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Rate of nosocomial MRSA transmission evaluated via contact screening

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Abstract

Background The prevention of methicillin-resistant S. *aureus* (MRSA) transmission in the healthcare setting is a priority in Infection Control practices. A cornerstone of this policy is contact tracing of nosocomial contacts after an unexpected MRSA finding. The objective of this retrospective study was to quantify the rates of MRSA transmission in different clinical settings.

Methods This multi-centre study included MRSA contact screening results from two regional hospitals and one academic hospital. MRSA contact tracing investigations from 2000 until 2019 were reviewed and post-contact screening results were included of index patients with an MRSA-positive culture and their unprotected contacts. Available typing results were used to rule out incidental findings.

Results Of 27,377 contacts screened after MRSA exposure, 21,488 were Health Care Workers (HCW) and 4816 patients. Post-contact screening was initiated for a total of 774 index cases, the average number of screened contacts per index case was 35.7 (range 1 to 640). MRSA transmission was observed in 0.15% (41) of the contacts, 19 (0.09%) HCW and 22 (0.46%) patients. The number needed to screen to detect one MRSA transmission was 667. The highest risk of MRSA transmission occurred during patient-to-patient contacts, with transmission rates varying from 0.32 to 1.32% among the participating hospitals. No transmissions were detected in HCW (n=2834) in the outpatient setting, and the rate of transmissions among HCW contacts on the wards was 0.13% (19 of 15,874). Among 344 contacts of patients with contact precautions, no transmissions were detected.

Conclusions Reconsidering current MRSA contact tracing practices may lead to a more targeted approach with a lower number needed to screen.

Keywords MRSA, Infection control, Contact precautions, Nosocomial transmission, Antimicrobial resistance, Contact tracing

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Background

Worldwide, health care institutions struggle with the consequences of Methicillin-Resistant *Staphylococcus Aureus* (MRSA) infections and their implications for Infection Control strategies. *S.aureus* is a common cause of infections both in the community and in health-care facilities, but patients with MRSA infections are 64% more likely to die than patients with drug-sensitive infections [2, 17, 19].

Currently, in the Netherlands, the overall MRSA prevalence rate is estimated to be 2% (percentage of MRSA-positive isolates with respect to all *Staphylococcus aureus* isolates) (ISIS-AR, 2015-2019). This low percentage can partly be explained by the rigorous nationwide MRSA Search and Destroy (S&D) policy. The Dutch MRSA S&D policy in hospitals involves several interventions to detect and eliminate MRSA. The first step is the distribution of a questionnaire before admission to assess whether pre-defined risk factors are present in patients. Subsequently, all identified high-risk patients are preventatively subjected to contact precautions while awaiting culture results. The second step is strict isolation of each proven MRSA-positive patient in a single room until decolonization has been successfully established. A key component is the post-contact screening of any unprotected person who came into contact with an unexpectedly discovered MRSA carrier in order to prevent secondary nosocomial cases and outbreaks. To achieve this aim, all close contacts are identified by means of "contact tracing" and are microbiologically screened for MRSA (contact screening). However, some aspects of this S&D policy, including the post-contact tracing and screening, are labor- and time-intensive. Reducing the number of screened contacts may lower the total efforts and costs associated with this intervention.

The risk of nosocomial transmission after unprotected contact with an MRSA index patient is not well established and depends on multiple characteristics of the interaction. An optimal screening strategy to identify secondary cases of MRSA infection and carriage will ideally take these factors into account, in addition to local factors such as the prevalence of MRSA and the vulnerability of the patient population [6, 12].

This retrospective multi-centre study aimed to evaluate the transmission rates of MRSA following unprotected exposure, as identified through a post-contact screening program, spanning a 20-year period across two regional hospitals and one academic hospital in the Netherlands. The secondary aim was to identify potential settings associated with a higher rate of MRSA transmission, enabling the identification of high-risk settings.

Material and methods

Design and setting

This multi-centre retrospective study included MRSA contact tracing investigations from 2000 until 2019. All patients with an MRSA-positive culture and all unprotected contacts were included. The three participating hospitals were the Reinier de Graaf Gasthuis (RdGG), Haga Teaching Hospital (Haga) and Leiden University Medical Centre (LUMC). Two of these hospitals are secondary care level hospitals with respectively 30 000 (RdGG) and 40 000 (Haga) yearly admissions, and the third is a tertiary care level hospital (LUMC) with 21 000 yearly admissions.

