Rapid diagnostic testing of methicillin-resistant *Staphylococcus aureus* carriage at different anatomical sites: costs and benefits of less extensive screening regimens

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Abstract

Multiple body site screening and pre-emptive isolation of patients at risk for methicillin-resistant *Staphylococcus aureus* (MRSA) carriage are considered essential for control of nosocomial spread. The relative importance of extranasal screening when using rapid diagnostic testing (RDT) is unknown. Using data from a multicentre study evaluating BD GeneOhm^{TM} MRSA PCR (IDI), Xpert MRSA (GeneXpert) and chromogenic agar, added to conventional cultures, we determined cost-effectiveness assuming isolation measures would have been based on RDT results of different hypothetical screening regimes. Costs per isolation day avoided were calculated for regimes with single or less extensive multiple site RDT, regimes without conventional back-up cultures and when PCR would have been performed with pooling of swabs. Among 1764 patients at risk, MRSA prevalence was 3.3% (n = 59). In all scenarios the negative predictive value is above 98.4%. With back-up cultures of all sites as a reference, the costs per isolation day avoided were €15.19, €30.83 and €45.37 with 'nares only' screening using chromogenic agar, IDI and GeneXpert, respectively, as compared with €19.95, €95.77 and €125.43 per isolation day avoided when all body sites had been screened. Without back-up cultures costs per isolation day avoided using chromogenic agar would range from €9.24 to €76.18 when costs per false-negative RDT range from €5000 up to €50 000; costs for molecular screening methods would be higher in all scenarios evaluated. In conclusion, in a low endemic setting chromogenic agar screening added to multiple site conventional cultures is the most cost-effective MRSA screening strategy.

Keywords: Back-up cultures, cost-effectiveness, extranasal screening, MRSA screening, multiple site screening, rapid diagnostic testing
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Introduction

Nosocomial infections caused by antibiotic-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), are a global healthcare problem, resulting in increased mortality and high healthcare costs [1–4]. There is considerable geographical variation in the prevalence of nosocomial MRSA infections. In countries with successful nationwide infection control policies for MRSA, such as in Scandinavian countries and the Netherlands, reported MRSA rates among *S. aureus* bloodstream infections are still around 1% [5]. In countries without such infection control programmes MRSA prevalence has been reported to be as high as over 55% [6,7].

Screening and pre-emptive isolation of patients at high-risk for MRSA carriage is considered an essential part of the search and destroy policy. The screening strategy requires sampling of multiple body sites. In the Netherlands, swabs of the anterior nares, throat, perineum and, if present, wounds, catheter insertion sites and sputum are recommended for MRSA screening, according to a national protocol [8]. Until recently screening methods, using conventional microbiological culture techniques, had a diagnostic delay of 3–5 days, during which screened but uncolonized patients remained pre-emptively isolated. Rapid diagnostic testing (RDT), using molecular methods or chromogenic agars, can offer results within 24 h (or even faster), albeit at extra costs [9]. Naturally, sensitivity of MRSA screening increases with the number of body sites tested, but there is no consensus on the choice of anatomical sites to be sampled and the relative importance of extranasal screening is unknown [10–14]. We, therefore, determined costs and effects of different MRSA screening regimes using RDT, by varying the number of body sites tested and whether or not conventional back-up cultures were included.

Materials and Methods

Study design and setting

A prospective multicentre study was performed in 14 Dutch hospitals (five university hospitals, nine teaching hospitals) between December 2005 and June 2008. All patients at risk of MRSA colonization and fulfilling the criteria for pre-emptive isolation were eligible. In addition to conventional cultures, RDT of MRSA was performed directly on patient material with decisions on isolation measures based on PCR results. Two real-time PCR assays were subsequently evaluated: BD GeneOhm^{TM} MRSA PCR (BD Diagnostics, San Diego, CA USA) between December 2005 and May 2007 ('IDI study'), and Xpert MRSA assay (Cepheid, Sunnyvale, CA, USA) between April 2007 and June 2008 ('GeneXpert study'). Within the framework of the IDI study, a nested prospective cohort study was performed in 10 of the 14 hospitals, between February 2006 and May 2007, to determine effects of screening with a chromogenic agar plate (MRSA-ID, bioMérieux, Marcy-l'Etoile, France) ('chromogenic study'). However, the results of chromogenic agar testing were not used to change isolation measures, as these decisions were always based on BD GeneOhm^{TM} MRSA PCR results. The institutional review board was informed but approval was not needed for this study. The effects of RDT on pre-emptive isolation duration and costs have been published elsewhere [9].

