Department of Clinical Microbiology, Lillebaelt Hospital
Department of Regional Health Research
Faculty of Health Sciences, University of Southern Denmark

PhD Thesis

Mette Assenholm Kristensen

Management and care of MRSA

Decolonization treatment, psychosocial health, and cross-sector collaboration

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Supervisors

Jens Kjølseth Møller, Professor, MD, PhD, DMSc (Main supervisor)
Department of Clinical Microbiology
Lillebaelt Hospital, University of Southern Denmark

Hanne Irene Jensen, Professor, PhD, MHSc, CCN.
Department of Anesthesiology and Intensive Care
Lillebaelt Hospital, University of Southern Denmark

Christian Backer Mogensen, Professor, MD, PhD
Department of Emergency Medicine
Hospital of Southern Jutland, University of Southern Denmark

Jens Søndergaard, Professor, MD, PhD
Research Unit of General Practice
University of Southern Denmark

Assessment Committee

Chairman of the committee and moderator of the defense
Niels Nørskov-Lauritsen, Clinical professor, MD, PhD, DMSc.
Clinical Research, University of Southern Denmark

Morten Lindbæk, Professor emeritus, MD, PhD
Department of General Practice
University of Oslo

Mette Damkjær Bartels, Clinical associate professor, MD, PhD
Department of Clinical Microbiology,
Hvidovre Hospital, University of Copenhagen

CONTENTS

PREFACE

This thesis explores methicillin-resistant *Staphylococcus aureus* (MRSA) care from three different perspectives: Decolonization treatment of MRSA carriage, psychosocial health, and MRSA consultations in general practice with specialist assistance through a video connection.

My path into science and MRSA care began in 2006 when I was employed as a young project nurse in a PhD project. The project evaluated a large MRSA outbreak in Vejle County. I visited citizens with MRSA in their homes to test their environments and MRSA status. They constituted a new patient group for me, and I was surprised by the personal stories they shared with me. A patient was banned from entering the GP's clinic; every visit was instead carried out in the parking lot. Another patient could not bear keeping doors in her house closed because she had spent a long period of her hospitalization in isolation. Later in my career as an infection control nurse, I met patients with MRSA needing hospital care. I realized the challenge of preventing MRSA infections in vulnerable groups of patients and the burden on asymptomatic MRSA carriers. In the Region of Southern Denmark (RSD), the MRSA care program is carried out in general practice. However, it may not be easy for practice staff to acquire appropriate experience in providing MRSA care due to the very few cases handled per general practitioner. Together with my colleagues in the Infection Control Unit at Lillebaelt Hospital, I offer advice on MRSA care to practice staff, but it is difficult to evaluate the overall effects of our work. Therefore, I began to work on a PhD protocol in 2019 to formulate ways to explore these important issues. Then, I enrolled as a PhD student in 2020.

Unfortunately, we did not succeed to carry out the planned randomized controlled study aimed to increase the efficiency of decolonization treatment and increase psychosocial health among MRSA-positive individuals through a telehealth intervention. The reason for this was the slow inclusion of participants in the shared videoconference due to COVID-19 and restrictive inclusion criteria.

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LIST OF PAPERS

Paper I: **The association between socioeconomic factors and the success of decolonization treatment among individuals diagnosed with methicillin-resistant *Staphylococcus aureus*: A cohort study from 2007–2020**
Kristensen MA, Abrantes JS, Jensen HI, Mogensen CB, Søndergaard J, Møller JK.
Published in Infection Control & Hospital Epidemiology. 2023.

Paper II: **Mental health, stigma, and illness perception among individuals diagnosed with methicillin-resistant *Staphylococcus aureus* - a longitudinal cohort study**
Kristensen MA, Jensen HI, Mogensen CB, Søndergaard J, Møller JK.
Manuscript in preparation to be submitted

Paper III **A framework for methicillin-resistant Staphylococcus aureus consultations comprising cross-sectoral videoconferences between patient, general practice, and specialist expertise - a participatory design-inspired study**
Kristensen MA, Jensen HI, Mogensen CB, Søndergaard J, Møller JK.
Manuscript in preparation to be submitted to the Scandinavian Journal of Primary Health Care

LIST OF ABBREVIATIONS

AIDS	Acquired immune deficiency syndrome
B-IPQ	Brief Illness Perception Questionnaire
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Program
EARS-Net	European Antimicrobial Resistance Surveillance Network
EUCAST	European Committee on Antimicrobial Susceptibility
GLASS	Global Antimicrobial Resistance and Use Surveillance System
GP	General practitioner
HIV	Human immunodeficiency virus
MHI-5	Five-item Mental Health Inventory
MRSA	Methicillin-resistant *Staphylococcus aureus*
PCR	Polymerase chain reaction
REDCap	RESEARCH Electronic Data Capture
RSD	Region of Southern Denmark
SF-12	Medical Outcomes Study Questionnaire Short Form 12 Health Survey
SF-36	Medical Outcomes Study Questionnaire Short Form 36 Health Survey
WHO	World Health Organization

LIST OF DEFINITIONS

Collaborative practice	This occurs in healthcare when multiple health workers from different professional backgrounds provide comprehensive services by working with patients, their families, caregivers, and communities to deliver the highest quality of care across settings.
Cross-sector	This occurs when two or more organizations work together across sectors.
Equity	Each individual or group of people have different circumstances, but the exact resources and opportunities needed to reach an equal outcome are allocated.
Equality	Each individual or group of people is given the same resources or opportunities.
Illness perception	This is a person's thoughts and feelings about a health condition. Individual illness perceptions can change over time and often becomes more detailed and expand. Individual illness perception is influenced by factors such as mass media, culture, and earlier experiences.
Mental health	This describes the psychological distress and well-being experienced by general populations.
Methicillin	A semisynthetic penicillin used for the treatment of *Staphylococcus aureus* in the 1950s. It is no longer used clinically.
MRSA carrier	An individual who has MRSA on their skin, in their nose or throat, but is not infected or ill due to MRSA. The term may be synonymous with "being colonized."

MRSA decolonization	This is a process by which efforts are made to remove MRSA from the patient who is colonized or is carrying MRSA.
MRSA infection	This term indicates the presence of MRSA with associated symptoms and signs of infection.
MRSA infection, invasive	Isolation of MRSA from a normally sterile body site e.g., blood, cerebrospinal fluid, or bone.
Multidisciplinary	This describes the combination or involvement of several academic disciplines or professional specializations in an approach to a topic or problem.
Psychosocial health	This multidimensional term encompasses the mental, emotional, social, and spiritual dimensions of health.
Socioeconomic factors	These characterize the individual or group within the social structure and includes, for example, individual or family income, education, and occupational background.
Specialist resource	This is a person who specializes in or is devoted to a particular area of activity, field of research, etc.
Stigmatization	Stigmatization is a social process that reduces a person possessing an attribute that makes him different from others, a process whereby the person goes from whole and usual to tainted and discounted.

Telehealth	This term describes the use of electronic information and telecommunications technologies to support long-distance clinical healthcare, patient and professional health-related education, public health, and health administration. Technologies include videoconferencing, the internet, store-and-forward imaging, streaming media, and terrestrial and wireless communications.
Videoconference	This type of conference involves participants in different locations who communicate with each other using sound and vision.

CHAPTER 1 I INTRODUCTION

This chapter provides a general introduction to MRSA, socio-economic factors, illness perception, psychosocial health, collaborative practice in MRSA care programs, and a conclusion leading to the objectives of this PhD thesis. The chapter ends with the objectives and hypotheses for the PhD thesis.

1.1 *Staphylococcus aureus*

Staphylococcus aureus is a leading human pathogen and an important cause of both community- and hospital-acquired infections. Depending on its virulence and host factors, *Staphylococcus aureus* can cause a wide range of bacterial infections from superficial skin infections to multiple types of invasive infections [1,2]. *Staphylococcus aureus* colonizes the skin and mucosae. When the skin and mucosal barriers are disrupted, *Staphylococcus aureus* can gain access to the underlying tissues or bloodstream and subsequently cause metastatic spread to internal organs, bones, and sterile tissues [3]. Invasive *Staphylococcus aureus* infections are associated with a high 30 days all-cause mortality rate (roughly 20%), making early, safe, and effective treatment essential. In the pre-antibiotic era mortality rates were between 75% and 83%. *Staphylococcus aureus* bacteremia has been noted to account for a greater number of deaths compared with deaths caused by AIDS, tuberculosis, and viral hepatitis combined [4,5].

Resistant *Staphylococcus aureus* strains

After the introduction of penicillin in the 1940s, penicillin-resistant strains of *Staphylococcus aureus* rapidly emerged. In the late 1950s, a semisynthetic penicillin, methicillin, was developed. However, as early as 1961, the first strain of *Staphylococcus aureus* resistant to semisynthetic penicillin was isolated. These strains were named methicillin-resistant *Staphylococcus aureus* abbreviated MRSA [6]. The first epidemic caused MRSA clones spread across Europe during the 1960s and 1970s [7]. MRSA led to outbreaks of nosocomial infections and from the 1990s resistant *Staphylococcus aureus* was also reported as community-acquired [8,9]. Due to the potential nephrotoxicity of

methicillin, it is no longer marketed for human use, but the term methicillin-resistant *Staphylococcus aureus* continues to be used. *Staphylococcus aureus* has a remarkable ability to acquire resistance. Today, MRSA includes resistance to most β-lactam antibiotics and is often resistant to multiple other antibiotic classes. Strains of MRSA with reduced susceptibility to vancomycin and even vancomycin-resistant *Staphylococcus aureus* have been reported, contributing to further concerns regarding the spread of MRSA [10]. In Denmark, however, a continuing decreasing trend in resistance to penicillin has been observed. In 2021, 31% of *Staphylococcus aureus* bacteremias was sensitive to penicillin. The highest frequency of resistance to antimicrobials other than penicillin was observed for fusidic acid (13%), according to the DANMAP report [5].

The virulence of MRSA seems to be similar to that of Methicillin-Susceptible *Staphylococcus aureus* (have not acquired the mecA/mecC gene) but is not yet fully understood [11]. In more recent studies, accounting for confounders and competing efforts no increased in-hospital mortality has been reported. Some studies have shown a diminished probability of long-term survival for invasive MRSA infections compared to Methicillin-Susceptible *Staphylococcus aureus*. Other studies have shown no difference in all-cause mortality, infection-related mortality, or infection-related hospital readmissions, between patients who had MRSA bacteremia and those who had Methicillin-Susceptible *Staphylococcus aureus* bacteremia [12–15].

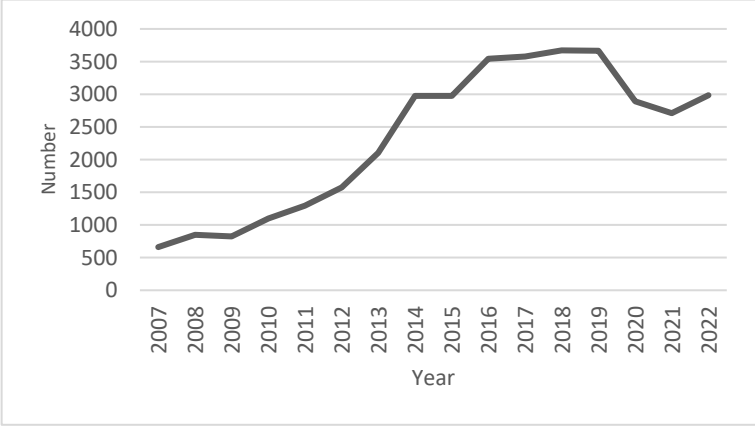
MRSA prevalence

MRSA prevalence varies geographically. In large parts of the Asia-Pacific region, the United States, and South America, more than 50% of *Staphylococcus aureus* isolates are confirmed as MRSA. In Africa, the prevalence of MRSA isolates ranges from 25% to 50%. In Russia, Australia, Canada, and parts of Central Europe, MRSA ranges from 10% to 25% [16]. In the Eastern part of Europe, the prevalence is between 5% to 15%. The highest prevalence in Europe is reported in the southeastern part of Europe for instance in Greece where the prevalence of MRSA isolates ranges from 50% to 74%. In

contrast, in the Nordic countries, France, Austria, and the Netherlands, the percentage of MRSA isolates is under 1% [17].

Following a period of high prevalence of MRSA in Denmark in the 1960s and 70s, it declined rapidly to a very low level in the 80s [18,19] but rose sharply again in 2003 [20]. Beginning in October 2006, the national notification of MRSA was implemented for both asymptomatic and symptomatic MRSA. The number of MRSA cases increased from 2007 to 2016 (however, testing also increased during this period compared to before 2006), after which the number of MRSA cases stabilized to about 3,600 cases a year from 2016 to 2019. From 2020 to 2022, the number of MRSA cases decreased, probably due to COVID-19 restrictions (e.g., social distancing, less international travel, and less contact with the healthcare system) [5]. For details, see Figure 1.

Figure 1: Number of MRSA cases (carriage and infections) from 2007 to 2022



Data source: Number and graphs, Statens Serum Institut.

In Denmark, 40 (1.6%) of the *Staphylococcus aureus* bacteremia cases discovered in 2021 were caused by MRSA. During the last decade, the proportion of bacteremia cases caused by MRSA has been between 1.3% (2012) and 2.9% (2014) [5], which is below most other European countries [21]. In 2019, the global burden associated with antimicrobial resistance was estimated to be nearly 5 million deaths and *Staphylococcus aureus* was one of

the six leading pathogens contributing to deaths associated with antibiotic resistance. The highest burden was in low-resource settings [22].

Risk of acquiring MRSA and transmission routes

The risk of MRSA colonization and infection is multifactorial. Host factors (e.g., age, comorbidity, surgery, prolonged antimicrobial therapy, bacterial load, immune status, and medical devices), living/working in a high-MRSA-prevalence setting (e.g., households, livestock farming, and hospitals), and socioeconomic factors (e.g., crowding, recent immigration, and low income) are frequently reported risk factors [2,23–26]. The duration of exposure and virulence characteristics also influence risk [27]. *Staphylococcus aureus* infections usually originate from asymptomatic colonization. Nares are traditionally regarded as the main *Staphylococcus aureus* colonization site, and in most cases, *Staphylococcus aureus* infections are considered endogenous in origin [28]. In addition, direct contact and indirect contact with environmental reservoirs (including dust) or contaminated hands have been described as a transmission route as well as spread via droplets [29].

Treatment of MRSA infections

MRSA infections are treatable, but the agents used are usually not part of empiric antimicrobial therapy. Depending on the severity of the infection, the patient's characteristics, the level of resistance, and the patient's clinical response, different treatments exist: 1) incision, and drainage treatment alone or combined with antimicrobial therapy, 2) oral systemic treatment, and 3) intravenous treatments. The length of systematic treatment varies from five days (community-associated skin and soft tissue infections) to four to six weeks (complicated bacteremia and endocarditis). More than one alternative agent exists for both complicated (e.g., parenteral linezolid, vancomycin, and daptomycin) and noncomplicated infections (e.g., oral linezolid, clindamycin, clarithromycin, rifampicin, and moxifloxacin). Parenteral, oral, or initial parenteral therapy, followed by oral therapies, is the route of administration of antibiotic therapy [30].

Surveillance and microbiological laboratory methods

Both national and international surveillance systems for MRSA exist, but serious data gaps have been reported in many low-income settings. GLASS was developed by the WHO to ensure homogeneous and global data completeness [31–33]. In Europe, EARS-Net is used for surveillance, and in Denmark, DANMAP publishes an annual surveillance report. In the report, MRSA is classified into three categories: 1) imported, 2) acquired in a Danish hospital, and 3) infection diagnosed outside hospitals. The last is further classified into two subcategories: community-onset or community-acquired infections. In Denmark, laboratory and clinical notification of all cases of MRSA was implemented in November 2006. Notification is required irrespective of whether citizens with MRSA display any symptoms [34].

According to Danish MRSA guidelines, the local departments of clinical microbiology perform laboratory testing for MRSA and submit isolates from new cases of MRSA to the reference laboratory for subtype determination [34]. In Europe, we use standards defined by EUCAST [35] when identifying MRSA and performing and interpreting antimicrobial susceptibility testing. Methicillin resistance can be detected both phenotypically and genotypically [16]. Phenotypical culture methods are considered the gold standard diagnostic method and are performed by, for example, the cefoxitin disk diffusion test, selective media, or chromogenic agar plates [36]. However, MRSA strains can also be detected by PCR. When using multiplex real-time PCR, the identification of MRSA, the analysis of selected virulence factors, and the identification of markers for human adaptation can all be conducted simultaneously [37–39]. Whole-genome sequencing is the most genotypically advanced method and is used primarily during outbreaks [40,41].

Strategies to prevent and control MRSA

In 2015, the WHO published a global action plan for the prevention of antimicrobial resistance. The overall goal is to ensure the successful treatment of infectious diseases with safe and effective medicine. The goal is divided into five subcategories: 1) to improve the awareness and understanding of

antimicrobial resistance; 2) to strengthen knowledge through surveillance and research; 3) to reduce the incidence of infection; 4) to optimize the use of antimicrobial agents; and 5) to ensure sustainable investment in countering antimicrobial resistance. On the priority list of bacterial and fungal pathogens, for the research and discovery of new antibiotics, MRSA is among the high-priority multidrug-resistant organisms. The list is published by the WHO [42]. On the European level, a One Health Action Plan against Antimicrobial Resistance was published in 2016 by the European Commission [43]. The Action Plan has since been followed by several initiatives, such as the investment of 5.1 billion € to provide funding to projects that aim to reduce the number of antimicrobial-resistant infections and improve vaccination rates [43].

Despite the above-mentioned efforts the strategies to prevent and control MRSA in the Nordic countries frequently include 1) the isolation of hospitalized patients colonized by or infected with MRSA, and 2) active surveillance cultures to identify possible reservoirs in patients at high risk of MRSA carriage at the time of hospital admission, and 3) decolonization treatment of MRSA carriage in hospitals and communities [34,44]. These strategies might have aided in maintaining low rates of nosocomial MRSA and the control of epidemics in Northern Europe [45–47]. However, each element is often part of a broader infection control program during epidemics. Furthermore, the effects of these programs have usually been studied through quasi-experimental before-and-after studies. Therefore, conclusions about their benefits are difficult to draw [48]. In addition, changes in the clonal complex from hyperendemic MRSA clones to clones with low survival and spread options might explain the low prevalence [18]. In situations of scientific uncertainty where the risks are high (e.g. serious or irreversible damage), it might be more favorable to act to support a healthier and safer world [49–51]. This approach is called the precautionary principle and is used in decision-making processes. There is no universally accepted definition of the precautionary principle. Most discussed is the degree of scientific uncertainty, ignorance (neglected research area), and the acceptable level of risk [52]. A frequently used definition was written by the European Commission in 2000: “Whether or not to invoke the precautionary

principle is a decision exercised where scientific information is insufficient, inconclusive, or uncertain and there are indications that the possible effects on the environment, or human, animal or plant health may be potentially dangerous and inconsistent with the chosen level of protection". The commission states that precautionary measures should be used with respect to other principles such as proportionality, non-discrimination, and comprehensive risk assessment [52]. However, there are conflicting viewpoints. From the One Health perspective, there is a one-sided focus on human health which can lead to unwanted outcomes and trade-offs e.g. culling of healthy animals [53]. Furthermore, guidelines within infection control based on the precautionary principle may occasionally be ineffective in decreasing the risk of infection, either because the risk is overestimated, the means are ineffective, or because routes of transmission are unknown [54]. Another downside of the use of precautionary principles is the potential disrespect for human and legal rights, which was discussed in several papers during the COVID-19 pandemic [55–58]. If a relatively high degree of scientific certainty is available, the proportionality principle can be used in design-making processes. To ensure proportionality there must be a balance between objectives and the means and a balance between the consequences of the means. Furthermore, this principle implies an obligation to appreciate the context, the mildest way of achieving the objective should be considered and there shall be respect for the dignity, human rights, and fundamental freedoms of individuals [56,57]. The Danish Communicable Disease Law ("Epidemiloven") enables the Danish government to protect society and individual citizens by eradicating, preventing, or containing the dissemination of infectious diseases in Denmark. Both the Danish Communicable diseases law and The International Health Regulations for Prevention of the transnational spread of infectious diseases rely on the proportionality principle [59,60]. Furthermore Dr Tedors Adhanon Ghebreyesus, the Director General of the WHO at the beginning of the COVID-19 pandemic said: "All countries must strike a fine balance between protecting health, minimizing economic and social disruption, and respecting human rights" [61]. To provide sufficient proportionality management during pandemics Julian März and colleagues argue that 1) restrictions to individual rights and freedom should

be adopted only to the extent to which they are necessary and effective in the promotion of a public health goal, 2) the public health benefits should be weighed against restrictions to individual rights and freedom, 3: all available, less intrusive courses of actions should be considered, 4) a continuous review of measures implemented should be provided and action should be taken if unexpected side-effect occurs or if the measures have become disproportionate, including in subgroups and particularly disadvantaged groups, 5) the measures should in lowest extent undermine rules and lows on human rights, and finally 6) evidence-based decision-making should be is a key element of good ethical pandemic management [57]. Harris and colleagues draw parallels between strategies to control COVID-19 and MRSA and argue that measures for COVID-19 management have been rebalancing harms and benefits during the pandemic contrary to the MRSA management, in which reaction towards a non-causal link between contact precautions and decreased MRSA incidence has been ignored. Furthermore, contact precautions are, according to Harris and colleagues, associated with several harms and suggest therefore that MRSA guidelines are revised so that harms do not outweigh benefits [62]. Nevertheless, there is an important difference in strategies towards COVID-19 and MRSA. During the COVID-19 pandemic harms and benefits imply the entire population for instance travel bans, school closures, vaccine mandates, and access to hospitals [57,63]. Whereas MRSA control measures only imply MRSA-diagnosed. Still, the suggestion on revising the recommendation on contact precautions according to the missing evidence for contact precautions, provided by Harris, might be in favor of ensuring proportionality within MRSA strategies. Ethics and the strategies for improving the patient experience among MRSA diagnosed will be further described in the introduction section 1.3 of this thesis.

Decolonization treatment

The eradication of MRSA carriage is usually achieved via the topical application of mupirocin 2% to the anterior nose twice a day combined with a daily 4% chlorhexidine gluconate bath and environmental cleaning for five days; however, various approaches exist [48]. A Cochrane review from 2003 found

insufficient evidence to support the use of topical or systemic antimicrobial therapy for eradicating MRSA or decreasing the risk of subsequent infections. Furthermore, potentially serious adverse events and the development of antimicrobial resistance can result from treatment. The settings of the studies were acute care hospitals and long-term care facilities and a total of 384 individuals were randomized in the five included studies [64]. Recently, an evidence-based guideline that primarily drew evidence from randomized controlled trials was published in the United Kingdom [36]. The guideline's main purpose is to provide advice for effective and safe healthcare services while reducing the risk of MRSA transmission in healthcare settings. The guidelines were largely developed for hospitals and did not include findings from randomized controlled trials that aimed to examine the evidence for decolonization in the communities. For inpatients (mainly surgical, dialysis, and intensive care), they found evidence of the effectiveness of topical treatment with mupirocin for nasal decolonization and chlorhexidine for body decolonization. Twelve randomized controlled trials showed strong evidence of the benefits of chlorhexidine for body decolonization. Furthermore, a meta-analysis of 10 randomized controlled trials showed strong evidence of the benefit of mupirocin for nasal decolonization. However, the guidelines state that complete eradication is not always possible, but temporary suppression may be sufficient in some circumstances [36]. Despite mupirocin nasal ointment and chlorhexidine body wash many other topical agents exist such as body wash with octenidine dihydrochloride (moderate evidence), povidone-iodine 5% or 7,5% (weak evidence) triclosan 1 % (weak evidence) and tea tree oil 5%, (weak evidence) [36,65].

A review from 2011 published in The Lancet adopted a broader perspective but examined only infection and not the prevention of the spread of MRSA as an outcome measure. The author concluded, "Decolonisation might reduce infection rates in patients undergoing hemodialysis or continuous peritoneal dialysis and could also be useful in patients with recurrent staphylococcal skin and soft tissue infections, although whether the same benefit occurs in those with recurrent community-acquired MRSA infections is uncertain" [48]. Systemic antimicrobial agents for instance rifampin and clindamycin (monotherapy or

combined) are less frequently used and are, as earlier described, not recommended due to weak evidence, serious adverse events, and the development of resistance to the agents used [64,66]. However, because no optimal decolonization treatment with long-term MRSA clearance in an outpatient setting is defined and because of the low evidence for the current use of systemic antibiotics for certain groups of MRSA carriers, a study from Sweden was recently carried out. The randomized controlled trial included 69 outpatients with pharyngeal MRSA carriage. One group received oral rifampicin in combination with clindamycin or trimethoprim for 7 days in combination with nasal mupirocin and chlorhexidine washing. The other group was treated with nasal mupirocin and chlorhexidine washing only. 61% of the group treated with systematic agents were cultured negative 6 months after the end of treatment. By contrast, only 12 % were cultured negative in the group receiving topical treatment [67]. Serious adverse events and the development of resistance to the agents used were not examined in the Swedish study.

Several observational studies have examined factors associated with treatment failure. A study found that the presence of wounds and throat carriage before decolonization treatment was associated with treatment failure among healthcare workers and hospitalized patients [68]. Also, perineal carriage, medical devices, chronic pulmonary disease, poor compliance with the decolonization protocol, dependence on activities of daily living, and MRSA carriage in household members have been associated with treatment failure [46]. In a recently published, from the Nederlands, low age, comorbidities, living in a refugee center, and not testing household members were all associated with treatment failure [69]. The number of decolonization treatments also seems like an important factor for MRSA clearance in outpatient settings in observational studies [68,70]. Furthermore, spontaneous clearance might occur over time. In one of the studies, patients were after two treatments offered the “wait-and-see” option and with this option, 20% spontaneously cleared their MRSA [68]. The Danish MRSA guideline does not provide evidence for recommendations regarding decolonization treatment including the recommendation of systemic antimicrobial agents [34]. For further description of the Danish treatment recommendations see section 2.3 MRSA care program in the RSD.

Outcomes of decolonization treatment

Decolonization treatment is often defined as successful when there is “no detection” of MRSA from a nasal or extra-nasal site after a given period of follow-up (e.g., 2–3 days [36] or 6 months [34]). However, no gold standard exists for either the measurement of adherence in follow-up samples or MRSA clearance. The clinical impact of decolonization treatment is often measured by the incidence of subsequent infections in the follow-up period and, less frequently, the spread of MRSA in healthcare institutions and the community. Finally, the emergence of resistance to eradication agents (especially to mupirocin and chlorhexidine) as a consequence of decolonization treatment is another important outcome that has been measured [44,48,64].

1.2 Socioeconomic factors

Socioeconomic factors in health research are often operationalized as factors pertaining to the economy, education, and occupation [71]. In addition, ethnic groups/migrants and residential crowding are considered when measuring socioeconomic factors and their relation to infectious diseases [72]. Racial disparities associated with higher attack rates and severe disease burdens are largely explained by socioeconomic factors [25]. Behind these measures are mediating factors in the association between socioeconomic position and health outcomes, such as health behaviors, environmental exposure, and psychosocial factors [73–75]. In general, resource-rich living conditions are associated with longer and healthier lives, and the risk of infection is associated with comorbidity and unhealthy lifestyles such as a high body mass index and smoking [76,77]. Two causal models are used to describe the relationship between socioeconomic factors and health: The social causation hypothesis and the health selection hypothesis. The social causation hypothesis argues that socioeconomic factors influence health via mediating factors such as resources, support, knowledge, or behavior. The health selection hypothesis argues that health influences socioeconomic factors, such as the loss of a job due to illness leading to poverty. Both causal models can contribute to health inequalities [78,79].

Socioeconomic factors and MRSA occurrence

Socioeconomic factors are likely to play an important role in the incidence of MRSA in high-income countries [80]. A higher incidence of MRSA is associated with overcrowding, homelessness, low income, and recent immigration [81]. In particular, low-income patients and patients without health insurance are a significant risk contributing to higher MRSA occurrence [82–85]. The impact on education is less clear. Low education was associated with higher MRSA rates according to a study conducted in the USA but this was not confirmed by a Swedish study [24,86]. The Swedish study was based on individual data instead of area-based data, which decreased the risk of information bias (misclassification). A study from the United Kingdom reported a notable increased risk of postoperative infections caused by MRSA, higher mortality rates, and length of hospital stay among individuals living in the most deprived areas [87]. Higher mortality rates and increased hospitalization might indicate that socioeconomic factors are not only risk factors for increases in MRSA occurrence but they might also influence the prospect of successful treatment.

Strategies to promote health equity

In 2005, the Global Commission on Social Determinants of Health was set up to marshal the evidence for action to promote health equity. Based on this work, which was finished in 2008, the WHO encouraged all countries to evaluate social inequality in health and to set goals for reducing inequality, with the specific aim of closing any health gaps [88]. This led to a 2011 Danish Health Authority report describing 1) the scope of inequality, 2) the causes of inequality 3) interventions to reduce inequalities, and 4) indicators to monitor health inequity [89]. In 2020, the first report measuring inequity in health was published and is planned to be repeated every four years. The report stated that social inequality in health is a growing problem in Denmark despite universal tax-supported healthcare [90]. The report is accompanied by theme reports, such as health efforts targeting socially disadvantaged citizens [91] and a literature review of research on inequality in the relationship between patient and provider in the healthcare system [92]. Several interventions are recommended to

reduce inequalities in infections in Europe, such as collecting sociodemographic variables and providing culturally sensitive health education and health promotion [72]. I did not identify studies that examined interventions to reduce inequalities in MRSA rates or treatment outcomes; however, researchers recommend identifying priority interventions to equalize MRSA incidence [24,82].

1.3 Illness perception and psychosocial health

For some time, concerns about psychosocial side effects have been raised in settings in which comprehensive preventive efforts to limit the spread of MRSA have been implemented [93]. The initial research was carried out in hospital settings and the main focus was on the use of isolation precautions. For example, a small qualitative study from Sweden showed that inpatients who had been isolated for at least one week described the isolation as traumatic and they felt vulnerable due to negative reactions from the nursing staff, family members, and other patients. Furthermore, the patients felt that they did not receive rehabilitation under the same conditions as other patients [94]. Several studies are in line with these findings [95,96]. When comparing MRSA with other multidrug-resistant organisms, patients with MRSA are more likely to experience stigmatization, depression, and anxiety symptoms. A recent quantitative study from the Netherlands that used data from questionnaires found no correlation between isolation precautions and perceived stigmatization among patients with multidrug-resistant organisms isolated for three days or more [97]. The authors argued that the intensive use of decolonization treatment and strict isolation procedures during hospitalization seems to result in stigmatization among MRSA carriers. In the Netherlands, contact plus airborne isolation precautions are required for MRSA, which includes mask wearing and door closure, whereas for most other multidrug-resistant organisms healthcare providers do not wear masks and doors can remain open [97]. Furthermore, it seems like the number of control measures influences the degree of stigmatization and quality of care [96], and several efforts are more common in terms of strategies to control MRSA compared to other multidrug-resistant organisms. A Danish qualitative study from 2018 examined 30 pig

farmers' experiences with MRSA guidelines during hospitalization and found that only a minority found the guidelines stigmatizing [98]. These diverse results may reflect the different MRSA strategies and methods of measurement among countries.