Infection control precautions

All participating hospitals have an MRSA infection control policy that conforms with the then prevailing national guidelines of the Netherlands (WIP '98-2012). Known MRSA carriers receive care under "strict isolation" precautions. These precautions involve placement in a single room with an anteroom and controlled air circulation, with personnel wearing gowns, gloves, and masks at all times. These precautions differ from the "contact isolation" precautions, which are less stringent. "Contact isolation" entails the use of gowns and gloves when there is direct patient contact, but an anteroom and universal masking are not required. "Contact isolation" precautions are applied to patients awaiting the results of the MRSA screening cultures or for other indications, such as ESBL carriage.

Upon admittance, each patient completes an MRSA screening questionnaire to evaluate the presence of nationally pre-defined MRSA risk factors. Patients identified with MRSA risk factors, as outlined in Table 1, are then microbiologically screened. In the period from 2000 until 2013, these patients were admitted in strict isolation pending the MRSA screening results. In case of an MRSA finding, no contacts were screened. That policy was updated in 2013, and since then, patients were admitted with contact precautions (CP) only whilst awaiting the

Table 1 Overview of nationally pre-defined risk factors from the Dutch guidelines in the study period

MRSA Risk factors warranting screening upon admission
A recent stay in a hospital abroad
An MRSA-positive household member
A history of MRSA carriage in the past
Contact with industrially farmed livestock
Adopted children from abroad with regular hospital contacts
Patient from an outbreak setting in a health institution
Recent exposure through unprotected contact with an MRSA carrier

results of microbiological screening and consequently these contacts were screened in case of MRSA. Patients without risk factors are not routinely screened for the presence of MRSA.

In the case of an unexpected MRSA finding in a clinical sample, the unprotected contacts of the index are microbiologically screened for transmission of MRSA. Unprotected contacts are defined as contacts without all the necessary isolation precautions, such as gloves, mask and gowns, including health care workers (HCW) that care for patients using contact isolation precautions instead of strict isolation precautions These contacts are screened once and as soon as it is known that they are at risk. However, no HCW are screened on the same day as the interaction with the index.

The selection of the contacts that need to be screened varies between different centres, as there are no strict national definitions. However, the guideline advises first to screen the contacts with close and more intense interactions and only to screen the remaining contacts in second instance. In LUMC and RdGG, the selection of contacts includes HCW with direct physical patient contact and patients who shared a room with an MRSA-positive patient. In Haga, all HCW with any kind of interaction are screened, including supporting staff such as meal service and cleaning staff. Also, in Haga, in case of doubt about the exact interactions of a specific MSRA-positive patient during admission, all the patients admitted to the same ward are considered contacts and are therefore screened.

MRSA carriers

During the whole study period, known MRSA carriers were placed in strict isolation upon admission to one of the participating hospitals, and consequently no contacts were screened.

All persons with at least one MRSA-positive finding are considered MRSA carriers. They are offered a decolonisation treatment. In addition, HCW are temporally relieved from patient duties awaiting clearance of their MRSA status after decolonisation.

Contact tracing investigations

Infection prevention files and contact tracing reports from 2000 to 2019 were reviewed to assess the results of MRSA contact tracing and screening initiated after the identification of MRSA-positive patients. In instances suggestive of matching secondary cases among HCW, any additionally screened contacts were included in the study. All other contact screenings with an HCW index were excluded from the study.

Three contact categories were defined: ward HCW, outpatient clinic HCW and patient-to-patient contacts. Details were collected regarding the index and the number, type and location of MRSA contacts. If known, the most invasive site of an index's first MRSA positive sample was recorded. In case of a secondary finding, microbiological typing data of the index isolate were compared to the contact isolate to confirm or exclude nosocomial transmission. The National Institute for Public Health and the Environment (RIVM) performed molecular typing as part of the voluntary national MRSA surveillance [4]. Typing methods varied during the study period, multiple locus variable number of tandem repeats analysis (MLVA), pulsed-field gel electrophoresis (PFGE), and spa typing were used. In cases in which no typing was performed, the antibiotic susceptibility results were compared. Non-matching isolates were considered incidental findings.

