

## Health-care workers: source, vector, or victim of MRSA?

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There is ongoing controversy about the role of health-care workers in transmission of methicillin-resistant *Staphylococcus aureus* (MRSA). We did a search of the literature from January, 1980, to March, 2006, to determine the likelihood of MRSA colonisation and infection in health-care workers and to assess their role in MRSA transmission. In 127 investigations, the average MRSA carriage rate among 33 318 screened health-care workers was 4·6%; 5·1% had clinical infections. Risk factors included chronic skin diseases, poor hygiene practices, and having worked in countries with endemic MRSA. Both transiently and persistently colonised health-care workers were responsible for several MRSA clusters. Transmission from personnel to patients was likely in 63 (93%) of 68 studies that undertook genotyping. MRSA eradication was achieved in 449 (88%) of 510 health-care workers. Subclinical infections and colonisation of extranasal sites were associated with persistent carriage. We discuss advantages and disadvantages of screening and eradication policies for MRSA control and give recommendations for the management of colonised health-care workers in different settings.

### Introduction

Hospitals worldwide are increasingly concerned by methicillin-resistant *Staphylococcus aureus* (MRSA). Whereas hospital-acquired MRSA (HA-MRSA) has been a concern for inpatients since the 1960s, the threat of community-associated MRSA (CA-MRSA) has recently been associated with young and healthy people without traditional risk factors.<sup>1-3</sup> CA-MRSA has started to spread from the community into hospitals, where outbreaks have occurred.<sup>1,4</sup> Since health-care workers are at the interface between hospitals, long-term care facilities, and nursing homes on the one hand and the community on the other, they may serve as reservoirs, vectors, or victims of MRSA cross-transmission (figure 1).

Although the role of health-care workers in sporadic, epidemic, and endemic MRSA transmission has been extensively described in individual reports, the only previous review was restricted to outbreak investigations.<sup>5</sup> Moreover, infection control practitioners and professional societies have reached different conclusions about the implications for daily practice.<sup>6-11</sup> In view of these uncertainties and current changes in the epidemiology of MRSA, more comprehensive approaches to controlling MRSA should be considered. We review the reported prevalence of MRSA colonisation in health-care workers and their role in MRSA transmission. Based on these results, we formulate recommendations for MRSA screening in personnel and for further management of colonised health-care workers.

### MRSA and health-care workers

We identified 169 original articles that reported either prevalence, risk factors, or management—including screening, decolonisation, and work-related consequences—of MRSA colonisation or infection in health-care workers from 37 countries. Most reports were from high-income countries, and included 102 outbreak investigations, 29 point prevalence studies, 32 prospective surveillance studies, and six case reports or case series. Notably, we did not identify any controlled intervention studies that specifically addressed the role of health-care

workers in MRSA transmission. 127 investigations, published in 120 articles, provided the number of health-care personnel tested. Characteristics of these studies are shown in table 1. A total of 33 318 health-care workers were screened with a median sample size per study of 101 health-care workers (range 3–5125). We did not attempt to grade the available evidence in the sense of a systematic review or perform a meta-analysis.

### *S aureus* prevalence in health-care workers

41 studies provided data on the carriage of methicillin-susceptible *S aureus* (MSSA) in health-care workers. 2508 (23·7%) of 10 589 health-care workers were found to carry MSSA (range 0–40%; 95% CI 10·7–36·7%). In 127 investigations with denominator data, the average MRSA prevalence was 4·6% (1545 of 33 318 health-care workers; range 0–59%; 95% CI 1·0–8·2%). Table 2 summarises the average prevalence of MRSA carriage in health-care workers from different settings.

18 investigations did not detect any MRSA in health-care workers; these studies had sampled health-care workers in acute hospitals (14 studies),<sup>1,12-24</sup> a long-term care facility and nursing home (two studies),<sup>25,26</sup>



Figure 1: Staphylococcal hand carriage is dependent on compliance with hand hygiene by health-care workers

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	Number of studies
<b>Location (hospital-based studies only)</b>	
ICU	34
ICU, ward	41
Ward	38
Burn unit	8
ICU, burn unit, ward	5
Unavailable	25
Others*	5
<b>Specialties (hospital-based studies only)†</b>	
Medicine and medical subspecialties	61
Surgery and surgical subspecialties	83
Maternity, obstetrics/gynaecology	13
Neonatal ICU and nurseries	26
ICU (not further specified)	9
Burn unit	14
Unavailable	22
<b>Population studied</b>	
Adults (excluding geriatrics)	101
Paediatrics	52
Geriatrics	15
<b>Setting (frequency of MRSA occurrence)</b>	
Endemic	27
Outbreak	95
Sporadic	18
Outbreak followed by endemicity	2
Endemic with superimposed outbreak	2
Unavailable	18

The sum of studies in each classification varies because criteria were not always unequivocal or reported in the original publication; sometimes, more than one category could be fulfilled in a single publication. ICU=intensive care unit. MRSA=meticillin-resistant *Staphylococcus aureus*. \*Includes various combinations of burn unit, ward, ICU, operating room, emergency room, outpatients, and administrative site. †More than one specialty reported for individual studies.

