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Chapter 1
General introduction
and outline of the thesis

General introduction

Staphylococcus aureus (*S. aureus*) is the leading hospital-acquired pathogen in hospitals throughout the world. Infection with *S. aureus* is associated with substantial morbidity and mortality – a trend that is increasing due to the widespread dissemination of methicillin-resistant *S. aureus* (MRSA).¹ MRSA is not more virulent than susceptible strains, but therapy is more problematic and it leads to an increased burden of disease.²

Staphylococcal infections occur regularly in hospitalised patients and can have severe consequences including postoperative wound infections, nosocomial pneumonia, catheter-related bacteraemia and endocarditis.³⁻⁶ A study of over seven million hospital admissions in the US estimated that 0.8% of all patients suffered from an infection caused by *S. aureus*, corresponding to a total of nearly 300,000 patients in US hospitals in 2003.⁷ After controlling for confounders the annual impact in the USA was estimated to be 2.7 million additional days in hospital, US\$9.5 billion excess costs, and at least 12,000 in-patient deaths. Since the consequences of these infections are immense, effective prevention strategies are essential.

Regarding prevention strategies, a distinction is made between MRSA and the sensitive variant (MSSA). In the Netherlands and Scandinavian countries a prevention strategy for MRSA, the 'MRSA Search and Destroy' (S&D) policy is applied since the end of the eighties to prevent transmission of MRSA in healthcare institutes.⁸ The main items of this policy are screening of patients and health care workers at risk for MRSA carriage and (pre-emptive) isolation. Furthermore, antibiotics are prescribed restrictively and prudently. This policy has resulted in the maintenance of the low MRSA incidence (0.11%), while in countries outside the Netherlands and Scandinavia, the MRSA incidences have increased dramatically since the eighties.⁹⁻¹⁰

For MSSA, there are no special precautions other than the general indications for wearing personal protective equipment (PPE). However, in case of wound infections which cannot be covered by a wound dressing, isolation is required.¹¹

The current preventive strategies effectively control cross-transmission of *S. aureus* in healthcare institutes. However, there are other problems to be dealt with. For MRSA, since the beginning of the new millennium two new variants emerged, the live-stock associated MRSA (LA-MRSA) and the community-acquired MRSA (CA-MRSA).¹²⁻¹³ In addition, for *S. aureus* in general, it is very important to focus also on infections caused by the patients' own flora because it was demonstrated that approximately 80% of *S. aureus* strains isolated from health-care associated infections are identical to the nasal strains found in these patients upon admission.¹⁴⁻¹⁶

In this thesis the effect of the current preventive strategies is studied. In addition, the challenges in the area of *S. aureus* (both MRSA and MSSA) epidemiology and control

are studied and put into perspective. Furthermore, cost analyses of preventive strategies are included.

The results and conclusions of these studies may contribute to further improvements in policies to prevent *S. aureus* carriage and/or infections.

Outline of the thesis

Chapter 2 describes the effectiveness of the MRSA 'Search and Destroy' policy in the Netherlands for the prevention of nosocomial transmission. Also the costs and benefits of this policy are calculated.

Chapter 2.1 describes the current MRSA sources in newly identified MRSA positive patients and health care workers in a large teaching hospital in the south of the Netherlands.

Chapter 2.2 calculates the costs and benefits of the MRSA 'Search and Destroy' policy.

Chapters 3 and 4 describe the current problems and challenges in the area of *S. aureus* epidemiology and control. Chapter 3 focuses on MRSA. Chapter 4 focuses on *S. aureus* in general (both meticillin-susceptible and resistant).

Chapter 3 describes two emerging variants of MRSA, the so-called livestock-associated MRSA (LA-MRSA) and the community-acquired MRSA (CA-MRSA).

Chapter 3.1 shows the increase of MRSA related to animal farming in a Dutch teaching hospital in the South of the Netherlands.

Chapter 3.2 describes the adaptation of the MRSA 'Search and Destroy' policy for MRSA positive and suspected patients in the outpatients' clinic.

Chapter 3.3 shows the transmission of CA-MRSA in a dancing group and among friends, resulting in severe skin and soft tissue infections.

Chapter 3.4 describes life-style associated risk factors for CA-MRSA carriage in the Netherlands based on a hospital-based case-control study.

Chapter 3.5 shows the presence of LA-MRSA (MC398) in individuals without direct contact to pigs or veal calves.

Chapter 3.6 focuses on the risk factors for transmission of CA-MRSA in households.

Chapter 3.7 shows that self-sampling is appropriate for detection of *S. aureus*.

Chapter 4 describes the risks for patients with nasal carriage of *S. aureus* to develop endogeneous *S. aureus* infections and the precautions the hospital have to take to prevent this. Furthermore, a cost-analysis of this precautions was performed.

Chapter 4.1 compares the rates of *S. aureus* infections in *S. aureus* nasal carriers after receiving nasal mupirocin ointment to rates in carriers not receiving this treatment.

Chapter 4.2 shows the comparison of two PCR-based methods and conventional culture for the detection of nasal carriage of *S. aureus* in pre-operative patients.

Chapter 4.3 summarises the new approaches to prevention of staphylococcal infection in surgery described in the literature.

Chapter 4.4 compares the real hospital costs for surgical patients with *S. aureus* nasal carriage with and without screening and subsequent treatment with mupirocin ointment in combination with chlorhexidine gluconated soap.

Chapter 4.5 shows mortality data of surgical patients with *S. aureus* nasal carriage treated with mupirocin ointment in combination chlorhexidine gluconated soap compared to carriers not receiving treatment.

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