Laboratory methods

For MRSA screening, nares, throat and rectal or perineal swabs were obtained from patients in addition to any present catheters or skin defects, while HCW submitted nares and throat swabs only, and skin defects if present.

Microbiological procedures varied over time and reflected the standards of the period. In the first years of the study, only cultures were applied for MRSA screening. Inventarisation swabs were incubated overnight in BHI enrichment broth with 2.5% NaCl and colistine and subcultered the next day on a blood and selective MRSA agar. Colonies suspect for *S.aureus* underwent further testing to confirm identification and antibiotic susceptibility. An isolate was considered MRSA in case of a positive cefoxitin screen combined with a positive PBP2A latex agglutination test. These isolates were referred to the national reference centre, RIVM, for confirmation, typing and surveillance purposes [18].

With the introduction of PCR MRSA screening methods at some point around 2008, all laboratories adopted a two-step approach. Screening specimens were incubated overnight in an enrichment broth. MRSA-negative samples would be distinguished by means of a PCR based on the detection of an *S. aureus*-specific gene target and the mec gene PCR on the broth sample, based on previously published protocols (for RdGG: [3]; for LUMC: [9]) and for Haga: [11]). Indeterminate or positive samples were subcultured for additional assessment. In case of growth of *S.aureus*-suspicious colonies, additional follow-up testing was applied to confirm identification and susceptibility. The previously mentioned PCR was performed on the isolate to confirm MRSA, and the sample was also referred to the national reference centre for confirmation and typing.

Statistics

For each category of exposure, the accuracy of the proportions of transmissions and negative contacts was estimated using Jeffrey's method. The proportion was calculated using Epitools. (Sergeant, ESG, 2018. Epitools Epidemiological Calculators. Ausvet. Available at: http://epitools.ausvet.com.au.) Jeffrey's method was chosen due to the small number of positive findings very close to zero, in which case the use of Fisher's exact test is less applicable for comparing proportions [5]. Fisher's exact test was used to calculate whether the proportion of MRSA transmissions differed significantly between patients with a positive clinical culture and carriage-only index patients.

Results

In the period from 2000 until the end of 2019, a total of 27,649 contacts were identified. For 272 contacts, the results of the cultures could not be obtained and therefore they were excluded from the study. All the remaining 27,377 contacts were included in the study. For the 27,377 included contacts, results were available of MRSA screening following an unprotected contact with an MRSA-positive patient. This total of 2777 included 3853 records with incomplete data. Among these, 2780 were healthcare workers of unknown type, with no information on whether the contact occurred in an outpatient setting or on a ward. Additionally, for 1073 contacts, no information was recorded regarding the setting or whether these contacts involved patients or healthcare workers. In a small minority of 7 instances, post-contact screening was expanded due to secondary findings to include additional contacts of an MRSA-positive HCW. This expansion was only implemented if the HCW and the index had a matching MRSA isolate.

MRSA-positive cultures were identified in 113 of the 27,377 cultured contacts, accounting for 0.41%. Molecular typing results suggested likely nosocomial transmission in 40 of these contacts, while transmission was ruled out in 72 cases. In one case, no additional typing results were available; consequently, this case was classified as a transmission in subsequent calculations, bringing the number of (assumed) transmissions to 41. Hence, among the 113 MRSA-positive contacts, 64% were deemed incidental findings without secondary transmission.

The overall number of contacts needed to screen (NNS) to detect one MRSA transmission was calculated to be 668 (27,377/41 =668).

The highest percentage of the secondary MRSA findings was due to patient-to-patient contacts, with transmission rates varying from 0.32 to 1.32% among the participating hospitals. No transmissions were detected in HCW in the outpatient setting, and the transmission rate among HCW contacts on the wards was 0.13% (19 of 15,874). A detailed overview is presented in Table 2. Among the 344 contacts of patients with contact precautions, no transmissions were detected (95% CI 0.00-0.007)

In the study period, post-contact screening was initiated for a total of 774 index cases, 225 in the LUMC, 421 in Haga and 128 in RdGG. The average number of screened contacts per index case was 35.7 (range 1–640). Of all the post-contact screenings, 45% had 10 or fewer contacts, whilst 1% had more than 220 contacts. Figure 1 illustrates the frequency of post-contact screenings categorized by the number of included contacts, providing an overview of the size and distribution of post-contact screenings.

Figure 2 presents an overview of the number of indices per hospital and screened contacts per year.