Microbiological analyses

Swabs from the anterior nares, throat, perineum and, if present, wounds, catheter insertion sites, sputum and urine samples (in the case of an indwelling urinary catheter) were obtained directly after meeting eligibility criteria. Swabs for PCR were taken first; subsequently, swabs were taken for conventional and chromogenic culture. Specimens for conventional microbiological cultures were processed according to the guidelines of the Dutch Society of Medical Microbiology [15]. After inoculation of agar plates for conventional cultures, specimens were plated directly on the selective chromogenic agar MRSA-ID, and interpreted after 18–24 h. Details of the molecular procedures are published elsewhere [9].

On a patient level, test results were considered positive if at least one RDT result was positive and were considered negative if the nasal swab was negative (and other sites were negative or non-conclusive). In the case of a non-conclusive PCR result of the nasal swab, the overall test result for that patient was considered non-conclusive; these patients were not taken into account for determination of test characteristics. Test characteristics for less extensive screening regimes were calculated regarding multiple site testing with conventional cultures (including broth enrichment) as the reference standard.

Study endpoint and cost analyses

The primary endpoint of the current analysis was the cost per isolation day avoided with less extensive RDT screening regimes (i.e. fewer body sites screened) as compared with the current Dutch search and destroy policy. We determined cost-effectiveness assuming isolation measures would have been based on RDT using screening regimes with single or less extensive multiple site testing, using screening regimes without conventional back-up cultures and when screening with PCR would have been performed with pool-

ing of swabs. Pre-emptive isolation days avoided when using less extensive screening regimes were calculated upon the hypothetical scenario that these screening regimes had been used in decision making on termination of isolation. The effect of pooling swabs is calculated for the scenario that all unresolved PCR results would have resulted in an unresolved pool (worst case scenario) and the scenario without unresolved results with pooling (best case scenario). Pooling of specimens *per se* was assumed not to influence sensitivity or specificity of the test.

Costs for RDT included costs for MRSA PCR or chromogenic agar and costs because of false-negative RDT results. Costs of one false-negative PCR results were estimated to be €1441.13 for the scenarios with back-up cultures (mean costs of contact screenings because of ten false-negative MRSA PCR results during the clinical study) [9]. Back-up cultures will guarantee that false-negative RDT results will be detected within 2–4 days after discontinuation of isolation measures. Additional costs because of false-negative RDT results without back-up cultures are unknown, but will depend on the rate of MRSA transmission and its possible consequences (e.g. outbreak, infections), and were, therefore, varied from €0 to €50 000. The number of avoided isolation days for the scenarios with back-up cultures are calculated and remained constant for the scenarios without back-up cultures. The additional isolation days between the day of the back-up culture result and the day of discharge for patients with false-positive MRSA PCR results were not included.

Results

Patient population

One thousand seven hundred and sixty-four patients were included in the study. The prevalence of MRSA carriage in high-risk patients, based upon conventional microbiological cultures, was 3.3% (n = 59 patients). Baseline characteristics of these patients using multiple site MRSA screening as performed in the prospective multicentre study are summarized in Table 1. Costs of screening tests and false-negative RDT results are presented in Table 2.