**Table 1: Characteristics of included studies**

ambulatory facilities (one study),<sup>27</sup> and in university medical students (one study).<sup>28</sup> No specific geographical region, type of study, time of publication, or sampling method was common to these 18 investigations, but remarkably, only two were done in an already endemic MRSA setting.<sup>16,19</sup>

#### Risk factors for MRSA in health-care workers

Individual risk factors for MRSA colonisation or infection in health-care workers, evaluated in more than 40 studies applying various study designs and stringency of evidence, are listed in panel 1. Poor infection control practices were implicated in both acquisition and transmission of MRSA by personnel,<sup>46,62,63</sup> but even good adherence to infection control (including masks) and hand hygiene did not entirely prevent transmission of MRSA from heavily colonised staff to patients.<sup>45</sup> Importantly, several studies identified no risk factors for MRSA colonisation.<sup>31,35,60,70-76</sup>

#### MRSA carriage and infection

Mean nasal MRSA carriage in health-care workers was 4.1% in 104 studies (range 0–59%; 95% CI 0.3–7.9%).<sup>1,12-28,63</sup> By contrast, data for MRSA carriage on other body sites were reported in fewer publications and those sites were often only cultured if MRSA had been found elsewhere on the body, if treatment failed, or if health-care workers relapsed. Carriage rates were 6.4% for hands (reported in 24 studies), 1.6% for perineum (seven studies), and 0.3% for pharynx (four studies). 48 (5.1%) of 942 surveyed health-care workers had symptomatic MRSA infection without reported fatalities. Skin or soft tissue infections were most frequent, followed by upper respiratory tract infections (figure 2). Although not always stated explicitly, most health-care workers were outpatients at the time of MRSA infection. However, in one case, a health-care worker with cystic fibrosis acquired MRSA post-operatively as a patient.<sup>52</sup> In 14 investigations in settings with epidemic or endemic CA-MRSA, MRSA was cultured from 70 (3.5%) of 2002 health-care workers and five (8.5%) of 59 were symptomatic.

#### Work restrictions for health-care workers with MRSA

In 28 studies, colonised or infected personnel were allowed to work without restrictions other than education and emphasis on hand hygiene and standard precautions. Five institutions instructed the health-care workers to work only in dedicated MRSA areas or where MRSA was present.<sup>15,30,49,76,77</sup> In 57 studies, colonised or infected health-care workers were temporarily removed from patient care for varying durations until documentation of negative follow-up cultures was obtained. Removal from patient care was implemented for longer periods if eradication failed,<sup>32,43</sup> if relapse occurred,<sup>49</sup> or if clear breaches in infection-control standards were observed, as was the case in a health-care worker with chronic sinusitis involved in an outbreak in an operating theatre.<sup>46</sup>

#### Decolonisation therapy

Infrequently, eradication treatment was not provided (11 studies), was optional (four studies)<sup>66,78-80</sup> or was optional for persistent carriers (three studies).<sup>35,51,81</sup> In two studies, eradication was given if there was no spontaneous clearance after 1 week<sup>54</sup> or 6 months.<sup>57</sup>

Eradication therapy varied between studies. Mupirocin with or without additional agents was used in 57 studies. 24 studies included at least one oral antibiotic agent with or without topical agents for the initial attempt at eradication. The most common antibiotic used was rifampicin (20 studies), followed by co-trimoxazole (14 studies). Three of these studies targeted extranasal carriage sites;<sup>32,65,69</sup> others used oral antibiotics only for infectious complications.<sup>45,54,72,82,83</sup> Reported duration of decolonisation therapy varied between 5 and 14 days (median 7 days).

Success rates of eradication therapy were high—449 (88%) of 510 health-care workers cleared colonisation. Duration of therapy did not affect treatment success and decolonisation occurred in 90% of health-care workers treated for 5 days, 82% for 7 days, 93% for 10 days, and 85% for 14 days. However, in many studies, follow-up was too short to detect late-onset relapse. Only 11 investigations stated that follow-up lasted at least 4 weeks after completion of therapy, suggesting that success of decolonisation might be overestimated in some studies. Additionally, there was marked heterogeneity between studies in terms of the definition of successful decolonisation, where mentioned, with differences noted in the length of follow-up and number and source of repeated specimen. 31 different criteria were applied in 42 investigations, limiting direct comparability between studies—a problem that was also encountered in a previous Cochrane review on MRSA decolonisation.<sup>84</sup>

24 reports described management of eradication failure: in 13 instances the initial regimen was repeated,<sup>29,32,47,49,64,67,71,72,85–87</sup> occasionally for longer periods<sup>45</sup> or until successful decolonisation;<sup>41</sup> oral antibiotics were added to the initial topical regimen in eight studies;<sup>31,33,38–40,43,60,65</sup> three groups successfully added mupirocin;<sup>47,61,88</sup> and one study reported treatment of eczema as the predisposing condition.<sup>30</sup>

### Transmission of MRSA from health-care workers to patients and close contacts

Transmission from health-care personnel to patients was evaluated in 106 studies. 27 studies reported clear molecular (eg, identical strain type) and epidemiological (eg, temporal and circumstantial associations with presumed direction of transmission) evidence of MRSA transmission from health-care workers to patients and another 52 studies considered transmission likely. One report describes an outbreak in a Welsh newborn nursery with an atypical MRSA strain, which was introduced from another ward by a healthy health-care worker who was a nasal carrier of that strain.<sup>42</sup> Subsequently, patient-to-patient transmission occurred, possibly via transiently colonised staff, and the outbreak ended with the removal of a health-care worker with infected hand eczema from patient care. Several other studies have reported termination of nosocomial MRSA outbreaks after successful decolonisation of health-care workers, although this was usually only one of several simultaneous interventions.<sup>89–92</sup>