To determine if clinical infections were more prone to nosocomial transmission than positive carriage sites alone (such as the nose/throat or rectum), we compared the transmission rates between the two groups. Clinical data regarding the initial site of MRSA infection or carriage for the index patients were available for most cases in two of the three hospitals, with the most invasive site recorded. For example, a patient with both a wound infection and throat carriage was categorized as a skin and soft tissue index case.

Analysis of the number of contacts involved showed that the 195 infection index cases led to the screening of 5558 ward HCW and 522 copatients, among whom 14 transmissions were detected, 8 in the HCW group and 6 in the copatient group. By contrast, the 111 carrier-only index cases resulted in the screening of 2451 ward HCW and 282 copatients, among whom 2 transmissions were detected, 1 in the HCW group and 1 in the copatient group. However, the p-value of Fisher's exact test was not statistically significant. The Supplementary file 1: table s2 provides an overview of the types of infections.

Index cases with proven transmission among their contacts varied considerably in their clinical characteristics. An overview of the index characteristics and the setting of the MRSA transmissions can be found in the supplement.

Discussion

This retrospective multi-centre study aimed to evaluate the transmission rates of MRSA following unprotected exposure, as identified through a post-contact screening program, spanning a 20-year period across two regional hospitals and one academic hospital in the Netherlands. The secondary aim was to identify potential settings associated with a higher rate of MRSA transmission, enabling the identification of high-risk settings.

Table 2 Overview of MRSA transmissions and incidental findings among screened contacts, sorted by setting and hospital

Type of contact	No. contacts	No. likely transmissions	No. incidental findings	NNS	Transmission rate (%)	CI 95%
All contacts*	27,377	41	72	667	0.15%	0.11–0.20%
HCW Clinic total	15,874	19	22	835	0.12%	0.07–0.2%
HCW Clinic LUMC	5648	8	8	706	0.14%	
HCW Clinic Haga	6935	10	14	694	0.14%	
HCW Clinic RdGG	3291	1	3	3291	0.03%	
HCW Outpatient total	2834	0	4	–		>0.001–0.09%
HCW Outpatient LUMC	712	0	0	–		
HCW Outpatient Haga	1751	0	4	–		
HCW Outpatient RdGG	371	0	0	–		
Patient total	4816	22	37	219	0.46%	0.29–0.68%
Patient LUMC	454	6	0	76	1.32%	
Patient Haga	4054	13	37	312	0.32%	
Patient RdGG	308	3	0	103	0.97%	
HCW unspecified	2780	0	8			
Non-specified	1073	0	1			

* 'All contacts' include 2780 HCW with unknown setting and 1073 contacts of unknown type.

For the 2780 HCW of unknown type, it was unclear if the contact occurred in an outpatient or ward setting. Similarly, no information was recorded for the unknown type contacts regarding the setting or whether they involved patients or HCW.

HCW Clinic: inpatient setting on the ward, HCW Outpatient: outpatient setting, Patient: patient-to-patient contacts, Number of Transmissions/Incidental Findings: This number is based on a comparison between the typing results of the detected MRSA isolates from the index cases and from their contacts. All matching isolates are considered likely transmissions, while the remaining cases are classified as incidental findings.

NNS: Number of contacts needed to screen to detect one transmission.

"–"indicates not applicable.

CI 95%: The accuracy of the proportions of transmission to contacts as calculated by means of Jeffrey's method

MRSA screening results were available for a total of 27,377 contacts after MRSA exposure, 21,488 of whom were HCW and 4816 were patients. A total of 41 (0.15%) secondary MRSA cases were detected. The number of contacts needed to screen to detect one MRSA transmission was 667. The highest rate of MRSA transmission was among patient-to-patient contacts. No transmission was detected among HCW contacts of outpatients with MRSA or of index patients who were treated in accordance with contact precautions.

The proportion of MRSA-positive contacts in this study is broadly consistent with the findings of most previous studies, which reported proportions of secondary cases ranging from 0.19 to 0.5% [2, 7, 10]. However, it differs greatly from the proportions reported by some other studies, which ranged from 4.7 to 12.6% [8, 13] This discrepancy can be explained by the fact that the studies that reported very dissimilar percentages used different methods to identify contacts than the present study.