Test characteristics

Using the results of conventional cultures as reference, sensitivity, specificity and positive and negative predictive values for detecting MRSA on a patient level were calculated for RDT screening regimes including 'nares only', 'nares and throat', 'nares and perineum', 'nares and skin' and all sites (Table 3). With less extensive screening regimes sensitivity decreases and specificity increases, which would avoid more isolation days. The percentages of avoided isolation days with single site testing of the nose, as compared with multiple site testing, would be 2.8%, 4.9% and 4.2% higher using BD GeneOhm^{TM} MRSA PCR, Xpert MRSA assay and MRSA-ID, respectively. In all scenarios the negative predictive value is above 98.4%.

TABLE 1. Baseline characteristics of multicentre study with multiple site testing [9]

	IDI study	GeneXpert study	Chromogenic study
No. of patients	853	911	428
MRSA carriage (%)	27/853 (3.2)	32/911 (3.5)	13/428 (3.0)
No. of RDTs	3113	3045	1485
No. of back-up cultures	3147	3345	1513
No. of false-negative RDT results	4	8	1
No. of avoided isolation days with RDT	1888	1782	672

TABLE 2. Cost of MRSA screening tests and false negative RDT results [9]

Resource unit	Cost/unit (€)
BD GeneOhm^{TM} MRSA PCR	56.22
Xpert MRSA assay	69.62
Chromogenic agar MRSA-ID	8.06
Conventional culture	7.11
Total costs per false-negative RDT result	1441.13

TABLE 3. Test characteristics of different RDT MRSA screening regimes

Sites screened with RDT	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Nose				
BD GeneOhm^{TM} MRSA PCR	69.2	98.4	58.1	99.0
Xpert MRSA assay	56.3	97.3	43.9	98.4
Chromogenic agar	61.5	98.8	61.5	98.8
Nose and throat				
BD GeneOhm^{TM} MRSA PCR	70.4	97.7	50.0	99.0
Xpert MRSA assay	65.6	96.1	38.2	98.7
Chromogenic agar	78.6	97.8	55.0	99.3
Nose and perineum				
BD GeneOhm^{TM} MRSA PCR	81.5	97.7	53.7	99.4
Xpert MRSA assay	68.8	95.5	36.1	98.8
Chromogenic agar	64.3	97.8	50.0	98.9
Nose and skin lesions[a]				
BD GeneOhm^{TM} MRSA PCR	73.1	97.9	52.8	99.1
Xpert MRSA assay	64.5	97.2	45.5	98.7
Chromogenic agar	76.9	97.8	52.6	99.3
All sites				
BD GeneOhm^{TM} MRSA PCR	85.2	96.5	44.2	99.5
Xpert MRSA assay	75.0	94.5	33.3	99.1
Chromogenic agar	85.7	96.6	46.2	99.5

PPV, positive predictive value; NPV, negative predictive value.
[a]Including wounds, i.v. lines, etc.

Costs per isolation day avoided with and without conventional back-up cultures

As compared with screening 'nares only', multiple site screening prevented four and six false-negative cases using BD GeneOhm^{TM} MRSA PCR (4/853, 0.5%) and Xpert MRSA

assay (6/911, 0.7%), respectively, at the (average) additional costs of €148.55 and €161.78 per patient. The costs for one prevented false-negative case with multiple site screening are, respectively, €31 680 and €24 564 when using BD GeneOhm™ MRSA PCR and Xpert MRSA assay. Chromogenic agar testing of multiple sites would have prevented four false-negative results (4/428, 0.9%), as compared with screening 'nares only' at the additional costs of €19.93 per patient. Mean costs for a false-negative RDT result were calculated to be €1441.13 [9]. Costs per isolation day avoided with less extensive screening regimes, but with conventional back-up cultures of all sites, are presented in Table 4.

If we assume that an unresolved PCR result from a single body site will also lead to an unresolved PCR result from pooled samples, then 13.1% and 15.5% of the patients would have remained in isolation when swabs were pooled for the IDI and GeneXpert test, respectively. The costs per isolation day avoided would have been €30.30 and €47.66 for BD GeneOhm™ MRSA PCR and Xpert MRSA assay in the IDI and GeneXpert study, respectively. If pooling of swabs would never reveal unresolved results, costs per isolation day avoided would be €27.57 and €41.36 for the BD GeneOhm™ MRSA PCR and Xpert MRSA assay, respectively.