Similar psychosocial stressors have been reported outside the hospital setting. Those living with MRSA in society describe stigmatization as wider ranging compared to within the hospital setting. For example, these people might be bullied by colleagues at work. Feeling dirty, guilty, and alone is also frequently reported in combination with being afraid of passing MRSA on to others [99,100]. The reason for the negative impact of MRSA going beyond the healthcare setting is unclear, but some studies have argued that public media, public debate, and opinions from representatives from the field of public health may induce public concern and stigmatization within society [98,99]. When stigmatization experiences are reported by setting, the hospital is most important compared to, for example, GPs' offices and sports settings [99]. Research on subgroups has shown some deviation from the main picture. The female sex and intensive MRSA decolonization treatment were associated with higher stigmatization scores [99]. Furthermore, pig farmers may experience both sector-wide (farming) and individualized stigmatization [98]. However, research in the field of psychosocial health and illness perception remains scarce, with studies having only a few participants, and the majority of the studies being qualitative. Unstudied areas included the importance of predisposed psychological health, personality features, living alone, and psychosocial health related to behavior, such as compliance with decolonization treatment. Furthermore, the generalizability of the study results may be low due to differences in the strategies used to prevent the spread of MRSA in hospitals and within society between and within countries.

Psychosocial health and behavior

Psychosocial health may along with other illness perceptions of MRSA, predict health behaviors and healthcare outcomes according to the theory of self-regulation [101,102]. In the MRSA context, for example, this involves test

behavior, disclosure, and compliance with decolonization treatment. Suboptimal adherence to MRSA guidelines may increase the risk of MRSA infections within the individual or the transmission of MRSA to vulnerable populations. The theory of illness perception is grounded in a paradigm of cognitive psychology in which a person's thoughts and feelings about a health condition can predict health behaviors and healthcare outcomes. The theory of self-regulation was developed by Howard Leventhal and colleagues over the last 30–40 years [101–103]. Individual illness perception can change over time and often becomes more detailed and expanded. Individual illness perception is influenced by, for example, mass media, culture, and earlier experiences. Even though these are individual perceptions, 90% of experiences can be classified into five areas: illness identity, cause, control, consequences, and timeline. This applies to a variety of disease conditions. The self-regulation process occurs in three phases: (1) illness perception, (2) coping strategies, and (3) evaluation. The model incorporates a continuous feedback loop in which the results of the appraisal process are feedback into the formation of the illness/threat representation and the adoption of coping responses [101].

Culture and illness perception

Illness perception is influenced by culture and explains why patients from other cultures might respond differently to MRSA compared to for example the native Danes. Fundamental differences have been noted between illness perceptions in egocentric cultures (Europeans and North Americans) and socio-centric cultures. Egocentric cultures are characterized by embracing the biomedical model of disease and illness whereas socio-centric cultures in general draw few distinctions between mind-body, religious, medical, spiritual, emotional, and social processes [101]. Although there are large individual variations in the causal attribution of a particular illness, patients from egocentric cultures are more likely to report symptoms that include details of duration, frequency, and intensity. In contrast, the causes of diseases, e.g. AIDS are in other cultures perceived as natural (e.g. God´s illness). These different perceptions may influence care-seeking behavior and adherence to healthcare treatment [101]. Throughout the world, societies have become increasingly multiethnic [104,105]. In Denmark,

15.4% of the population are immigrants or descendants [106] and, based on experience, the MRSA incidence is high among individuals from Eastern Europe working in pig farms and among individuals from the Middle East. According to the sociologist Geert Hofstede, cultural variations are largely explained by nationality. He explains cultural variations by six dimensions, which can serve as a basis for mutual understanding of cultural differences: 1) power distance, 2) uncertainty avoidance, 3) individualism versus collectivism, 4) masculinity versus femininity, 5) short versus long-term orientation, and 6) indulgence versus restraint. These cultural differences are also reflected in the relationship between doctors and patients. For example, are consultations shorter and there is less room for unexpected information exchanges in cultures with large power distances [107]. It is important to note that many national cultures may consist of various subcultures and stay somewhere in between each of the dimensions scales and not at an extreme position of the scale. In addition, each dimension should not be interpreted separately, but in conjunction with each other [105]. In nearly all cases, migrants and refugees move from a more collectivist society to a more individualist society. Migrants and refugees thus often experience a lower power distance, a more femininity-dominated culture, and a lower degree of uncertainty avoidance (tolerates uncertainty) in the new country they become citizens in [105]. Migrants and refugees often pass four acculturation phases (steps of cultural modification) when arriving in a new country 1) euphoria, 2) culture shock, 3) acculturation, and 4) stable state. Migrants and refugees usually also experience several other barriers such as discrimination, language, financial, occupational, or educational barriers which may influence negatively on care-seeking and health [104]. Furthermore, the burden of illness of migrants and refugees may be different from the native population in the receiving country. A recently published Danish study found that the majority of refugees had vitamin deficiencies, mental health problems, and reported headache and other types of pain [108]. The immunity against infectious diseases is also different [109] and the mortality from infectious diseases is higher compared to native Danes [110]. Finally, individuals who have recently immigrated are often placed in rural municipalities, which challenges mobilization and social relations with other refugees and local volunteers organizing activities [111].

Strategies for improving the patient experience

Since 2016, actions have been taken by Danish healthcare authorities to address the stigmatization against MRSA carriers using notification cards, according to published research [112,113]. Furthermore, they have taken actions to prevent the rejection of individuals with MRSA from obtaining healthcare services due to published Nordic research [114]. In Denmark, it is no longer a requirement to carry a personal MRSA card with the disclosure of information about MRSA positivity. Furthermore, additional discomfort from healthcare services and society should be avoided. Disclosure of MRSA status within healthcare has also been limited to hospitals, nursing homes, and home care. A recently published MRSA guideline from the United Kingdom recommends information during hospitalization to minimize anxiety and improve patient experience [36]. To effectively meet the health needs of refugees and migrants, WHO has published a global action plan [104]. This includes, as written in section 1.2, strategies to promote health equity in management of infectious diseases and encompasses culturally sensitive health education for healthcare workers [72]. In the RSD, a team of healthcare workers with additional cultural competencies promotes health equity in hospitals. Healthcare services for vulnerable ethnic minority patients are provided by The Migrant Health Care Clinic at Odense University Hospital. To limit language barriers video interpreting services are implemented in Denmark [115,116]. Furthermore, written information on MRSA decolonization treatment and livestock-associated MRSA is available in English, Arabic, Lithuanian, Polish, Romanian, Russian, and Ukrainian.

Ethics and strategies to prevent and control MRSA

There are ethical challenges connected to measures to prevent and control MRSA [117–120]. A qualified ethical analysis encompasses a balance between conflicting considerations: What are the expected benefits and what are the possible harms of an action? Is there an overweight of benefits compared to harms? Is there equality in the benefits? Is the violation of legal rights and autonomy minimized as far as possible? This analysis can increase the awareness

of different considerations, which emphasizes designing strategies that avoid or minimize potential harms most properly [121].

The main ethical challenges concerning antibiotic resistance outlined by Jasper Littmann and colleagues are at first the restrictions of individual liberty for the protection of public health. Second justice with regard to overuse and lack of access to antibiotics. Third, the use of antibiotics in veterinary medicine. Finally, justice and responsibility for the effectiveness of antibiotics for future generations [117].

The theoretical frameworks of ethics often include an analysis of the consequences of action and non-action [121]. In case of non-action in the short and long term, some of the following scenarios caused by MRSA might be possible: Increased risk for severe and untreatable infections, excess mortality, increased occupancy rates at hospitals, and increased cost due to hospitalization and treatment of infections. If action is taken, by using the search-and-destroy strategy, some of the following scenarios might be possible: Prevention and efficient treatment of severe MRSA infections in the present and in the future, and decreasing mortality due to MRSA. Furthermore, it minimizes the reservoir of MRSA in hospitals and the community. However, some negative consequences might also appear when the search-and-destroy strategy is implemented. For example, psychosocial problems such as less social contact, medicalization of healthy citizens including unnecessary concern and decision-making on how to act. Resource allocation issues, for instance, fewer resources for other preventive efforts, and time spent for both patients and healthcare providers on for example screening, decolonization treatment, and follow-up. Finally, a higher degree of harm might occur among frequently hospitalized individuals and in subgroups such as immigrants, individuals living in nursing homes, and individuals with dementia or mental illness. This results in an imbalance in harm related to the strategy. Overall there may be a risk of doing more harm than good, according to the theory of the precautionary principle [52], because the available evidence of MRSA carrier clearance [64] and isolation regimes [122–125] is low, which might lead to over-medicalization [126]. However, there are conflicting results of ethical analyses according to expected benefits and possible harmful ef-

fects when implementing a search-and-destroy strategy, which results in different suggestions on how to act ethically. Some argue that there are not strong ethical reasons for justifying the removal of active surveillance and contact precautions to control MRSA transmission [120]. Other argue that the missing evidence of contact precautions of patients with MRSA when hospitalized and the burdens identified due to this practice is unethical [127,128]. Finally, MRSA carriage has been related to a negative impact on well-being, autonomy, and health-associated justice. For example, autonomy has been at stake if carriers are pressed to undergo MRSA tests and eradication therapy they might have preferred to avoid [119]. Most agree that values such as well-being, autonomy, solidarity, liberty, privacy, justice, transparency, and equality are important. Nevertheless, it is difficult to prioritize different ethical considerations [121].
A practical framework for ethical decision-making in infection control is the four widely used principles of medical ethics articulated by Beauchamp and Childress [129]: Beneficence (the duty to do good), nonmaleficence (the duty to avoid harming), justice (the duty to treat equals equally), and autonomy (the duty to respect the patient's ability to control his or her life) [130]. Several initiatives, despite the search-and-destroy strategy, have been taken or suggested to respond to these principles. For instance, suggesting that research and interventions should be established to minimize potential adverse effects of the measures to control MRSA [120], suggesting adjusting guidelines continuously according to new evidence [128], and decreasing the overuse of antibiotics in veterinary medicine [43] but not at the expense of animal well-being [53]. Furthermore, initiatives to have a restrictive antibiotic policy [131], to develop new antibiotics for humans [132] and vaccines [133] have been initiated. However, the patient's autonomy concerning deciding the initial test for MRSA and decolonization treatment is, as far as I know, less considered. A Health Technology Assessment, about vaccination for human papillomavirus in young boys, suggested that parents were sufficiently informed that the vaccine also was given to prevent transmission of human papillomavirus to girls and within the homosexual environment. In other words, the information should take into account that the vaccine strategy also included a public health effort. Furthermore, the information given should prevent the feeling of being forced to

be vaccinated to induce autonomy [134]. However, in the Danish culture, which is characterized by a predominantly individualistic society [105], ethical values such as solidarity and responsibility as a supplement to autonomy might be important also to consider, when implementing MRSA strategies [135,136]. For a further description, of how to respond to principles articulated by Beauchamp and Childress, see section 1.2 in the paragraph describing strategies to promote health equity and the above paragraph describing strategies for improving the patient experience.

1.4 Collaborative practice in MRSA care programs

To ensure coordination between hospitals and the primary care sector, the Danish Health Authority recommends that the measures taken against MRSA in each region be coordinated between departments of clinical microbiology, the Danish Patient Safety Authority, GPs, municipal health services, and other relevant stakeholders. For example, they might collectively establish a special regional MRSA unit [34]. In the RSD, the regional MRSA unit coordinates MRSA guidelines for general practice and hospitals. Furthermore, the MRSA unit publishes a yearly surveillance report. As the standard, the practice staff is responsible for the communication and initiation of decolonization treatment in collaboration with the patient and the patient's household. However, it may be challenging for general practice staff to handle MRSA care programs due to the low MRSA prevalence in Denmark. Approximately every two years, practice staff in the RSD meet patients with MRSA. Additionally, practice staff may face difficulty because Danish MRSA guidelines are complex [34]. In Germany, physicians from the primary healthcare sector showed significant variation in knowledge and level of activity regarding MRSA. Thus, 42 % of the responding physicians stated that there was not enough information available on MRSA and that knowledge about MRSA among patients was generally low. The authors stated that this might hinder the success of decolonization treatments [137].

Strategies for improving MRSA care programs

Few studies have described interventions to improve the management and care of MRSA carriers. In Germany, the Authorities of Public Health have established a network for dealing with multidrug-resistant organisms that offers a help-desk service to healthcare professionals, patients, and the wider public. The study showed that even though information about MRSA was widely available on the internet, healthcare professionals and patients asked for interactive dialogue with a specialist. Patients called the help desk because of the insufficient expert knowledge offered by healthcare professionals, and healthcare professionals called for assistance on how to handle preventative efforts, such as decolonization treatment. The authors concluded that further research needs to investigate whether there are systemic failures in the education and training of healthcare professionals [138]**.**

Multidisciplinary team meetings

Enhancing access to specialist care in general practice is one way to increase GPs' competency. A way to bring the GP, the hospital specialist, and the patient together is through multidisciplinary team meetings. When patients participate in shared meetings, their medical history becomes clearer to the health practitioners, making care decisions and planning more streamlined beneficial. The identified barriers to patient participation are that some clinicians feel uncomfortable discussing certain aspects of care and that clinicians must be aware of using non-professional terminology during the meeting [139]. However, patients seem to value participating in multidisciplinary team meetings [140,141]. Most of these meetings are held within organizations (e.g., a hospital setting). In a study of patients with cancer, GPs participated in hospital meetings (multidisciplinary and cross-sector). The GPs found these meetings useful for complex patient care situations but also asked for more optimized organizational time management [142].

Access to specialist care by telehealth

More optimized organizational time management may occur if modern tools are used to assist GPs. In recent years, electronic email consultation services

between GPs and hospital specialists have become common to streamline care and improve access to specialist consultations [143–146]. The downside is that electronic consultations do not involve real-time problem-solving. Typically, a GP gets a specialist text message answer in return between two and seven days after sending the text message. Furthermore, these specialist services do not include the patient in the consultation, and they are designed for non-complex cases [147]. In general, video telehealth seems to contribute to improved healthcare quality, enhanced patient participation, and broadened access to specialist care. Additionally, it seems to be time and cost effective [148,149]. Still, there are unanswered questions and important conditions to consider in its use in general practice, such as the effect of new technologies on different population groups [150]. Despite the rapid emergence of new technologies, peer-to-peer videoconferences in general practice clinics are still rare. However, in a study carried out in the Netherlands, the patient, a hospital specialist, and providers from primary healthcare were brought together through a videoconference carried out in the patient's home, with access to specialist care provided through a video connection. However, in only 1 out of 17 cases were both the patient and the professionals connected simultaneously. In the remaining cases, interprofessional contact was restricted to backstage work after the consultation [151]. A recent Danish study used multidisciplinary video consultation to improve the coherence and coordination of rehabilitation in cancer care and succeeded in having a shared meeting. Patients with cancer, a GP, and a hospital oncologist participated in the consultations. The patient could be located either in the hospital with the oncologist or at the general practice clinic. This shared meeting was initiated and managed by the hospital. The patients reported high levels of satisfaction. Furthermore, the meeting was perceived as patient-centered, and the roles during the meeting were clearly defined. GPs and oncologists were overall positive, although less pronounced, compared to patients [152].

1.5 Conclusion leading to the objectives of the thesis

Staphylococcus aureus is one of the most common causes of bloodstream infections, resulting in significant morbidity and mortality. The MRSA proportion

in *Staphylococcus aureus* isolates from blood ranges from 1% to 4% in low-prevalence countries such as Denmark and up to 25% to 49% in high-prevalence countries in Europe. MRSA is therefore an important pathogen in the European region [21]. One of the measures used to prevent MRSA infections and the spread of MRSA is decolonization treatment [36,44]. Treatment failure has been associated with several factors e.g. skin lesions, foreign-body materials, MRSA isolates resistant to mupirocin, throat carriage, wounds being present, and noncompliance with treatment recommendations [46,68]. The incidence of MRSA is higher among individuals with lower socioeconomic status [24]. However, it is not known whether socioeconomic status is a risk factor for treatment failure or whether social inequality affects the outcome of decolonization treatment.

MRSA has been linked to poor mental health and social implications in hospital and community settings [98,99,153]. However, differences in the psychosocial consequences of being infected and being a carrier have only been examined lightly. Furthermore, we do not know if these consequences are long lasting among MRSA carriers.

To prevent the spread of MRSA to vulnerable populations, authorities in Denmark recommend collaboration among stakeholders in MRSA care [34]. Travel and transportation distance complicate the integration of primary and specialist care. Face-to-face consultation through a video connection is still rare in clinical practice, but it might be beneficial for patients, practice staff, and specialists in the MRSA context. Additionally, there is very little research on how MRSA care programs are presently organized. These abovementioned knowledge gaps led to the objectives of this PhD thesis.

1.6 Objectives

Paper I: **The association between socioeconomic factors and the success of decolonization treatment among individuals diagnosed with methicillin-resistant *Staphylococcus aureus*: A cohort study from 2007–2020**

The objective was to examine the following:

- Cumulative incidence proportion of adherence to MRSA follow-up swab sampling.
- Cumulative incidence proportion of the success of decolonization treatment.
- Whether socioeconomic factors were associated with adherence to MRSA follow-up swab sampling after 1 and 6 months.
- Whether socioeconomic factors were associated with successful decolonization treatment.

We hypothesized that one or more of the socioeconomic factors included were associated with higher adherence to MRSA follow-up swab sampling and a higher rate of successful decolonization treatment.

Paper II: **Mental health, stigma, and illness perception among individuals diagnosed with methicillin-resistant *Staphylococcus aureus* - a longitudinal cohort study**

The objective was to examine the following:

- The rate of clear and suggestive stigmatization and the rate of poor mental health among individuals colonized or infected with MRSA 1, 6, and 12 month(s) after the MRSA diagnosis.

- The scores within the subdomains of stigmatization, mental health, and illness perception among individuals colonized or infected with MRSA 1, 6, and 12 month(s) after the MRSA diagnosis.
- The association between stigmatization, mental health, and illness perception among patients with either MRSA infection or carriage 1 month after the MRSA diagnosis.
- The association between stigmatization, mental health, and illness perception at 6 and 12 months following colonization or infection with MRSA compared to 1 month after the MRSA diagnosis.

We hypothesized that self-reported stigmatization, poor mental health, and having a more threatening perspective on MRSA were associated with MRSA infection and that stigmatization, poor mental health, and having a more threatening perspective on MRSA would decrease during the first year after the MRSA diagnosis.

Paper III **A framework for methicillin-resistant Staphylococcus aureus consultations comprising cross-sectoral videoconferences between patient, general practice, and specialist expertise - A participatory design-inspired study**

The objective was as follows:

- Develop and test a framework for enhancing access to specialist care through cross-sector videoconferencing during MRSA consultations in general practice.

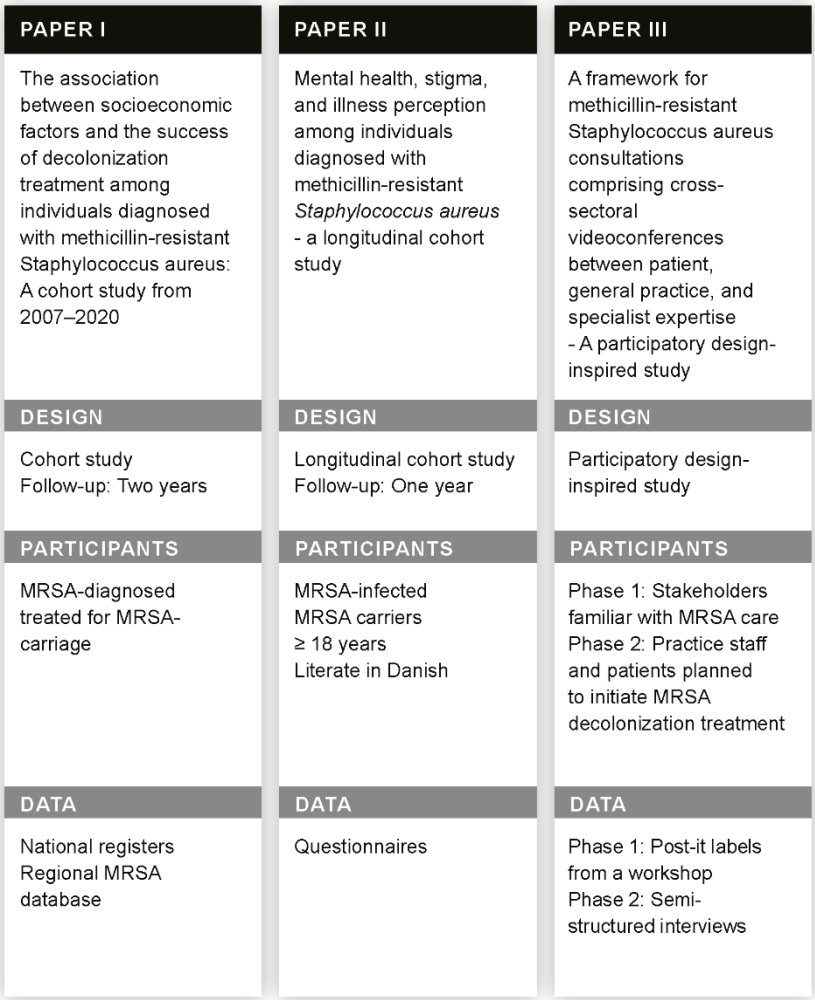
CHAPTER 2 I MATERIALS AND METHODS

This section begins with a summary of the materials and methods used in the studies reported in Papers I–III. Furthermore, ethical considerations, approvals, data management, and settings pertinent to the three papers are described. The description of key materials and methods is divided into three subsections corresponding to each of the three papers included in the PhD thesis. For a complete overview, please read Papers I–III, which can be found in the Appendix.

2.1 Summary of materials and methods

A summary of the materials and methods used in the three papers included in this thesis is shown in Figure 2.

Figure 2: Summary of the materials and methods in Papers I–III.



2.2 Code of conduct for research integrity, permissions, and ethics

We created a protocol describing all three studies and a detailed protocol for each study. Funding agreements did not limit our ability to analyze and publish data independently. Before collecting the data, we obtained permission to store the data according to the guidelines of the RSD [154]. Permission was registered in the Record of Data Processing Activities in the RSD with identifier

20/25135. In Paper I, we were unable to obtain consent from the participants. The study was instead approved by the Danish Patient Safety Authority (Identifier S-31-1521-375). We also obtained approval to access patient records for the identification of patients in Papers II and III (Identifier S-31-1521-375). Approval from the patient's GP to send the questionnaire was obtained by telephone for each potential respondent. Patients gave their consent when filling in the online questionnaire. Patients who participated in Paper III received oral and written project information and a link to sign the informed consent form using NemID (a common secure electronic login developed by the public authorities in Denmark). Written project information was sent by email to the general practice. The practice staff gave oral consent at the beginning of the recorded qualitative interviews. The region's research counseling unit was the facilitator of the abovementioned approvals, including in the obtaining of consent from the study participants.

According to the Regional Committees on Health Research Ethics for Southern Denmark (Project-ID: S-20192000-155), it was not necessary to obtain ethical approval for this project. However, we were aware of the potential implications for patients who filled out the online questionnaire, such as individuals who experienced psychosocial stressors during the MRSA care program. Therefore, we decided to add a "no opinion" response option to the questionnaire to measure stigmatization, and further respondents could skip questions. Due to the way the study was organized, it was not possible for us to carry out any debriefing after answering the questionnaire.

During the analysis, data from the interviews and questionnaires were stored in a safe and secure analysis platform provided by the research support unit in RSD. Register data were similarly stored and analyzed on Statistics Denmark's platform. Only the PhD student had access to data at these secure data storage facilities. Audio files were temporarily stored on a drive at Lillebaelt Hospital with an approved entry (but not double-password entry, and activity was not logged) for the infection control nurse performing the interviews before the data were transferred to the analysis platform. During data collection, the questionnaire data were managed by RedCap, which is a secure database [155]. The data were anonymized when they were transferred from RedCap to the analysis

platform. The register data used in Paper I were pseudo-anonymized (unique identifier numbers) when analyzed using the analysis platform. For analysis, Stata version 17 (StataCorp, College Station, Texas, USA) and NVivo 12 (QSR International, 2014) were used. Descriptions of data extracts, logbooks, and do-files were saved. Each document enabled the identification of the persons who conducted the work concerned. Furthermore, data will be stored for five years from the date of publication in a storage repository available at the research support unit in RSD, making reproduction of the research possible in accordance with the code of conduct for research integrity [156]. All three studies were recommended by the Regional Committee of Multipractice Studies in General Practice. Collaborative research was carried out. In Papers I and II, all four departments of clinical microbiology in the RSD participated, and in Paper III, the collaboration was carried out between the Hospital of Southern Jutland and Lillebaelt Hospital. Mainly nurses and physicians were involved in the research process. However, patients with MRSA experience participated in the creation of the study protocol for the three studies, a workshop, and in the development of the questionnaire. The patients involved were very dedicated and had a broad perspective on MRSA for instance experiences related to severe MRSA infections and stigmatization within the community. However, their main focus was to improve MRSA care in MRSA consultations and to minimize stigmatization. Furthermore, technical personnel (videoconferencing), epidemiologists, statisticians, data managers, and researchers adept at qualitative methods were involved during the research process. The attribution of authorship for the three papers was based on the Vancouver guidelines. Part of the research has been published, and part of the findings has been communicated with the research community. I will continue this process and also communicate the research to professional practitioners and society at large.

2.3 Setting

The Region of Southern Denmark

The three studies were carried out in the RSD. The population of the region is approximately 1.2 million people living in 22 municipalities. Most of the main

towns in municipalities in the RSD have less than 50,000 inhabitants, and the metropolitan city is located in Odense municipality. The area is served by four somatic hospital units (Odense University Hospital, Hospital of Southern Jutland, Hospital of South West Jutland, and Lillebaelt Hospital), which altogether consist of 13 somatic hospitals. The four departments of clinical microbiology are located at Odense University Hospital, Aabenraa Hospital, Esbjerg Hospital, and Vejle Hospital. The area has approximately 795 GPs working in 357 clinics [157]. For details, see Figures 3 and 4.

Figure 3: Map of the RSD. Symbols indicate the sites of the departments of clinical microbiology.

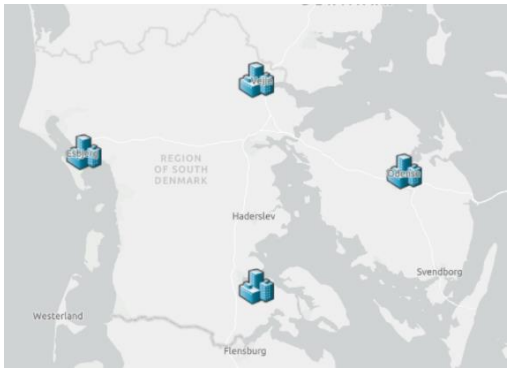
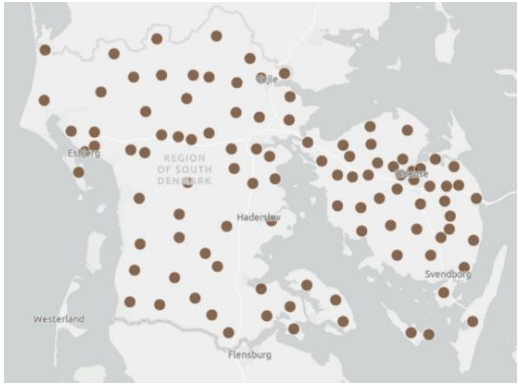
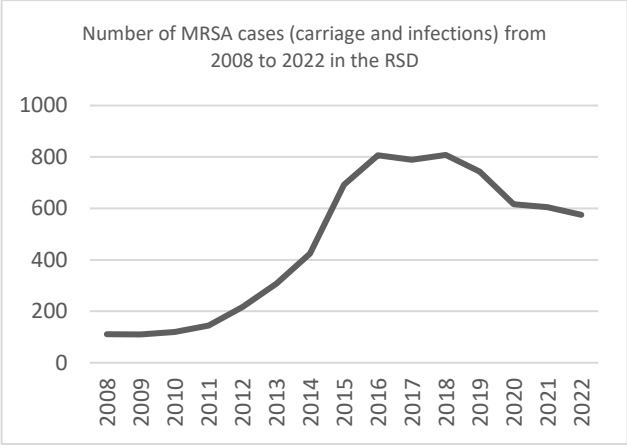


Figure 4: Map of the RSD. Symbols indicate the site of general practice clinics.



The RSD comprises approximately 20–25% of the total MRSA cases in Denmark. MRSA cases in the RSD from 2009 to 2022 are shown in Figure 5.

Figure 5: Number of MRSA cases (carriage and infections) from 2008 to 2022



Data source: The regional MRSA database in the RSD

Two nosocomial outbreaks in the RSD occurred within the study period of Paper I. A very large ST22 outbreak in the former Vejle county occurred from December 2002 to March 2008, and the CC398 (human variant) outbreak occurred in a maternal ward at Kolding Hospital in 2016 [41,158].

General practice clinics

In Denmark, the number of GPs per 1000 population is 0.99, and 98% of Danish citizens are listed with a GP [159]. Danish general practice care is based on the tradition of a strong doctor-patient relationship and continuity of care [160]. GPs provide generalist healthcare and play an important role as gatekeepers between the primary and specialized healthcare systems. Approximately 4% of patients seen are referred to hospitals, 2% to community specialist care, and 2–3% to auxiliary services (e.g., physiotherapists). GPs work as private contractors and are remunerated by public health authorities through a mixed capitation and fee-for-service system [159,161,162]. Danish GPs offer face-to-face, remote, two-way video, email, and telephone consultations [159]. However, video

consultations account for only 1.2% of all consultations. In comparison, email consultations account for 25% and telephone consultations for 26% [163].

Departments of clinical microbiology

The four departments of clinical microbiology in the RSD serve hospital departments and the primary healthcare sector with microbiological diagnostics and counseling. The department is staffed with laboratory technicians, physicians, molecular biologists, and infection control nurses. All four departments in the RSD offer microbiological diagnostics of MRSA including resistance testing.

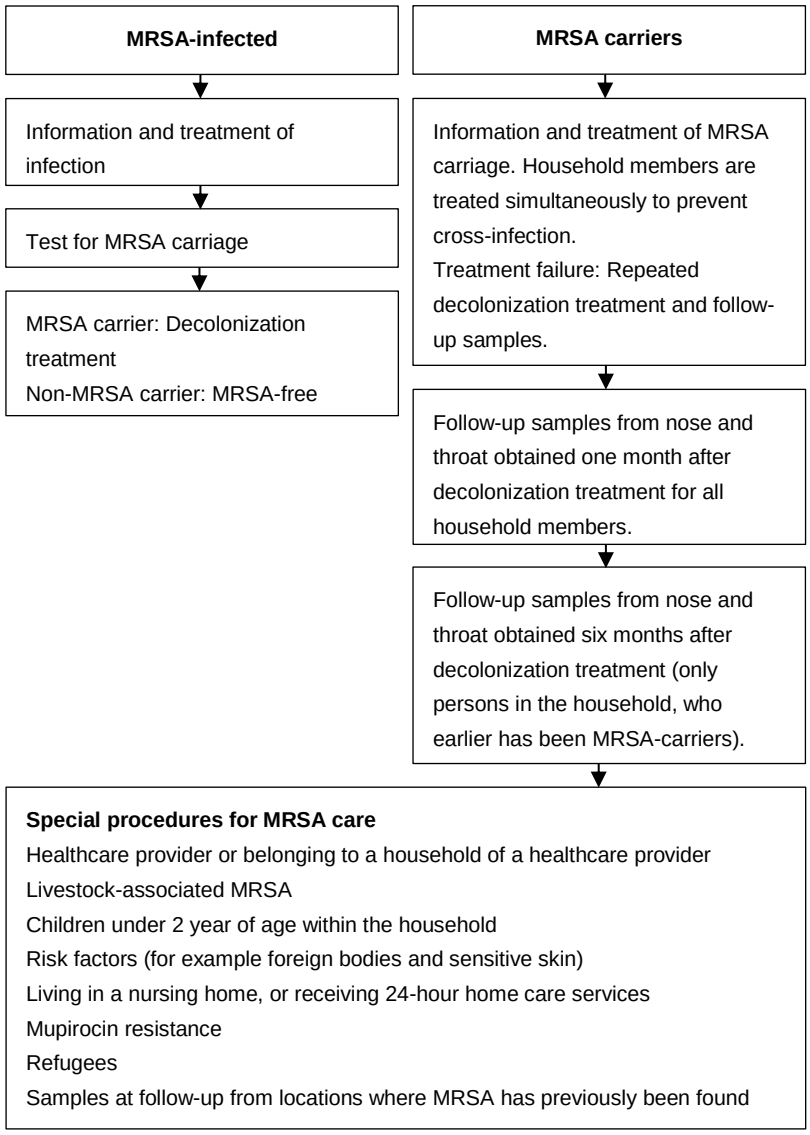
Advice given is registered in a medical journal and is available only to staff working in the departments of clinical microbiology. They submit MRSA isolates to the National Reference Laboratory (Statens Serum Institut) for monitoring and genetic typing according to national MRSA guidelines. Odense University Hospital hosts the regional MRSA coordinating unit. The exchange of clinical information about MRSA between practice staff and the departments of clinical microbiology is managed by telephone and a regional electronic requisition and laboratory reporting system. Email or face-to-face consultations are not available. The surveillance of MRSA is managed by a regional MRSA database. The database contains the results of MRSA samples and is updated electronically in real time from the laboratory information system. A web application provides access to the MRSA database for infection control units in the RSD.

