Riems, Germany

cating that MRSA does not replace methicillin-sensitive strains of *S. aureus* (MSSA) in an otherwise unchanged overall incidence [5]. It is estimated that around 150,000 patients in European health care facilities are infected with MRSA every year and that about 44% of all infections in health care facilities of the EU member states are caused by MRSA [5].

Due to the massive increase of MRSA in hospitals and in the population as well as the simultaneously escalating pressure for rationalization in the health care system, interest in the economic context has continuously increased due to the growing evidence that a management based on networking is necessary for the prevention and control of MRB not only from the medical and ethical point of view, but also already in mid-term of individual- and macro-economic sense [6].

Cost factor MRSA

It has been reported in the available literature that the costs of MRSA-infections are 1.2 to 2.8 times higher than the costs of infections caused by methicillin-sensitive strains of *S. aureus* [7], [8], [9], [10], [11]. MRSA-infections can be of a localized or, of a severe and systemic nature, like the MRSA-sepsis. The cost of nosocomial MRSA-infections depends on their respective clinical manifestation. Wernitz et al. [12] have calculated that the cost of MRSA-pneumonia with around € 29,000 is particularly high whereas much lower cost are generated by MRSA-septicemia (appr. € 13,500), SSI (appr. € 11,300) and urinary tract infections (appr. € 4,500). Apart from the treatment of the MRSA-infection, the main cost driving factors are the prolonged hospitalization and necessary isolation of the patient, additional diagnostic and hygiene measures as well as necessity to deploy more staff for these patients.

In this context it is of interest to look at the results of a Canadian study on 20 MRSA-patients in which the average additional cost per patient amounted to \$ 14,360. The average prolongation of hospitalization was 14 d for these patients. Prolonged hospitalization was responsible for 95% of the additional costs, whereas therapeutic and diagnostic measures accounted only for 1% and 4% of the additional costs, respectively [13].

According to an analysis of relevant studies, MRSA-infections can cause average costs of \$ 35,367. This brings MRSA-infections to second place in the ranking of costs generated by nosocomial infections behind sepsis (\$ 38,703) but well ahead of pneumonia (\$ 17,677) and SSI (\$ 15,646) [14].

A retrospective case-control study performed on an intensive care unit in France compared the costs between 27 patients with and 27 patients without MRSA. As a result, average stay was 18 d for patients with MRSA and 14 d for patients without MRSA ($p=0.02$). Average costs for an MRSA-patient were \$ 30,225 and thus about one third higher than the average costs for a control-patient which were reported to \$ 20,959 ($p=0.004$) [15].

The financial burden of MRSA

The additional annual cost of nosocomial MRSA-infections for the health care system of the EU countries is estimated to be around € 380m [5]. The total financial burden for the German economy has been calculated from Wernitz and Veit [1] to be about € 146m. The health insurance DAK calculated even a minimum financial burden of € 610,277,836 [16].

This burden is considerable especially when taking into account that consequential costs associated with rehabilitation, insurance claims and additional cost items that may arise as a result of long term morbidity are not included. In this context it has been shown that, depending on the clinical manifestation, MRSA-infections may cause financial losses for the treating health care facilities of up to € 22,000 per patient under DRG-conditions [12]. This data demonstrates that efficient strategies for the prevention of MRSA-infections are absolutely essential.

Cost reduction by active screening

Surveillance data from 199 German hospitals for 2009 showed that 72.52% of 28,195 MRSA-cases were brought into the hospital by the patients themselves [2]. In addition it is assumed that a pre-existing colonization with MRSA is an independent predictive factor for the development of an MRSA-infection [17], [18]. However, a high percentage of MRSA-carriers can be discovered by active screening [19]. It has been shown that the intranasal application of Mupirocin leads to a significant reduction of nosocomial *S. aureus* infections of nasal carriers ($p=0.02$) [20]. Correspondingly, published data show that active screening and decontamination of colonized patients can lead to significant savings. Thus, the cost incurred for the initial screening of 539 patients (=1.5% of all admitted patients within 19 months) has been reported to be € 26,241 in a study published in year 2005 [12] – this cost factor seems low when considering that only one single MRSA-infection not avoided by screening and decontamination can cause costs of the same magnitude. In consequence, further calculations within the framework of this study showed that 35 nosocomial MRSA-infections and associated additional costs of about € 200,000 could be saved through screening. After deducting the expenses for initial screenings, this resulted in a net saving of about € 175,000 in 19 months. Similar results have been found by Jernigan et al. [21] already in 1995 who conducted a cost-to-benefit analysis for MRSA-screenings in a 700 beds university hospital in Virginia. As a result, MRSA-screening led to a net saving of about \$ 462,000.