Additional costs because of false-negative RDT results without back-up cultures are unknown and were therefore varied from €0 up to €50 000 per case. In this scenario, screening multiple sites with chromogenic agar is most beneficial (Fig. 1). 'Nares only' screening is favourable over multiple site screening as long as average costs per false-negative RDT result remain below €30 000 when using BD GeneOhm™ MRSA PCR and below €25 000 when using the Xpert MRSA assay (Fig. 2).

TABLE 4. Costs per isolation day avoided for the scenario with conventional back-up cultures of all sites

	Sites screened with RDT		
	Nose	Nose and throat	All sites
BD GeneOhm™ MRSA PCR	€30.83	€56.14	€95.77
Xpert MRSA assay	€45.37	€79.12	€125.43
Chromogenic agar	€15.19	€16.29	€19.95

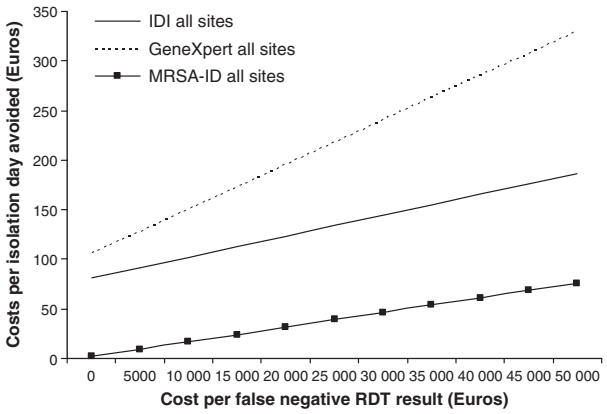

FIG. 1. Costs per isolation day avoided for multiple site testing without conventional back-up cultures. RDT, rapid diagnostic testing.