MRSA care program in the RSD

The RSD has implemented national guidelines for preventing the spread of MRSA [34]. The first guideline was published in 2006 and revised in 2012 and the latest edition was published in 2016. The primary changes in the 2012 guidelines were added information on the management of livestock-associated MRSA and that follow-up swabs should be taken at 6 months instead of 12 months after decolonization treatment. In 2016, a section on how to avoid stigmatization and a more detailed description of the disclosure of MRSA were added.

MRSA care programs provide treatments for MRSA infections, decolonization treatments, and follow-up swabs to evaluate the effects of decolonization treatments. In Denmark, MRSA carriage is treated with a topical application of 2% mupirocin to the anterior nose twice a day, combined with daily bathing with 4% chlorhexidine gluconate and environmental cleaning for five days. In cases of throat carriage, the treatment period is extended to 10 days. To avoid cross-transmission, MRSA carrier treatment is offered to household members. Treatment is free of charge. Treatment is not recommended for children below the age of two years or individuals with day-to-day contact with live pigs [34]. Due to living conditions, decolonization treatment is, as a general rule, not offered to refugees before they are issued a residence permit, as well as a place of residence and an assignment to a general practice clinic [164]. Post-treatment MRSA follow-up swabs are recommended 1 and 6 months after treatment. Specific guidelines for follow-up exist for healthcare providers, those living in nursing homes, and individuals who require 24-hour home care services. Decolonization treatment is considered effective when samples taken from the nose, throat, and earlier positive sites are negative six months (or later) after decolonization treatment, although hospitalized persons need supplementary negative samples from the perineum to be declared free of MRSA. Individuals infected are only recommended to initiate decolonization treatment if the test is positive for MRSA in swabs taken from the nose, throat, or perineum after completion of the treatment [34]. If two treatment attempts fail supplementary systemic treatment should be considered by the Department of Clinical Microbiology. If it is not possible to eradicate carriage whole-body washing with chlorhexidine soap 1-2 times a week should be initiated and prolonged as long the person is MRSA-positive [34]. For a detailed description of the MRSA care programs see Figure 6.

Figure 6: MRSA care programs in Denmark



Typically, in the RSD, the general practice clinics manage the MRSA care program and inform the patient. The information includes an explanation of:

- The purpose of presenting the personal MRSA card and that it is voluntary to use the card;
- How to reduce the risk of transmitting MRSA to others;
- MRSA only rarely causes serious infections in healthy people.

If the patient is discharged before the test result is available or the patient tests positive at a specialist doctor's clinic, the MRSA card and information letter are forwarded to the general practice [34].

In the RSD, the four departments of clinical microbiology assist in advising the doctor in charge of the patient. The assistance includes advice concerning the antibiotic treatment of a possible infection, decolonization treatment, and follow-up sampling. Regional guidelines for the MRSA care program are published by clinical microbiology departments and are available on electronic platforms for healthcare workers. In a few regions in Denmark, MRSA care programs are organized by an MRSA unit centralized to the secondary healthcare sector, according to local agreements [70].

2.4 Paper I

The association between socioeconomic factors and the success of decolonization treatment among individuals diagnosed with methicillin-resistant *Staphylococcus aureus*: A cohort study from 2007–2020

To examine decolonization treatment and socioeconomic factors, we conducted a cohort study using prospectively collected register-based information at the individual level for MRSA-diagnosed individuals (asymptomatically colonized or infected with MRSA) in the RSD. MRSA-diagnosed individuals were identified using the regional MRSA database and included MRSA-diagnosed individuals in the RSD who initiated decolonization treatment in the period from 2007 to 2018. The follow-up time was two years. We excluded individuals who died, moved from the region, or left Denmark within two years of follow-up. We included MRSA-diagnosed patients who were treated for 5 or 10 days (throat carriers) with 2% mupirocin nasal ointment (Bactroban® Nasal)

from 2007 to 2018. Patients were included in the study from the day the prescription of the initial decolonization treatment was redeemed.

Outcome measurement and analysis

Information from a patient's medical record stored by a general practice is not transferred to national registers in Denmark. Instead, we obtained the prescription redemption dates for 2% mupirocin nasal ointment from the Danish National Prescription Registry. Furthermore, we collected information on MRSA samples from a regional MRSA database comprising patient IDs, sampling dates, test results, and sampling sites. We measured adherence to follow-up samples by including data on samples from the nose and throat only. We categorized the data into sets of nose and throat samples taken on the same date and calculated the time since the decolonization treatment was finished. We did not take any specific guidance for follow-up into account (Figure 6) due to missing data, such as being a healthcare provider, living in a nursing home, or receiving a 24-hour home care service. We defined successful adherence after one month as follow-up swabs from the nose and throat (same date) 1–5 months after decolonization treatment, and successful adherence after six months as follow-up swabs taken from the nose and throat (same date) 6–12 months after decolonization treatment. Successful decolonization treatment was defined as a set of negative MRSA samples from the nose and throat at least six months after completing the decolonization treatment and before the end of the two-year follow-up. We used household crowding, education, family income, occupation, length of residence in Denmark, and population density as markers of socioeconomic status.

We used a cluster-based logistic regression model to examine the association between socioeconomic factors and adherence to follow-up samples and MRSA clearance. We adjusted for age, sex, MRSA diagnosed in the household, throat carriage, and the number of decolonization treatments. For the robustness of the analysis, and due to the low occurrence of somatic disorders, mental disorders, the use of foreign bodies, and systemic antibiotics, these variables were not included in the adjusted analysis. Information on cases with a relapse

of MRSA after successful decolonization treatment was not included in the analysis. $P < 0.05$ (two-sided) was deemed statistically significant. Individuals lost to follow-up were excluded from the analysis.

For details see Paper I, Appendix 1.

2.5 Paper II

Mental health, stigma, and illness perception among individuals diagnosed with methicillin-resistant *Staphylococcus aureus* - a longitudinal cohort study

Aside from the examination of decolonization treatments and socioeconomic characteristics, we prospectively collected data on illness perception, stigmatization, and mental health from questionnaires. We used a longitudinal cohort study design and measured outcomes of interest at 1, 6, and 12 months after the MRSA diagnosis. We identified participants from a regional MRSA database comprised of MRSA samples submitted to the four departments of clinical microbiology in the RSD. We enrolled participants from September 2020 to September 2021. We included MRSA-infected individuals and MRSA carriers aged 18 years or older. We excluded patients from other regions in Denmark, patients not literate in Danish, and patients without the mental capacity to fill in questionnaires. Furthermore, we excluded patients who reported being MRSA free when answering the questionnaire because data on MRSA clearance were not available in the regional MRSA database or the laboratory system in the departments of clinical microbiology. Because there was no patient contact with MRSA diagnosed in the departments of clinical microbiology in the RSD, the questionnaire was mailed through a public electronic mailbox system called e-Boks. If there was no response, two reminders were sent at intervals of one week.

Outcome measurement and analysis

Throughout the course of three months, I reviewed research literature and collected comments from stakeholders, and patients familiar with MRSA care programs. This knowledge was considered when choosing questionnaires. We ended up using three existing questionnaires, which had previously been used in the study field of MRSA and which measured illness perception, stigmatization, and mental health [99,165].

To measure illness perception we used the Danish version of the B-IPQ [166]. The items in the B-IPQ encompass consequences, timeline (acute-chronic), amount of perceived personal control, treatment control, identity (symptoms), concern regarding the illness, coherence of the illness, and emotional representation.

To measure stigmatization, we used a 10-item stigma scale developed by Wright (four-point scale) [167]. The scale includes four subscales: 1) personalized stigma (three items), which measures the consequences of others knowing about one's MRSA status, including rejection, loss of friends, and avoidance of others; 2) disclosure concerns (two items), which measures issues related to whether individuals tell others about their diagnosis; 3) negative self-image (three items), which measures one's feelings towards oneself such as shame, guilt, and self-worth; and 4) concern with public attitudes (two items), which measures participants' perceptions of the public attitudes toward those living with MRSA. Due to research results suggesting, that healthcare settings are particularly important in promoting stigmatization [99], we added a question on stigmatization from healthcare at the end of the original questionnaire. We did not change the response options. We translated the English version into Danish using a three-step translation process. The translations were conducted by independent professional translators, bilingual translators familiar with everyday language, and bilingual specialists in infection control. The English version was translated into Danish. The accepted Danish version was then blindly back-translated into English by new translators. A panel constructed the final Danish version of the questionnaire [168].

To measure mental health we used the Danish version [169,170] of the MHI-5 [171]. The scale includes the following four subscales: 1) anxiety (one item), 2) depression (one item), 3) emotional control (one item), and 4) general positive affect (two items).

The questionnaire data were calculated as per the instructions [166,171–173] and analyzed as continuous data (mean, 95% confidence interval). Stigmatization scores were categorized into “no stigmatization” (score 40–75), “suggestive of stigmatization” (score 76–110), and “clear stigmatization” (score 111–160) [174–177]. The mental health score was dichotomized as poor mental health (<60) and normal mental health ($\geq$60), as per instruction [171]. We used linear regression models to examine the association between MRSA carriers and individuals with MRSA infections. To examine the associations between time points (1, 6, and 12 months) and the outcome of interests (mental health, stigmatization, and illness perception), we used linear mixed-effects models, in which all available information was included in the model, to reduce the risk of selection bias and include information for as many participants as possible. Following the literature, we adjusted for gender, education level, stigmatization score/mental health score, and livestock-associated MRSA [98,99].

For details, see Paper II, Appendix 2.

2.6 Paper III

A framework for methicillin-resistant Staphylococcus aureus consultations comprising cross-sectoral videoconferences between patient, general practice, and specialist expertise – a participatory design-inspired study

Occurring concurrently with the examination of decolonization treatment and psychosocial health, we worked on a new framework for MRSA care programs. We initiated the work in August 2020 and used a participatory-inspired study design. The participatory design method has roots in action research and focuses on making designs that fit the actual needs of end users. The active

involvement of relevant stakeholders can take many forms but the core element is to equalize the power between designers and users to facilitate mutual learning. To enhance user participation several activities can be used and a traditional way to categorize them is under the umbrella terms of telling, making, and acting activities. Telling activities are used at the beginning of a participatory design study. These activities can facilitate participants to express their needs and experiences. Examples include fieldwork, interviews, literature studies, and “personas.” Next, user participation is facilitated by making activities that induce quick adjustments and the evaluation of new ideas on the spot. This includes activities such as creative workshops and dilemma games. Finally, acting out possible future scenarios via mock-ups or clinical practice facilitates the understanding of end users’ perspectives [178,179].

Jane Clemensen and colleagues developed a participatory design method for health science that includes four phases: 1) need assessment, 2) idea generation, 3) testing and retesting, and 4) evaluation [178]. We divided the study into two phases. Phase 1 included both need assessment and idea generation. Phase 2 included testing in a clinical pilot study. We did not assess the effectiveness or quality of care (evaluation). In Phase 1, we developed a framework for MRSA care programs carried out by using cross-sector videoconferences (corresponding to need assessment and idea generation). In Phase 2, we tested the framework in clinical practice (corresponding to testing and retesting). In Phase 1, we included patients with personal experiences of being MRSA positive as well as healthcare providers with expertise in general medicine, infection control, and infectious diseases. In Phase 2, we included Danish-speaking patients who were about to begin decolonization treatment in primary healthcare for MRSA carriage, and the participating patients' practice staff. We identified patients through the microbiological laboratory database used in the included settings (the departments of clinical microbiology at the Hospital of Southern Jutland and Lillebaelt Hospital).

In Phase 2, we used the videoconference system Webex, which is used for videoconferences in the secondary healthcare sector in the RSD. Practice staff

can use the system through a browser and do not need any specific software downloads or licenses. The Department of Clinical Microbiology used a screen from Cisco (TRANBJERG DX80). The Cisco screen was connected to a computer by a DP-HDMI cable making screen-sharing options available. A unique link to the web-based conference was sent electronically via a secure email to the general practice clinics. To connect, the practice staff needed to type in a meeting code. The system provides a secure connection with no third-party data processing. In most cases, the practice staff used a static computer combined with a microphone/speaker and a webcam attached to the top of the computer screen. Tablets, smartphones, or laptops could be used as well. Practice staff were supported by the Health Innovation Center of Southern Denmark, and the Department of Clinical Microbiology was supported by the videoconference team from the hospital's Department of Information Technology at Lillebaelt Hospital. To avoid interpersonal variation, the same infection control nurse carried out the videoconferences. We used the one-way text messaging option in the hospital medical patient journal (from the Department of Clinical Microbiology to general practice clinics) to write summaries of the shared meetings.

Outcome measurement and analysis

We used qualitative methods to develop and test the framework for enhancing access to specialist care through a cross-sector videoconference in clinical practice.

Phase 1

In Phase 1, we carried out a workshop to identify needs and generate ideas. To enhance user participation, we used the telling activities "Personas" and "The User Journey," as well as the "Think-Pair-Share" template. During the two-hour workshop, needs and ideas (individual, pair, and shared) were written on post-its. Post-its were grouped into themes by participants during the workshop. After the workshop, the results were summarized, and a framework for the shared videoconference was constructed. A summary of the workshop data and the framework were reviewed by the workshop participants (making activity). When

the framework was accepted, we composed a guideline to carry out a cross-sector videoconference for MRSA consultations based on the newly developed framework, practical aspects of telehealth [180], and the Danish MRSA guidelines [34]

Phase 2

In Phase 2, we tested the framework in clinical practice (acting activities), and we interviewed patients and general practice staff. The PhD student constructed a semi-structured interview guide. To ensure impartiality, an infection control nurse who was not involved in the project conducted semi-structured telephone interviews between 2 and 7 days after the shared MRSA consultation. To avoid interpersonal variation, the same infection control nurse carried out all interviews. We used the theory of qualitative research interviewing by Kvale and Brinkmann [181]. A transcription guide (see Paper III, Appendix 3) and an analysis guide were created. The interviews were recorded and subsequently transcribed in Danish. To structure and shorten the transcript, text lines were coded. For further text reduction, the codes were merged into themes and sub-themes. During the process, annotations in NVivo were used to write comments on the understanding (self-understanding and common-sense level) of specific text lines. Next, we used matrices to summarize and condense the data material. The analysis process initially focused on what the participants seemed to perceive as the meaning of their own statements (self-understanding), leading to a common-sense understanding. In the final step, the theoretical understanding of the statements and their interrelationships was examined using the theory of *relational coordination* [182]. This theoretical framework defines relational coordination as a process of coordinating work between professionals, which encompasses four communication dimensions (frequent, timely, accurate, and problem-solving) and three relational dimensions (shared knowledge, shared goals, and mutual respect). These dimensions work against, for example, specialized knowledge and finger-pointing behavior. Fostering high levels of relational coordination across organizations in particular, clinical pathways (protocols or guidelines used to integrate work around the needs of a process), boundary spanners

(integrate work around the needs of a process), patient rounds (real-time interaction among people who are engaged in the same work), and information systems (systems designed to provide a common infrastructure of information for administrative and clinical information) have been pointed out by Gittell to connect with external providers who are engaged in caring for the same patients, as well as the patients' families. These components are expected to be more effective when used in conjunction with one another. Building these supply partnerships enables healthcare providers to deliver more efficient and higher-quality patient care than they can on their own [182]. For details, see Paper III, Appendix 3.

CHAPTER 3 I RESULTS

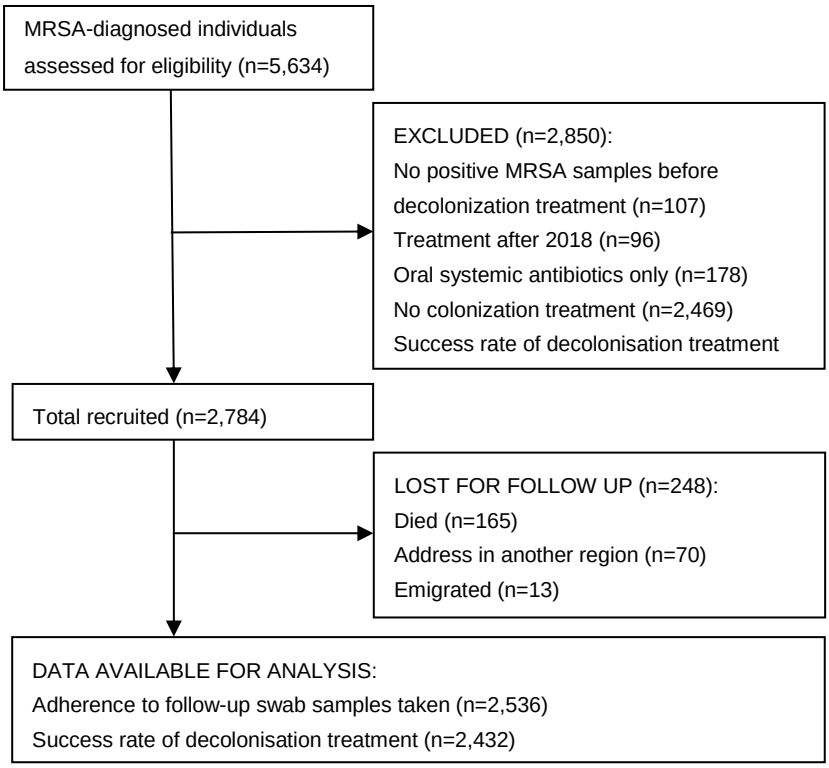
In this chapter, a short description of the study population and key results is presented. For more details, please read Papers I–III in the Appendix.

3.1 Paper I

The association between socioeconomic factors and the success of decolonization treatment among individuals diagnosed with methicillin-resistant *Staphylococcus aureus*: A cohort study from 2007–2020

We identified 5,634 MRSA-diagnosed individuals between 2007 and 2018. The main cause of exclusion was no decolonization treatment (n = 2,743). We included 2,536 individuals in the analysis of adherence and 2,432 in the analysis of the success rate of MRSA clearance. The largest group of included individuals was below the age of 34. Gender was almost equally distributed. The majority of MRSA-positive participants had only one course of treatment (n = 1,548, 61%). Somatic disorders, foreign bodies, and mental disorders ranged from 1 to 2.3%. Approximately half of the study population had one or more culture-positive household contacts. The study flowchart is shown in Figure 7.

Figure 7. Study population flow, Paper I. Reprinted from Assenholm Kristensen et al., *Infection Control & Hospital Epidemiology,* 2023. Discrepancies from the reprint: "Lost to follow-up"=248 and "Emigrated"=13 due to incorrect numbers in Paper I.



When comparing the baseline socioeconomic characteristics of treated and non-treated individuals in a sensitivity analysis, decolonization treatment was less likely to be initiated when individuals were between the ages of 0 and 35, recent immigrants, male, and employed.

We examined adherence to MRSA follow-up swabs in 2,536 individuals and MRSA decolonization treatment in 2,432 individuals. The adherence to MRSA follow-up swabs 1 month after treatment was 66%, and it decreased to 30% after 6 months. Living in predominantly urban (160–900^{+} inhabitants per km^{2}) or intermediate municipalities (76–159 inhabitants per km^{2}) or having retired was

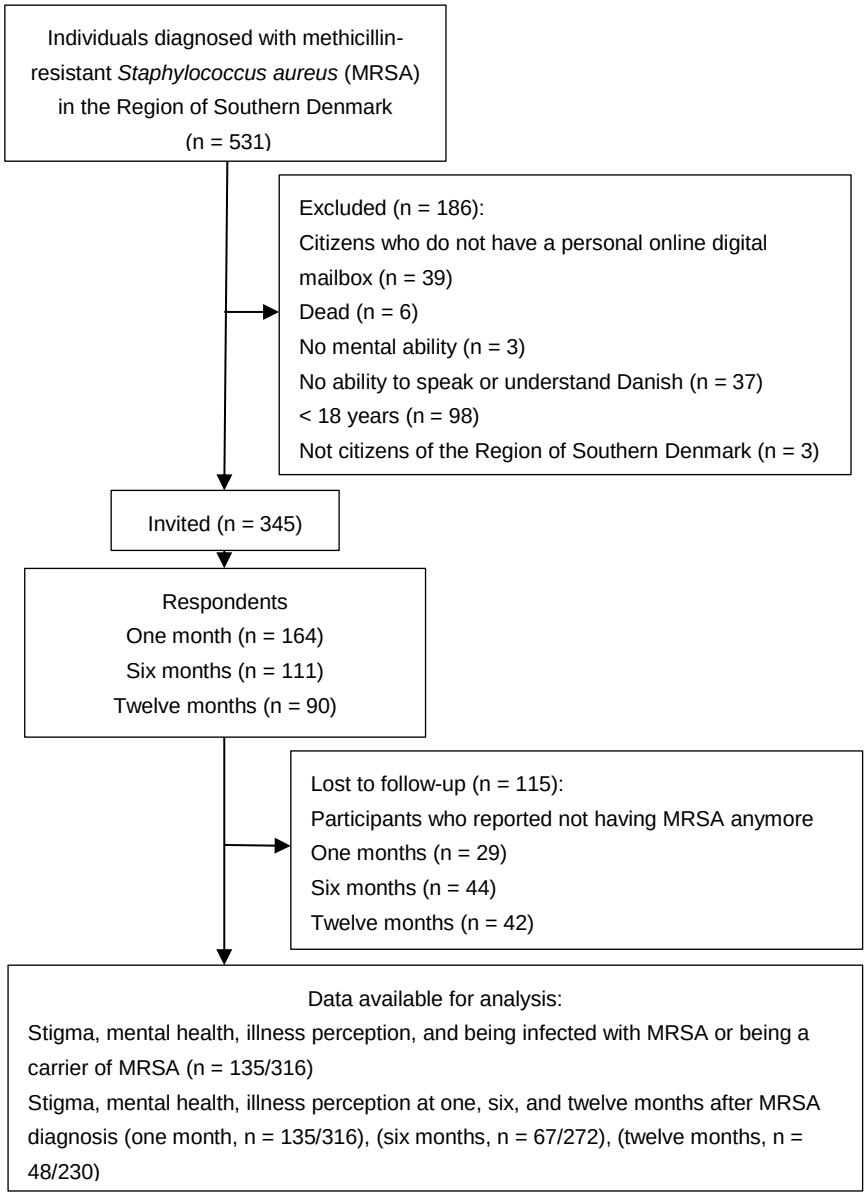
associated with a significantly higher rate of adherence to tests for colonization. The MRSA clearance rate after decolonization treatment was 36% two years after initiating treatment. Early retirement, being more educated, and living in intermediate municipalities or predominantly urban municipalities were associated with a higher success rate. However, low income, unemployment or welfare payments, short length of residence in Denmark, and household crowding were not associated with lower rates of adherence to follow-up swab sampling or with lower rates of successful decolonization treatment.

3.2 Paper II

Mental health, stigma, and illness perception among individuals diagnosed with methicillin-resistant *Staphylococcus aureus* - a longitudinal cohort study

From September 2020 to September 2021, 531 individuals in the RSD were diagnosed with MRSA. After excluding those who did not meet the criteria, we invited 345 patients to participate in the study. The main reason for exclusion was being under 18 years of age. A total of 164 questionnaires were returned (48%) one month after diagnosis, but 29 reported being MRSA free at the time of return, thereby leading to the inclusion of 135 individuals (43%). After 6 and 12 months, the response rates for MRSA-positive individuals were 25% (67 individuals) and 21% (48 individuals), respectively. Furthermore, 10 patients did not respond to the questionnaire at one month but responded at six and twelve months. Gender and hospital affiliation (department of clinical microbiology) were almost equally distributed among respondents and non-respondents. When comparing age groups, the younger population was less represented among the respondents. The majority of the respondents were under 65 years of age, retired or employed, or married. Only a few respondents perceived their health as poor or very poor. The study flowchart is shown in Figure 8.

Figure 8. Study population flow, Paper II. Reprinted from a manuscript in the review process; Appendix 2.



We examined stigmatization, mental health, and illness perception in 135 individuals with MRSA 1 month after the MRSA diagnosis, 67 individuals after 6 months, and in 48 individuals after 12 months. The rate of clear stigma was 11–13% during the follow-up period of 1 year. The rate of poor mental health was 16–24%. Subdomains within the stigma scale defining a less favorable MRSA-related stigma state were disclosure and public attitudes. The subdomain within the mental health scale defining a less favorable mental health state was general positive affect (well-being). For subdomains in the illness perception questionnaire, treatment control, timeline, and personal control denoted a more threatening perspective of MRSA. Being infected with MRSA as opposed to being a MRSA carrier was associated with a more threatening perspective of consequences and identity (symptoms). However, we found no difference in psychosocial health between individuals and carriers. Having MRSA 6 months later compared to 1 month later was associated with a more threatening view of the control of treatment. Furthermore, having MRSA 12 months later compared to 1 month was associated with a more threatening view of the timeline of being MRSA positive. For details, see Paper II, Appendix 2.

3.3 Paper III

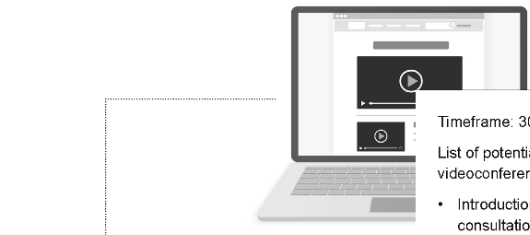
A framework for methicillin-resistant Staphylococcus aureus consultations comprising cross-sectoral videoconferences between patient, general practice, and specialist expertise - A participatory design-inspired study

In the workshop, seven stakeholders participated: one patient, three GPs, two infection control nurses, and one infectious disease specialist. We completed eight consultations, and eight patients and seven practice staff members were interviewed. Patient interviews lasted for 15–25 minutes, and those for practice staff lasted 8–19 minutes. Three nurses and four GPs were interviewed. The patients were aged 32–52 years, the majority of patients were women, and 63% initially had a MRSA infection. The patients from the two hospital settings included were almost equally distributed. Furthermore, the following characteristics were represented: Livestock-associated MRSA, different family

sizes, families with children under the age of two years, patients with eczema, pregnancy, and working in healthcare.

The developed framework consisted of tasks for healthcare providers before and after the cross-sector videoconference and the videoconference itself. For details see Figure 9. Please note that only the main communication channel is shown in images with symbols.

Figure 9. Framework for the cross-sector videoconference, Paper III. Reprinted from the manuscript in preparation; Appendix 3.



Timeframe: 30 minutes

List of potential themes during the cross-sectoral videoconference for MRSA consultations

- Introduction and purpose of the shared consultation
- A summary of the patient's MRSA care program
- Questions (patient and family) and delivery of written information in print or electronically
- Information matching patient's needs (livestockassociated MRSA, MRSA in newborns and children up to two years of age, healthcare workers, pregnancy, individual risk factors such as e.g., eczema or wounds, frequent hospitalization, psychosocial issues)
- Planning of the MRSA care program (treatment of any clinical infections, clarifying carrier status, treatment of for example wound/eczema, decolonization treatment, MRSA follow-up swabs one and six months after treatment, closing the MRSA care program)
- Considering the need for further support due to life circumstances or complexity (involvement of municipalities e.g. social nurse, telephone conversation with specialist expertise in MRSA, consultation with the practice staff)
- Summarizing the output of the videoconference to facilitate a common understanding of agreements

- The practice staff invites and informs the patient by phone.
- The infection preventionist send a consultations guide to the practice staff before consultations including a list of potential themes to address during the videoconference and task to be accomplished before and after the consultations including links to MRSA guidelines.
- To avoid interprofessional talk, the practice staff can call the Departments of Clinical Microbiology before the shared videoconference.
- The infection preventionist also sends the list of potential themes to address during the shared consultation to the patient.

- After the consultation, the infection preventionist writes a summary in the hospital's electronic patient record with a copy sent electronically to the general practice.
- The infection preventionist is available for advice by telephone for patients and practice staff.
- After the shared videoconference the practice staff ensures that consultations for MRSA follow-up swabs are booked, writes prescriptions for MRSA decolonization treatment for all family members, and after treatment reacts in case of treatment failure, and closes the MRSA care program when the family is effectively treated (considered MRSA-free).

The main focus of the developed framework was to solve real-time patient needs and plan the MRSA care program. The content of the framework consisted of a list of potential themes to discuss during the shared videoconference including a summary of the MRSA care program, questions, information matching the patient's needs, planning of the MRSA care program, and consideration of the need for further support. The timeframe was a double consultation in the general practice working structure. To maximize time efficiency, tasks that were not relevant to all participants were accomplished separately before or after the shared consultation. A summary of the shared meetings was made available to all participants. Pilot testing of the framework in a real-world setting showed that MRSA care is a complex process that benefits from cross-sector collaboration. Relationships between participants were characterized by mutual respect and shared knowledge, and the communication was characterized as problem-solving and accurate. Few practice staff perceived the shared consultation as time consuming, and they asked for a clearer description of roles and responsibilities. The main barrier identified by a few patients was the wish for face-to-face consultations with the infection control nurse, but contrary to the practice staff, patients found the cross-sector videoconference time efficient.

CHAPTER 4 I DISCUSSION

In this chapter, the results of Papers I–III are compared to existing literature, and the strengths and limitations are described. Aside from the key strengths and limitations, additional topics, not available in the three original papers, are discussed. Furthermore, the results of Papers I–III, are linked. A meta-view of the key limitations is presented at the end of the chapter.

4.1 Paper I

4.1.1 Comparison with existing literature

Paper I, describes the examination of 2,536 MRSA carriers in a cohort study, who initiated MRSA decolonization treatment between 2007 and 2018. Normally, income and liquid assets are strongly associated with health through the affordability of healthcare, a healthy diet, good housing quality, and a safe environment. In these cases, there is no psychological burden of being poor, which is associated with chronic stress, lower levels of social cohesion, and generalized distrust [183]. However, we found no association between income and adherence to control swabs and MRSA clearance. In Denmark, patient copayments are required to acquire prescription drugs in primary healthcare. In 2023, the first 140 € worth of prescription drugs per year is paid in full by each patient. Then, reimbursements covering increasing percentages of costs in increments of 50%, 75%, and 85% are issued until out-of-pocket expenditures are capped at 509 € [184]. However, due to local agreements in the RSD, decolonization treatment is free of charge. A decolonization treatment (topical application of 2% mupirocin combined with daily bathing with 4% chlorhexidine for five days and with supplies such as lotion and washcloths) cost approximately 60 € or 64 USD. Depending on the family size and the number of treatments, the total costs might be a challenge for low-income families. The lack of association between income and low adherence to MRSA clearance might therefore be explained by the initiative of free decolonization treatments in the RSD.