Rationale for the pharmaceutical industry

RIEMSER Arzneimittel AG, being a part of the health care system, has a vital and ethical interest in the optimization

of care within the healthcare system in order to ensure that it remains affordable. Nosocomial infections with MRB cause extensive additional costs that may have a destabilizing effect on the healthcare system and they are therefore in conflict with this interest. The above data show, that the additional costs are primarily caused by increased employment of the medical infrastructure and resources such as prolonged hospitalization and more intensive care provided by staff rather than by use of antibiotics or diagnostic medicinal products provided by pharmaceutical companies. As a pharmaceutical company cannot profit from this it is more reasonable to support the development of new structures for the prevention and control of MRB and to become a relevant partner within this structure and to develop further in this field. The previously described results are encouraging since they demonstrate that even relatively simple and cost efficient measures such as an MRSA-screening can lead to considerable cost savings and even protect the patients against severe infections.

Cooperation of the relevant partners

Currently available knowledge about the risk factors enhancing the emergence and transmission of MRB clarifies that no single health care facility can eradicate these bacteria on its own within an isolated setting. Many risk factors are beyond the influence of an individual facility. The establishment of an effective prevention and control strategy requires the cooperation and networking between all relevant actors and competencies of the health care system.

The selection pressure caused by antibiotics for example is a relevant risk factor for the development of multi-resistance [22], which can be counteracted to primarily by controlled usage of antibiotics [23]. Therefore, controlled changes of treatment strategies within one health care institution or between different health care institutions (“antibiotic cycling”) are necessary to prevent multi-resistance.

The mutual exchange of knowledge and therapeutic experience as well as an understanding of the local resistance situation are prerequisites for the successful establishment of such a change strategy. Another example illustrating the necessity for extensive cooperation is the fact that the duration of decontamination and recovery of MRSA-patients may be longer than their hospitalization [24], [25]. Based on this knowledge, adequate follow-up measures within the ambulatory environment have to be established in order to ensure successful decontamination after the patient has left the hospital – under the reasonable assumption that MRSA patients require an individual case management which has to begin in hospital and needs to be continued after the patient has left the hospital until all factors inhibiting full recovery are eliminated. The spreading of relatively new epidemic *S. aureus* strains causing very progressive courses of

diseases in otherwise healthy patients previously at low risk (community onset) bears the potential hazard that these species establish themselves as new nosocomial pathogens [26], [27], [28]. In this context we need to ask on the basis of which cooperation the transmission of these in part extremely aggressive forms of bacteria from outpatients into health care facilities can be stopped.

These examples, exclusively from an infective-epidemiological point of view, already demonstrate the necessity for an interdisciplinary networking for the prevention and control of MRB.

The primary target is the establishment of an optimal strategy for the prevention, diagnosis and treatment of infections caused by MRB which includes all relevant partners in the healthcare system and gives them the opportunity to participate in the generation of additional value. Providing an individualized and integrated therapy under efficient utilization of the medical infrastructure is the most important parameter for patients. Health care institutions must be able to profit from rapid access to therapeutic standards, an effective utilization of the resources and the reduction of additional costs. Improved cost-to-benefit relations and the chance to conduct reliable analyses of the cost driving factors are the key factors for the health payers. For a pharmaceutical company, planning reliability resulting from a stable and affordable healthcare system is especially important since only such a system will provide the environment necessary for value adding innovations.

Essential for the cooperation is the sharing of knowledge and experience for the benefit of all partners. The resulting transfer of knowledge will allow a continuous evolution of the system and the participating partners.

The pharmaceutical company Riemser Arzneimittel AG recognizes HIC@RE as an infrastructure project in which this integration and networking through the participation of relevant partners shall be realized in order to establish an integrated care of patients with a maximum of efficiency in one of the strategic core competencies of the company.

Apart from the therapy of infections caused by MRB and the increasingly important *Clostridium-difficile* associated diarrhea, the expertise of RIEMSER Arzneimittel AG also includes the therapy of the drug-resistant tuberculosis.

Notes

Conflicts of interest

The authors declare that they have no competing interests.