Sherertz and colleagues<sup>48</sup> linked a single health-care worker with an upper respiratory tract MRSA infection to an outbreak involving eight of 43 patients from a surgical intensive care unit (ICU). The investigators confirmed increased staphylococcal airborne dispersal in experimentally induced rhinovirus infection.<sup>48</sup> Inter-departmental or inter-hospital MRSA transfer has been reported in several instances after staff have

started new positions or changed wards within an institution.<sup>31,54,55,61,66,76,87,93</sup> Likely or proven transmission of MRSA to patients from health-care workers without clinical or subclinical symptoms was reported in 44 studies. 27 (25%) of the 106 investigations could not prove transmission between health-care workers and patients. MRSA isolates of patients and health-care workers were clonally related in 63 (93%) of the 68 studies

	Number of health-care workers with MRSA	Number of health-care workers tested	Prevalence of MRSA in health-care workers
Location (hospital vs non-hospital)			
Hospitals	1404	25 884	5.4%
Non-hospitals	42	1236	3.4%
Location within hospitals			
ICU	154	3309	4.7%
General ward	128	2032	6.3%
Burn unit	38	1326	2.9%
Baseline prevalence of MRSA among patients			
Outbreaks of MRSA	863	22 289	3.9%
MRSA endemic	389	4782	8.1%
MRSA sporadic	98	2234	4.4%
Medical specialty			
Medicine and medical subspecialties	49	1200	4.1%
Surgery and surgical subspecialties	74	1651	4.5%
Age-groups (patients)			
Adults	601	12 888	4.7%
Geriatrics	50	946	5.3%
Paediatrics	111	3187	3.5%
Type of health-care workers			
Medical staff	79	991	8.0%
Nursing staff	186	2499	7.4%
MRSA isolation practices			
Contact precautions or gowns and gloves	531	9429	5.6%
No contact precautions or gowns and gloves	373	11 362	3.3%
Private room or cohorting of patients			
Private room or cohorting	306	12 576	2.4%
No private room or cohorting	586	7586	7.7%
Geographic regions			
Northern Europe (including the Netherlands)	101	1910	5.3%
Western Europe	291	10 851	2.7%
Southern Europe	151	3121	4.8%
Eastern Europe	8	511	1.6%
North America	328	7886	4.2%
South America	13	201	6.5%
Africa	105	678	15.5%
Middle east	136	2233	6.1%
South and central Asia	17	513	3.3%
East Asia	132	1005	13.1%
Australia, New Zealand	196	2017	9.7%
Total	1545	33 318	4.6%

ICU=intensive care unit.

Table 2: Prevalence of MRSA in health-care workers

**Panel 1: Risk factors for MRSA in health-care workers****MRSA carriage***Comorbidities*

- Cutaneous lesions or conditions (eg, dermatitis, eczema, psoriasis, pemphigus)<sup>16,29-44</sup>
- Sinusitis, rhinitis (chronic, allergic, infectious)<sup>32,45-48</sup>
- Chronic otitis externa, earlobe dermatitis<sup>40,49,50</sup>
- Recent urinary tract infection<sup>51</sup>
- Cystic fibrosis<sup>52</sup>

*Other endogenous factors*

- Recent antibiotic use<sup>16,46,51,53</sup>

*Work-related factors*

- Previous work abroad<sup>31,54,55</sup>
- Work experience (eg, student health-care worker, longer duration of service)<sup>30,56,57</sup>
- Area of service (eg, medicine, surgery, long-term care facilities, decreasing risk from ward to ICU to operating theatre)<sup>56-58</sup>
- Employment in areas of high patient MRSA prevalence<sup>56,57</sup> (eg, patients from high-prevalence countries)<sup>31,50,54,55,59-61</sup>
- Close contact with patients (eg, dressing changes, wound contact)<sup>32,34,51,56</sup>
- Poor attention to infection control (eg, poor hand hygiene)<sup>46,62,63</sup>
- High work load<sup>41</sup>

**MRSA persistence despite eradication**

- Comorbidities: cutaneous lesions/conditions<sup>30,40</sup>
- Sites of colonisation: pharynx, rectum, perineum, extensive skin<sup>41,60,64-66</sup>
- Household and environmental contamination<sup>39,67</sup>
- Mupirocin resistance<sup>68</sup>

**Relapse after eradication**

- Sites of colonisation: pharynx, rectum, genitals (vagina, prepuce), skin, ear lobes<sup>39,60,66</sup>
- Infections: upper respiratory tract infection, chronic otitis externa<sup>48,49,69</sup>
- Mupirocin resistance<sup>68</sup>

that examined this association, and unrelated in only five (7%) studies.<sup>74,79,94-96</sup>

Transmission to health-care workers' family members was reported in eight studies.<sup>39,43,46,57,66,67,73,97</sup> Eveillard and co-workers<sup>57</sup> found a 29% MRSA prevalence among family members of colonised health-care workers with identical pulsed field gel electrophoresis patterns. Only one of the reviewed studies failed to identify MRSA carriage among close contacts of colonised staff.<sup>47</sup>

**Stages of MRSA carriage**

Three types of MRSA carrier status can be distinguished for health-care workers:<sup>51</sup> non-carriers; persistent carriers, who are chronically colonised with the same strain; and intermittent or transient carriers, who are colonised with varying strains for short time periods.