Retirement or early retirement was associated with either higher adherence to control swabs and higher MRSA clearance rates. As a standard, occupation

influences health through the general position and prestige in a society that a job can provide and also through physical and mental health risks in the workplace [79]. In our study, a minor part of the study population was aged above 65 (13%), including the 65+ groups, when measuring occupation, which might be misleading. The elderly are retired and are no longer exposed to current work conditions. Furthermore, we could not measure whether these groups were never employed or had various employments [79,185]. An explanation might therefore be that a higher age and more frequent illness within these groups affect adherence and treatment rates instead of occupation. Age was a strong confounding in our analysis and potential residual confounding might have occurred due to the categorization of age. Higher age and comorbidity increase the risk of MRSA infections, which might influence illness perceptions. Having a more threatening view of MRSA carriage may have increased adherence to control swabs and also resulted in higher rates of MRSA clearance. As described in Section 1.4, the illness perception of MRSA can predict health behavior and healthcare outcomes according to the theory of self-regulation [101,102].

Having a higher educational level was associated with higher rates of MRSA clearance in our study. This knowledge might be particularly important for further interventions. Even though standard materials are available, a particular group seems to need further guidance. When we developed the shared videoconference for MRSA consultations, we found that even healthcare providers found MRSA care complex and diffuse, leaving individuals with a lower education with a huge challenge. In contrast to the above-mentioned information bias in our occupation data, an individual's highest attained level of education is generally achieved in early adulthood and is therefore relatively constant throughout life [79,186]. As discussed in Paper I, higher education is positively associated with health and is driven by the cognitive ability to process complex information [187].

4.1.2 Strengths and limitations

Paper I has several strengths. First, we evaluated the risk of selection bias in a sensitivity analysis. This was of particular importance due to the large number of

individuals who did not undergo decolonization treatment. Second, a large sample size gave us the statistical power to examine associations and adjust for relevant confounders, which provided greater precision. Two earlier published studies in Denmark that examined successful decolonization, included only 358 [70] and 143 individuals [188]. We were able to explore the large population because of the regional MRSA database, which contained the necessary information on MRSA samples, making manual data processing unnecessary. Third, the use of register data is cost and time efficient for both researchers and participants. However, register data can be considered both a strength and a limitation. Registers have high data completeness, and the data are prospectively collected, but the information is collected with a different purpose than answering a specific research question, leading to a risk of information bias. Another possible risk of information bias is, that we used registry data on the prescription of mupirocin nasal ointment to estimate completed decolonization treatment. Access to medical records containing information on treatment, noncompliance, etc., could have made it possible for us to compare the two different data collection methods, as performed in other studies to validate register data [189]. Finally, due to the long follow-up, negative samples taken might be caused by spontaneous MRSA clearance rather than the effect of treatment. No standard exists for how to estimate MRSA clearance rates. However, if we had included anatomical locations where MRSA had previously been found and specific follow-up times for the subgroups, our estimates may have been more valid. Finally, cohort design precludes, as the standard, any conclusion regarding a causal relationship because the design does not fully prevent influence from confounders (known or unknown). For example, the MRSA clearance rate might have decreased during the years from 2007 to 2018 due to changes in the prescription of antibiotics, staff competencies, and competing efforts such as isolation or screening. Potential confounders such as cultural differences are difficult to measure and we do not know the relevance of these confounders. According to Bradford Hill, a strong association (e.g., a risk ratio > 5) substantially decreases the risk of confounding [190]; however, no associations in our study were above 5.

4.2 Paper II

4.2.1 Comparison with existing literature

Paper II, describes a longitudinal cohort study examining stigmatization, mental health, and illness perception in 135 individuals with MRSA 1 month after the initial MRSA diagnosis, 67 individuals after 6 months, and 48 individuals after 12 months. A recent review and meta-analysis examined the broader psychological impact of pandemic lockdowns on the general population using longitudinal studies. The study was carried out at the beginning of the pandemic and therefore did not include results on repeated or prolonged lockdowns. They concluded that the psychological impact of COVID-19 lockdowns is small in magnitude and highly heterogeneous, suggesting that lockdowns do not have uniformly detrimental effects on mental health and that most people are psychologically resilient to their effects. Subgroup analyses indicated that depression and anxiety consistently showed small but significant effects of lockdown [191]. The outcomes measured were relatively broad, covering anxiety and depression, social support (not stigmatization), loneliness, general distress, negative affect, and suicide risk [191]. However, when compared to research on infectious diseases (e.g., HIV/AIDS), the picture is different. Contrary to the abovementioned review and meta-analysis, this group was diagnosed with an infectious disease. Thus, a recently published systematic review and meta-analysis found that more than a quarter of adolescents with HIV had depression [192]. The examination of the association between HIV-related stigmatization and healthcare outcomes in people living with HIV/AIDS showed that there are significant associations between HIV-related stigmatization and higher rates of depression, lower social support, and lower levels of adherence to antiretroviral medications and access to and usage of health and social services. The outcome measures assessed were mental health (depressive symptoms, emotional and mental distress, anxiety), quality of life, physical health, social support, adherence to antiretroviral therapy, access to and usage of health/social services, and risk behaviors [193]. Rump and colleagues also found a correlation between stigmatization and mental health among individuals with MRSA [99]. However, the two outcomes were measured

at the same time, making any conclusion regarding a causal relationship particularly difficult to draw. In our study, 24% of the respondents were classified as having poor mental health. The scales cover depression, anxiety, emotional control, and general positive affect (well-being), and are therefore not completely comparable to measuring depression alone. When we compare our results to the general population in Denmark, the percentage of those with poor mental health in our study was slightly higher compared to the results from the Danish National Representative Health and Morbidity Study from 2021, in which 17.4% of the general population had low scores on the mental health scale. The national study used the SF-12, which contains the same questions as the MHI-5, but it measures mental health with only two questions (MHI-3 (depression) and MHI-4 (general positive affect)) [194,195]. The MHI-5 is a short version of the original 38-item version of the Mental Health Inventory questionnaire [196]. The MHI-5 is a part of the SF-36, which measures eight general health concepts, including mental health [197]. The lower levels of adherence to control swabs and lower rates of MRSA clearance found in Paper I might, despite the results from Paper I, also be explained by the above-mentioned relationship between HIV-related psychosocial stressors and lower levels of adherence and inefficient treatment outcomes.

4.2.2 Strengths and limitations

The primary strength of Study II was that we used validated questionnaires. Mental health was measured with the MHI-5 [171] using the Danish version which is a part of the first validation and translation of the Danish version of SF-36 [169,170]. We used the B-IPQ to measure illness perception [166]. The B-IPQ is a generic nine-item questionnaire developed to assess cognitive and emotional representations across diverse patient groups. The B-IPQ is a short version of the 84-item revised illness perception questionnaire [198]. Stigmatization was measured with a Danish translation of a 10-item stigma scale developed by Wright and colleagues in 2007 (four-point scale) [167]. The revised version is a short version of the 40-item Berger Stigma Scale questionnaire from 2001 [173]. However, most MRSA studies have measured stigmatization through qualitative methods [94,98,100,112,153], which is an

advantage when studying complex phenomena, such as stigmatization [181]. The downside is that comparisons, frequency, and change over time are more difficult to capture. Still, only one study [99] prior to our present study measured stigmatization with a questionnaire, and it is appropriate to consider whether the questionnaire covers the stigmatization phenomenon when studying individuals with MRSA. As previously mentioned, the questionnaire used was developed to measure stigmatization in patients with HIV. A recently published systematic review examined the psychometric properties of the Berger HIV stigma scale and found that the questionnaire appeared to be a reliable and valid measure of HIV-related stigmatization. The evidence supporting its validity came from 36 studies, most of which were conducted in North America and Europe [199]. Even though the questionnaire is reliable and valid it also has to measure the condition of interest [200]. Earlier addressed concerns are that HIV is a chronic and potentially life-threatening health condition in contraction to MRSA carriage, which is usually a treatable condition that rarely results in health problems [99]. However, a review that compared health-related stigmatization measurements in different disciplines, found that stigmatization was remarkably similar across different health conditions, cultures, and public health programs. Overall, van Brakel and colleagues concluded that the development or use of generic instruments to assess health-related stigmatization is possible [201]. Since their review in 2006, the COSMIN methodology for assessing content validity has been published, which could be taken into account in future studies of MRSA-related stigmatization, such as interviewing patients [200] and not only contextualizing using theoretical analysis [99]. Furthermore, in that process, it is important to examine whether qualitative or quantitative methods are most suitable for measuring MRSA-related stigmatization.

Aside from the use of validated questionnaires another strength of our study is its longitudinal design. The nature of the longitudinal design is to collect data on more than one time-point to examine changes over time. Furthermore, our study involved the largest study population to date within this field, which made adjusted analysis and analysis for subdomains within mental health and stigmatization possible. However, considering the small sample sizes, especially during follow-up, our study was likely underpowered, resulting in

imprecise estimates with wide confidence intervals. To provide a more unbiased outcome, we used the mixed effect model (uses all available information from respondents who do not provide data from all events). However, if data are missing not at random, which is likely, the outcome might still be influenced by some selection bias [202]. Furthermore, it should be noted that cohort studies are prone to loss to follow-up, which is potentially a major source of selection bias. Bias is introduced if both the exposure and factors related to the outcome affect participation, [203], which was likely in our study. Perhaps we could have increased the number of respondents by hand delivering each questionnaire, such as during an MRSA consultation. However, this was not possible because of the organizational structure of our study. Finally, as described in Section 4.1.2, the cohort design precluded any conclusion regarding a causal relationship, which also applies to Paper II.

4.3 Paper III

4.3.1 Comparison with existing literature

Paper III, describes the development of a framework for a cross-sector videoconference for MRSA consultations in general practice clinics and the pilot testing of the framework in clinical practice. We involved seven stakeholders familiar with MRSA care programs when developing the framework and pilot tested the framework eight times in clinical practice. Most caregivers found the video link easy to use, however in a few cases, the experience was the opposite. A GP explained it in this way*: "*The way the link was communicated to us was bad in the sense that the secretary hadn't got the video link right in the medical record, so it was a bit of a hassle for me. I ended up looking in an old email and then I found the link*".* If the link had already been placed in the medical record by the infection control nurse, no parallel work occurred. According to Gittell, we need to develop shared systems designed to provide a common infrastructure of information for both administrative and clinical information [182]. Thus far, only doctor-patient video consultation through the application My Doctor is available in Denmark [204] but a common infrastructure for peer-to-peer cross-sector video meetings has not yet been developed.

Furthermore, the laboratory database is not set up for electronic text messages for general practice apart from the final laboratory reports, and only one-way messages are available through the hospital's electronic patient records. This means that access to specialist care in general practice through a video connection and text messages is at a very premature level in Denmark, particularly between practice staff and staff from the clinical microbiology departments in the RSD. To future-proof the Danish healthcare system, which is seeing an increased aging population and fewer healthcare providers, the national strategy for digitalization of the healthcare system includes large-scale digitalization. Although enhancing access to specialist knowledge in general practice is not a present focus area, virtual consultations aim to provide flexible solutions, and making health services available regardless of geographical area and proximity to home is part of the current strategy [205]. For example, in Australia, three-way consultations between a remote specialist, a patient, and a primary care provider are implemented for remote and rural areas [206]. Reducing geographical inequality enhances the rate of successful decolonization treatments, and as discussed in Paper I, such inequality can be mitigated by cross-sector videoconferences.

Normally, conventional consultations in general practice are based on the patients' agenda [207,208] as opposed to consultations in the secondary healthcare sector. The complexity of consultations in general practice increases, for example, because of the transfer of activities from secondary to primary care and increasingly complex clinical guidelines [209]. Our framework for cross-sector videoconferences consists of a list of potential themes to discuss, which reflects the structure of a consultation in the secondary healthcare sector. This more systematic approach met the patient's needs and the requirements for high-quality planning of the MRSA care program. Previous research has not examined the relationship between consultations and potentially listed themes to address in general practice; therefore, our results should be confirmed by other studies.

In Paper I, we found that lower education was associated with lower success rates of decolonization treatment. We did consider the need for further support

during videoconferencing; however, in some cases, patients may benefit from a more tailored care pathway [210]. Gittell argued that boundary spanners, who integrate work around the needs of a process, contribute to higher performance in healthcare. Boundary spanners are synonymous with case managers or navigators; they coordinate the whole case, including taking care of social work [182]. In an example from Australia, a study in general practice aimed to help address navigation problems faced by patients from culturally and linguistically diverse communities by using bilingual community navigators. They found that the patients had inadequate health literacy, faced cultural and language barriers, and had difficulties navigating health and social services. To succeed, bilingual community navigators should be trained and supervised, with clear role definition and manageable workloads, and not used as interpreters [211]. In Denmark, initiatives such as outreach work and tailored care pathways are integrated into the GP´s collective agreement to promote equality [212].

In Paper II, we found that individuals with MRSA may experience rejection from healthcare services, stigmatization, and poor mental health. We addressed psychosocial issues if relevant during the shared consultation, and providing information and answering patients' questions were part of the shared consultations. These steps were taken to minimize psychosocial stressors [36,99]. However, only patients who met the criteria to be prescribed decolonization treatment were invited to participate. Only about 49% received decolonization treatment in the RSD, according to the results of Paper I. This leaves a large group of patients who might have benefitted from participating in the cross-sector videoconference.

A literature review examined and identified strategies to reduce stigmatization. The interventions were grouped according to the levels of McLeroy's social-ecological framework: 1) intrapersonal, 2) interpersonal, 3) organizational/institutional, and 4) governmental/structural level [213]. The authors argued that interventions should be multi-targeted and oriented at multiple levels.They also noted that stigmatization is powerfully reinforced by culture and that its effects are not easily overcome by the coping actions of individuals alone. However, patient-centered care is important. When empowering persons, they become aware of the barriers and their human

rights, which can establish priorities regarding the need for institutional and national change [213]. Taking this into account, the cross-sector videoconference should be supplemented with other initiatives, such as organizational and governmental initiatives. Furthermore, we were not aware of specific strategies for particularly vulnerable groups. Harris and colleagues discussed the disproportionate negative impacts of MRSA care. They argued that vulnerable groups, such as hospitalized patients, refugees, and aged care facility residents, experience additional side effects, such as isolation when hospitalized [127]. Study participants from these vulnerable groups were likely under-represented in Study II, making it difficult to examine inequity in stigma and poor mental health. Furthermore, in Study III, we were not especially aware of these patient groups in society.

Many telemedicine interventions are “add-on” interventions [214] in line with our intervention. However, for organizations managing MRSA care in the secondary sector, cross-sector videoconferences might be resource efficient. We did not identify substantial parallels in MRSA care, but often, some communication had already been initiated at the hospital, if MRSA had been identified in the hospital setting. Furthermore, the practice staff might have already informed the patient ahead of a shared consultation. To maximize resource efficiency, tasks that were not relevant to all participants were accomplished separately before or after the shared consultation.

4.3.2 Strengths and limitations

One of the strengths of Paper III is that it was a two-center study, which increased transferability. However, as discussed in Paper III, elderly and more vulnerable patients did not participate in the study and only two of the hospital units in RSD participated, which raises a note of caution concerning transferability. Furthermore, it was challenging to recruit participants due to strict inclusion criteria and the COVID-19 pandemic (fewer visits to general practices and a decrease in the number of MRSA cases), resulting in only small-scale testing with eight shared consultations. Another limitation is that the research team or an independent researcher did not directly observe users when testing

the videoconferencing intervention. Additionally, the interviews were only examined by the first author (PhD student), who had also been a central participant in the consultations. Reflections from other researchers and data from various sources could have enhanced the breadth of the analysis and increased objectivity. Participatory design methods presuppose that designers and the same users meet over time for mutual learning, mutual respect, and project commitment [179]. Instead, we used interviews. Alternatively, questionnaires could have been used to examine relation coordination as in earlier work in general practice in Denmark [215], thus making quantitative research possible. Iterations within the design cycle were also a concern with only small-scale workshops and real-use settings without refinement or retesting of the shared consultation. An extended iterative approach could have improved the cross-sector videoconference. For example, a relatively short workshop made it difficult to foster mutual learning, which could have impacted important information for the development of the framework.

To succeed with implementation, the “design-after-design” approach is recommended to make it possible to change and adjust continuously. In other words, the product is not finished, and the process is not “closed” after the product is ready for implementation. The product should be developed as part of a universal strategy to take hold within organizations, and it should be part of a standard system that can be modified to address special needs (building blocks) [179]. As mentioned in Section 4.2.3, access to specialist care in general practice through a video connection is still in its nascent stage in Denmark. The research in the field of videoconferences is in line with missing the design-after-design process, leaving the field with knowledge gaps regarding the scaling-up and sustainability of video consultations in healthcare [216].

To choose the most efficient and cost-effective technologies, an assessment tool for telemedicine applications has been developed. The assessment tool is based on the Health Technology Assessment. The parameters assessed include the clinical effectiveness of technology, patient perspectives, and economic and organizational aspects. The assessment tool unique for technologies addresses supplementary topics, such as patients’ perceptions of

the technology in a separate domain [217,218], which we addressed when interviewing patients. Still, according to the participatory methods used [178] and the abovementioned assessment tool, our study only examined a few aspects of the use of the cross-sector videoconference, which did not include e.g. the underlying working conditions when using videoconferences in organizational analysis. When examining the clinical effectiveness of technology in randomized controlled trials, the use of CONSORT-EHEALTH is recommended [219,220].

Overall, this PhD thesis provides evidence and enriches the study of preventing the spread of MRSA from a broad perspective. Evidence and a broad perspective are important when implementing ethically justifiable MRSA guidelines and when working with the proportionality principle instead of the precautionary principle [127]. In addition, missing evidence and inadequate methods when understanding a particular phenomenon and its causes can induce over-medicalization [126]. It should be noted that the precautions principle is an important risk management tool in public health; for instance, issues caused by uncertain science, complexity, and cultural differences [50]. However, the precautionary principle has dominated the recommendations regarding contact precautions in hospital care and guidelines must be adjusted according to new evidence to compose ethically justifiable MRSA guidelines [128]. However, whether the remaining strategies, to prevent the spread of MRSA, are dominated by the precautionary principle has not yet been studied.

4.4 Meta-view of key limitations

A meta-view of the key limitations, in the three papers included in this thesis, is shown in Figure 10 to 12.

Figure 10: Paper I, meta-view of internal and external validity, and the possible influences on the results

Specific follow-up times

Weakness: We did not examine the specific follow-up times (day 1, 14, 21) on MRSA-positive patients in hospitals, residents of assisted living facilities/persons receiving care, and healthcare staff who were MRSA-positive.

Influence: Preclude findings on the cumulative incidence proportion of adherence to specific follow-up times among MRSA-positive patients in hospitals, residents of assisted living facilities/persons receiving care, and healthcare staff who were MRSA-positive.

Essence: The results on the cumulative incidence proportion of adherence to MRSA follow-up swabs apply for standard follow-up times (posttreatment follow-up at 1 and 6 months) only.

Information on decolonization treatment

Weakness: We used registry data on the prescription of 2% mupirocin nasal ointment to estimate completed decolonization treatment. Mupirocin might have been prescribed for other reasons than MRSA carriage.

Influence: The risk of being allocated to the wrong group (treated instead of non-treated) is considered minimal.

Essence: Low risk of information bias (non-differential).

Occupation category

Weakness: We included retirement and early retirement as an occupation category even though this group is not exposed to working conditions and their earlier working conditions are unknown.

Influence: An explanation of increased successful decolonization treatment and adherence towards control swab sampling might instead of occupation be a higher burden of illness in general within this 65+ group and therefore an increased risk of severe MRSA infections leading to preventive efforts such as an increased focus on becoming MRSA-free.

Essence: Other factors than retirement and early retirement might be associated with the increased successful decolonization treatment and adherence towards control swab sampling within these groups of retired persons.

Characteristics of treated and non-treated

Weakness: 49% did not undergo MRSA decolonization treatment. To consider if the patients, who underwent treatment were different from those who did not undergo decolonization treatment, we conducted a sensitivity analysis comparing demographics and socioeconomic characteristics on the date of the patients first positive MRSA sample (date of MRSA diagnosis).

Influence: It is most likely that the main group of non-treated individuals is related to livestock MRSA (no treatment indication according to the Danish guidelines) and not to differences in socioeconomic factors. However, there is a risk of underestimating associations between socioeconomic factors, and adherence to MRSA follow-up swabs taken after 1 and 6 months due to the overrepresentation of individuals who immigrated to Denmark within the last five years in the group of non-treated compared to treated. This also applies to the associations between socioeconomic factors and successful decolonization treatment.

Essence: Associations between socioeconomic factors (recently immigrated) and adherence to MRSA follow-up swab sampling, and successful decolonization treatment might be underestimated.

Confounding

Weakness: The study was a cohort study, which induces a risk of confounding. To reduce the risk of confounding a cluster-based logistic regression model was carried out. Strong associations (risk ratio> 5) were not found in the current study, which increases the risk of confounding.

Influence: Due to the risk of known and unknown confounders, conclusions regarding causal relationships between adherence to MRSA follow-up swab sampling after 1 and 6 months should be presented with large reservations. This also applies to the causal relationships between socioeconomic factors and successful decolonization treatment.

Essence: Conclusions regarding causal relationships should be presented with large reservations.

Figure 11: Paper II, meta-view of internal and external validity, and the possible influences on the results

Low response rate

Weakness: A sensitivity analysis was carried out to examine the characteristics between respondents and non-respondents, but only a few data were available on non-respondents making a comprehensive sensitivity analysis infeasible.

Influence: The younger population (18 to 40 years old) responded less frequently to the questionnaire (65% did not respond), which may lead to a risk of selection bias. The younger population has in general few healthcare contacts and a lower risk of severe infections, leading to an expected lower degree of having a threatening view of MRSA, being stigmatized, and having a poor mental health state.

Essence: Due to the risk of selection bias, the psychosocial burdens and the illness perception related to the MRSA diagnosis are likely to be overestimated.

Large-scale drop-out during follow-up

Weakness: To prevent selection biases we carried out a mixed-effect model analysis (uses all available information from respondents who do not provide data from all events).

Influence: Dropouts might **not** have occurred at random: The characteristics of the lost participants might not be similar over time which can lead to an under- or overestimated degree of stigmatization, poor mental health, and having a threatening view of MRSA. Most likely it is an overestimation over time, due to those perceiving negative consequences of having MRSA might have been overrepresented in answering the questionnaires at all three time points.

Essence: There is a risk of selection bias, which is most likely to overestimate the psychosocial burdens and illness perception related to the MRSA diagnosis.

Few respondents with a poor or very poor health state

Weakness: Selection bias might have occurred.

Influence: This group of patients often experiences additional side effects, such as isolation when hospitalized, which might lead to an underestimation of perceived stigmatization, poor mental health, and having a threatening view of MRSA in the study.

Essence: There is a risk of selection bias, which most likely leads to underestimating the psychosocial burdens and the illness perception related to the MRSA diagnosis.

Self-reported data only

Weakness: Information bias might have occurred e.g. on information of MRSA clearance or MRSA infection. Data from national registries could have provided more valid information.

Influence: Using self-reported data may both under- and overestimate the results due to the patients' perhaps erroneous perceptions e.g. on MRSA clearance or MRSA infection.

Essence: The risk of information biases due to self-reported data may either under- or overestimate the results.

Measurement of complex phenomena by questionnaires

Weakness: Qualitative methods are an advantage when studying complex phenomena such as mental health and stigmatization. However, the analysis of sub-domains induces a more detailed and nuanced description of a phenomenon e.g. the stigmatization scale, which included personalized stigma, disclosure concerns, negative self-image, and public attitudes.

Influence: The use of quantitative methods might simplify the measurement of complex phenomena and might therefore induce information bias (low content validity). However, when examining sub-domains the risk of information bias is reduced.

Essence: There is a risk of low content validity when measuring complex phenomena.

Small sample size

Weakness: Only 135 participated in the study at 1 month, 67 participated at six months and, 48 participated at twelve months.

Influence: Reduced statistical precision might lead to type II error especially when analyzing data from the timepoint at six and twelve months.

Essence: There is a risk of type II error.

Confounding

Weakness: We used a linear regression model which reduces the risk of confounding. However, there is limited knowledge about confounders within this research field.

Influence: Due to the risk of known and unknown confounders, conclusions regarding causal relationships between MRSA carriers and MRSA infections should be presented with large reservations. This also applies to the causal relationships between having MRSA at one month compared to six and twelve months after the MRSA diagnosis.

Essence: Conclusions regarding causal relationships should be presented with large reservations.

External validity

Weakness: Those aged below 18 and those who were not literate in Danish were not included in the study. Furthermore, few respondents had a poor or very poor health state and the younger population (18 to 40 years old) responded less frequently to the questionnaire.

Influence: No information is available on the degree of stigmatization, poor mental health, and illness perception among children. Furthermore, there are also limited insights on these measurements on groups from other cultures than the Danish. Thereby potential cultural and age-related differences, in the degree of stigmatization, poor mental health, and having a threatening view of MRSA, may not be noticed.

Essence: The result might not be generalizable to individuals aged below 18, those who are not literate in Danish, the younger population (18 to 40 years old), and individuals having a poor or very poor health state.

Figure 12: Paper III, meta-view of undesirable or hidden skewness, transferability, and the possible influences on the results.

Predetermined intervention

Weakness: It was predetermined that specialist expertise should be delivered through a video connection. Furthermore, the infection control nurse (specialist expertise) should be placed in the hospital and the patient, the patient's family, and the practice staff should be located at the general practice clinic. According to the theory of participatory design, predetermined interventions are not recommended therefore the study was a participatory design-inspired study only.

Influence: Other interventions suitable for management of MRSA care in low prevalence settings, comprising complexity but no need for special medical equipment, might have been superior or equivalent compared to the cross-sectoral videoconference in the present study.

Essence: Other ways to manage MRSA care might be superior or equivalent compared to the cross-sectoral videoconference.

Limited use of the iterative approach in the design process

Weakness: Iterations were limited due to one small-scale workshop and due to small-scale testing of the cross-sectoral videoconference, which was not refined or retested after the first test in clinical practice.

Influence: There is a risk that not all possible scenarios for the cross-sectoral videoconference were discussed. Therefore important perspectives, needs, and ideas from end-users might not have been included leading to a model not fitting the actual needs of all end-users e.g. the needs of specific patient groups (e.g., elderly or patients without indication for decolonization treatment).

Essence: A more intensive use of the iterative approach could have ended up with a more sufficient understanding of the needs of end-users and a broader perspective on how to manage MRSA care most appropriately.

Subjectivity and reflexivity

Weakness: Subjectivity arises when the effect of the researcher is ignored. The researchers' background and position will affect the results of qualitative studies. To account adequately for the effects of the PhD student, who had the primary responsibility of the study, her background and position were discussed. To create adequate distance from the study setting, interviews were performed by an independent infection control nurse. Reflexivity was maintained by looking at the data and the interpretation for competing conclusions. Despite the above-mentioned strategies to improve objectivity and reflexivity, the pursuit of diversity and contradictions might be limited.

Influence: Preconceptions from the PhD student about the positive effect of bringing specialist competencies of MRSA care into general practice might have overestimated the effect of the cross-sectoral videoconference despite several efforts to promote objectivity and reflexivity.

Essence: Preconceptions might have led to an overestimating effect of the cross-sectoral videoconference, and essential perspectives of the cross-sectoral videoconference might have been neglected.

Transferability

Weakness: The research aims to produce information that can be shared and applied beyond the study setting, however, elderly, and more vulnerable patients did not participate in the study and the study was carried out in a setting in which general practice is the main healthcare provider in MRSA care programs. This raises a note of caution concerning transferability. However, we included a diverse study population, when testing the cross-sectoral videoconference in clinical practice.

Influence: The study findings might not provide transferable results for elderly, vulnerable patients(e.g. homeless) and patients not literate in Danish or in settings in which MRSA care programs are carried out by a MRSA specialist in a hospital setting. However, the results are transferable for individuals with the following characteristics: Live-stock-associated MRSA, different family sizes, families with children under the age of two, patients with eczema, pregnancy, and working in healthcare. Groups of patients, which were represented in the study.

Essence: Caution concerning transferability for especially elderly, vulnerable patients not literate in Danish.

CHAPTER 5 I PERSPECTIVES AND CONCLUSION

In this chapter, perspectives and a conclusion for Papers I–III are presented. Perspectives are divided into implications for future research and implications for clinical practice and are listed only. For a complete overview, please read Papers I–III in the Appendix.

5.1 Perspectives

5.1.1 Implications for future research

Paper I

- To validate register measurement methods for assessing the success rate of decolonization treatment by comparing register data with data from medical records containing information on treatment, non-compliance, and MRSA samples.
- To examine how to measure geographical inequality in MRSA management and care.
- To examine how to increase the efficiency of decolonization treatment.

Paper II

- Further development of the measurement of stigmatization and mental health among individuals diagnosed with MRSA with a particular focus on content validity.
- To examine whether stigmatization, poor mental health, and a threatening view of MRSA influences test behavior, disclosure, and non-compliance with decolonization treatment.
- To examine interventions at the intrapersonal, interpersonal, institutional, and governmental levels, aimed to decrease stigmatization and rejections from healthcare services among individuals diagnosed with MRSA.
- To confirm or reject that stigmatization, poor mental state, and having a threatening view of MRSA do not decrease over time among individuals diagnosed with MRSA.

Paper III

- To examine interventions on the intrapersonal level, which also includes efforts to decrease the vulnerability of disadvantaged people and stigmatization, and compensate for geographical inequality. All patients, not only those with an indication for decolonization treatment, should be included in the intervention.
- To examine these interventions' clinical efficiency (e.g., infections, decolonization treatment, inequality, and psychosocial health) and cost efficiency in a randomized controlled trial study design.

5.1.2 Implications for clinical practice

- Provide information about the possibility of re-colonization after decolonization treatment.
- Increase health literacy in vulnerable individuals with MRSA undergoing decolonization treatment.
- Continuing the initiative of free MRSA decolonization treatment in the RSD
- Provide interventions to reduce stigmatization and poor mental health among individuals diagnosed with MRSA; Interventions can be provided at an intrapersonal, interpersonal, institutional, and governmental level with particular awareness of vulnerable groups (e.g., residents in nursing homes or hospitalized populations).
- Strengthen the collaboration between hospitals and general practice clinics in MRSA management and care, especially in low population density areas and urban deprived areas.
- Prevent infections caused by MRSA to decrease additional burdens of illness.

5.2 Conclusion

The overall conclusion is that adherence to follow-up swabs and the success rate of MRSA decolonization treatment are presently sub-optimal in the RSD. A higher success rate of MRSA decolonization was associated with being able to

retire early, having a higher education, and living in more densely populated areas. Furthermore, MRSA-infected individuals perceived MRSA as more threatening than MRSA carriers; however, infected individuals and carriers both perceived the same levels of poor mental health and stigmatization, which did not decrease over time. Finally, both practice staff and patients experienced a few disadvantages with the cross-sector videoconferencing intervention; however, the majority found the model useful when a physical meeting was not possible. Research should address how to increase the efficiency of MRSA clearance and how to minimize and equitize psychosocial downsides and socioeconomic and geographical health inequalities.

CHAPTER 6 I META-VIEW

In this chapter, a meta-view of the three papers included in this thesis is shown in Figure 13.