We also observed a variation in transmission percentages between the hospitals which participated in the present study. This variation may be partially explained by differences between screening protocols. For instance, if the interactions of the patient during admission are uncertain, the policy in the Haga Hospital is to screen not only roommates but also all the other patients on the same ward. Including a larger number of contacts with very limited interactions will probably lower the overall transmission rate. By contrast, limiting the selection of screened patients will increase the probability of missing a transmission, but the net effect on the detected transmission rate remains unknown. It is not possible to attribute all the differences in the numbers of secondary cases between the centres to differences between the contact tracing protocols.

An important limitation of this study is its retrospective design. Incomplete administrative data resulted in incomplete records, which may have led to an underestimation of the transmission rates in certain settings or to other unknown effects. To mitigate this limitation, we utilized multiple sources and archives, such as laboratory logs and outbreak reports, to capture all nosocomial transmission events. In addition, the retrospective nature of the study means that various typing methods have been used over the years, which potentially introduced variability into the results. For a more accurate evaluation of local contact screening practices, prospective registration is recommended. Another limitation is the limited generalizability of the results to other countries. The Netherlands is a high-resource setting that endeavours

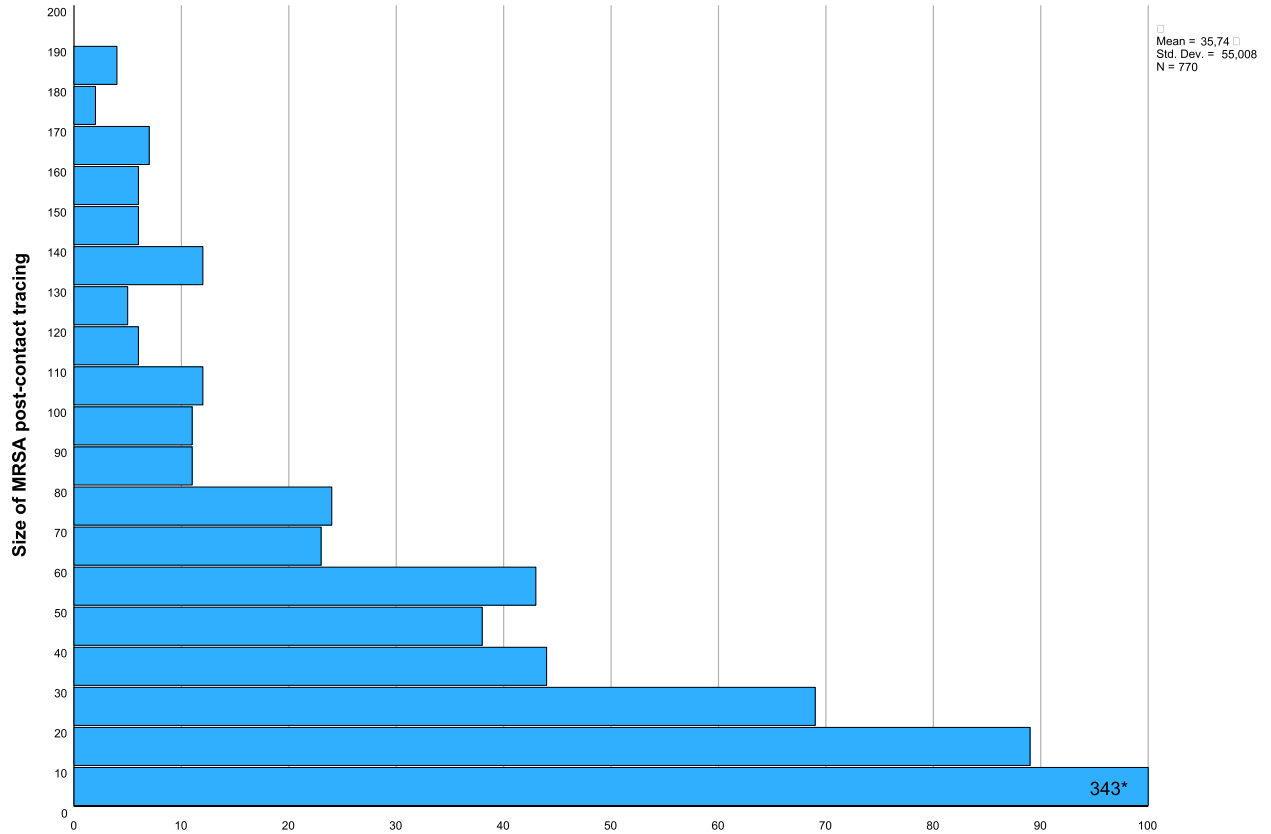


Fig. 1 Frequency of post-contact screenings shown by number of included contacts. The bar graph illustrates the frequency of initiated post-contact screenings. The bars indicate the frequency categorized by the size of each screening. The y-axis represents the size of the screenings in increments of 10 contacts, while the x-axis shows the frequency in which screenings of each size were initiated. *post-contact screenings of up to 10 contacts have been initiated 343 times. For clarity, the x-axis is visually limited to 100

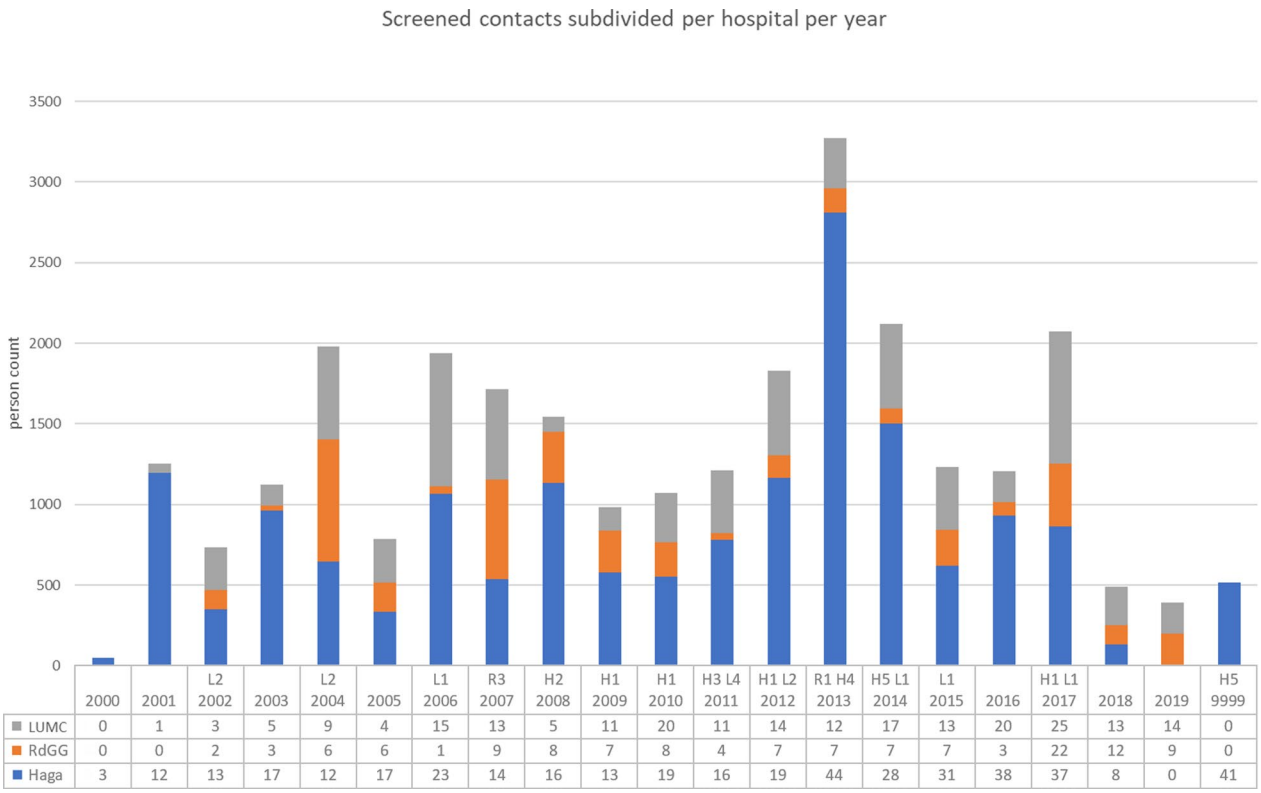
high compliance with basic hygiene practices and hospital hygiene guidelines. Therefore, the findings may not be directly applicable to settings with different resources and hygiene practices.