Cookson and colleagues<sup>51</sup> collected nasal swabs from 26 nurses working in a dedicated MRSA ward before and after each shift for 7 weeks. Transient carriage after a shift, which was lost before the next shift, was identified in 12 (46%) nurses and was mainly nasal. Short-term carriage, defined as two consecutive positive swabs, was less common and identified in four (15%) nurses. Only one nurse (4%) had persistent carriage, defined as three or more consecutive positive swabs.

There are few longitudinal studies on the natural evolution of health-care workers' colonisation with MRSA that are unaffected by decontamination attempts. Although persistent carriage of MRSA in health-care workers dominated in several studies,<sup>32,53,70,71,78</sup> other studies revealed higher proportions of transient or intermittent carriage,<sup>24,60,79,88,92,98-104</sup> or similar proportions of persistent and non-persistent carriage.<sup>35,45,85,105,106</sup> As a caveat, misclassification bias cannot be excluded because transient or intermittent carriers may have been mistakenly reported as persistent carriers. Conversely, transient carriage of MRSA among health-care workers could also have been missed because of its short duration and erratic occurrence.

Transient carriage, although associated with lower organism burden than persistent carriage,<sup>107</sup> is frequently implicated in cross-transmission between patients if no alternative source can be found among health-care workers or in the environment.<sup>41,51,104,108-110</sup> By contrast, obtaining cultures of health-care workers during or immediately after work hours might lead to inappropriately assuming persistent carriage and unnecessarily submitting the implicated health-care worker to eradication therapy, work restrictions, and stigmatisation.<sup>111</sup> Grundmann and colleagues<sup>112</sup> detected a 15% transmission rate from MRSA-positive patients to the hands of personnel after removal of gloves,<sup>112</sup> similar to a rate of 17% from MRSA-colonised patients to gloves of health-care workers reported by McBryde and colleagues.<sup>113</sup> A previous study by Thompson and co-workers<sup>24</sup> found that eight out of ten staff acquired MRSA transiently (eliminated after simple handwashing) after wound dressing changes.<sup>24</sup> In a French geriatric department with endemic MRSA, the range of monthly incidence of nasal MRSA in health-care personnel was 0-3.3%. Only one of 193 health-care workers was colonised for 3 months or longer.<sup>101</sup>

Although many body sites such as hands, rectum, perineum, axillae, vagina,<sup>114</sup> gastrointestinal tract,<sup>115</sup> and intact or inflamed skin are frequently colonised for varying time periods, the main reservoir of MRSA is the anterior nares.<sup>63,110,116-120</sup> Staphylococcal hand carriage is usually transient and greatly dependent on hand hygiene compliance.

Persistent carriage of MRSA among health-care workers was rarely reported, and was more common in personnel with extranasal carriage,<sup>45,51,64-66,110</sup> possibly affected by unsuccessful eradication therapy and associated

publication bias. Although pharyngeal carriers tend to have fewer organisms on the skin and are less likely to cause airborne dispersal,<sup>110</sup> undetected or refractory pharyngeal carriage of staff was considered responsible for repeated outbreaks.<sup>60</sup> Personnel with nasal or throat MRSA carriage can become “cloud health-care workers” during upper respiratory tract infections with substantially increased dispersal into the air.<sup>48</sup> Increased aerial dispersal of *S aureus* has also been reported during tetracycline treatment.<sup>121</sup> Even outside these special circumstances, masks may be able to reduce nasal, pharyngeal, or hand colonisation with MRSA in health-care workers.<sup>63</sup> Burn patients or patients with large open wounds are at particularly high risk for staphylococcal colonisation or infection via the airborne route.<sup>6,35,122,123</sup>

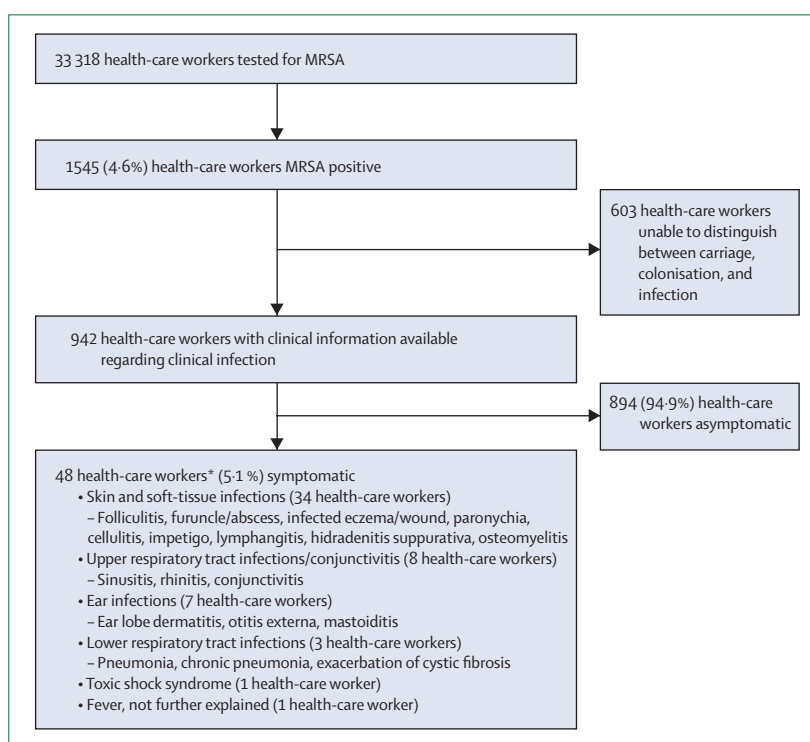
Although active infection with MRSA is reported infrequently in health-care workers and most infections are mild or even subclinical, some infections such as chronic sinusitis or dermatitis tend to become chronic and are associated with higher rates of persistent colonisation, eradication failure, or post-treatment relapse.<sup>39,40,45–47,49</sup>