Figure 13: Meta-view of Papers I–III

PAPER I	PAPER II	PAPER III
The association between socioeconomic factors and the success of decolonization treatment among individuals diagnosed with methicillin-resistant Staphylococcus aureus	Mental health, stigma, and illness perception among individuals diagnosed with methicillin-resistant *Staphylococcus aureus*	A framework for methicillin-resistant Staphylococcus aureus consultations comprising cross-sectoral videoconferences between patient, general practice, and specialist expertise
DESIGN	**DESIGN**	**DESIGN**
Cohort study Follow-up: Two years	Longitudinal cohort study Follow-up: One year	Participatory design-inspired study
PARTICIPANTS	**PARTICIPANTS**	**PARTICIPANTS**
MRSA-diagnosed treated for MRSA-carriage	MRSA-infected MRSA carriers Age ≥ 18 years Literate in Danish	Phase 1: Stakeholders familiar with MRSA care Phase 2: Practice staff and patients planned to begin MRSA decolonization treatment
DATA	**DATA**	**DATA**
National registers Regional MRSA database	Questionnaires	Phase 1: Post-it labels from a workshop Phase 2: Semi-structured interviews

RESULTS
2,536 individuals were included in the analysis of adherence to follow-up swab sampling. The adherence to MRSA follow-up swab sampling 1 month after treatment was 66% and 30% after 6 months. Higher rates of adherence to follow-up swab sampling were associated with living in predominantly urban (160–900^{+} inhabitants per km^{2}) or intermediate municipalities (76–159 inhabitants per km^{2}) or having retired. 2,432 individuals were included in the analysis of the success rate of decolonization treatment. The rate of successful decolonization treatment was 36% two years after completed treatment. Early retirement, being more educated, and living in intermediate municipalities or predominantly urban municipalities were associated with a higher success rate.

RESULTS
135/316 individuals (response rate 43%) were included 1 month after being diagnosed with MRSA. 67/272 individuals (response rate 25%) were included 6 months after being diagnosed with MRSA. 48/230 individuals (response rate 21%) were included 12 months after being diagnosed with MRSA. From 1 to 12 months after the MRSA diagnosis the rate of perceived stigmatization and poor mental health state was: Clear stigma: 11–13% Abandoned from healthcare: 8–19% Poor mental health: 16–24% The primary type (subdomain) of stigmatization was: “Disclosure” and “public attitude” The primary type (subdomain) of poor mental health was: “Well-being” The primary type (subdomain) of having a threatening view of MRSA was:

RESULTS
Phase 1 Seven stakeholders were included. The framework was organized as structured and included: A shared consultation (30 minutes), which consisted of a list of potential themes to discuss: A summary of the MRSA care program, questions from patients and household members, information matching the patient’s needs, planning of the MRSA care program, and consideration of the need for further support. A summary of the conclusions of the shared meeting was made available to all participants through the electronic patient record. Tasks that were not relevant for all participants were accomplished separately before and after the shared consultation, e.g. to book consultations for follow-up or interprofessional talk between practice staff and the infection control nurse.

RESULTS, CONT.	RESULTS, CONT.	RESULTS, CONT.
Low income, unemployment or welfare payments, recent residence in Denmark, and household crowding were not associated with lower rates of adherence to follow-up swab sampling or with lower rates of successful decolonization treatment.	"Low treatment control", "long time-line", and "low personal control". Being MRSA-infected was associated with having a more threatening perception of MRSA in terms of increased levels of symptoms and perceived consequences compared to MRSA carriers. Being MRSA-infected was not associated with higher degrees of stigmatization or poor mental health state compared to MRSA carriers. However, the associations were borderline significant. Having MRSA at 6 months compared to 1 month after being diagnosed with MRSA was associated with lower treatment control of MRSA. Having MRSA at 12 months compared to 1 month after being diagnosed with MRSA was associated with a longer time-line for having MRSA.	Phase 2 Eight consultations (eight patients and seven practice staff) were included. Interviews with patients and practice staff showed that MRSA care is a complex process that benefits from cross-sector collaboration. Relationships between participants were characterized by mutual respect and shared knowledge, and the communication was characterized as problem-solving and accurate. Few of the practice staff perceived the shared consultation as time-consuming, and they asked for a clearer description of roles and responsibilities. The main barrier identified by a few patients was the wish for face-to-face consultations with the infection control nurse, but contrary to the practice staff, patients found the cross-sector videoconference time efficient.

CONCLUSIONS	CONCLUSIONS	CONCLUSIONS
Adherence to follow-up swab sampling and the success rate of MRSA decolonization treatment are sub-optimal in the RSD. A higher success rate of MRSA decolonization was associated with being able to retire early, having a higher education, and living in more densely populated areas.	MRSA-infected individuals perceived having MRSA as more threatening than MRSA carriers. However, both infected individuals and carriers perceived the same levels of poor mental health and stigmatization, which did not became less over time.	Both practice staff and patients experienced a few disadvantages with the cross-sector videoconferencing intervention. However, the majority found the model useful when a physical meeting was not possible.

PERSPECTIVES

Implications for research:

- Increase the efficiency of MRSA clearance.
- Minimize and equitize psychosocial downsides among MRSA carriers and MRSA-infected.
- Minimize socioeconomic and geographical health inequalities in MRSA care.

Implications for clinical practice:

- Increase health literacy in vulnerable individuals with MRSA undergoing decolonization treatment.
- Continuing the initiative of free MRSA decolonization treatment in the RSD.
- Provide interventions to reduce stigmatization and poor mental health; Interventions can be provided at an intrapersonal, interpersonal, institutional, and governmental level with particular awareness of vulnerable groups (e.g., residents in nursing homes or hospitalized populations).
- Strengthen the collaboration between hospitals and general practice clinics in MRSA management and care, especially in low population density areas and urban deprived areas.
- Prevent infections caused by MRSA to decrease additional burdens of illness.

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SUMMARY

Methicillin-resistant *Staphylococcus aureus* (MRSA) causes morbidity and mortality worldwide. To prevent the spread of MRSA, most European countries have implemented a strategy that includes case finding, contact precautions during hospitalization, and the decolonization treatment of MRSA carriers. A downside of this strategy is stigmatization, poor mental health, and reduced quality of care among MRSA carriers. Information about MRSA, decolonization treatment, and MRSA follow-up swabs is mainly provided by practice staff in the Region of Southern Denmark. It might be a challenge to acquire and maintain MRSA competencies in general practice, due to low MRSA prevalence and guideline complexity. In the Region of Southern Denmark, the effect of decolonization treatment has not been studied and internationally it is not known whether there is a socio-economic inequality in the effect of decolonization treatment. Psychosocial consequences and illness perception between infected and carriers have been sparsely examined and further, we do not know if these consequences are long-lasting. In addition, there is very little research into how MRSA care programs are organized. This PhD thesis consists of one published paper and two manuscripts. The published paper (Paper I) and the two manuscripts (Paper II and Paper I) are based on three studies conducted from 2020 to 2022 in the Region of Southern Denmark using three different study populations.

The primary objective of Paper I was to examine whether socioeconomic factors were associated with successful decolonization treatments. The study was a co-hort study featuring data from Danish national registers and a regional MRSA database. We included 2,536 individuals who initiated MRSA decolonization treatment between 2007 and 2018. Each person had a follow-up of 2 years. We found that adherence to follow-up swabs was 66% 1 month and 30% 6 months after decolonization treatment. The success rate of decolonization treatment was 36%. Early retirement, being more educated, and living in municipalities with a high population density were associated with a higher success rate of MRSA clearance.

In Paper II, the objective was to investigate stigmatization, mental health, and illness perception among patients with either MRSA infection or MRSA carriage 1 month after the MRSA diagnosis and to investigate the association between stigmatization, mental health, and illness perception at 6 and 12 months compared to 1 month after MRSA diagnosis. We used a longitudinal cohort design based on data from the questionnaires. We included 135 individuals with MRSA and each individual had a follow-up of 1 year. Participants included were literate in Danish, over 17 years of age, and residents in the Region of Southern Denmark. In total, 11% of the participants perceived a clear stigma, 19% had been abandoned by healthcare services, and 24% had a poor mental health state. Carriers and infected individuals perceived the same level of poor mental health and stigmatization. However, being infected was associated with higher levels of symptoms and perceived consequences. We found no changes in stigmatization or mental health state within the first year of diagnosis. However, an increased timeline for continued MRSA positivity and a more threatening view of the control of treatment was found.

The objective of Paper III was to develop a framework for cross-sector videoconferencing and to pilot test this framework in MRSA consultations in clinical practice. In the cross-sector videoconference, an infection control nurse participated in the MRSA consultation. A participatory design-inspired study was conducted to ensure systematic user involvement. To develop the framework for the cross-sector videoconference, we conducted a workshop for stakeholders who were familiar with MRSA care programs. Subsequently, this framework was pilot tested in clinical practice. In the pilot test, we included eight patients diagnosed with MRSA who planned to initiate decolonization treatment and the participating patients' practice staff. The result was a structured framework whose main focus was to solve real-time patient needs and plan the MRSA care program. The pilot test showed that MRSA care is complex and that it benefits from cross-sectional collaboration. The relationship during the cross-sector videoconference was characterized by mutual respect and shared knowledge, and the communication was characterized as problem-solving and accurate.

Few among the practice staff perceived the shared consultation as time consuming and asked for a clearer description of roles and responsibilities. The main barrier identified by a few of the patients was the wish for face-to-face consultations with the infection control nurse, but contrary to practice staff, the patients found the cross-sector videoconference time efficient.

The overall conclusion is that adherence to follow-up swabs and the success rate of MRSA decolonization treatment were suboptimal. A higher success rate of MRSA decolonization was associated with being able to retire early, having a higher education, and living in more densely populated areas. Furthermore, MRSA-infected individuals perceived MRSA as more threatening than MRSA carriers; however, infected individuals and carriers perceived the same levels of poor mental health and stigmatization, which did not decrease over time. Finally, both practice staff and patients experienced a few disadvantages with the cross-sector videoconferencing intervention; however, the majority found the model useful when a physical meeting was not possible. Future research should aim to discover ways to increase the efficiency of MRSA clearance and minimize psychosocial downsides and socioeconomic and geographical inequalities.

RESUMÉ

Methicillin-resistent *Staphylococcus aureus* (MRSA) kan medføre øget sygelighed og dødelighed. For at forebygge smittespredning med MRSA har de fleste europæiske lande derfor iværksat tiltag, herunder undersøgelse for MRSA i udvalgte grupper, isolation under hospitalsindlæggelse samt behandling af MRSA-bærertilstand. En negativ konsekvens af forebyggelsesindsatsen er risiko for stigmatisering, et dårligere mentalt helbred samt reduceret behandlings- og pleje kvalitet blandt personer med MRSA-bærertilstand. I Region Syddanmark varetages information, bærerskabsbehandling og de efterfølgende kontrolundersøgelser i almen praksis. Det kan være en udfordring at tilegne sig og fastholde kompetencer i almen praksis, da MRSA-prævalensen er lav og retningslinjen kompleks. I Region Syddanmark er effekten af bærerskabsbehandlingen ikke undersøgt, og internationalt vides det ikke, om der er socioøkonomisk ulighed i effekten af bærerskabsbehandlingen. Forskellen mellem psykosociale konsekvenser og sygdomsopfattelsen blandt personer med enten infektion eller bærerskab er sparsomt undersøgt, og det vides ikke om konsekvenserne ændres over tid. Derudover er der meget få undersøgelser af, hvordan MRSA-forløb varetages hensigtsmæssigt organisatorisk. Denne Ph.d. afhandling er baseret på en artikel udgivet i et internationalt tidsskrift og to manuskripter. Grundlaget for artiklen (artikel I) og manuskripterne (artikel II og artikel III) er tre studier, der blev udført fra 2020-2022 i Region Syddanmark med tre forskellige studiepopulationer.

Det primære formål med artikel I var at undersøge, om socioøkonomiske faktorer var associeret med effekten af bærerskabsbehandlingen. Studiet var et kohorte studie, hvor data fra en regional MRSA database og nationale registre blev anvendt. Vi inkluderede 2536 personer, som var påbegyndt bærerskabsbehandlingen mellem 2007 og 2020. Hver person blev fulgt i 2 år. Undersøgelsen viste, at compliance til den opfølgende undersøgelse for MRSA var 66% efter 1 måned og 30% 6 måneder efter bærerskabsbehandlingen. 36% var MRSA-fri. At være efterlønsmodtager, høj uddannet og at være bosiddende i en tætbefolket kommune, var associeret med en højere behandlingseffekt.

I artikel II var formålet at undersøge stigmatisering, mentalt helbred samt sygdomsforståelse blandt personer med henholdsvis MRSA infektion og bærerskab 1 måned efter MRSA-diagnosen. Derudover var formålet at undersøge stigmatisering, mentalt helbred og sygdomsforståelse 1 måned efter påvist MRSA sammenlignet med 6 og 12 måneder efter påvist MRSA. Vi anvendte et longitudinelt kohorte studie baseret på spørgeskemadata. Vi inkluderede 135 personer med MRSA, og hver person havde en opfølgningsperiode på 1 år. Deltagerne var dansktalende, over 17 år og bosiddende i Region Syddanmark. 11% oplevede tydelig stigmatisering, 19% var blevet afvist fra behandlinger i sundhedsvæsenet, og 24% oplevede at have et dårligt mentalt helbred 1 måned efter, de havde fået påvist MRSA. Personer med MRSA infektioner oplevede flere symptomer, og at MRSA i højere grad påvirkede deres liv, men der var ingen forskel i graden af stigmatiseringen eller mentalt helbred blandt bærere og infektiøse. Derudover var der ikke forskel i graden af stigmatiseringen eller mentalt helbred i løbet de 12 måneder, dog var der en forventning om en forlænget varighed af, at være MRSA-positiv og tiltroen til vellykket behandling af MRSA var reduceret.

Formålet med artikel III var at udvikle en drejebog for en tværsektoriel videokonference, og teste drejebogen for MRSA konsultationer i klinisk praksis. I den tværsektorielle videokonference deltog en hygiejnesygeplejerske i MRSA konsultationen, som fandt sted i almen praksis. For at sikre systematisk brugerinvolvering blev der anvendt et participatory design inspireret studie. For at udvikle drejebogen til den tværsektorielle videokonference blev der afholdt en workshop for interessenter i MRSA-forløb. Efterfølgende blev drejebogen pilot-testet i klinisk praksis. Vi inkluderede 8 patienter, der var diagnosticeret med MRSA, og hvor der var indikation for at påbegynde bærerskabsbehandling og patientens lægehus. Resultatet var en struktureret drejebog, hvis primære formål var at imødekomme patientoplevede behov samt planlægge MRSA-forløbet. Pilot-testen viste, at MRSA-forløb er komplekse, og at det var fordelagtig med et tværsektorielt samarbejde. Relationen mellem deltagerne var karakteriseret af gensidig respekt ved at generere fælles viden.

Kommunikationen var karakteriseret ved at være nøjagtig og problemløsende. Enkelte blandt praksispersonalet oplevede, at den fælles konsultation var forbundet med et øget tidsforbrug, og at der manglende en tydelig afklaring af rolle- og ansvarsfordelingen mellem praksispersonalet og hygiejnesygeplejersken. Den væsentligste barriere, set fra patienternes perspektiv, var at få af patienterne foretræk at hygiejnesygeplejersken var fysisk tilstede, men modsat praksispersonalet syntes patienterne, at videokonferencen var tidseffektiv.

Den overordnede konklusion af de tre studier er, at compliance til kontrolpodninger samt effekten af bærerskabsbehandlingen var suboptimal. En højere effekt af bærerskabsbehandlingen var associeret med muligheden for at gå på efterløn, have en høj uddannelse og bo i områder med højere befolkningstæthed. Derudover oplevede patienter med infektion MRSA som mere truende sammenlignet med MRSA koloniserede, men begge grupper oplevede samme grad af stigmatisering og dårligt mentalt helbred, hvilket ikke aftog over tid. Både praksispersonale og patienter oplevede, at der var nogle få ulemper ved at anvende den tværfaglige videokonference. Hovedparten fandt dog modellen brugbar, når et fysisk møde ikke var muligt. Fremtidig forskning bør fokusere på, hvordan man øger effekten af MRSA bærerskabsbehandlingen, og hvordan man minimerer psykosociale konsekvenser samt uligheden i socioøkonomi og geografi.

APPENDIX

1. Paper I: Published version, Infection Control & Hospital Epidemiology
2. Paper II: Version in preparation to be submitted
3. Paper III: Version in preparation, Scandinavian Journal of Primary Health Care

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SHEA

Original Article

The association between socioeconomic factors and the success of decolonization treatment among individuals diagnosed with methicillin-resistant *Staphylococcus aureus*: A cohort study from 2007 to 2020

Mette Assenholm Kristensen MHSc[1,2], Julia Skov Abrantes BSc[3], Hanne Irene Jensen PhD[2,4], Christian Backer Mogensen PhD[2,5], Jens Søndergaard PhD[6] and Jens Kjølseth Møller DMSc[1,2]

[1]Department of Clinical Microbiology, Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark, [2]Department of Regional Health Research, University of Southern Denmark, Odense, Denmark, [3]Department of Quality, Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark, [4]Department of Anesthesiology and Intensive Care, Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark, [5]Department of Emergency Medicine, Hospital Sønderjylland, University Hospital of Southern Denmark, Aabenraa, Denmark and [6]Research Unit of General Practice, Department of Public Health, University of Southern Denmark,Odense, Denmark

Abstract

Objectives: To examine associations between socioeconomic factors and (1) adherence to methicillin-resistant *Staphylococcus aureus* (MRSA) posttreatment follow-up swab sampling after 1 and 6 months and (2) successful decolonization treatment.

Design: Cohort study with 2 years of follow-up. Data on patients diagnosed with MRSA were extracted from a regional MRSA database and national registries. We used a cluster-based logistic regression model to estimate the adjusted odds ratios (aOR) and 95% confidence interval (CI) for associations between socioeconomic factors and decolonization treatment.

Setting: Danish primary health care.

Results: The rate of adherence to posttreatment follow-up swab sampling among 2,536 cases 1 month after decolonization treatment was 66% (95% CI, 64%–68%), and it decreased to 30% (95% CI, 28%–32%) after 6 months. Living in intermediate municipalities (76–159 inhabitants/km2) or having retired were associated with completed posttreatment follow-up swabs 1 month after decolonization treatment: aOR, 1.40 (95% CI, 1.2–1.74) and aOR, 2.67 (95% CI, 1.16–6.13), respectively. The rate of successful decolonization treatment 2 years after initiating treatment was 36% (95% CI, 34%–38%). Factors associated with successful decolonization treatment included individuals with higher education (aOR, 1.62; 95% CI, 1.22–2.15), early retirees (aOR, 1.63; 95% CI, 1.12–2.38), those living in intermediate municipalities (ie, 160–900+ inhabitants/km2; aOR, 1.35; 95% CI, 1.08–1.68), and those living in predominantly urban municipalities (ie, 160–900+ inhabitants/km2; aOR, 2.04; 95% CI, 1.5–2.76).

Conclusions: Disparities in the effect of decolonization treatment and adherence to MRSA follow-up sampling among MRSA-positive individuals appear to be largely explained by the level of education, area of residence, and employment status.

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Antimicrobial drug resistance poses a major global threat to human health. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a leading cause of death associated with antimicrobial resistance.[1] MRSA carriage also has considerable social and psychological consequences for those diagnosed with it.[2] Despite better overall health, health inequalities still exist in European countries.[3] Studies have reported higher rates of communicable diseases among people with lower socioeconomic status.[4,5] In some high-income countries, antibiotic-resistant infections are likelier among the unemployed and low-income populations living in deprived neighborhoods.[4,6] Therefore, social factors related to infectious diseases have also become a public health priority in high-income countries to limit the disease burden on individuals and to decrease the spread of infectious diseases in communities and healthcare systems.[7] Overcrowding, low education, an urban living environment, and recent immigration seem to increase MRSA rates.[8,9] Length of education is strongly linked to health literacy skills and, consequently, to the ability to act upon health information. Furthermore, low health literacy is strongly associated with poor adherence to treatment.[10,11]

Author for correspondence: Mette Assenholm Kristensen, E-mail: mette.assenholm.kristensen@regionsyddanmark.dk

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Denmark has small-scale social and economic inequalities. The public healthcare system is mainly tax funded and free for all citizens.[12] To maintain a low prevalence of disease caused by MRSA in Denmark, national guidance on preventing the spread of MRSA includes offering sampling for MRSA and decolonization treatment for MRSA-positive individuals.[13] All household members of MRSA carriers are also offered decolonization treatment.[13] Risk factors for failed MRSA carriage decolonization treatment are typically based on individual risk factors (eg, skin lesions and throat carriage).[14] However, little is known about the importance of socioeconomic factors for adherence to follow-up swab sampling and MRSA cure rates after decolonization treatment. Therefore, we examined whether socioeconomic factors are associated (1) with adherence to MRSA posttreatment follow-up swab sampling after 1 and 6 months and (2) with successful decolonization treatment. We hypothesized that low socioeconomic status is associated with lower rates of adherence to MRSA posttreatment follow-up swab sampling and a lower success rate of decolonization treatment of MRSA carriage.

Methods

Study design and setting

We conducted a cohort study using prospectively collected register-based information at the individual level for MRSA-diagnosed individuals (asymptomatically colonized or infected with MRSA) in the Region of Southern Denmark (RSD) (population, ~1.2 million). The follow-up time was 2 years. Based on the first Danish national guidance on preventing the spread of MRSA from 2006 and a national reorganization (Danish Municipal Reform) of all municipalities and regions in 2007, we chose the study period 2007–2020. In the RSD, decolonization treatment and follow-up swab sampling are mainly handled by general practice staff, with guidance from the department of clinical microbiology upon request. MRSA carrier treatment is free for all household members. Public interpretation services are available for foreign-speaking citizens. The main part of the study period was conducted in an endemic setting with a low prevalence of MRSA (ie, 49.5 asymptomatic colonization or clinically apparent infections with MRSA per 100,000 inhabitants).[15] However, 2 nosocomial outbreaks have been described.[16,17] The Danish national guidance on preventing the spread of MRSA was revised in 2012 (ie, primary changes: livestock MRSA added, routine follow-up swab sampling should be taken at 6 months instead of 12 months after decolonization treatment) and in 2016 (minor revision). In Denmark, all citizens with a permanent residence are assigned a 10-digit Central Personal Register number, which is used in all Danish public registries, allowing the linkage of data on individuals. Furthermore, families are assigned a unique family identifier.[18]

This study has been reported according to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for antimicrobial stewardship.[18] Permission to store data was registered in Record of Data Processing Activities in the RSD (no. 20/25135), and the study was approved by the Danish Patient Safety Authority (no. S-31-1521-375). It was not necessary to obtain ethical approval for this project (no. S-20192000-155).

Participants

We included MRSA-diagnosed patients who were treated for 5 or 10 days (throat carriers) with 2% mupirocin nasal ointment (Bactroban nasal) in the primary healthcare sector from 2007 to 2018. Patients were included from the day the prescription of the initial decolonization treatment was redeemed. Information on cases with later colonization or infection with MRSA (relapse) after successful decolonization treatment was not included in the analysis. We excluded individuals who died, moved from the region, or left Denmark within 2 years of follow-up. In the analysis of success rate, we excluded participants who did not have post-treatment follow-up swab samples taken after 6 months. MRSA-diagnosed individuals were identified using a regional MRSA database. Statistics Denmark replaced Central Personal Register numbers with unique identifier numbers (pseudo-anonymized), and the study population (MRSA-diagnosed individuals) was matched with national registry data.

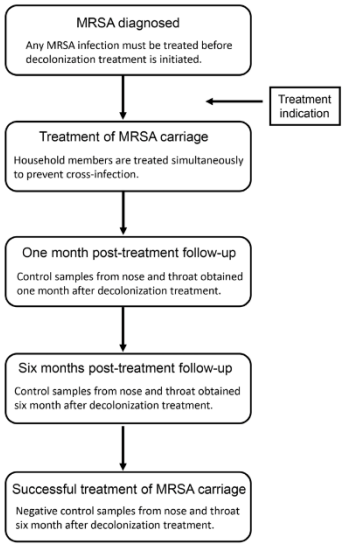

Fig. 1. Treatment of MRSA carriage: Posttreatment follow-up and successful decolonization treatment.

Decolonization

In Denmark, MRSA carriage is treated with a topical application of 2% mupirocin to the anterior nose twice a day, combined with daily bathing with 4% chlorhexidine gluconate and environmental cleaning for 5 days. In cases of throat carriage, the treatment period is extended to 10 days and retreatment is recommended in case of treatment failure. Treatment is not recommended for children aged <2 years or for individuals with day-to-day contact with live pigs. There is no general recommendation to test household

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Table 1. Variables Describing Socioeconomic Factors

Variable	Definition	Data Administrator and Data Source
Disposable family income	The amount of money that the household has available for spending and saving after income taxes and interest expenses has been accounted for.	Statistics Denmark: The Income Statistics Register
Highest education completed	The highest education that a person has completed at any given point in time.	Statistics Denmark: The Population Education Register
Employment status	Attachment to the labor market from age 15 years. Includes all persons having an income during the year chargeable to income tax in Denmark.	Statistics Denmark: The Register-based Labour Force Statistics
Length of residence in Denmark	Years since immigration to Denmark or birthdate if born in Denmark	The Danish Civil Registration System
Household crowding	Residential size (m^2) and the number of individuals living at the same address (family identifier).	Statistics Denmark: The Central Register of Buildings and Dwellings and The Danish Civil Registration System
Population density	Inhabitants per square kilometer	Statistics Denmark: The Danish Civil Registration System and an analyst note published by Local Government Denmark describing inhabitants per square kilometer for each municipality in Denmark

members before beginning treatment. Posttreatment MRSA follow-up swab samples are recommended 1 and 6 months after treatment. MRSA carriage treatment is considered effective when swab samples taken from the nose and throat are negative 6 months (or later) after decolonization treatment.[13]

Outcome and exposure variables

For each patient with laboratory-confirmed MRSA, we collected information on sampling dates and laboratory results of all samples examined for MRSA in the regional MRSA database, which includes samples taken within hospitals and the community. Laboratory examinations of MRSA were done using either rapid screening of samples with polymerase chain reaction (PCR) and/or routine culture methods for detection of MRSA in clinical samples according to the European quality standard.[16,17] MRSA posttreatment follow-up swab sampling was defined as sets of MRSA cultures from the nose and throat 1 and 6 months after decolonization treatment. Successful decolonization treatment was defined as a set of negative MRSA samples from the nose and throat at least 6 months after completing the decolonization treatment and before the end of the 2-year follow-up. Figure 1 briefly describes the process and definitions for treatment and posttreatment follow-up swab sampling and successful decolonization treatment. We obtained the prescription redemption dates for 2% mupirocin nasal ointment and possible systemic antibiotic treatment with a combination of 2 antibiotics given perorally for MRSA carriage in Denmark (eg, fusidic acid, rifampicin, and clindamycin) from the National Prescription Registry.

For each MRSA-diagnosed patient, we retrieved information on exposure variables on socioeconomic status from 4 validated national registries available in Statistics Denmark and reports published by Local Government Denmark (an interest organization of the 98 Danish municipalities) describing inhabitants per square kilometer for each municipality.[19–24] The definitions of each explanatory variable examined are listed in Table 1. We considered these socioeconomic measures to cover important factors, in agreement with earlier studies.[4,6,8,25] Categories for household crowding were based on former similar studies.[26] The cutoff for groupings of family income (tertiles), education, and occupation was based on recommended categories from Statistics Denmark and the Odense Patient Data Explorative Network. The population density was classified into 3 categories: 0–75 inhabitants/km^2 (predominantly rural municipality), 76–159 inhabitants/km^2 (intermediate municipality), and 160–900+ inhabitants/km^2 (predominantly urban municipality).

Confounder variables and participant characteristics

Confounders were variables of importance for successful decolonization treatment in earlier studies.[14] The number of decolonization treatments and systemic antibiotics was measured during an individual's 2-year follow-up. Information about foreign bodies and somatic disorders was collected 5 years retroactively from study entry. The remaining variables were measured in the same year in which the first decolonization treatment was given. Data on somatic and mental disorders (ICD codes) and foreign bodies (treatment codes) were obtained from the National Patient Registry covering all admissions and outpatient visits to Danish hospitals.[27,28] Data on systemic antibiotics and repeated decolonization treatment were obtained from the National Prescription Registry.[29] The variable "MRSA-diagnosed in the household" was created using information on household relations (unique family identifier) and MRSA-diagnosed individuals identified from the regional MRSA database. Data on throat carriage were also obtained from the MRSA database.

Statistical analysis

We descriptively estimated the cumulative incidence proportion of adherence to follow-up swab samples taken 1 and 6 months after decolonization treatment and successful decolonization treatment. All proportions were calculated with a 95% confidence interval (CI). Using the unadjusted odds ratio (OR) with 95% CI, we assessed the association between socioeconomic factors (ie, household crowding, education, family income, occupation, length of residence in Denmark, and population density) and (1) adherence to MRSA posttreatment follow-up swab sampling 1 and 6 months after decolonization treatment and (2) successful decolonization treatment, univariate analyses. To estimate the adjusted OR, we used a cluster-based logistic regression model. In this multivariable model, we adjusted for age, sex, MRSA diagnosed in the household, throat carriage, and number of decolonization treatments. Due to

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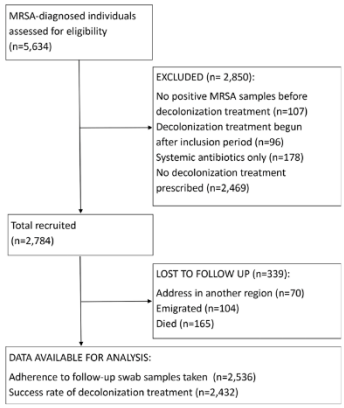

Fig. 2. Participants flow diagram.

the low occurrence of somatic disorders, mental disorders, use of foreign bodies, and systemic antibiotics, these variables were not included in the adjusted analysis. *P* values < .05 (2-sided) were deemed statistically significant. Individuals lost to follow-up were excluded from the analysis. Statistical analyses were conducted using Stata version 17 software (StataCorp, College Station, TX).

Results

We extracted 5,634 MRSA-diagnosed individuals from the regional MRSA database. The main cause of exclusion was no treatment (n = 2,743). When comparing baseline socioeconomic characteristics of treated and untreated individuals, decolonization treatment was less likely to be initiated when individuals were aged 0–35 years, were recent immigrants, were male, and were employed (Supplementary Files 1 and 2 online). We included 2,536 individuals in the analysis of adherence and 2,432 individuals in the analysis of the success rate of MRSA clearance (Fig. 2). Table 2 shows the baseline demographic and clinical characteristics. The largest group of individuals was aged <34 years. Sex was almost equally distributed. Overall, 1,548 (61%) of MRSA-positive participants had only 1 course of treatment. Somatic disorders, foreign bodies, and mental disorders ranged from 1% to 2.3%. Approximately half of the study population had 1 or more culture-positive household contact.

The rate of adherence to national guidelines advising MRSA follow-up swab sampling taken 1 month after treatment was 66% (95% CI, 64%–68%), and it decreased to 30% (95% CI, 28%–32%) after 6 months. Examining the relationship between socioeconomic factors and adherence to MRSA posttreatment follow-up swab sampling 1 month after decolonization treatment, we found that living in intermediate municipalities and being retired were associated with significantly higher rates of adherence (Table 3a) compared to predominantly rural municipalities. A significantly higher degree of adherence to MRSA follow-up swab sampling 6 months after decolonization treatment was only associated with living in areas with >160 citizens/km^2 (Table 3b).