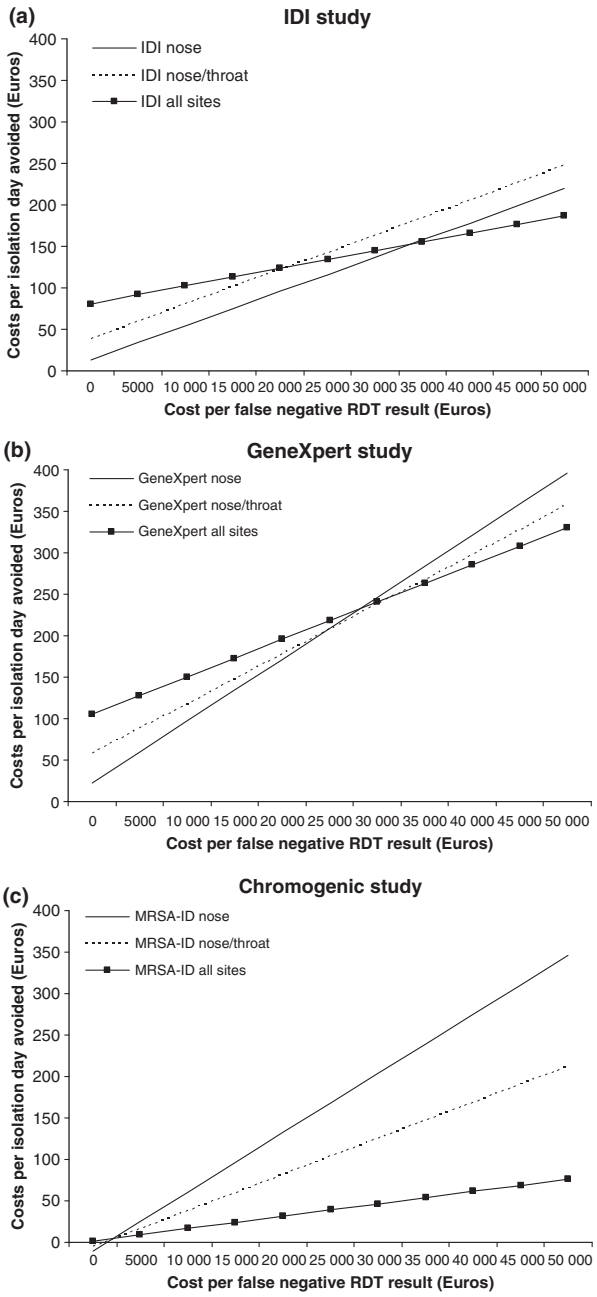

FIG. 2. Costs per isolation day avoided for RDT testing without back-up cultures using BD GeneOhm™ MRSA PCR (a), Xpert MRSA assay (b) and chromogenic agar (c). RDT, rapid diagnostic testing.

Discussion

Although multiple site screening strategies will be more sensitive than 'nares only' screening, the latter strategy appeared to be most cost-effective when using RDT in a multicentre study performed in low endemic settings. With conventional back-up cultures of all sites as a reference, the costs per isolation day avoided were €15.19, €30.83 and €45.37 with 'nares only' screening using chromogenic agar, BD GeneOhm™ MRSA PCR and Xpert MRSA assay, respectively, as compared with €19.95, €95.77 and €125.43 per isolation day avoided when all body sites had been screened (as recommended) with these three tests, respectively. Without conventional back-up cultures to adjust for any false-negative RDT results, predicted costs per isolation day avoided using chromogenic agar would range from €9.24 to €76.18 when costs per false-negative RDT range from €5000 up to €50 000, and (with current pricing levels) costs for molecular screening methods would be higher in all scenarios evaluated.

The anterior nares are considered the most important screening site for colonization with *S. aureus,* both methicillin-sensitive (MSSA) and MRSA [16–18], although some studies suggest that the throat is the most common colonization site [14,19]. Screening extranasal sites in addition to the nares increases the sensitivity to detect MRSA carriers, with 2–34% of MRSA carriers being detected through extranasal screening only [10,12,13]. With conventional cultures and broth enrichment as reference, sensitivities of multiple site RDT were suboptimal, being 85.2%, 75.0% and 85.7% for BD GeneOhm™ MRSA PCR, Xpert MRSA assay and chromogenic agar, respectively. Our findings now demonstrate that in such a setting (with back-up cultures being performed anyway) 'nares only' screening with RDT is more beneficial than molecular RDT of samples obtained from multiple body sites, increasing the costs per isolation day avoided, with €64.94 and €80.06 for BD GeneOhm™ MRSA PCR and Xpert MRSA assay, respectively. For chromogenic agar screening the additional costs for multiple site screening are limited.

Cost-effectiveness of a control policy based on screening and pre-emptive isolation is determined by the costs of the screening method and the savings generated by reductions in isolation days and transmission events (leading to further screening, isolation and infections). Although RDT of MRSA with molecular methods has been shown to reduce MRSA bloodstream infections, its use is not associated with a decrease in MRSA acquisition rates or surgical-site infections when compared with culture screening [20]. Also, cost-effectiveness of MRSA PCR remains to be determined [9,21–23]. In a low endemic setting, chromogenic agar screening is probably cost-effective but molecular screening is not [9]. Based on our experience in hospitals with low levels of MRSA, it can be expected that also in countries with endemic MRSA, multiple body site screening with chromogenic agar will have a sensitivity that is comparable to that of molecular RDT, but at lower costs. Naturally, longer turn-around times (about 32 h for chromogenic agar as compared with 14–22 h for molecular methods) [9,24–29] are an important drawback of chromogenic agar testing, but with current pricing of molecular tests, it is uncertain whether the shorter turn-around time will outweigh the higher costs.