### MRSA carriage and outbreaks

Several studies have described outbreaks of MRSA among patients associated with colonised health-care workers. From 1992 to 2002 at Utrecht University Hospital (Netherlands), where strict isolation procedures were in place, colonisation with MRSA was identified in less than 1% of health-care workers.<sup>31</sup> Spread to other areas of the hospital could usually be prevented if the index case had been identified, but was common when the source remained unknown. Importantly, health-care personnel served not only as vectors but were also index cases in at least four of 17 outbreaks.<sup>31</sup> Notably, carriage levels among staff varied even for outbreaks with the same genotypes—eg, between 0.9% and 7% for EMRSA-16.<sup>32,97,106</sup>

Using a mathematical model, Grundmann and colleagues<sup>112</sup> predicted the occurrence of MRSA clusters in ICU patients, assuming that nosocomial MRSA transmission was limited to staff-to-patient contact via hands. While most parameters were measured, the probability of health-care worker-to-patient transmission was fitted as 0.01 to the data. The basic reproductive number ( $R_0$ ), in the absence of infection control and staff cohorting, was calculated as ten, indicating ten incident cases after admission of a single MRSA case solely from staff acting as vectors. The real-life case reproductive number ( $R_n$ ), was more than one (ie, risk for nosocomial transmission), despite routine infection control in periods of understaffing, which were also temporally associated with MRSA clusters.

Persistently colonised or infected staff can be the source of MRSA clusters among patients if they are not identified or treated appropriately.<sup>40,45–47,60</sup> Identification of these health-care workers as a source of transmission can be difficult and is probably under-reported. Although an



**Figure 2: Prevalence of carriage and risk of infection with MRSA in health-care workers**

\*Some health-care workers developed more than one symptom or clinical manifestation. All infections were caused by MRSA.

epidemiological or molecular link was detected in most studies that evaluated health-care workers, several others were not able to confirm clonal relatedness between patient and personnel strains despite an epidemiological association.<sup>74,79,94–96</sup> It is therefore imperative to undertake epidemiological studies and to characterise MRSA strains molecularly to identify the definitive source of an MRSA outbreak.<sup>5</sup>

### MRSA carriage in settings with endemic MRSA

MRSA carriage of health-care workers was lower during outbreaks (3.9%) compared with endemic settings (8.1%), although heterogeneity between studies prevented direct comparisons. Shorter duration of outbreaks, greater attention to hand hygiene, and attempts to eliminate carriage among patients and health-care workers may contribute to lower rates during outbreaks. By contrast, health-care systems with endemic MRSA are overwhelmed by high numbers of carriers with lower awareness of the threat of the bacteria.<sup>36,124</sup> Compliance with hand hygiene and contact precautions among health-care workers were repeatedly shown to be poor in hospitals with endemic MRSA,<sup>125–127</sup> with understaffing as an important predictor of poor compliance<sup>125,126,128</sup> and increased MRSA rates.<sup>129</sup>

In regions with high MRSA prevalence, there is an increasing likelihood that both patients and staff are colonised with MRSA and that several MRSA strains

circulate simultaneously.<sup>130</sup> Despite clonal relatedness, there may be no epidemiological connection between staff and patient isolates if a single or few clones predominate in the local community. This might be particularly true for CA-MRSA.<sup>2,131</sup>

### CA-MRSA and health-care workers

The role of health-care workers in CA-MRSA transmission is still poorly studied;<sup>75</sup> they may be the source or vectors of cross-infection,<sup>132</sup> they may become secondarily colonised or infected from patients,<sup>133</sup> or their colonisation may be unrelated to colonisation in patients.<sup>134</sup> Although rates of CA-MRSA colonisation appeared to be similar to HA-MRSA in our review, there was a higher proportion of infection, highlighting the direct hazard to medical personnel.<sup>133</sup> This finding was confirmed in a recent report from an HIV-outpatient clinic in Baltimore (MD, USA), where CA-MRSA caused extensive environmental contamination, and infections with identical strains in two (3%) of 70 health-care workers with patient contact, but nasal MRSA carriage in only three (2%) of 138 health-care workers.<sup>135</sup> By contrast, asymptomatic nasal carriage with CA-MRSA occurred in six (5.8%) of 104 health-care staff at a German nursing home,<sup>75</sup> confirming a previously reported community reservoir of CA-MRSA in asymptomatic people.<sup>136</sup>