The cumulative incidence proportion of successful decolonization treatment was 36% (95% CI, 34%–38%). Postsecondary school (short-cycle tertiary education or university degree completed), living in predominantly urban and intermediate municipalities, and individuals who retired early (voluntary early retirement of individuals partly depending on self-financing and age >60 years) were associated with a significantly higher rate of successful decolonization treatment (Table 4).

Table 2. Baseline Demographic and Clinical Characteristics for Individuals Treated for MRSA Carriage[a]

Demographic and Clinical Characteristics	Total (N = 2,536) No. (%)
Age group	
0–34 y	1,311 (51.7)
35–49 y	449 (17.7)
50–64 y	423 (16.7)
65–79 y	266 (10.5)
≥80 y	72 (2.8)
Sex	
Male	1,210 (48)
Female	1,311 (52)
Throat carriage	1,394 (55)
MRSA diagnosed in a household	
1 individual	1,426 (56.2)
2 individuals	618 (24.4)
3 individuals	292 (11.5)
≥4 individuals	185 (7.3)
Unknown carriage household	15 (0.6)
Decolonization treatment	
1 treatment	1,548 (61.0)
2 treatments	640 (25.2)
3 treatments	227 (9)
≥4 treatments	121 (4.8)
Systemic antibiotic decolonization treatment[b]	294 (11.6)
Somatic disorder	
Diabetes mellitus	26 (1.0)
Chronic obstructive pulmonary disease	50 (2)
Chronic skin disease	33 (1.3)
Chronic wounds	25 (1)
Renal disease	19 (0.8)
Mental disorder	57 (2.3)
Foreign bodies	55 (2.2)

Note. MRSA, methicillin-resistant *Staphylococcus aureus*.
[a]Decolonization treatment: mupirocin nasal ointment 2% and body wash using chlorhexidine soap 4% for 5 or 10 days (throat carriage).
[b]Rifampicin, fusidic acid, clindamycin.

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Table 3a. Cluster Analysis in a Multivariable Logistic Regression Model Analyzing the Association Between Socioeconomic Factors and Adherence to MRSA Posttreatment Follow-Up Swab Sampling After 1 Month[a]

	Incidence Proportion (N = 2,536)	Crude Analysis 1 Month		Adjusted Analysis[b] 1 Month	
Variable	No. (%)	OR (95% CI)	*P* Value	aOR (95% CI)	*P* Value
Employment status					
Employed	1,160 (62)	1 (reference)		1 (reference)	
Student	183 (67)	1.28 (0.92–1.78)	.15	1.28 (0.85–1.91)	.23
Unemployed or welfare payment	225 (70)	1.44 (1.06–1.96)	.02	1.27 (0.90–1.77)	.17
Early retirement[c]	174 (67)	1.28 (0.91–1.79)	.16	1 (0.67–1.49)	.98
Retirement	310 (75)	1.92 (1.44–2.55)	<.001	2.67 (1.16–6.13)	.02
Other[d]	484 (70)	1.43 (1.14–1.79)	.002	1.16 (0.87–1.53)	.31
Data missing	0 (0.0)				
Household income					
Low tertile	841 (64)	1 (reference)		1 (reference)	
Middle tertile	840 (67)	1.14 (0.93–1.39)	.21	1.10 (0.86–1.41)	.46
High tertile	840 (69)	1.22 (0.99–1.49)	.06	1.24 (0.96–2.59)	.10
Data missing	15 (0.6)				
Student					
Lower secondary school	656 (67)	1 (reference)		1 (reference)	
Upper secondary school	863 (63)	0.87 (0.70–1.07)	.19	0.95 (0.74–1.21)	.66
Postsecondary school	378 (69)	1.13 (0.86–1.49)	.37	1.15 (0.84–1.56)	.39
Unknown	639 (68)	1.08 (0.86–1.37)	.50	1.19 (0.91–1.56)	.20
Data missing	0 (0.0)				
Household crowding					
≤20 m^2 per person	2,179 (67)	1 (reference)		1 (reference)	
>20 m^2 per person	239 (70)	0.85 (0.64–1.14)	.28	1.06 (0.71–1.6)	.77
Data missing	118 (4.7)				
Population density					
0–75 inhabitants/km^2	840 (63)	1 (reference)		1 (reference)	
76–159 inhabitants/km^2	1,283 (70)	1.37 (1.14–1.64)	.001	1.40 (1.12–1.74)	.003
160–660 citizens per inhabitants/km^2	398 (64)	1.07 (0.83–1.37)	.62	1.06 (0.79–1.42)	.69
Data missing	15 (0.6)				
Length of residence in Denmark					
≤5 y	533 (67)	1 (reference)		1 (reference)	
>5 y	1,988 (67)	0.99 (0.81–1.21)	.99	0.94 (0.31–1.23)	.68
Data missing	15 (0.6)				

Note. MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; CI, confidence interval; aOR, adjusted OR.
[a]Follow-up swab samples from nose and throat (same date) 1–5 months after decolonization treatment.
[b]Adjusted for age, sex, number of decolonization treatments, MRSA-diagnosed in the household, and throat carriage.
[c]Voluntary early retirement of individuals partly depending on self-financing and age >60 years.
[d]Other includes individuals who have no connection to the labor market or with little connection to the labor market. Individuals in the other group do not receive welfare payments or education. Children aged <5 years are included in this group.

Discussion

In this cohort study, we evaluated decolonization treatment for MRSA carriage in 2,536 individuals over a study period of 13 years. The adherence to posttreatment follow-up swab sampling after 1 month was 66%, which decreased to 30% after 6 months. Retirement and living in predominantly urban and intermediate municipalities were associated with significantly higher rates of adherence to posttreatment follow-up swab sampling. The MRSA clearance rate after decolonization treatment was 36% 2 years after initiating treatment. Living in predominantly urban and intermediate municipalities, having retired early, and having a higher education were associated with more successful rates of decolonization treatment.

Individuals who had completed postsecondary school were likelier to achieve successful decolonization treatment. Higher

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Table 3b. Cluster Analysis in a Multivariable Logistic Regression Model Analyzing the Association Between Socioeconomic Factors and Adherence to MRSA Posttreatment Follow-Up Swab Sampling After 6 Months[a]

	Incidence Proportion (N = 2,536)	Crude Analysis 6 Months		Adjusted Analysis[b] 6 Months	
Variable	No. (%)	OR (95% CI)	*P* Value	aOR (95% CI)	*P* Value
Employment status					
Employed	1,160 (25)	1 (reference)		1 (reference)	
Student	183 (32)	1.37 (0.97–1.92)	.07	1.26 (0.86–1.87)	.24
Unemployed or welfare payment	225 (30)	1.28 (0.93–1.75)	.13	1.16 (0.82–1.65)	.41
Early retirement[c]	174 (39)	1.89 (1.36–2.63)	<.001	1.34 (0.90–1.99)	.15
Retirement	310 (42)	2.10 (1.62–2.73)	<.001	1.26 (0.59–2.71)	.55
Other[d]	484 (0.28)	1.15 (1.62–2.72)	.25	1.06 (0.79–1.41)	.71
Data missing	0 (0.0)				
Household income					
Low tertile	841 (31)	1 (reference)		1 (reference)	
Middle tertile	840 (28)	0.85 (0.69–1.05)	.14	0.90 (0.69–1.17)	.42
High tertile	840 (30)	0.94 (0.76–1.15)	.54	1.01 (0.78–1.32)	.93
Data missing	15 (0.6)				
Education					
Lower secondary school	656 (31)	1 (reference)		1 (reference)	
Upper secondary school	863 (28)	0.89 (0.71–1.11)	.29	1.02 (0.80–1.31)	.84
Postsecondary school	378 (35)	1.20 (0.92–1.58)	.18	1.33 (0.98–1.79)	.06
Unknown	639 (28)	0.87 (0.69–1.11)	.27	1.11 (0.84–1.47)	.45
Data missing	0 (0.0)				
Household crowding					
≤20 m^2 per person	2,179 (30)	1 (reference)		1 (reference)	
>20 m^2 per person	239 (34)	0.82 (0.62–1.08)	.16	0.80 (0.51–1.23)	.31
Data missing	118 (4.7)				
Population density					
0–75 inhabitants/km^2	840	1 (reference)		1 (reference)	
76–159 inhabitants/km^2	1,283	1.28 (1.05–1.56)	.01	1.22 (0.96–1.54)	.10
160–900+ inhabitants/km^2	398	1.92 (1.49–2.48)	<.001	1.79 (1.32–2.44)	<.001
Data missing	15 (0.6)				
Length of residence in Denmark					
≤5 y	533 (26)	1 (reference)		1 (reference)	
>5 y	1,988 (31)	1.31 (1.06–1.63)	.01	1.80 (0.82–1.43)	.59
Data missing	15 (0.6)				

Note. MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; CI, confidence interval; aOR, adjusted OR.
[a]Follow-up swabs from nose and throat (same date) 6–12 months after decolonization treatment.
[b]Adjusted for age, sex, numbers of decolonization treatments, MRSA-diagnosed in the household, and throat carriage.
[c]Voluntary early retirement of individuals partly depending on self-financing and an aged >60 y.
[d]Other includes individuals who have no connection to the labor market or with little connection to the labor market. Individuals in the other group do not receive welfare payments or education. Furthermore, children aged <5 years are included in this group.

education is associated with characteristics such as health literacy, prestige, and problem-solving skills, which have important health effects.[10] A substantial proportion of the Danish population perceives difficulties related to understanding health information and engaging with healthcare providers.[30] MRSA studies indicate that patients actively seek information about decolonization treatment when help-desk access is provided and that information increases knowledge about MRSA.[31,32] Furthermore, individuals who can retire early might have additional advantages such as time and still being healthy, thereby explaining why this group achieves a higher level of MRSA clearance.

Interestingly, living in predominantly urban municipalities was associated with a higher rate of adherence to posttreatment control sampling and a higher success rate of MRSA clearance. This finding may be due to the benefits of an urban living environment outweighing the possible higher risk of MRSA transmission in

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Table 4. Cluster Analysis in a Multivariable Logistic Regression Model Analyzes the Association Between Socioeconomic Factors and Successful Decolonization Treatment[a]

	Incidence Proportion (N = 2,432)	Crude Analysis		Adjusted Analysis[b]	
Variable	No. (%)	OR (95% CI)	*P* Value	aOR (95% CI)	*P* Value
Employment status					
Employed	1,103 (31)	1 (reference)		1 (reference)	
Student	178 (35)	1.16 (0.83–1.63)	.37	1.16 (0.80–1.69)	.43
Unemployed or welfare payment	219 (40)	1.44 (1.06–1.93)	.02	1.29 (0.94–1.78)	.11
Early retirement[c]	167 (50)	2.15 (1.55–2.99)	<.001	1.63 (1.12–2.38)	.01
Retirement	298 (50)	2.18 (1.68–2.83)	<.001	1.88 (0.79–4.47)	.15
Other[d]	467 (34)	1.1 (88.0–1.39)	.40	1.13 (0.85–1.50)	.41
Data missing	0 (0.0)				
Household income					
Low tertile	806 (37)	1 (reference)		1 (reference)	
Middle tertile	806 (35)	0.88 (0.71–1.09)	.23	0.89 (0.69–1.14)	.34
High tertile	805 (37)	0.99 (0.80–1.23)	.94	1.04 (0.81–1.35)	.75
Data missing	15 (0.6)				
Education					
Lower secondary school	624 (36)	1 (reference)		1 (reference)	
Upper secondary school	826 (37)	1.01 (0.81–1.25)	.96	1.15 (0.91–1.47)	.42
Postsecondary school	363 (45)	1.51 (1.16–1.96)	.002	1.62 (1.22–2.15)	.001
Unknown	619 (33)	0.88 (0.70–1.12)	.30	1.18 (0.90–1.55)	.23
Data missing	0 (0.0)				
Household crowding					
≤20 m^2 per person	2092 (37)	1 (reference)		1 (reference)	
>20 m^2 per person	237 (40)	0.88 (0.67–1.16)	.37	0.82 (0.55–1.23	.34
Data missing	103 (4.2)				
Population density					
0–75 inhabitants/km^2	802 (30)	1 (reference)		1 (reference)	
76–159 inhabitants/km^2	1,239 (37)	1.28 (1.05–1.56)	.01	1.35 (1.08–1.68)	.008
160–900+ inhabitants/km^2	379 (47)	1.92 (1.49–2.48)	<.001	2.04 (1.5–2.76)	<.001
Data missing, no. (%)	15 (0.6)				
Length of residence in Denmark					
≤5 y	513 (31)	1 (reference)			
>5 y	1904 (38)	1.37 (1.11–1.69)	.003	1.11 (0.85–1.43)	.45
Data missing	15 (0.6)				

Note. MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; CI, confidence interval; aOR, adjusted OR.
[a]Decolonization treatment: mupirocin nasal ointment and body wash using chlorhexidine soap 4% for 5–10 days. Successful decolonization treatment. MRSA-negative follow-up swab samples from nose and throat (same date) at least 6 months after completion of treatment to the end of the 2-year follow-up period.
[b]Adjusted for age, sex, number of decolonization treatments, MRSA-diagnosed in the household, and throat carriage.
[c]Voluntary early retirement of individuals partly depending on self-financing and age >60 y.
[d]Other includes individuals who have no connection to the labor market or with little connection to the labor market. Individuals in the other group do not receive welfare payments or education. Furthermore, children aged <5 years are included in this group.

crowded communities. Low-quality health care is a frequent problem in rural areas. Numerous problems associated with low-quality healthcare in rural areas emerge as deficiencies in the provision of continued and coordinated care. Problems occur because of shortcomings in interprofessional communication, a general lack of resources, or patients requiring more specialized care.[33] Some of the predominantly rural municipalities in our study have been struggling with shortages of physicians in hospitals and among general practitioners.

In our study, we obtained a MRSA clearance rate of 36%. A causal effect of decolonization treatment on MRSA clearance has been reported in 2 small studies of selected MRSA-positive patients. A Swedish study found a success rate after 6 months of 61% among patients treated once with topical treatment and

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systemic antibiotics. Patients receiving topical treatment had a success rate of 13%.[34] In another study, the success rates were 74% in the treated group and 32% in the untreated group after 3 months.[35] The low long-term decolonization effect of 36% in our study cohort may be partly explained by the low number (11.6%) of individuals receiving systemic antibiotics together with the topical treatment. Long-term decolonization effects, the impact of repeated courses of treatment, possible side effects of decolonization treatments evaluated in randomized controlled trials, and organizational matters remain understudied.[36] More successful decolonization treatment has been reported when MRSA management is handled by a specialist team or in an outpatient setting with close cooperation with the inpatient sector, but none of these studies had control groups, and the aim of the studies was not to compare organizational differences.[37,38]

One strength of this study is that it comprises a large community cohort based on individual data and an observational period of 2 years for each person included. However, this study has some limitations that should be considered when interpreting our findings. First, we included only registry data on the prescription of mupirocin nasal ointment to estimate the completed decolonization treatment. Clinical data from general practice were not routinely transferred to national registries in Denmark. This limited our ability to determine other factors that may have contributed to the observed difference such as validation of the data collection method for initiated and completed decolonization treatment. Furthermore, we could not measure sociocultural differences or stage-of-life characteristics. Second, some of the socioeconomic measures considered were highly correlated with each other. For example, a high education level could be correlated with other socioeconomic factors, such as a high income. This raises concerns about collinearity. However, previous evidence has shown that the correlation between different socioeconomic factors was not strong enough to be grouped as 1 measurement.[10] Third, ~50% of MRSA-diagnosed individuals were excluded due to no treatment. The sensitivity analysis revealed that decolonization treatment was less likely to be initiated if the individuals were males, were employed, lived in predominantly rural municipalities, and had recently immigrated to Denmark. The RSD is a high-density farming area and persons with day-to-day contact with live pigs do not initiate decolonization treatment, which may explain some of the high proportions of untreated individuals. However, limited access to healthcare in rural areas is frequently reported.[33] Furthermore, immigrants with a risk of severe disease from MRSA may be less likely to initiate treatment. In a Danish study, mortality rates from infectious diseases were higher among refugees and immigrants compared to native Danes. The study also stated that a lack of information on consulting general practitioners and language barriers may impair access to healthcare services.[39] Furthermore, individuals who have recently immigrated are often placed in rural municipalities, which challenges mobilization.[40] This raises a concern for inequity in MRSA morbidity and mortality for individuals who have immigrated to Denmark within the last 5 years. Finally, a few associations in our study were relatively weak (adjusted OR < 1.5), though it is difficult to assess the clinical significance because research on the number needed to treat to reduce infections or to prevent transmission of MRSA in the community is lacking in the literature.[36]

To generalize the findings on rural areas it should be noted that most travel distances are short in Denmark.[12] Rural districts within the municipalities often have a maximum of 30 minutes of driving by car to the nearest general practitioner or hospital.

Our findings have some implications for future research. The surprising benefits of living in predominantly urban municipalities require further study. Furthermore, it is unclear whether the low rate of follow-up sampling and successful decolonization treatment in our study was due to the data collection method, the present organization of MRSA care in primary healthcare, or ineffective decolonization treatment regimens.

In conclusion, we found low rates of adherence to MRSA follow-up sampling and low rates of successful decolonization treatment. Lower decolonization rates and lower adherence to follow-up tests were not linked to overcrowding, low income, unemployment, or recent immigration. Further, disparity in the effect of decolonization treatment and adherence to MRSA follow-up sampling among MRSA-positive individuals appear largely explained by the level of education, area of residence in predominantly urban and intermediate municipalities, and employment status.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2023.32

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Conflicts of interest. All authors report no conflicts of interest related to this article.

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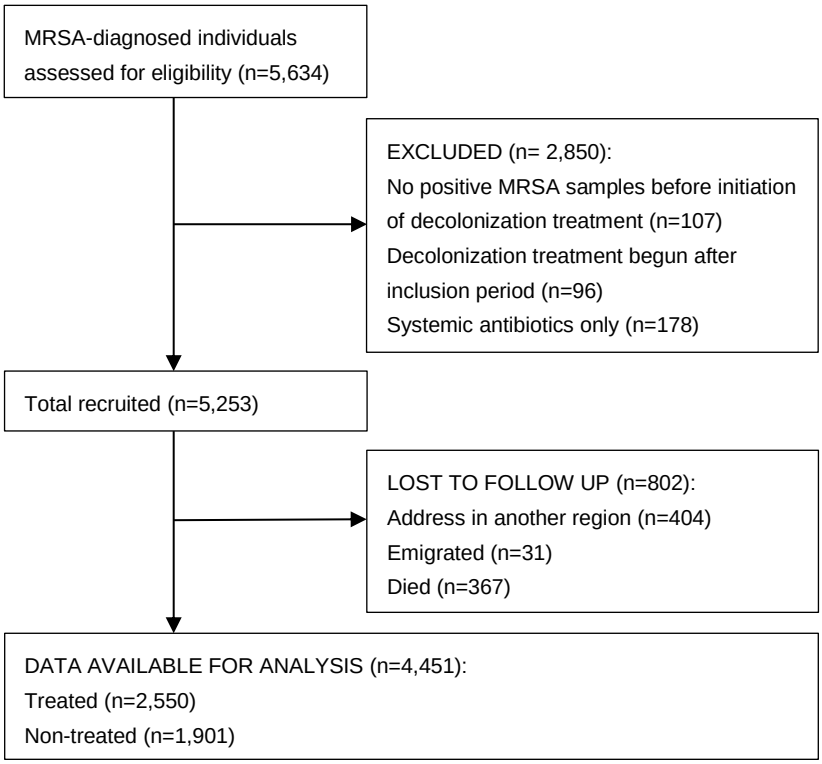
Supplementary materials



Baseline[a] demographic and socioeconomic characteristics of treated[b] or non-treated methicillin-resistant *Staphylococcus aureus* positive individuals

	Number (%)		
N=(4,451)	Treated (n=2,550)	Non-treated (n=1,901)	P-value[c]
Age group			0,000
0-34 years	1,330 (52)	1,098 (58)	
35-49 years	437 (17)	392 (21)	
50-64 years	427 (17)	217 (11)	
65-79 years	269 (11)	111 (6)	
80^{+} years	74 (3)	42 (2)	
Sex			0,000
Male	1,218 (48)	1,170 (62)	
Female	1,319 (52)	690 (36)	
Missing	13	41	
Employment status			0,000
Employed	1,183 (46)	1,080 (57)	
Student	177 (7)	97 (5)	
Unemployed or welfare payment	203 (8)	109 (6)	
Early retirement[d]	176 (7)	63 (3)	
Retirement	313 (12)	134 (7)	
Other[d]	497 (19)	411 (22)	
Data missing	1 (0,04)	7 (0,4)	
Household income			0,000
Low tertile	835 (33)	631 (33)	
Middle tertile	856 (34)	610 (32)	
High tertile	846 (33)	619 (33)	
Data missing	13 (0,5)	41 (2)	
Education			0,000

Lower secondary school	670 (26)	413 (22)	
Upper secondary school	862 (34)	650 (34)	
Post-secondary school	373 (15)	234 (12)	
Unknown	645 (25)	604 (32)	
Household crowding			0,001
≤ 20 m^2 per person	232 (9)	162 (9)	
> 20 m^2 per person	2179 (85)	1,584 (83)	
Data missing	139 (5)	155 (8)	
Population density			0,000
0-75 inhabitants per square kilometer	849 (33)	693 (36)	
76-159 inhabitants per square kilometer	1,287 (50)	913 (48)	
160-660 inhabitants per square kilometer	401 (16)	254 (13)	
Data missing	13 (0,59	41 (2)	
Length of residence in Denmark			0,000
≤ 5 years	553 (22)	583 (31)	
> 5 years	1984 (78)	1,277 (67)	
Data missing	13 (0,5)	41 (2)	

a: First positive MRSA test registered for an individual
b: Decolonization treatment: Mupirocin nasal ointment 2% and body wash using chlorhexidine soap 4 % for five or ten days (throat carriage)
c: Chi-squared test
d: Voluntary early retirement of individuals depending on partly self-financing and an age above 60.
e: Other includes individuals who have no connection to the labor market or with little connection to the labor market. Individuals in the other group do not receive welfare payments or education. Furthermore, children under the age of five years are in this group.

Article type: Original Article

Mental health, stigma, and illness perception among individuals diagnosed with meticillin-resistant *Staphylococcus aureus* - a longitudinal cohort study

Mette Assenholm Kristensen[1,2], Hanne Irene Jensen[2,4] , Christian Backer Mogensen[2,5] , Jens Søndergaard[6] and Jens Kjølseth Møller[1,2]

[1]Department of Clinical Microbiology, Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark.
[2]Department of Regional Health Research, University of Southern Denmark, Odense, Denmark.
[3]Department of Quality, Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark.
[4]Department of Anesthesiology and Intensive Care, Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark.
[5]Department of Emergency Medicine, Hospital Sønderjylland, University Hospital of Southern Denmark, Aabenraa, Denmark
[6]Research Unit of General Practice, Department of Public Health, University of Southern Denmark, Odense, Denmark.

Corresponding author
Mette Assenholm Kristensen
Beriderbakken 4, 7100 Vejle, Denmark
E-mail: mette.assenholm.kristensen@rsyd.dk
Tel: +45 22740923
ORCID: https://orcid.org/0000-0001-8676-6661

Short running title: Stigma and illness perception in MRSA cases
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Abstract: **249 words**
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Supplementary material: 1 table, 1 figure

Summary

Background: Prevention of meticillin-resistant *Staphylococcus aureus* (MRSA) transmission includes case finding, isolation when hospitalized, and decolonization treatment for asymptomatic carriers. However, patients may experience psychosocial stressors related to this strategy.

Aim: To examine stigma, mental health, and illness perception in individuals diagnosed with MRSA one month after getting an infection or being diagnosed as a carrier, and at one month compared with six and twelve months after diagnosis, respectively.

Methods: A longitudinal cohort study comprising adults in Southern Denmark diagnosed with MRSA in 2020–2021. We used three internationally standardized questionnaires to measure stigma, mental health, and illness perception.

Findings: One month after MRSA diagnosis, 135 (43%) MRSA-positives responded to the questionnaire. Hereof, 11% perceived clear stigma, 24% had poor mental health, and 19% were denied healthcare services. We found no change in mental health and stigma state among carriers and infected, and no changes in stigma and mental health state within the first year of diagnosis. Being infected was associated with higher levels of symptoms and higher levels of perceived consequences: adjusted mean difference 1.9 (95% confidence interval (CI): 1.0;2.7), and 1.3 (95% CI: 0.2;2.4), respectively. A significantly longer perceived timeline for having MRSA was found twelve months after the diagnosis compared to one month after the diagnosis, adjusted mean difference 1.4 (95% CI 0.3;2.4).

Conclusions: Individuals perceived MRSA infection as being more threatening than MRSA carriage but no difference was found in stigma and mental health state. These psychosocial stressors did not decrease during the one-year follow-up.

Introduction

Meticillin-resistant *Staphylococcus aureus* (MRSA) is listed as one of the priority antibiotic-resistant pathogens by the World Health Organization, and urgent actions are required to address the threat of MRSA to human health [1,2]. One of the recommended efforts is to reduce the incidence of infection through infection control measures [3]. Scandinavian countries and the Netherlands have implemented the “search and destroy policy” to prevent the transmission of the increasing number of MRSA cases. The strategy includes case finding, isolation when hospitalized, and decolonization treatment for asymptomatic carriers in endemic settings [4,5]. However, certain patients experience psychosocial stressors related to this strategy [6–8]. A study has found that 56% of MRSA carriers reported stigma and that educational level, female sex, and intensive MRSA eradication therapy were associated with higher levels of stigma. Stigma was experienced most frequently in healthcare settings, and stigma and mental health scores were inversely correlated [9]. Due to the lack of high qualitative evidence warnings against over-interpreting the significance and generalizability of these findings have been suggested [10]. Furthermore, these studies have not addressed the long-term consequences. More negative illness beliefs are associated with higher levels of psychological consequences [11], but thus far there has been no comparison between MRSA-infected individuals and MRSA carriers. Increased knowledge could clarify the scope and type of interventions that need to be initiated for example systemic changes like loosening the isolation restrictions or person-oriented initiatives like consultations addressing psychosocial issues. For individuals with MRSA, this might lead to increased social contact. For society, it might affect test activity or the initiation of decolonization treatment.

The primary objective of this study was to investigate the association of stigmatization, mental health, and illness perception among patients with either MRSA infection or MRSA carriage one month after the MRSA diagnosis. The secondary objective was to assess the association between stigma, mental health, and illness perception at six and twelve months compared to one month after MRSA diagnosis.

Methods

Study design

We conducted a longitudinal cohort study using prospectively collected information from a questionnaire survey. We enrolled participants from September 2020 to September 2021. Each individual had a follow-up time of twelve months. The online questionnaire was mailed one, six, and twelve months after the MRSA diagnosis. If there was no response, two reminders were sent at intervals of one week.

Setting and participants

We included MRSA-infected and MRSA carriers above 18 years of age. For identification, we used new cases diagnosed with MRSA identified through samples submitted to the four departments of clinical microbiology in the Region of Southern Denmark (RSD). The RSD comprises approximately 20%–25% of the total MRSA cases in Denmark. We excluded patients from other regions in Denmark, patients not literate in Danish, and patients without mental capacity to fill in questionnaires. Furthermore, we excluded patients who reported being MRSA-free when answering the questionnaire. In the RSD, departments of clinical microbiology provide, on request, advice to the doctor in charge of the patient (typically the general practitioner) concerning the antibiotic treatment of a possible infection, decolonization regime, and subsequent control sampling. In this study, participants provided consent by responding to the questionnaire. The region's research counseling unit evaluated the declaration of consent used. We obtained permission to store data from the RSD (20/25135), and access to patient records was approved by the Danish Patient Safety Authority (S-31-1521-375). It was not necessary to obtain, ethical approval according to the Regional Committees on Health Research Ethics for Southern Denmark (S-20192000-155).

Data collection

We collected data on patient characteristics and outcome variables of mental health, stigmatization, and illness perception (Supplementary File A1). We used

electronic questionnaires managed by the software program REDCap (RESEARCH Electronic Data Capture), Vanderbilt University, version 10.0.28 [12]. Questionnaires were sent through a public digital mailbox system. Respondents were allowed to skip any questions in the questionnaire.

Measuring illness perception

We used the Danish version of the Brief Illness Perception Questionnaire (B-IPQ) [13,14]. B-IPQ is a generic nine-item questionnaire developed to assess cognitive and emotional representations across diverse patient groups. B-IPQ is a short version of the 84-item revised illness perception questionnaire (IPQ-R) [15]. The items in the B-IPQ encompass consequences, timeline (acute-chronic), amount of perceived personal control, treatment control, identity (symptoms), concern regarding the illness, coherence of the illness, and emotional representation. The items are rated using a single-item scale, with responses from 0–10 and descriptors (none or extreme) that either end with 0 representing no perceived threat in items 1, 2, 5, 6, and 8 and highest perceived threat in items 3, 4, and 7. In all questions, we replaced the word “illness” with “MRSA” as recommended when applying the B-IPQ to specific conditions. The Danish scale from 1-10 was changed to the original scale of 0–10 to compare our results with those of international studies.

Measuring stigma

Stigma was measured using a 10-item stigma scale developed by Wright (four-point scale) [16]. This revised version is a short version of the 40-item Berger Stigma Scale questionnaire originally developed for patients diagnosed with the human immunodeficiency virus (HIV) [17]. The multi-item scale includes four subscales: 1) personalized stigma (three items), which measures the consequences of others knowing about one’s MRSA status, including rejection, loss of friends, and avoidance of others; 2) disclosure concerns (two items), which measures issues related to whether or not individuals tell others about their diagnosis; 3) negative self-image (three items), which measures one’s feelings towards oneself such as shame, guilt, and self-worth; 4) concern with public attitudes (two items), which measures participants’ perceptions of the

public attitudes toward those living with MRSA. An extra response option of “no opinion” was added to the original stigma scale because of the sensitivity of the questions (treated as missing value). In addition, HIV in the original questionnaire was replaced with MRSA. Lower scores define a more favourable MRSA-related stigma state. We translated the English version to Danish using a three-step translation process. The translations were conducted by independent professional translators, bilingual translators familiar with everyday language, and bilingual specialists in infection control. The English version was translated into Danish. The accepted Danish version was then blindly back-translated into English by new translators. A panel constructed the final Danish version of the questionnaire [18]. We added a question on stigmatization from healthcare at the end of the original questionnaire with the same response options.

Measuring mental health

Mental health was measured using the five-item RAND Mental Health Inventory questionnaire (MHI-5) [19] using the Danish version [20,21]. MHI-5 (six-point scale) is a short version of the original 38-item version of the Mental Health Inventory (MHI-38) questionnaire [22]. The MHI-5 is a part of the Medical Outcomes Study 36-item short-form survey (SF-36) [23]. The scale includes the following four subscales: 1) anxiety (one item), 2) depression (one item), 3) emotional control (one item), and 4) general positive affect (two items). Scores range from 0–100, with higher scores reflecting better mental health. Lower scores are interpreted as “feelings of nervousness and depression all of the time”. High scores indicate “feels peaceful, happy, and calm all of the time” [19]. Moreover, “During the last month” was changed to “During the period of being MRSA-positive”.