References

1. Wernitz M, Veit S. Der Einfluss von MRSA auf die deutsche Volkswirtschaft. Management Krankenh. 2005;6:16.

2. Nationales Referenzzentrum für Surveillance von nosokomialen Infektionen. Modul MRSA-Krankenhaus-Infektions-Surveillance-System (MRSA-KISS) [Version: 6. Mai 2010]. Berlin: Charité-Universitätsmedizin; 2010. Available from: <http://www.nrz-hygiene.de/surveillance/kiss/mrsa-kiss/>
3. Staphylococcus aureus resistance trends: 1999-2006. In: Grundmann H, Ed. European Antimicrobial Resistance Surveillance System (EARSS) – Annual Report 2006. Bithoven (NL): EARSS; 2007. p. 55-56. Available from: http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/Documents/2006_EARSS_Annual_Report.pdf
4. Boyce JM, White RL, Spruill EY. Impact of methicillin-resistant Staphylococcus aureus on the incidence of nosocomial Staphylococcal infections. *J Infect Dis.* 1983;148(4):763. DOI: 10.1093/infdis/148.4.763
5. Köck R, Becker K, Cookson B, van Gemert-Pijnen JE, Harbarth S, Kluytmans, Mielke JM, 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. *Eurosurveill.* 2010;15(41):12-20. Available from: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19688>
6. Hübner NO, Hübner C, Kramer A. Ökonomische Aspekte des Hygienemanagements von MRSA. *Gesundheitswes.* 2009;71(11):771-6. DOI: 10.1055/s-0029-1241891
7. Capitano B, Lesham OA, Nightingale CH, Nicolau DP. Cost effect of managing methicillin-resistant Staphylococcus aureus in a long-term care facility. *J Am Geriatr Soc.* 2003;51(1):10-6. DOI: 10.1034/j.1601-5215.2002.51003.x
8. Engemann JJ, Carmeli Y, Cosgrove SE, Fowler VG, Bronstein MZ, Trivette SL, Briggs JP, Sexton DJ, Kaye KS. Adverse clinical and economic outcomes attributable to methicillin-resistance among patients with Staphylococcus aureus surgical site infection. *Clin Infect Dis.* 2003;36(5):592-8. DOI: 10.1086/367653
9. Kopp BJ, Nix DE, Armstrong EP. Clinical and economic analysis of methicillin-susceptible and -resistant Staphylococcus aureus Infections. *Ann Pharmacother.* 2004;38(9):1377-82. DOI: 10.1345/aph.1E028
10. Reed SD, Friedman JY, Engemann JJ, Griffiths RI, Anstrom KJ, Kaye KS, Stryjewski ME, Szczech LA, Reller LB, Corey GR, Schulman KA, Fowler VG. Costs and outcomes among hemodialysis dependent patients with methicillin-resistant or methicillin-susceptible Staphylococcus aureus bacteremia. *Infect Control Hosp Epidemiol.* 2005;26(2):175-83. DOI: 10.1086/502523
11. Abramson MA, Sexton DJ. Nosocomial methicillin-resistant and methicillin-susceptible Staphylococcus aureus primary bacteremia: at what costs? *Infect Control Hosp Epidemiol.* 1999;20(6):408-11. DOI: 10.1086/501641
12. Wernitz MH, Keck S, Swidsinski S, Schulz S, Veit SK. Cost analysis of a hospital-wide selective screening program for methicillin-resistant Staphylococcus aureus (MRSA) carriers in the context of diagnosis related groups (DRG) payment. *Clin Microbiol Infect.* 2005;11(6):466-71. DOI: 10.1111/j.1469-0691.2005.01153.x
13. Kim T, Oh PI, Simor AE. The economic impact of methicillin-resistant Staphylococcus aureus in Canadian hospitals. *Infect Contr Hosp Epidemiol.* 2001;22(2):99-104. DOI: 10.1086/501871
14. Stone PW, Larson E, Kowar LN. A systematic audit of economic evidence linking nosocomial infections and infection control interventions: 1900–2000. *Am J Infect Contr.* 2002;30(3):145-52. DOI: 10.1067/mic.2002.121099
15. Chaix C, Durand-Zaleski I, Alberti C, Brun-Buisson C. Control of endemic methicillin-resistant Staphylococcus aureus. A cost-benefit analysis in an intensive care unit. *JAMA.* 1999;282(18):1745-51. DOI: 10.1001/jama.282.18.1745