### MRSA and household transmission

Both CA-MRSA and HA-MRSA have spread to close contacts of health-care workers.<sup>45,46,57,66,67,73,97,137–139</sup> Not only does this entail risks for family members,<sup>140</sup> but can also lead to further spread of MRSA.<sup>39,43,97</sup> This may be particularly relevant for easily transmissible strains<sup>43</sup> such as EMRSA-15<sup>67</sup> or EMRSA-16.<sup>97</sup> Moreover, the home environment can become contaminated with MRSA, which may occasionally require commercial cleaning or complete removal of contaminated material.<sup>39,67,137</sup>

### Screening of health-care workers

A recent review of MRSA outbreaks found a strong association between patient and health-care worker carriage and recommended that screening efforts should focus on health-care workers with symptomatic infection.<sup>5</sup> However, screening of infected health-care workers only will likely miss a large number of asymptomatic personnel capable of transmitting MRSA to patients, since staphylococcal dispersal is mainly dependent on whether the person is a nasal carrier.<sup>141</sup> There was no marked difference in skin colonisation and environmental contamination between nasal carriers with and without minor purulent staphylococcal skin infections.<sup>141</sup> By contrast with Vonberg and colleagues,<sup>5</sup> who identified only three MRSA outbreaks with likely transmission from asymptomatic health-care workers to patients, our search revealed 18 studies with proven and 26 studies with likely transmission to patients from health-care workers who were not clinically infected with MRSA.

Our results further suggest that screening of health-care workers should not be restricted to outbreak settings because there is a trend for higher colonisation rates in settings with endemic MRSA. By contrast with the common opinion that health-care workers are usually victims rather than the source of MRSA transmission,<sup>89,142</sup> we identified 79 studies that supported a causal role of health-care workers in transmission of MRSA to patients.

### Eradication of MRSA carriage

Decolonisation of health-care workers as part of a multifactorial approach has contributed to successful termination of nosocomial MRSA outbreaks,<sup>89–92</sup> which appears easier and more cost effective if applied early before MRSA becomes endemic in an institution.<sup>143–145</sup> In a systematic review, nasal mupirocin was found to be safe and effective, leading to eradication of staphylococci in 130 (91%) of 143 health-care workers at 48–96 h post-treatment; 96 (74%) of 130 successfully decolonised health-care workers still had negative nasal cultures at 4 weeks' post-treatment.<sup>146</sup> Although this study was done in MSSA carriers, no difference would be expected in MRSA carriers, since the efficacy of mupirocin is not impaired by meticillin-resistant strains.<sup>147</sup> Our review confirms the high success rates of MRSA decolonisation regimens including mupirocin. Preliminary data suggest that mupirocin is also effective for decolonisation of CA-MRSA in health-care workers.<sup>134,135</sup>

Despite higher rates of treatment failure with nasal mupirocin in patients with extranasal MRSA carriage, successful eradication from the skin has been shown, particularly if combined with chlorhexidine body washes.<sup>119,148</sup> In a direct comparison, nasal mupirocin versus oral co-trimoxazole plus nasal fusidic acid, both in addition to chlorhexidine, resulted in similar treatment efficacy, but mupirocin was easier to use.<sup>149</sup> A Dutch study concluded that nasal mupirocin without antiseptic body wash was effective against pharyngeal, but not perineal, colonisation<sup>150</sup> despite low pharyngeal mupirocin concentrations.<sup>151</sup> Recently, a 7-day regimen of nasal mupirocin, chlorhexidine body wash, and oral rifampicin and doxycycline resulted in successful MRSA eradication at 3 months' post-treatment in 64 (74%) of 87 patients regardless of the presence of extranasal MRSA colonisation.<sup>152</sup>

### Documentation of eradication and follow-up

Although not recommended or specifically mentioned in British and US guidelines,<sup>6,153,154</sup> Dutch<sup>10</sup> and German<sup>8</sup> guidelines emphasise removal of nasal carriers from patient care for at least 48 h after initiation of eradication therapy<sup>10</sup> or proven eradication.<sup>8,10</sup> Within 2–3 days of starting mupirocin, MRSA is usually eradicated from the nares;<sup>66,89,144,155</sup> therefore, some institutions do not require health-care workers to be removed from patient contact.<sup>32,34</sup>

The timing and number of follow-up cultures required remains controversial. They largely depend on the goals

of decolonisation therapy and the local MRSA prevalence with associated likelihood of reinfection. In settings of high endemicity or frequent outbreaks, decolonisation therapy aims to reduce MRSA prevalence (rather than achieve MRSA eradication) and obtain outbreak termination. Therefore, shorter follow-up periods may be preferred because they likely reflect the true effect of decolonisation therapy rather than the chances of reinfection. By contrast, when MRSA prevalence is low and outbreaks are rare, the goal of decolonisation therapy is to prevent MRSA from becoming endemic and to ensure that health-care workers remain free of MRSA after decolonisation. In these settings extended follow-up may be indicated.