Statistical analysis

Statistical analyses were performed using Stata/BE version 17.0 (StataCorp, Texas, USA). Questionnaire data was calculated as per instruction [13,14,17,19] and analyzed as continuous data (mean, 95% confidence interval). In accordance with literature, stigma scores were categorized into “no stigma” (score 40–75), “suggestive of stigma” (score 76–110), and “clear

stigma" (score 111–160) [24–27]. The results from the added item "cancellation of planned healthcare appointments on account of being MRSA positive were presented as single-item data. In addition, mental health score was dichotomized as poor mental health (<60) and normal mental health (≥60), as per instruction [19]. Furthermore, we used linear regression models to examine the association between MRSA carriers and MRSA infections. To examine the associations between time points (one, six, and twelve months) and the outcome of interests (mental health, stigmatization, and illness perception) we used linear mixed-effects models. Following existent literature, we adjusted for gender, educational level, stigmatization score/mental health score, and livestock-associated MRSA [9,28]. P-values of less than 0.05 (two-sided) were deemed statistically significant.

Results

During the study period, 531 individuals were found to be diagnosed with MRSA; from among these 345, patients were invited to participate in the study. The main reason for exclusion was being aged below 18 years (Figure 1). A total of 164 questionnaires were returned (48%) one month after diagnosis, but 29 reported being MRSA-free, at the time of return, thereby leading to the inclusion of 135 individuals (43%). After six and twelve months, the response rates for MRSA-positive were 25% and 21%, respectively (Figure 1). Gender and hospital affiliation were almost equally distributed among responders and non-responders. When comparing age groups the younger population was less represented among the respondents (Supplementary Table A2). Further, ten patients did not respond to the questionnaire at one month but responded at six and twelve months.

The characteristics of the respondents at one month are presented in Table I. Those who responded to the questionnaire mainly included participants aged under 65, those who were retired or employed, and married individuals. Only a few participants perceived their health as very poor. Further, "Suggestive stigma" and "clear stigma" were perceived by 21% and 11% of the participants after one month, by 20% and 11% of the participants after six months, and by 17% and 13% of the participants after twelve months, respectively. The extend

of poor mental health was 24% after one month and 16% and 20% after six and twelve months, respectively. Among the respondents, 19% agreed or strongly agreed with the statement “I have had treatment in health care canceled due to MRSA”. After six months, 12% agreed with this statement and after twelve months, 8% of the responders agreed with this statement.

There was no difference between MRSA carriers and those infected with MRSA in perceived stigmatization and mental health. Examining the association between stigma, mental health, illness perception, and having MRSA infection or being an MRSA carrier one month after MRSA diagnosis, we found significantly higher scores of consequences and identity (symptoms) among responders with MRSA infections compared to MRSA carriers (Table IIa,b,c). Furthermore, issues related to whether or not individuals tell others about their diagnosis (disclosure) were the most dominant subcategory of perceiving a less favourable MRSA-related stigma state. The second most dominant subcategory was related to statements on the two questions measuring public attitudes: “Most people think that a person with MRSA is disgusting” and “Most with MRSA are rejected when others find out”. For mental health, the most dominant subscale was general positive affect (well-being) for perceiving a less favourable mental health state, which is related to the question “Been a happy person”. Treatment control (“How much do you think your treatment can help your MRSA?”), timeline (“How long do you think MRSA will continue?”), and personal control “How much control do you feel you have over MRSA?” were the domains which induced a threatening perspective of MRSA to the greatest extent (Supplementary Figure A3). Examining the association between one and six months we found that the respondents had a more threatening view of the control of treatment (“How much do you think your treatment can help your MRSA?”) six months after the MRSA diagnosis compared to one month after the diagnosis. A significantly longer perceived timeline (“How long do you think MRSA will continue?”) for having MRSA was found twelve months after the diagnosis compared to one month after the diagnosis (Table III).

Discussion

We found that MRSA-infected patients experienced the MRSA condition as more threatening in perceived illness identity (symptoms) and consequences compared to MRSA carriers. At baseline (one month), all those who were diagnosed with MRSA perceived public attitudes and the disclosure of being MRSA-positive as the most important subdomain for having a higher level of stigmatization. For the same group, the most important subdomain for having a lower level of mental health state was general positive affect (well-being). Moreover, we found lower levels of belief in the treatment control of MRSA after six months compared to one month after the MRSA diagnosis and a prolonged perspective of the timeline for continuing to have MRSA at twelve months compared to one month.

Since 2016, the Danish MRSA guidelines state that those diagnosed with MRSA have the same rights to receive healthcare services as everyone else [29]. In this context, we were surprised to find that 19% of the responders reported rejections from healthcare services and that 11% were classified as being subject to clear stigma with scores above 111. Furthermore, in a previous study among MRSA carriers from the Netherlands, 14% reported clear stigma and the mean stigma score was 80. We found lower mean stigma scores both in carriers (60) and in infected (73). The Dutch study measured stigma with the original 40-item Berger HIV Stigma Scale; items rated as “no opinion” were replaced with a calculated individual mean [9]. We used a shorter version of the questionnaire and replaced “no opinion” with “missing value”, which might explain the measured difference. As in an earlier published study [30], we also found an additional burden in those who were infected with MRSA. The study addressed patient illness perceptions in in-patients with severe MRSA infection and severe non-MRSA infection. In addition, 79% believed that their infection was very serious and 76% believed that their infection also had major consequences on their life. MRSA-infected responders were more worried than responders with a non-MRSA infection with regard to passing their infection on to their families. However, there were no significant differences between those who were not infected with MRSA and those infected with MRSA in feelings of

anger or concern regarding the future. The authors suggest that it is the infection, and not the MRSA, which is the main concern [30].

We have been unable to find other studies describing a follow-up of a cohort of MRSA-positive patients for a year after the first positive test. We found a lower belief in the treatment control of MRSA and in having MRSA for a short period of time. Initially, numerous patients tend to assume that it is easy to get rid of MRSA, but the fact is that the duration of time it may take to be MRSA-free might be long and occasionally unsuccessful. A Swedish study found that 28% of patients were not treated successfully for MRSA carriage even after two years of diagnosis [31] Furthermore, a Danish study revealed that only 358 patients out of 688 were treated for carriage [32], and it is likely that not all patients were informed of this shortly after the first positive test result. Further, we did not find any change in stigma or mental health state during the one-year follow-up. These findings are in line with previous literature for example, on those who are HIV-positive, thereby revealing HIV-infected, that the risk of disclosure is an ongoing issue for patients rather than just an issue at the time of diagnosis [33]. Furthermore, new-onset or persistent depression may occur during the first year after HIV diagnosis [34]. Since HIV and MRSA are not similar this comparison must be interpreted with caution.

Our study has a few limitations. The response rate was low and only limited data on non-responders were available. The sensitivity analysis revealed that most of the respondents were above 40 years of age. Lower age groups may perceive lower levels of stigma [9], which might have led to overestimated stigma scores in this present study. On the contrary, only a few of the responders reported having very poor health, which may cause the psychosocial stressors related to healthcare less substantial. In addition, the questionnaire was in Danish, thereby limiting participation only to people who were literate in Danish. This may limit insights into cultural differences which is of importance considering that a substantial proportion of MRSA cases in Denmark may exist among non-ethnic Danes. Although there are no studies on the Danish population studies exist among migrants in Europe and, the prevalence of MRSA carriage or MRSA infection is 7.8% [35]. Moreover, individuals born outside Sweden have an increased risk of having MRSA [36],

and in Canada, English-speaking residents have MRSA infections less frequently [37]. It also should be noted that a large proportion of the responders had livestock-associated MRSA. For example, pig farmers may experience both individualized and sector-wide stigma. The sector-wide stigma in farming includes criticism of pig farmers for being socially irresponsible and for risking public health [28]. To help this specific group and to limit the spread of livestock-associated MRSA, a national helpdesk has been established in Denmark, which may likely have contributed to a reduced burden of psychosocial stressors among pig farmers and their households.

Further, having low psychosocial functioning might limit resources and influence test behavior and treatment compliance. Previous studies suggest using standard precautions instead of prevention by isolation when MRSA patients are admitted to hospitals, allocation of more resources to isolated patients, and improvement of social contact when isolated [6,38,39]. It has also been suggested that healthcare workers must also be better educated, both for those handling isolation precautions and for those responsible for decolonization treatment [6–8]. Our findings highlight the need for research on the consequences of MRSA behavior and research on interventions to reduce psychosocial stressors in community and hospital settings. The most fundamental intervention is to address the rejection from healthcare facilities at a structural level. To help individuals, the main intervention in MRSA care is to manage disclosure concerns and decrease the timeframe for perceiving psychosocial stressors.

Conclusions

Individuals infected with MRSA perceive MRSA as more threatening than MRSA carriers, but there was no difference in psychosocial stressors. Further, individuals with persistent MRSA positivity continued to experience psychosocial stressors one year after diagnosis; Moreover, there was a reduced belief in the effectiveness of MRSA treatment and that MRSA positivity lasted only for a short duration.

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Conflicts of interest statement

The authors report no conflicts of interest.

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Tables and figures overview with legends

Table I. Baseline demographic, clinical, and social characteristics one month after diagnosis of meticillin-resistant *Staphylococcus aureus* (MRSA)

N = 135	Number (%)	
	Carriers of MRSA n = 96	Infected with MRSA n = 39
Age group		
18–40 years	39 (41)	12 (31)
41–64 years	46 (48)	19 (49)
≥65 years	11 (11)	8 (21)
Gender		
Female	42 (44)	21 (54)
Male	54 (56)	18 (46)
Marital status		
Married	57 (59)	19 (49)
Cohabitant	23 (24)	8 (21)
Single (separated, divorced)	4 (4)	3 (8)
Single (widow)	0 (0)	3 (8)
Single (unmarried)	12 (13)	6 (15)
Size of the family		
1–2 persons	50 (52)	22 (56)
3 persons or more	45 (47)	17 (44)
Missing values	1 (1)	0 (0)
Children under two years in the household		
Yes	9 (9)	4 (10)
No	87 (91)	35 (90)
Education		
Student	4 (4)	1 (3)
Primary school	18 (19)	9 (23)

Trade-based education	32 (33)	7 (18)
Lower secondary school	5 (5)	6 (15)
Upper secondary school	22 (23)	9 (23)
Post-secondary school	12 (13)	3 (8)
Missing values	3 (3)	4 (10)
Employment		
Student	3 (3)	2 (5)
Employed	66 (69)	19 (49)
Self-employed	14 (15)	3 (8)
Long-term sick leave	1 (1)	1 (3)
Unemployed	3 (3)	4 (10)
Disability pensioner	4 (4)	0 (0)
Retired	5 (5)	10 (25)
Health care worker		
Yes	11 (11)	5 (13)
No	85 (89)	34 (87)
Self-rated health		
Very poor	0 (0)	3 (8)
Poor	1 (1)	3 (8)
Fair	9 (9)	6 (15)
Good	50 (52)	17 (44)
Very good	36 (38)	10 (26)
Livestock-associated MRSA		
Yes	42 (44)	6 (15)
No	44 (46)	25 (64)
Do not know	10 (10)	8 (21)

Table IIa: The association between stigma, mental health, illness perception, and having MRSA infection or being an MRSA-carrier one month after MRSA diagnosis

N=135	MRSA infected Mean (95% CI) n=39	MRSA carrier Mean (95% CI) n=96	Crude analysis[a] Mean difference (95% CI)	P-value	Adjusted analysis[b] Mean difference (95% CI)	P-value
Stigma, 40-160 score[c]						
Total score	73.2 (61.0;85.5)	60.3 (52.8;67.8)	12.9 (-0.5;26.4)	0.06	4.6 (-9.8;18.9)	0.52
Missing/no opinion n (%)	13 (33)	42 (44)				
Personalized stigma	64.8 (55.0;74.6)	55.3 (49.5;61.2)	9.5 (-1.1;20.1)	0.08	1.7 (-10.9;14.3)	0.79
Missing/no opinion n (%)	3 (8)	23 (24)				
Disclosure	83.5 (70.1;97.0)	76.5 (67.6;85.4)	7.1 (-8.9;23.1)	0.38	2.4 (-14.9;19.6)	0.78
Missing/no opinion n (%)	5 (13)	17 (18)				
Negative self-image	71.4 (57.8;85.0)	65.7 (57.4;74.4)	5.6 (-9.9;21.1)	0.48	-3.9 (-19.6;11.7)	0.61
Missing/no opinion n (%)	4 (3)	10 (10)				
Public attitudes	77.9 (65.5;90.4)	65.9 (56.9;74.7)	12.1 (-3.4;27.6)	0.12	-1.6 (-18.2;15.1)	0.85

a: Simple linear regression analysis, reference group: MRSA carrier

b: Multiple linear regression analysis, reference group: MRSA carrier. Adjusted for gender, education level, livestock-associated MRSA, employment status and mental health score/stigma score.

c: Stigma-scale: Lower scores define a more favorable MRSA-related stigma state.

Table IIb: The association between mental health and having MRSA infection or being an MRSA-carrier one month after MRSA diagnosis

N=135	MRSA infected Mean (95% CI) n=39	MRSA carrier Mean (95% CI) n=96	Crude analysis[a] Mean difference (95% CI)	P-value	Adjusted analysis[b] Mean difference (95% CI)	P-value
Mental health, 0-100 score[d]						
Total score	71.7 (62.8;80.5)	81.5 (77.1;85.9)	-9.82 (-18.6;-1.01)	0.03	1.3 (-7.3;10.0)	0.76
Missing n (%)	8 (21)	7 (7)				
Anxiety	69.7 (59.1;80.4)	84.8 (79.8;89.9)	-15.11 (-25.4;-4.9)	0.004	0.3 (-11.1;11.8)	0.96
Missing n (%)	2 (5)	5 (5)				
General positive affect	62.4 (51.4;73.5)	73.8 (67.5;80.1)	-11.4 (-23.4;0.7)	0.06	0.8 (-12.2; 13.7)	0.91
Missing n (%)	2 (5)	4 (4)				
Depression	76.2 (67.5;84.9)	83.7 (78.3;89.2)	-7.5 (-17.6;2.6)	0.14	2.0 (-9.6;13.6)	0.73
Missing n (%)	2 (5)	5 (5)				
Emotional control	88.1 (80.8;95.4)	90.7 (86.8;94.6)	-2.6 (-10.1;5.0)	0.50	2.4 (-8.4;13.3)	0.65
Missing n (%)	2 (5)	5 (5)				

a: Simple linear regression analysis, reference group: MRSA carrier

b: Multiple linear regression analysis, reference group: MRSA carrier. Adjusted for gender, education level, livestock-associated MRSA, employment status and mental health score/stigma score.

:d. Five-item RAND Mental Health Inquiry (MHI): Higher scores define a more favorable mental health state

Table IIc: The association between illness perception, and having MRSA infection or being an MRSA-carrier one month after MRSA diagnosis

N=135	MRSA infected Mean (95% CI) n=39	MRSA carrier Mean (95% CI) n=96	Crude analysis[a] Mean difference (95% CI)	P-value	Adjusted analysis[b] Mean difference (95% CI)	P-value
Illness perception, 0-10 score[e]						
1. Consequences	3.8 (2.6;5.0)	1.5 (1.0;2.0)	2.3 (1.2;3.4)	0.50	1.3 (0.2;2.4)	0.02
Missing n (%)	0	0				
2. Timeline	3.4 (2.5;4.4)	3.9 (3.2;4.6)	-0.5 (-1.7;0.8)	0.46	-0.8 (-2.3;0.6)	0.26
Missing n (%)	0	2 (2)				
3. Personal control	5.5 (4.4;6.5)	5.9 (5.1;6.7)	-0.4 (-1.9;1.0)	0.54	0.3 (-1.3;1.9)	0.70
Missing n (%)	0	3 (3)				
4. Treatment control	5.8 (4.7;7.0)	4.7 (3.9;5.5)	1.11 (-0.3;2.6)	0.13	1.3 (-0.4;2.9)	0.14
Missing n (%)	0	4 (4)				
5. Identity	2.8 (1.8;3.8)	0.6 (0.2;0.9)	2.3 (1.5;3.1)	<0.001	1.9 (1.0;2.7)	<0.001
Missing n (%)	0	2 (2)				
6. Concern	4.1 (2.9;5.2)	2.6 (1.9;3.3)	1.5 (0.2;2.7)	0.03	0.5 (-0.9;1.9)	0.49
Missing n (%)	0	1 (1)				
7. Coherence	6.82 (5.9;7.8)	7.2 (6.4;7.9)	-0.3 (-1.6;1.0)	0.60	-0.3 (-1.7;1.2)	0.71
Missing n (%)	0	2 (2)				
8. Emotional representation	3.3 (2.2;4.3)	1.91 (1.30;2.53)	1.2 (0.2;2.5)	0.02	0.7 (-0.6;2.0)	0.30
Missing n (%)	0	2 (2)				

a: Simple linear regression analysis, reference group: MRSA carrier

b: Multiple linear regression analysis, reference group: MRSA carrier. Adjusted for gender, education level, livestock-associated MRSA, employment status and mental health score/stigma score.

e: Brief-IPQ (B-IPQ): Brief Illness Perception Questionnaire, higher scores on items 1,2,5,6, and 8 denote a more threatening view of the illness, while higher scores on items 3,4, and 7 denote a less threatening view of the illness.

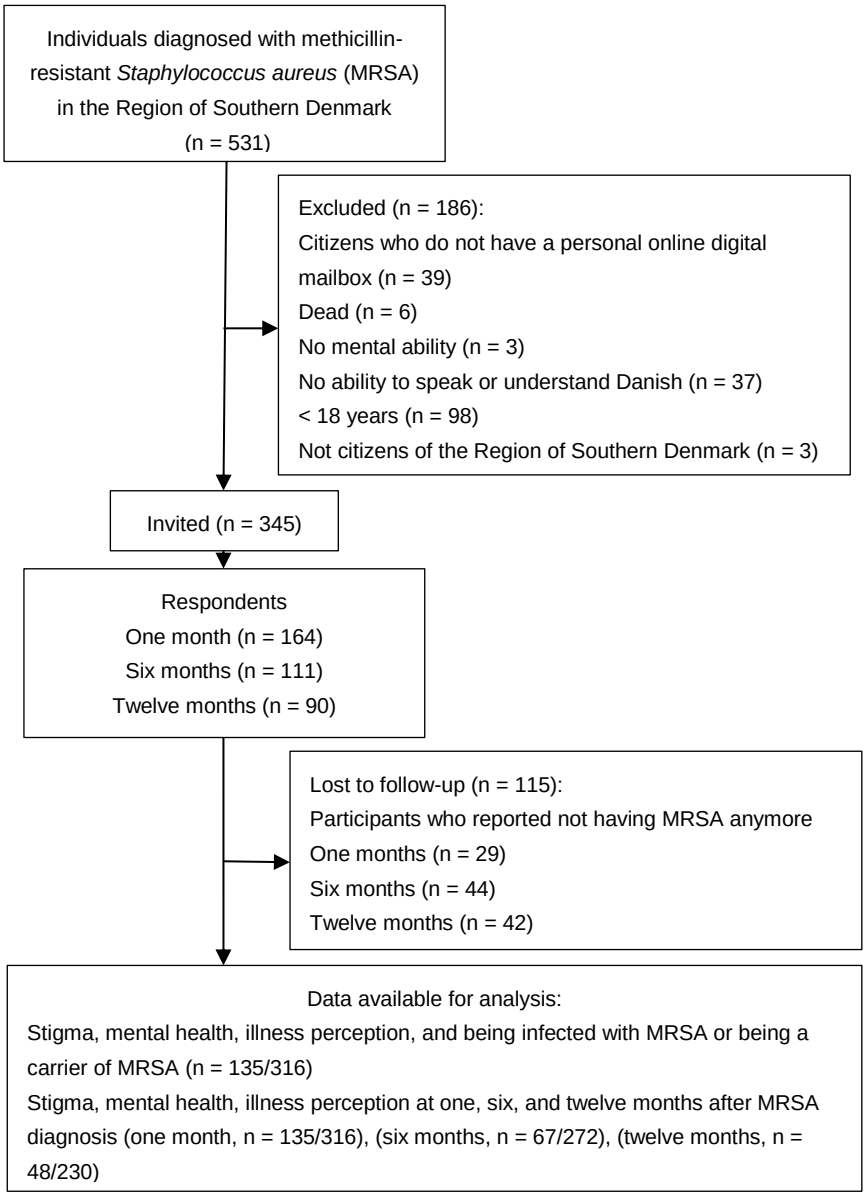
Table III: The association between stigma, mental health, and illness perception, at one month compared to six, and twelve months after meticillin-resistant *Staphylococcus aureus* (MRSA) diagnosis

N = 135	Association between one and six months				Association between one and twelve months			
	Crude analysis[a] Mean difference (95% CI)	P-value	Adjusted analysis[b] Mean difference (95% CI)	P-value	Crude analysis[a] Mean difference (95% CI)	P-value	Adjusted analysis[b] Mean difference (95% CI)	P-value
Stigma, score ranging from 40–160								
Total score	-1.1 (-7.0;4.9)	0.72	0.4 (-6.9;7.8)	0.91	-3.0 (-10.0;3.9)	0.39	-0.8 (-9.2;7.6)	0.85
Personalized stigma	0.5 (-4.5;5.4)	0.85	-0.7 (-6.8;5.5)	0.83	-3.0 (-8.8;2.7)	0.30	-3.9 (-11.0;3.2)	0.28
Disclosure	4.4 (-4.3;13.2)	0.32	4.9 (-5.8;15.7)	0.37	-0.2 (-10.4;10.0)	0.97	2.9 (-9.4;15.2)	0.64
Negative self-image	-0.1 (-7.6;7.4)	0.98	1.0 (-8.3;10.3)	0.83	2.4 (-6,3;11.1)	0.59	6.2 (-4.4;16.7)	0.25
Public attitudes	1.7 (-6.4;9.9)	0.68	1.4 (-9.0;11.7)	0.80	-1.8 (-11,3;7.7)	0.71	1.6 (-10.1;13.4)	0.78
Mental health, score ranging from 0–100								
Total score	2.9 (-0.7;6.6)	0.11	0.8 (-3.7;5.3)	0.73	1.1 (-3,1;5.3)	0.61	-2.1 (-3.7;5.3)	0.73
Anxiety	4.7 (-0.4;9.8)	0.07	1.1 (-5.2;7.5)	0.73	4.9 (-0.9;10.8)	0.10	0.6 (-6.3;7.9)	0.86
General positive affect	5.5 (1.0;11.9)	0.10	0.6 (-6.7;7.8)	0.88	-0.9 (-8.4;6.6)	0.82	-6.4 (-14.7;2.0)	0.13
Depression	-0.4 (-0.6;5.8)	0.90	-3.1 (-10.4;4.3)	0.41	0.6 (-6.5;7.7)	0.88	-4.7 (-13.1;3.8)	0.28
Emotional control	2.0 (-2.1;6.2)	0.34	2.0 (-3.1;7.2)	0.44	3.1 (-1.8;8.0)	0.21	3.46 (-2.5;9.4)	0.25
Illness perception scored in a range of 0–10								
1. Consequences	-0.2 (-0.7;0.3)	0.39	0.4 (-0.2;1.0)	0.15	-0.3 (-0.8;0.3)	0.30	0.4 (-2.3;1.1)	0.22
2. Timeline	0.8 (0.0;1.6)	0.05	0.9 (-0.0;1.8)	0.06	1.2 (0.2;2.1)	0.01	1.4 (0.3;2.4)	0.01
3. Personal control	0.3 (-0.5;1.2)	0.41	0.0 (-1.02;1.04)	0.98	1.0 (-0.-0.1;1.8)	0.07	0.5 (-0.6;1.7)	0.37
4. Treatment control	-1.4 (-2.4;-0.4)	0.005	-1.3 (-2.5;-0.2)	0.0	-1.0 (-2.1;0.1)	0.08	-0.8 (-2.1;0.5)	0.24
5. Identity	-0.4 (-0.8;0.1)	0.09	0.1 (-0.5;0.6)	0.84	-0.1 (-0.6;0.4)	0.69	0.1 (-0.5;0.7)	0.69
6. Concern	-0.2 (-0.8;0.4)	0.48	-0.1 (-0.7;0.6)	0.86	-0.7 (-1.4;0.1)	0.02	-0.6 (-0.7;0.6)	0.86
7. Coherence	-0.1 (-0.9;0.6)	0.77	-0.2 (1.1;0.6)	0.602	0.3 (-0.6;1.1)	0.52	0.1 (-1.1;0.6)	0.86
8. Emotional representation	-0.0 (-0.6;0.6)	0.96	0.6 (-0.2;1.1)	0.20	-0.5 (-1.8;0.1)	0.12	-0.1 (-0.8;0.7)	0.89

a: Mixed fits, linear mixed-effects model, reference group: one month after MRSA diagnosis.

b: Mixed fits, linear mixed-effects model, reference group: one month after MRSA diagnosis. Adjusted for gender, education level, livestock-associated MRSA, employment status, and mental health score/stigma score

Figure 1: Flow diagram for inclusion of participants



Supplementary materials

A1

Stigma scale

Please answer the questionnaire by ticking the box with which you agree the most:

	Strongly disagree	Disa-gree	Agree	Strongly agree	No opinion
I feel that I am not as good a person as others because I have MRSA					
Having MRSA makes me feel unclean					
Most people think that a person with MRSA is disgusting					
Having MRSA makes me feel I'm a bad person					
Most with MRSA are rejected when others find out					
I am very careful who I tell that I have MRSA					
I have been hurt by how people reacted to learning I have MRSA					
I worry that people who know I have MRSA will tell others					
I have stopped socializing with some due to their reactions					
Have lost friends by telling them I have MRSA					
I have had treatment in health care canceled due to MRSA					

Mental health scale

During the period of being MRSA-positive please mark the box to which you agree the most:

	Almost all the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of time
Been a very nervous person						
Felt calm and peaceful						
Felt downhearted and blue						
Been a happy person						
Felt so down in the dumps that nothing could cheer you up						

The Brief Illness Perception Questionnaire

For the following questions, please circle the number that best corresponds to your views:

1. How much does your MRSA affect your life?

0	1	2	3	4	5	6	7	8	9	10
No affect at all										Severely affects my life

2. How long do you think MRSA will continue?

0	1	2	3	4	5	6	7	8	9	10
A very short time										Forever

3. How much control do you feel you have over MRSA?

0	1	2	3	4	5	6	7	8	9	10
Abso-lutely no control										Extreme amount of control

4. How much do you think your treatment can help your MRSA?

0	1	2	3	4	5	6	7	8	9	10
Not at all										Extreme-ly helpful

5. How much do you experience symptoms from your MRSA?

0	1	2	3	4	5	6	7	8	9	10
No symp-toms at all										Many severe symp-toms

6. How concerned are you about your MRSA?

0	1	2	3	4	5	6	7	8	9	10
Not con-cerned at all										Extreme-ly con-cerned

7. How well do you feel you understand your MRSA?

0	1	2	3	4	5	6	7	8	9	10
Don´t understand at all										Understand very clearly

8. How much does MRSA affect you emotionally? (e.g. does it make you angry, scared, upset, or depressed?)

0	1	2	3	4	5	6	7	8	9	10
Not at all affected emotionally										Extremely affected emotionally

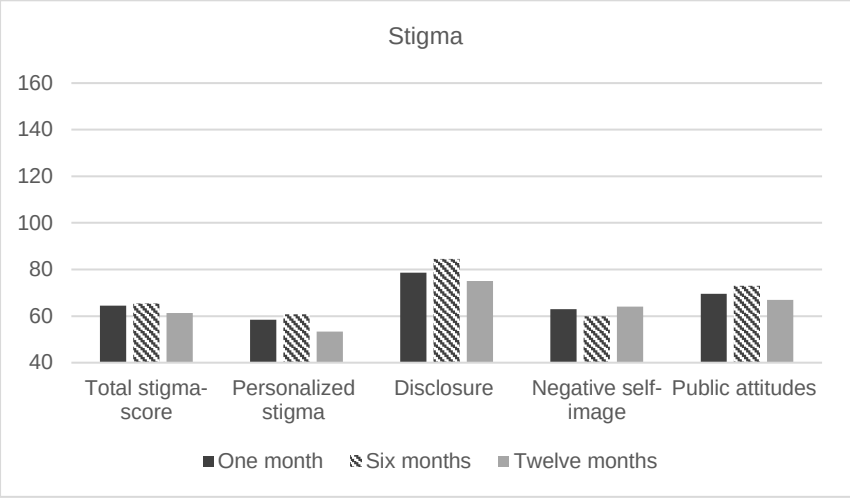
Please list in rank order the three most important factors that you believe caused your MRSA. The most important causes for me:

1. _____
2. _____
3. _____

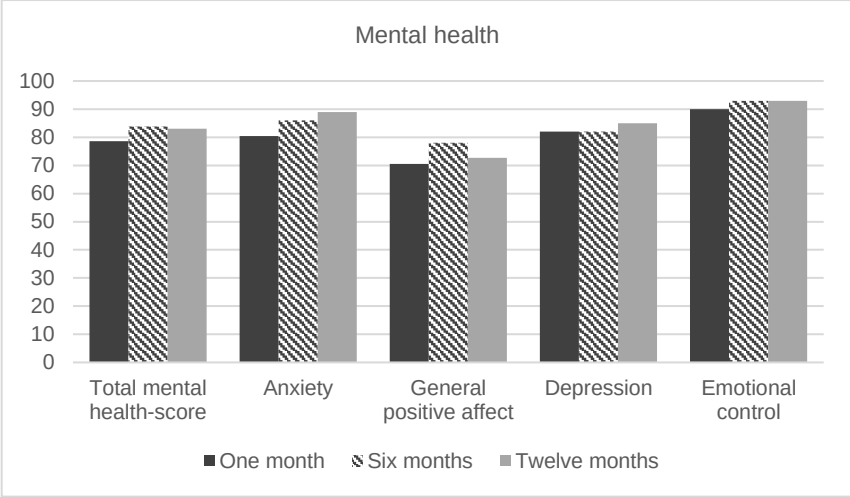
Supplementary Table A2: Baseline demographic characteristics of responders and non-responders among individuals diagnosed with meticillin -resistant *Staphylococcus aureus*

N = (345)	Number (%)	
	Responders (n = 164)	Non-responders (n = 181)
Age group		
18–40 years	61 (37)	117 (65)
41–64 years	78 (48)	48 (26)
≥65 years	25 (15)	16 (9)
Gender		
Male	85 (52)	100 (55)
Female	79 (48)	81 (45)
Hospital		
Odense University Hospital	61 (37)	62 (34)
Hospital South West Jutland	39 (24)	39 (22)
Hospital of Southern Jutland	32 (19.5)	45 (25)
Lillebaelt Hospital	32 (19.5)	35 (19)

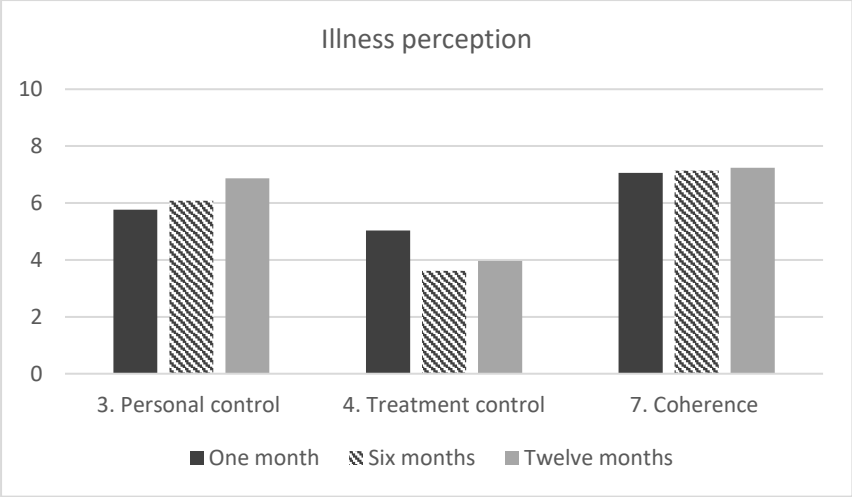
Figure A3: Subcategories of stigmatization, mental health, and illness perception among individuals diagnosed with methicillin-resistant *Staphylococcus aureus* one, six, and twelve months after the diagnosis



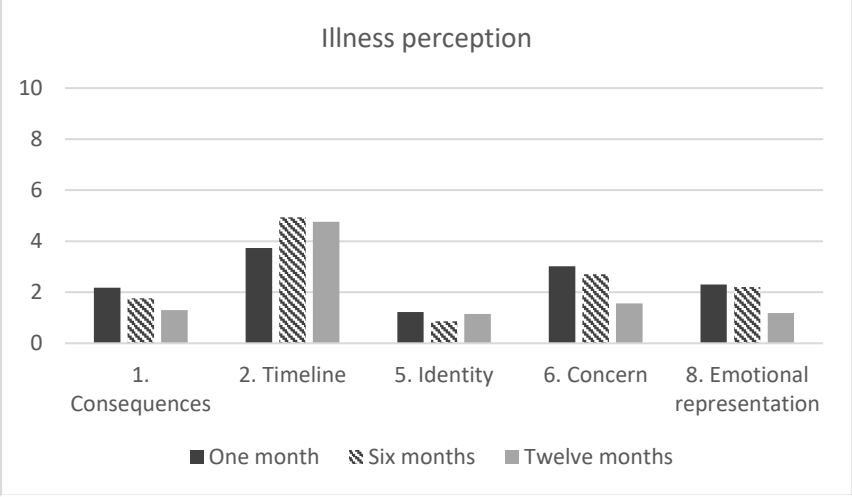
Stigma-scale, score: 40-160. Lower scores define a more favourable MRSA-related stigma state.
Number of observations in total stigma-score one month: n = 80, six months: n = 46, twelve months: n = 30



Five-item RAND Mental Health Inquiry (MHI), score: 0-100. Higher scores define a more favourable mental health state. Number of observations in total mental-score one month: n = 125, six months: n = 67, twelve months: n = 44



Brief-IPQ (B-IPQ): Brief Illness Perception Questionnaire. Higher scores on items 3,4, and 7 denote a less threatening view of the illness.
Number of observations in personal control one month: n = 132, six months: n = 66, twelve months: n = 47



Brief-IPQ (B-IPQ): Brief Illness Perception Questionnaire, higher scores on items 1,2,5,6, and 8 denote a more threatening view of the illness
Number of observations in consequences one month: n = 135, six months: n = 67, twelve months: n = 47

A framework for methicillin-resistant Staphylococcus aureus consultations comprising cross-sectoral videoconferences between patient, general practice, and specialist expertise - A participatory design-inspired study

Mette Assenholm Kristensen[1,2], Hanne Irene Jensen[2,4] , Christian Backer Mogensen[2,5] , Jens Søndergaard[6] and Jens Kjølseth Møller[1,2]

[1]Department of Clinical Microbiology, Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark.
[2]Department of Regional Health Research, University of Southern Denmark, Odense, Denmark.
[3]Department of Quality, Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark.
[4]Department of Anesthesiology and Intensive Care, Lillebaelt Hospital, University Hospital of Southern Denmark, Vejle, Denmark.
[5]Department of Emergency Medicine, Hospital Sønderjylland, University Hospital of Southern Denmark, Aabenraa, Denmark
[6]Research Unit of General Practice, Department of Public Health, University of Southern Denmark, Odense, Denmark.