According to our findings, several factors seemed to increase the probability of MRSA transmission. We observed that MRSA transmission was only likely after contact on a clinical ward, either between patients or between an inpatient and a nurse who cared for that patient. No MRSA-positive contacts were detected among outpatient contacts. We hypothesize that such interactions are usually brief and do not involve close physical contact, which makes transmission less likely. This finding is in accordance with observations of other authors, who showed that MRSA transmission was facilitated by a longer duration and a greater intensity of contact [15, 16].

Another factor, albeit not statistically significant, was the trend that contact with a carrier led to fewer secondary cases than contact with an MRSA index an infection. An important limitation for this observation was the lack of data for carriers only, as it was not always known why carriers were screened. In case of a known risk factor and pending screening results, compliance with basic hygiene precautions may be higher, which may lower the chance of transmission.

The highest risk of MRSA acquisition was found in contacts between patients sharing a room. This higher transmission risk was also described by Moore et al and Ng et al in studies that focused on inpatients' roommates [13, 14]. A probable explanation is that sharing a room with an MRSA carrier leads to continuous exposure to an MRSA-colonized environment, which results in a higher transmission risk. These factors could be of special interest in settings with lower overall basic hygiene precautions as the magnifying role of environmental colonization and clinical infections may be mitigated by strict adherence to basic precautions.

The quantity of incidental findings may be influenced by differences in background MRSA carriage, as opposed to nosocomial transmission rates. In several instances, incidental MRSA findings among screened contacts were



	2000	2001	L2 2002	2003	L2 2004	2005	L1 2006	R3 2007	H2 2008	H1 2009	H1 2010	H3 L4 2011	H1 L2 2012	R1 H4 2013	H5 L1 2014	L1 2015	2016	H1 L1 2017	2018	2019	H5 9999
LUMC	0	1	3	5	9	4	15	13	5	11	20	11	14	12	17	13	20	25	13	14	0
RdGG	0	0	2	3	6	6	1	9	8	7	8	4	7	7	7	7	3	22	12	9	0
Haga	3	12	13	17	12	17	23	14	16	13	19	16	19	44	28	31	38	37	8	0	41

Fig. 2 Overview of screened contacts per year and divided per centre. The bar graph shows the total number of screened contacts per year. The table displays the number of index cases per year and per hospital, with the upper row showing the likely transmissions. H-Haga ziekenhuis, R- Reinier de Graaf Gasthuis, L-Leiden University Medical Centre, 9999=Unknown year of occurrence

more prevalent than transmissions. This finding indicates that despite current risk-based screening practices, some MRSA cases remain undetected. However, the incidental carriage rate remained consistently low. Currently, there is no insight into the carriage percentages of MRSA in different demographic groups in the Netherlands. We assume that these percentages vary widely, as incidental MRSA findings may be considered a proxy parameter for MRSA carriage. In the Haga Hospital in The Hague, the incidentally found MRSA outnumbered the detected transmissions. The three hospitals included in this study serve different patient populations, and the cause of the high percentage of incidental findings of MRSA among HCW in the Haga Hospital is unknown. Further research should explore the effects of alternative screening strategies if the background carriage rate significantly outnumbers the transmission risk. Local carriage rates may thus have important implications for developing and evaluating current screening practices.

Conclusions

This study revealed that over the past 20 years, MRSA transmission to HCW occurred at a rate of only 1 to 2 per 1000 contacts in the three participating hospitals, exclusively on clinical wards. Interestingly, the study found a tendency towards reduced transmission rates in situations where contact precautions are implemented, in outpatient settings, and among carriers, although this trend lacks statistical significance. Further investigation into optimal hospital hygiene practices for these specific groups is necessary.

The efficacy of MRSA contact screening should be carefully evaluated. Based on our findings, it may be more efficient to focus post-contact screening efforts exclusively on contacts of inpatients. Revisiting current MRSA preventative practices, informed by local data, may help to develop a more targeted and effective approach.

Supplementary Information

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Supplementary material 1

Author contributions
Study conception and design by MMK and KEV. Data investigation, data collection and curation were performed by MMK CG and MB. LK and NB contributed data analysis and interpretation. JW aided with statistical methodology. KEV provided supervision, revising the manuscript critically together with NB

for important intellectual content. The first draft of the manuscript was written by MMK and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Declarations

Ethical approval
This is a retrospective observational study. The METC-LDD Research Ethics Committee has waived ethical approval.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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