### Treatment failure and relapse

Risk factors for eradication failure are mainly colonisation of extranasal sites or subclinical infections.<sup>39,41,45,46,60,64–66,156,157</sup> In a few instances, health-care workers even underwent tonsillectomy or other surgical interventions to achieve definitive eradication of MRSA carriage.<sup>45,111,158</sup> Mupirocin resistance, which occurs at increased rates after widespread application of the drug,<sup>18</sup> is an additional risk factor for treatment failure and relapse.<sup>157,159</sup>

### Recommendations

Health-care worker screening should take place irrespective of the presence of risk factors or purulent infections as part of pre-employment examination,<sup>55,130,160,161</sup> or even periodically<sup>162</sup> and unannounced before a work shift to avoid detecting only transient carriers.<sup>5,11,111</sup> Recently, similar or higher percentages of pharyngeal than nasal *S aureus*<sup>163,164</sup> and MRSA carriage<sup>163,165</sup> have been reported, particularly in healthy people.<sup>163–165</sup> By contrast, throat screening for MRSA in ICU patients did not significantly improve diagnostic accuracy,<sup>166</sup> possibly reflecting strain or population differences. Since eradication regimens differ depending on whether MRSA is present at extranasal sites, we recommend screening of both anterior nares and throat with separate swabs. If health-care workers are at high risk of MRSA colonisation, have a positive culture, or if optimum sensitivity of screening is desired, additional screening cultures using broth enrichment should be obtained from perineum (or rectum) and chronic skin lesions.<sup>31,110,116,117,167</sup>

Implementing routine health-care worker screening is not feasible in many health-care settings because of its high cost. However, in regions with low MRSA prevalence such as Scandinavia, the Netherlands, and western Australia, close health-care worker surveillance is practised routinely.<sup>15,31,54,130,145</sup> We recommend screening of health-care workers during outbreak investigations and during early stages of an institutional epidemic when MRSA prevalence is still low or when a new MRSA strain is propagating rapidly. In settings with endemic MRSA or limited resources, priority should be

#### Panel 2: Practical management of health-care worker screening and decolonisation therapy of MRSA carriers

##### Establishing a leadership committee

- Hospital epidemiologist, members of departments of infectious disease, microbiology, occupational medicine, hospital management, human resources, and relevant clinical departments including nursing
- Responsible for decisions/policies on screening, information, decolonisation therapy, and leave of absence

##### Policies established before screening

- Indications for health-care worker screening (eg, pre-employment or outbreak)
- Measures involving screening (who, when, and what source material)
- How to deal with colonised health-care workers (notification, counselling, eradication therapy, and removal from patient care)
- Allocation of resources (costs, locum cover)

##### Screening procedures

- All health-care workers epidemiologically associated with MRSA outbreak or with any MRSA case if sporadic MRSA occurrence
- Pre-employment screening
- Unannounced screening before work shift
- Swabs of anterior nares and throat (with or without perineum, skin lesions)
- Use of enrichment cultures

##### Information given to health-care workers

- Notification of colonisation status
- Counselling by experienced infection control practitioners

##### Decolonisation therapy for MRSA carriers and follow-up

- Mupirocin 2% nasal twice daily for 7 days
- Chlorhexidine 4% bath/shower to skin and hair for 7 days
- Recommendations for daily changes of bed linen and clothing, washing laundry at least at 60°C
- Correction/treatment of predisposing conditions
- Addition of chlorhexidine gluconate 0.2% spray or gargle for pharyngeal carriage
- Addition of oral combination therapy for gastrointestinal carriage or infected health-care workers (rifampicin and co-trimoxazole or fusidic acid)
- Removal of colonised health-care workers from patient care for 48 h (nasal carriers) or until documented eradication (extranasal carriers)
- Culture of all previously colonised sites: three times, 48 h apart, starting 48 h after completion of therapy
- Long-term follow-up at 4 weeks (and 12 weeks for extranasal carriers)

Modified from the guidelines of the Heinrich-Heine University, Düsseldorf, Germany.<sup>11</sup>

given to staff in high-risk units such as ICUs, burn units, or surgical wards (especially cardiovascular and orthopaedic surgery).<sup>168</sup> Conversely, health-care workers

### Panel 3: Advantages, disadvantages, and ethical considerations of health-care worker screening and decolonisation

#### Advantages

- Assessment of full extent of MRSA spread
- Interruption of transmission of MRSA to patients
- Reduction of MRSA prevalence in patients (endemic MRSA)
- Termination of outbreaks, eradication of MRSA (sporadic MRSA)
- Reduction of burden of *S aureus* infections
- Reduction of glycopeptide use
- Long-term cost savings
- Reduction of individual risk of clinical MRSA infection in health-care worker
- Decreased risk of transmission to close contacts/ community reservoir
- Patient and public confidence

#### Disadvantages

- Disruption of patient care
- False reassurance of non-colonised or non-identified health-care workers
- Increased work load for non-colonised health-care workers with potential threat to staff-patient ratios
- Side-effects of decolonisation treatment
- Immediate costs (screening, eradication, locum cover)
- Concerns about uneconomical/unjustified use of resources
- Tensions between health-care workers and infection control team

#### Ethical considerations

- Stigmatisation
- Feelings of guilt of health-care workers towards patients and close contacts
- Threat to staff morale

#### Other considerations

- Sick versus special leave for health-care workers who are removed from clinical duties
- Health-care workers should not be responsible for cost of eradication treatment
- Maintaining anonymity of health-care workers during testing and eradication

undergoing surgical procedures should be evaluated for MRSA carriage and potential eradication treatment.<sup>169</sup>

Practical recommendations for health-care worker screening and the management of identified MRSA carriers are summarised in panel 2.