Corresponding author
Mette Assenholm Kristensen
Beriderbakken 4, 7100 Vejle, Denmark
E-mail: mette.assenholm.kristensen@rsyd.dk
Tel: +45 22740923
ORCID: https://orcid.org/0000-0001-8676-6661

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Abstract: **249 words**
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Supplementary material: 1 figure

Abstract

Objective: To develop and pilot test a cross-sectoral videoconference for Methicillin-resistant *Staphylococcus aureus* (MRSA) consultations in general practice with the use of specialist expertise.

Design: A participatory design-inspired study comprising a workshop for end-users to develop a framework for a cross-sector videoconference and pilot test the framework in clinical practice. Post-its from the workshop were categorized into themes and reviewed and a framework was created. The framework was used in the pilot test and evaluated with semi-structured interviews.

Setting: General practices in the catchment areas of Lillebaelt Hospital and Hospital of Southern Jutland.

Subjects: End-users involved in MRSA care.

Main outcome measures: End-users' perspectives on a framework for a cross-sectoral videoconference and end-users' perspectives of the use of the framework in clinical practice.

Results: The framework included tasks before, during, and after the videoconference and aimed to be patient-centered and to plan the MRSA care program. The framework was structured with potential themes to address. The pilot test showed that MRSA care was perceived as complex and benefited from shared MRSA consultations. In particular, mutual respect, shared knowledge, and problem-solving communication had a high value among the participants. However, a few practice staff found the videoconference time-consuming. In contrast, patients found it time-saving and a few patients preferred face-to-face consultation with the infection preventionist.

Conclusion: With a structured and patient-centered framework for the shared MRSA consultation with specialist assistance from an infection preventionist,

the majority of practice staff and patients found the MRSA consultation in general practice clinics useful.

Introduction

According to the Danish guidelines, treatment and follow-up on MRSA carriage are mainly handled by general practitioners (GPs) unless a regional MRSA clinic exists [1]. In the Region of Southern Denmark, decolonization treatment and subsequent control sampling are managed by general practice. However, it might be difficult for practice staff to develop routines in MRSA care because of the complexity of the MRSA guidelines and the limited number of patients with MRSA seen by most GPs [2]. Videoconferences are now more widely used as a consequence of the COVID-19 pandemic and most healthcare providers in Denmark have access to the necessary equipment and are confident with its use. Moreover, there is strong political pressure to increase the use of video consultations in healthcare in Denmark [3,4]. Securing access to hospital specialists in general practice through videoconferences may improve patient outcomes. In a study, patients with cancer, the GP, and a hospital oncologist participated in a videoconference. The patients reported high satisfaction and GPs and oncologists were overall positive although less pronounced than the patients [5]. However, peer-to-peer videoconferences between hospital specialists and practice staff are still uncommon in Denmark. Likewise, two-way video consultations between practice staff and patients account for only 1.2% of all consultations in general practice in Denmark [6].

Few studies have described interventions to improve the management and care of MRSA carriers. However, The German Authorities of Public Health have established a help-desk service for healthcare professionals, patients, and the wider public [7]. Even though information about MRSA was widely available on the internet, the study showed the need for an interactive dialogue with a specialist for healthcare professionals and patients [7]. Text messages consultations between general practice and hospital specialists are widely used [8,9]. A downside is that these consultations do not offer real-time problem-solving, do not include the patient, and may be inefficient for more complex care programs [10]. Cross-sector videoconferences might be a better alternative and improve access to and collaboration with medical specialists increasing levels of

medical competence in general leading to improved diagnosis, treatment, and follow-up to patients whether in hospital or in primary health-care [11]. Therefore our study aimed to develop a framework for a cross-sectoral videoconference with specialist expertise for MRSA consultations in general practice and to pilot-test this framework in clinical practice.

Material and methods

Study design

The study was inspired by a participatory design methodology. The methods attempt to create a platform for active participation of end-users in the development of new designs including information technology [12]. We followed the four-step method developed by Clemensen and colleagues 1: needs assessment, 2: ideas generation, 3: testing and retesting, and 4: evaluation [13]. However, in our study, we only carried out needs assessment and ideas generation in Phase 1, and testing in Phase 2 (Figure 1). To develop a framework for the cross-sectoral videoconference for MRSA consultations in general practice, we held a workshop to identify needs and generate ideas (Phase 1). To be noted, it was predetermined that the specialist expertise was a remote sitting infection preventionist (IP) and that the patient, the patient's family, and the practice staff all were located at the general practice clinic. Afterward, this framework was pilot-tested (Phase 2), see Figure 2. The study period was from October 2020 until December 2022. Workshops and videoconferences were, to avoid interpersonal variation, conducted by the first author, who is an experienced IP, currently working as a PhD student.

Setting and participants

The study was carried out at the Department of Clinical Microbiology, Lillebaelt Hospital in collaboration with the Hospital of Southern Jutland. Both hospitals are located in the Region of Southern Denmark.

Phase 1

Participants in the workshop included former patients with MRSA, and healthcare providers with expertise in general medicine, infection control, and infectious diseases.

Phase 2

Recruitment of patients for the pilot test of the videoconferences was based on information about new MRSA-positive patients extracted from a regional MRSA database comprising laboratory data on MRSA samples. We included patients belonging to the catchment areas of the Hospital of Southern Jutland and Lillebaelt Hospital. We included the index cases in the family and individuals with indication for decolonization treatment within 2–3 months. Furthermore, participants should be mentally able to cooperate, able to understand and speak Danish, and able to participate in the videoconference in general practice. An IP contacted the practice staff of patients eligible for participation by phone. If the practice staff accepted to participate, they contacted the patients and informed them orally. The IP provided oral project information to practice staff and written information for both patients and practice staff. We used the Cisco Webex meeting system for the videoconference. The videoconference was an add-on to the existing practice, where the departments of clinical microbiology provides written material and guidance via telephone on MRSA care to general practice. The assistance is provided by a clinical microbiologist or by an IP. IPs in Denmark are generally nurses who have spent at least two years as registered healthcare provider and have had training and a certification exam covering microbiology, epidemiology, infection control, and hospital hygiene. Practice staff (nurses or GPs) inform individuals with MRSA, prescribe the decolonization treatment of MRSA carriers, and perform follow-up control sampling. However, MRSA patients often serve as their own care coordinators navigating the MRSA care program in the Region of Southern Denmark.

Data collection and data analyses

Phase 1

The two-hour-long workshop included a presentation of the most frequent patient characteristics (personas) and the typical MRSA care program (user journey). During the workshop, needs and ideas (think, pair, and share) were written on post-its, which were grouped into themes by participants during the workshop. After the workshop, the first author summarized the workshop data and constructed the framework for the videoconference. The summary of the workshop data and the framework were reviewed by the workshop participants. The first author composed a guideline and a checklist as supplementary material to carry out the cross-sectoral videoconference for MRSA consultations based on the framework, practical aspects of telehealth [14], and the Danish MRSA guideline [1].

Phase 2

Based on the results of Phase 1 we conducted the cross-sectoral videoconference for MRSA consultations, where the patients and GP were placed in the GP consultation room, with the IP appearing on the practice staffs computer screen. Between 2–7 days after the MRSA consultation, semi-structured telephone interviews of the participants were performed. To ensure impartiality, the interviews were performed by an IP from the Department of Clinical Microbiology at Lillebaelt Hospital, who not was directly involved in the study project. The first author constructed the semi-structured interview guides (Supplementary A1), a transcription guide, and an analysis guide, and analyzed the qualitative interviews. Analysis of the qualitative interviews was managed using NVivo 12 (QSR International, 2014). The theory of qualitative research interviewing by Kvale and Brinkmann was used [15]. Interviews were recorded and subsequently transcribed. The analysis process initially focused on what the participants seemed to perceive as the meaning of his or her own statements (self-understanding), leading to a common-sense understanding. To structure and reduce the transcript text, lines were coded. For further text reduction, the codes were merged into themes and subthemes. During the process annotations in NVivo were used to write comments on the understanding (self-understanding and common-sense level) of specific text lines. Next, the framework matrice in NVivo to summarize and condense the

data material was used. In the final step, the theoretical understanding of the statements and their interrelationships was examined using Jody Gittell's theory on relational coordination [16]. Relational coordination is a process of coordinating work between professionals, which encompasses four communication dimensions (frequent, timely, accurate, problem-solving) and three relational dimensions (shared knowledge, shared goals, mutual respect). Fostering high levels of relational coordination across organizations, in particular, clinical pathways (protocols or guidelines to integrate work), boundary spanners (case managers), patient rounds (meetings), and shared information systems (administrative and clinical) are essential. These components are expected to be more effective when used in conjunction with one another [16].
The quotations were translated into English by a translation bureau. Participant names were changed to unique patient, nurse, and GP numbers.

Ethical approval, participant consent, and data security
We obtained permission to store data from the Region of Southern Denmark (20/25135) and access to patient records was approved by the Danish Patient Safety Authority (S-31-1521-375). Ethical approval was not necessary according to the Regional Committees on Health Research Ethics for Southern Denmark (S-20192000-155). Data analysis was conducted in a secure analysis environment. The patients received oral and written project information and a link to sign the informed consent form by use of NemID (a public secure electronic user login developed by the national authorities in Denmark). Written information and a link for the videoconference were sent by e-mail to general practice. The practice staff gave oral consent at the beginning of the recorded qualitative interview. The study was reported according to the Standard for Reporting Qualitative Research (SRQR) guideline [17].

Results
Phase 1
In the workshop participated seven end-users, which included one patient, three GPs, two IPs, and one infectious disease specialist. The developed framework

for the cross-sector videoconference consisted of a list of the potential themes to be discussed during the consultation and tasks to solve before and after the consultation for either the IP or the practice staff for example documentation or writing referrals. The timeframe was a double consultation (30 minutes) according to the organizational structure in general practice. The consultation was planned shortly after the MRSA diagnosis. Questions from patients had a high priority during the consultation. Real-time dialogue by phone after the consultations to handle unsolved needs from practice staff and patients was also a part of the developed framework. For details, see Figure 2.

Phase 2

We completed eight consultations when pilot-testing the cross-sectoral videoconference. Afterward eight patients and seven practice staff (three nurses and four GPs) were interviewed. Patient interviews lasted for 15–25 minutes and 8–19 minutes for practice staff. Patient characteristics are displayed in Table I. Analysis revealed in three main themes: Collaboration, shared knowledge, and barriers.

Collaboration. Practice staff found that they handled MRSA care in videoconferences markedly differently from their usual practice. One general GP expressed it this way: *"*We're a little quick to say *drive down to the pharmacy.* They have these packages and they tell you everything you need to know" (GP1). Further, the traditional way of the use of guidelines was stated: "I have used the material that I have been able to find" (Nurse2). The majority of practice staff used the excuse of obtaining specialist advice by phone on concrete questions that arose during the MRSA care in general practice: "There are some questions that I have to say I need to follow up on, and I will have to come back to them and give my answer" (GP2). However, when the structure was changed and an IP actively participated in a real-time dialogue with the patient and the practice staff it was overall described as useful for the MRSA care program. A GP phrased it in this way*: "*The consultation worked incredibly well. The patient felt really well taken care of. And the fact that the three of us could talk. There was a nice atmosphere if you can say that about a

consultation. It was a good environment to do it in, I think" (GP3). The participants experienced the relationship between the participants during the videoconference as respectful of one another's competencies. Professional identities, specialized knowledge, and status differentials did not influence communication negatively. A patient expressed it in this way: "I actually thought it worked well because they were good at supporting each other. My own nurse knows what she needs to know as part of her job, and the external person, if you can call her that, she knows her specialty to the max" (Patient4) and a GP said: "I don't really think that it is interfering with what we do. I don't see it that way. I feel it is a help" (GP1).

Shared knowledge. The participants considered the videoconference as thorough, focused on patients' needs, and forward-looking. A patient stated: "When the video call was finished, the agreement was made directly with the doctor about when we would come back for the test. So when you left, you had a plan for everything" (Patient8). A GP explained it in this way: "Patients got answers to their questions and help with the things they felt were a problem in this situation" (GP2). Most often the information was passed from the MRSA specialist to the practice staff and the patient. Questions addressed were for example socializing with grandchildren, job situation, disclosure of MRSA-positivity, contagiousness, and how to become MRSA-free. The practice staff had an important role in contributing with information with regard to the medical history of each patient and the household. A patient experienced the competencies specific to the primary healthcare sector in this way: "My doctor sat by my side to support and help me, also by telling me about my husband's illness" (Patient6). Most patients and practice staff found the session educational. They thought MRSA care was diffuse, which made the practice staff insecure in their professional competencies. A nurse described the educational role in this way: "The infection preventionist was good at talking very understandably about what MRSA is and how treatment would proceed if that's what we chose to do. She was good at communicating it so that we ordinary people could understand it too" (Nurse2). In a few cases, the new information during the videoconference contributed to a changed course of the

practice staff's actions. A nurse expressed it this way: “I thought the whole family would just have to be put on treatment to get rid of MRSA, but as she was part of the conversation, she could explain that no treatment was needed when the person was not yet free of infection and because the child was under two years old. Then you have to wait until the infection has been treated and the child turns two. I didn't know that” (Nurse2). The interviews reflected that the written communication in the patient record after the consultation and the possibility of handling future case-specific questions by phone made timely and accurate communication possible: “There was a clear description of what we had gone through. Nothing was missing. I was also given a number to call if I had any questions and patients were given a number to call. I think it was rounded off well” (GP2). The complicity of MRSA care was described in several ways by the practice staff. Most of them experienced that the patients and patients' families had a lot of questions regarding MRSA, reflecting the growth and specialization of MRSA care programs. A nurse expresses it in this way: “Who should be treated and how many members of the family need a swab and who doesn’t need a swab? That's where it gets a little tricky for me. Those who work on a pig farm and those who are going to surgery. I think there are many variations anyway” (Nurse2).

Barriers. Both patients and practice staff wanted a more thorough written description of the agenda for the videoconference and a clarification of roles and responsibilities before the videoconference. A GP explained it in this way: “I was a bit unsure at first whether it was me who was going to run the consultation or whether it was the infection preventionist and what we were going to talk about” (GP2). In addition, the patients were preoccupied with getting written information on MRSA before the meeting. A patient stated it in this way: **“**I would have liked to have had the material before the consultation so I could have read about MRSA. I feel best when I am prepared for a meeting, because then I can ask my questions properly” (Patient6). Most patients valued access to specialist healthcare that would not otherwise be possible. However, the impersonal nature of communication through an electronic system was a concern among a few patients. Furthermore, in the case of big families, it was

difficult for everyone to be seen on the screen. In addition, stationary computer screens made it difficult for the patient to show for example eczema to the IP by video. A patient expressed the impersonal nature of communication through an electronic system as followed: “Video conferencing is not quite the same as sitting in front of someone. It's easier to talk when you're sitting next to each other” (Patient1). However, most caregivers were positive about communication by video even though they did not have any experience in the use of videoconference in their practice: **“**It's also about making the most of the possibilities that exist today - that you can have these video meetings. I haven't done that before, but we shouldn't be so afraid. There may be others who work this way, I just haven't done it before, but it was a boost to my work” (Nurse 2). In addition, most caregivers found the link easy to use, however in a few cases, the experience was the opposite. A GP explained it in this way: “The way the link was communicated to us was bad in the sense that the secretary hadn't got the video link right in the record, so it was a bit of a hassle for me. I ended up looking in an old email and then I found the link” (GP3). A few of the practice staff mentioned that the videoconferences were time-consuming. However, this barrier was first mentioned after specific questions addressing negative perspectives on the videoconference: “If there are any drawbacks, it's probably that it takes longer. You certainly need to be prepared for that” (GP2). On the contrary, most patients found the intervention time efficient and believed that it was a clear advantage that the MRSA care program was carried out in general practice. Further, patients benefitted from the improved access to specialist care: “I definitely think this is the best option because it's local, so I don't have to spend a whole lot of time on it. At the same time, I'm sure you get the correct information because you're talking to a specialist in the field” (Patient2).

Discussion

In this study, we created a framework for the simultaneous presence of a patient, practice staff, and an IP in a video-based MRSA consultation. The framework was structured to solve patient needs and carry out an action plan for the MRSA care program among individuals who were planning to receive decolonization treatment. Tasks needing only one profession were carried out

before or after the shared consultation. Care for patients with MRSA was perceived as complex and overall patients and practice staff benefited from the cross-sectoral collaboration. The relationship during the videoconference was characterized by mutual respect and shared knowledge, and the communication was characterized as problem-solving and accurate. Identified barriers included from the practice staff perspective that a few found the cross-sectoral videoconference time-consuming. In contrast, patients found the cross-sectoral videoconference time-saving but a few patients preferred face-to-face consultation with the IP. Further, a few patients called for written information on MRSA sent before the shared consultation. Both patients and practice staff preferred a clear agenda for the meeting and clarification of roles.

It was a strength that we had user involvement, which is the core of the participatory design method. We involved users as active partners when developing the framework for the videoconference and by testing it in a real-world setting. Furthermore, a strength of the study was the inclusion of different characteristics among the participating families with MRSA. For example families with children under two years of age, individuals working in healthcare, and individuals with risk factors such as eczema. However, three patients dropped out after inclusion. A homeless individual, a young pregnant woman, and a non-Danish family. These individuals might have added a different perspective on the present analysis of the videoconference and tested the robustness of the design for these groups in society. It should also be mentioned that females and the younger age groups were over-represented in the study population. A study from Sweden showed the elderly's ambivalence towards e-health: reluctant curiosity, a wish to join, and a need for information and learning support [18]. This highlights the need to include a diverse study population in studies of telemedicine and to adjust future interventions to the needs of these specific patient groups. It is also a limitation that the number of videoconferences held in the pilot study is small and that the analysis of the interviews only was performed by the first author solely, which may limit the breadth and depth of the analysis.

According to Gittell, meetings provide a convenient forum for high-quality communication among the participants, helping to strengthen shared goals,

shared knowledge, and mutual respect. Furthermore, supplementing meetings with case managers, clinical pathways, and shared information systems, these meetings can be short, focused, and efficient [16]. However, both shared information systems and the use of case managers are relatively weak elements in the developed framework in the present study. Case managers may, to benefit the most, coordinate the whole case across the organization's boundaries [16], which might be a consideration to implement for further improvement of the present framework, for example, when used in groups of vulnerable patients. So far a shared information system is only available in practice for doctor-patient video consultation through the application “My Doctor” in Denmark [19]. A common infrastructure for peer-to-peer cross-sectorial video meetings has yet to be developed. In Australia, however, three-way consultation between a remote-sitting specialist, a patient, and a primary-care provider is implemented in remote and rural areas [20].

Our results are predominantly in line with the previously mentioned Danish study involving cancer patients and GPs [5] and a study from the United Kingdom. The latter study examined the interaction between patients, practice staff, and a specialist, during diagnosis and decision-making in a videoconference. The cross-boundary collaboration enabled practice staff to develop their skills and actively participate in diagnosis and decision-making. However, they found that interprofessional interaction resulted in limited patient involvement in decision-making [21]. We also found that the practice staff develop their skills and actively participated in the planning of the patients' MRSA care program. Furthermore, the practice staff felt capable of continuing the MRSA care program on their own. However, our intervention was focused on patient needs. To limit interprofessional communication during the videoconference, the practice staff was informed of MRSA guidelines before the shared consultation. Furthermore, the practice staff could phone the IP before and after the consultation, which may have encouraged more patient-centered consultations. One of the main barriers that the practice staff pointed out in our study was the clarification of roles among the healthcare professionals during the videoconference. Results from a review that aimed to examine what makes cross-sectoral partnerships work, showed that vague structures and unclear

roles harmed productivity [22]. This is also in line with the use of clinical pathways (protocols or guidelines to integrate work around the needs of a process) according to Gittell [16]. To structure our framework, the shared MRSA consultations included potential themes to be addressed for example information matching patient needs (e.g. livestock-associated MRSA, healthcare providers) and consideration of the need for additional support (e.g. social nurse, extra consultation in general practice). These efforts might benefit from further improvements to increase clarification of roles.

Our study differs from most of the present studies in the field of interactive telemedicine, because the majority of these studies focus on the use of telemedicine in direct patient care, i.e., studies in which the patient is remote from the clinician [23]. When comparing the content and quality of video, telephone, and face-to-face consultation in primary care, a study found that video consultation may only be suitable for simple problems. In terms of consultation length, content, and quality, a videoconference appeared only similar to a telephone consultation. Face-to-face consultations were most "information rich" [24]. Mascia and colleagues also explored face-to-face versus video communication. They concluded that the use of easy-to-use electronic-based communication tools can hinder the quality of group discussion and debate [25]. Thus, these studies indicate that many prefer face-to-face meetings to videoconferences, as a few patients in our also favored. In our framework, however, we avoid limitations applicable to two-way video consultations between practice staff and patients. For example poorer access for people who are unable to use online technologies [26].

Further research is needed before the routine implementation of the cross-sectoral videoconference. After the needs assessment, ideas generation, testing, and retesting of a telemedicine solution, an evaluation should be carried out according to participatory design methods in telemedicine research. The evaluation should include an assessment of the effectiveness of care examined in clinical trials and cost-effectiveness studies [13]. Furthermore, we will recommend, due to limitations in the representativeness of patients included, that future research and implementation of specialist competencies through video in general practice should be aware of patients with special needs such

as the elderly or patients needing interpreting services. Finally building access to specialist care in the primary healthcare sector through cross-sectoral video consultations might be beneficial for other low-prevalent diseases seen in primary healthcare or in cases of complex disease management.

In conclusion, with a structured and patient-centered framework for the shared MRSA consultation with specialist assistance from an infection preventionist, the majority of practice staff and patients found the MRSA consultation in general practice clinics useful.

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Conflicts of interest

The authors report no conflicts of interest.

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Table I. Patient characteristics

Patient	Affiliated laboratorium[1]	Age (years)	Sex[2]	Initial infection	Livestock-associated	Family size	Small children in family[3]	Eczema	Pregnancy	Healthcare worker
1	SHS	44	F	Yes	-	4+	-	-	-	-
2	SHS	33	F	-	-	3	Yes	-	-	-
3	SHS	35	M	Yes	-	2	-	Yes	-	-
4	SLB	43	M	Yes	Yes	4+	-	-	-	-
5	SLB	32	F	Yes		2	-	-	Yes	-
6	SHS	52	F	Yes	-	3	-	-	-	-
7	SLB	32	F	-	-	4+	Yes	Yes	-	Yes
8	SHS	33	F	-	Yes	3	-	-	-	-

[1] SLB: Lillebaelt Hospital, SHS: Hospital of Southern Jutland
[2] F=female, M=male
[2] Below two years of age

Figure 1. The participatory design process

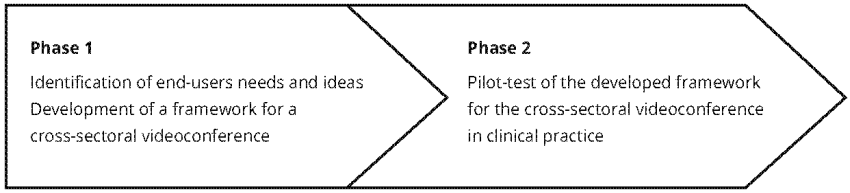

Figure 2. Framework for the cross-sectoral videoconference system for MRSA consultations

Supplementary A1

Interviewguide til telefoninterviews med patienter

Forskningsspørgsmål	**Interviewspørgsmål**
Introduktion	Tak for medvirken Intervieweren præsenterer sig kort Kort om rammerne for interviewet • Varighed ca. 15-20 min. • Anonymt • Samtalen bliver optaget Har du spørgsmål inden vi starter?
Er interventionen brugbar og accepteret set fra patientens perspektiv?	Hvad har været vigtigt for dig i forhold til MRSA og hjælp fra dit lægehus? Hvordan har dit forløb ellers været? Har du oplevet, at der er blevet taget hånd om det du gerne ville have hjælp til? – hvordan – kan du give nogle eksempler? Hvordan havde du det med at konsultationen foregik i dit lægehus og ikke på sygehuset? Hvordan synes du bookingen til konsultationen fungerede (den konsultation hvor hygiejnesygeplejersken var med via video)? Hvordan oplevede du selve konsultationen? Kan du huske, hvad I talte om? Var der noget du manglede? Hvordan oplevede du tidsrammen? Var der spildtid (inkl. ventetid)? Vil du benytte dig af muligheden for en telefonsamtale med en hygiejnesygeplejerske efter den fælles konsultation? Hvorfor/hvorfor ikke?
Er det brugbart og accepteret at anvende specialistressourcer i	Hvordan oplevede du, at der var en ekstra person (hygiejnesygeplejerske) med via video?

almen praksis via videoforbindelse set fra patientens perspektiv?	Hvordan bidrog hygiejnesygeplejersken? Gav det noget ekstra som du havde brug for? Hvorfor ikke? /Hvorfor ikke? Kan du give nogle eksempler?
Hvilke barriere og incitamenter er der ved interventionen set fra patientens perspektiv?	Hvordan synes du denne form for samarbejde mellem lægehuset og hygiejnesygeplejerskerne på sygehuset fungerer? Hvilke ulemper synes du, der er? Ville det gøre, at du ikke har lyst til at tage i mod tilbuddet en anden gang? Oplevede du nogle klare fordele ved, at sygehuset og lægehuset samarbejder på denne måde? Hvis du ønsker at tage i mod tilbuddet en anden gang – hvad ville årsagen så være? Var der noget, du oplevede som ubehageligt? Hvordan? Har du forslag til, hvordan hjælpen fra dit lægehus og sygehuset kunne blive bedre?
Afrunding på interviewet	Har du spørgsmål eller kommentarer til noget af det, vi har talt om? Er der noget jeg ikke har spurgt om, men som du synes er vigtigt at få med?

Supplementary A1, cont.

Interviewguide til telefoninterviews med sundhedspersonale

Forskningsspørgsmål	**Interviewspørgsmål**
Introduktion	Tak for medvirken Intervieweren præsenterer sig kort Kort om rammerne for interviewet • Varighed ca. 10 min. • Anonymt • Samtalen bliver optaget • Samtykke via lydoptagelse: Du spørger om den praktiserende læges navn, og om de vil give mundtligt samtykke til at interviewet anvendes til pågældende forskningsprojekt (det skal med på lydoptagelsen, som dokumentation!). Har du spørgsmål inden vi starter?
Er interventionen brugbar og accepteret set fra lægehusets perspektiv?	Helt overordnet; hvad synes du om konceptet? Hvad synes du om indholdet i videokonsultationen? Fik vi talt om de vigtigste ting? Hvad var det vigtigste? Var tiden passende? (Spildtid/ventetid) Hvordan har den skriftlige kommunikation fungeret (fx formidling af videolink, og korrespondancenotater)? Forventer du at få behov for telefonisk rådgivning efter den fælles konsultation? Hvis ja – hvilke områder forventer du, at skulle have rådgivning om?
Er det brugbart og accepteret at anvende specialistressourcer i	Hvad synes du om samarbejdet og de opgaver du havde?

almen praksis via videoforbindelse set fra lægehusets perspektiv?	Er der brug for samarbejdet omkring patienter med MRSA? / I så fald hvor meget sparring er der brug for? Hvordan havde du det med, at der deltog en specialist i konsultationen med patienten? Er der nogle klare fordele ved det? Er der nogle klare ulemper? Hvordan oplevede du kvaliteten af fagligheden fra sygeplejersken? Hvad synes du om korrespondancenotaterne fra hyg. spl? (Det at de laves, og hvor hurtigt de er tilgængelige)
Hvilke barriere og incitamenter er der ved interventionen set fra lægehusets perspektiv?	Ville du vælge at bruge konceptet, hvis du fik det tilbudt en anden gang? Hvorfor? Kan du komme i tanken om noget, der kunne gøre at du fravalgte det (telefonisk og skriftlig rådgivning er tilstrækkeligt, økonomiske eller tekniske forhold)? Synes du grundlaget for at tilbyde konceptet er på plads, eller har du forslag til ændringer?
Afrunding på interviewet	Har du spørgsmål eller kommentarer til noget af det, vi har talt om? Er der noget jeg ikke har spurgt om, men som du synes er vigtigt at få med?

University of Southern Denmark
Campusvej 55
DK-5230 Odense

Phone: +45 6550 1000
sdu@sdu.dk
www.sdu.dk