16. Helfrich J. Multiresistente Erreger aus Sicht der Kostenträger. Auftaktveranstaltung Expertengruppe Multiresistente Erreger im Krankenhaus – Neue Standards für Patientensicherheit. Berlin; 2008.
17. von Eiff C, Becker K, Machka K, Stammer H, Peters G. Nasal carriage as a source of Staphylococcus aureus bacteremia. *N Engl J Med.* 2001;344:11-6. DOI: 10.1056/NEJM200101043440102
18. Safdar N, Bradley EA. The risk of infection after nasal colonization with staphylococcus aureus. *Am J Med.* 2008;121(4):310-5. DOI: 10.1016/j.amjmed.2007.07.034
19. Diller R, Sonntag AK, Mellmann A, Grevener K, Senninger N, Kipp F, Friedrich AW. Evidence for cost reduction based on preadmission MRSA screening in general surgery. *Int J Hyg Environ Health.* 2008;211(1-2):205-12. DOI: 10.1016/j.ijheh.2007.06.001
20. Perl TM, Cullen JJ, Wenzel RP, Zimmerman MB, Pfaller MA, Sheppard D, Twombly J, French PP, Herwaldt LA; Mupirocin and The Risk of Staphylococcus aureus study team. Intranasal Mupirocin to prevent postoperative Staphylococcus aureus infections. *New Eng J Med.* 2002;346(24):1871-7. DOI: 10.1056/NEJMoa003069
21. Jernigan JA, Clemence MA, Stott GA, Titus MG, Alexander CH, Palumbo CM, Farr BM. Control of methicillin-resistant Staphylococcus aureus at a university hospital: One decade later. *Infect Control Hosp Epidemiol.* 1995;16(12):686-96. DOI: 10.1086/647042
22. Monnet DL, MacKenzie FM, Lopez-Lozano JM, Beyaert A, Camacho M, Wilson R, Stuart D, Gould IM. Antimicrobial drug use and methicillin-resistant Staphylococcus aureus, Aberdeen, 1996–2000. *Emerg Infect Dis.* 2004;10(8):1432-41.
23. Kollef MH. Bench-to bedside review: antimicrobial utilization strategies aimed at preventing the emergence of bacterial resistance in the intensive care unit. *Crit Care.* 2005;9:459-64. DOI: 10.1186/cc3757
24. Vriens MR, Blok HE, Gigengack-Baars AC, Mascini EM, van der Werken C, Verhoef J, Troelstra A. Methicillin-resistant Staphylococcus aureus carriage among patients after hospital discharge. *Infect Control Hosp Epidemiol.* 2005;26(7):629-33. DOI: 10.1086/502592
25. Robicsek A, Beaumont JL, Peterson LR. Duration of colonization with methicillin-resistant Staphylococcus aureus. *Clin Infect Dis.* 2009;48(7):910-3. DOI: 10.1086/597296
26. Otter JA, French GL. Nosocomial transmission of community-associated methicillin-resistant Staphylococcus aureus: an emerging threat. *Lancet Infect Dis.* 2006;6(12):753-5. DOI: 10.1016/S1473-3099(06)70636-3
27. Saiman L, O'Keefe M, Graham PL, Wu F, Saïd Salim B, Kreiswirth B, LaSala A, Schlievert PM, Della Latta P. Hospital transmission of community-acquired methicillin-resistant Staphylococcus aureus among postpartum women. *Clin Infect Dis.* 2003;37(10):1313-9. DOI: 10.1086/379022
28. D'Agata EMC, Webb GF, Horn AM, Moellering RC, Shigui Ruan JR. Modeling the invasion of community-acquired methicillin-resistant Staphylococcus aureus into hospitals. *Clin Infect Dis.* 2009;48(3):274-84. DOI: 10.1086/595844

Corresponding author:

Dr. Berno Müller

RIEMSER Arzneimittel AG, Medical Science & Operations,
An der Wiek 7, 17493 Greifswald – Insel Riems, Germany,
Phone: +49 (0) 38351-76-0, Fax: +49 (0) 38351-76-778
dr.mueller@riemser.de

Please cite as

Müller B, Becker J. HIC@RE ... and its relevance for a company like RIEMSER. *GMS Krankenhaushyg Interdiszip.* 2011;6(1):Doc22.
DOI: 10.3205/dgkh000179, URN: urn:nbn:de:0183-dgkh0001790

This article is freely available from

<http://www.egms.de/en/journals/dgkh/2011-6/dgkh000179.shtml>

Published: 2011-12-15

Copyright

©2011 Müller et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by-nc-nd/3.0/deed.en>). You are free: to Share – to copy, distribute and transmit the work, provided the original author and source are credited.