#### Treatment failure and relapse

For treatment failure or relapse of nasal colonisation, we recommend one or more repeated courses of nasal mupirocin and chlorhexidine washes, and treatment of

risk factors. Treatment for persistent throat colonisation might include additional rifampicin plus a second oral agent.<sup>97</sup> If decolonisation repeatedly fails immediately following completion of therapy, mupirocin resistance should be excluded.<sup>157,159</sup> No alternative standard therapy has been established in the event of mupirocin resistance, but several combinations of topical and systemic antibiotics have been used successfully.<sup>68,170,171</sup>

Eradication failure or frequent relapses in patients with chronic infections or extranasal colonisation should be treated with oral combination therapy. Household contacts, home environment, and pets must be ruled out as unrecognised reservoirs. If these are colonised or contaminated with MRSA, eradication therapy and thorough cleaning is advised.<sup>67</sup>

#### General considerations before screening

Screening and eradication of health-care workers' MRSA status should always be part of a comprehensive infection control policy including staff education and emphasising high compliance with hand hygiene and contact precautions.<sup>172</sup> Care must be taken to avoid feelings of guilt or stigmatisation among colonised health-care workers and to avoid disrupting the relationship between health-care workers and the infection control team.<sup>32,57,68,123,142,169</sup> If a health-care worker is removed from patient care, it should not be regarded as sick leave,<sup>123</sup> although frequently practised because of a lack of alternatives.<sup>31,32</sup> In analogy to needle-stick injuries, MRSA carriage or infection in a health-care worker should be considered an occupational hazard and injury according to local legislation, thereby abating negative career consequences. Accordingly, neither the colonised health-care worker nor their health insurance should be responsible for covering costs and instead the occupational health department should be actively involved. Particularly for temporary staff, who receive no payment while taking (forced) leave of absence, human resources might assist in compensating for loss of income.

A recent survey showed that legal rights and consequences for health-care workers colonised with MRSA differ geographically. European and Swiss infection control experts reported that 21% and 26% of colonised health-care workers, respectively, were forced to undergo decolonisation therapy at least once; 36% and 62% health-care workers, respectively, were removed from clinical duties; and 9% and 35% health-care workers, respectively, were forced to take leave of absence.<sup>173</sup>

The many anticipated advantages<sup>125,172,174</sup> and potential disadvantages<sup>97,60,169</sup> for staff screening and eradication are summarised in panel 3.

#### Limitations

We aimed to provide a broad overview of experiences over different time periods and geographical areas, and therefore accepted considerable heterogeneity in the

quality of the reviewed literature. Since many of the included publications were case series or outbreak investigations with limited numbers of MRSA-positive health-care workers, the level of evidence is variable, but they are nonetheless of hypothesis-generating or practical importance. Publication bias is conceivable in opposing directions depending on expectations, perceived opinions, and current epidemiology, which vary over time and in different areas. For example, it might be of great interest to publish high carriage rates in health-care workers at times of generally low MRSA prevalence, or, alternatively, low carriage rates while MRSA is on the rise in the general population or as indication of a successful “search and destroy” policy.

### Future research

Since the epidemiology of CA-MRSA is still poorly understood in terms of duration of carriage, transmissibility, attack rates, and possible eradication, future investigations will have to clarify the role of health-care workers as reservoirs and vectors of CA-MRSA in health-care facilities.<sup>138</sup> We are aware of the funding constraints and shortages in staff and laboratory facilities in resource-poor environments<sup>175</sup> in the face of frequently high MRSA prevalence.<sup>73,176</sup> Feasibility of some of our recommendations also depends on availability of decolonisation treatments and proof of eradication, and particularly on the capacity to temporarily remove colonised personnel from clinical duties. To provide better assistance for guidelines, more accurate data and particularly well-designed intervention studies are needed, including surveillance data on mupirocin resistance.

### Conclusions

The reviewed literature supports different roles of health-care workers in association with MRSA. About 5% of health-care workers become colonised with MRSA, of whom approximately 5% develop clinical disease. Based on the published evidence,<sup>127,177</sup> health-care workers are likely to be important in the transmission of MRSA, most frequently acting as vectors and not as the main sources of MRSA transmission. Thus, good hand hygiene practices remain essential to control the spread of MRSA.<sup>127,177</sup> Health-care workers as persistent reservoirs of MRSA in health-care institutions are rare but nonetheless important. Finally, health-care workers may also be innocent bystanders without any role in transmission to patients. This scenario might become increasingly frequent with rising prevalence of MRSA in the community. These roles are not exclusive and occasionally difficult to differentiate. Although no single approach to dealing with MRSA in health-care workers will work universally, aggressive screening and eradication policies seem justified in outbreak investigations or when MRSA has not reached highly endemic levels.

### Search strategy and selection criteria

We searched Medline and Current Contents for mainly English, French, and German articles (including English abstracts of other language articles) published between January, 1980, and March, 2006, on the prevalence, risk factors, and management of MRSA colonisation or infection in health-care workers. Combinations of the following terms were used: “MRSA”, “oxacillin”, “methicillin”, “personnel”, “healthcare worker”, and “healthcare workers”. We also searched an internet-based database of nosocomial outbreaks (<http://www.outbreak-database.com>), and scanned references, review articles, and personal files for other potentially relevant articles.

### Conflicts of interest

SH has received consulting fees from 3M, BioMerieux, and Roche Diagnostics. WCA declares that he has no conflicts of interest related to this review.

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