Pooling of patient samples in the laboratory may increase sensitivity, as compared with single site testing, while avoiding expenses of multiple testing. Depending on whether we incorporate inhibition of test procedures, calculated costs per avoided isolation day would have ranged between €27.57 and €30.30 for BD GeneOhm™ MRSA PCR and between €41.36 and €47.66 for the Xpert MRSA assay, which is considerably lower than €95.77 and €125.43, when all sites were tested separately. Yet, pooling samples may reduce sensitivity, which has been demonstrated for conventional cultures [30], BD GeneOhm™ MRSA PCR [31] and Xpert MRSA assay [32]. Furthermore, pooling may increase the rate of inhibition for the BD GeneOhm™ MRSA PCR and for the Xpert MRSA assay [32,33], yet technical adjustments of the procedure (e.g. dilution of the sample or an extra heating step) have been shown to reduce this effect [31–33].

Our study has several limitations, such as the hypothetical nature of the consequences of the different screening regimes. In a scenario without back-up cultures, false-positive RDT results would increase the number of isolation days because without back-up cultures isolation will be continued until discharge. The additional isolation days between the day of the back-up culture result and the day of discharge were not taken into account in our analyses. However, as the number of false-positive cases will decrease with less extensive screening regimes and because specificity was already very high, this omission did not change our conclusions. Another limitation is that our study was performed in hospitals in the Netherlands, and may not be fully generalizable to hospitals with higher MRSA prevalence levels in other countries. Further research in countries with a high MRSA prevalence is needed to determine this. In addition, colonization patterns of healthcare-acquired MRSA may well differ from those of community-acquired MRSA (CA-MRSA) [34], and the relative importance of extranasal screening might be different for CA-MRSA. Human-derived CA-MRSA isolates are only sporadically encountered in Dutch hospitals.

Our results demonstrate that in a low endemic setting chromogenic agar screening added to conventional microbiological cultures of samples from multiple body sites as back up is the most cost-effective MRSA screening strategy. When more expensive molecular methods (with shorter turnaround times) are to be used, 'nares only' screening with PCR is recommended when performed in addition to conventional microbiological cultures of samples from multiple body sites as back up.

Transparency Declaration

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References

1. Cosgrove SE, Sakoulas G, Perencevich EN, Schwaber MJ, Karchmer AW, Carmeli Y. Comparison of mortality associated with methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* bacteremia: a meta-analysis. *Clin Infect Dis* 2003; 36: 53–59.
2. Engemann JJ, Carmeli Y, Cosgrove SE *et al.* Adverse clinical and economic outcomes attributable to methicillin resistance among patients with *Staphylococcus aureus* surgical site infection. *Clin Infect Dis* 2003; 36: 592–598.
3. Reed SD, Friedman JY, Engemann JJ *et al.* Costs and outcomes among hemodialysis-dependent patients with methicillin-resistant or methicillin-susceptible *Staphylococcus aureus* bacteremia. *Infect Control Hosp Epidemiol* 2005; 26: 175–183.
4. Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y. The impact of methicillin resistance in *Staphylococcus aureus* bacteremia on patient outcomes: mortality, length of stay, and hospital charges. *Infect Control Hosp Epidemiol* 2005; 26: 166–174.
5. EARSS database RIVM. European Antimicrobial Resistance Surveillance System. (2005). Available at: http://www.rivm.nl/earss/database/. (last accessed 9 March 2010).
6. National Nosocomial Infections Surveillance (NNIS). System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004; 32: 470–485.
7. Styers D, Sheehan DJ, Hogan P, Sahm DF. Laboratory-based surveillance of current antimicrobial resistance patterns and trends among *Staphylococcus aureus*: 2005 status in the United States. *Ann Clin Microbiol Antimicrob* 2006; 5: 2.
8. Werkgroep Infectiepreventie. [MRSA, Ziekenhuis.]. (2008) Available at: http://www.wip.nl/free_content/richtlijnen/mrsa%20ziekenhuis080310.pdf (last accessed 9 March 2010).
9. Wassenberg MW, Kluytmans JA, Box AT *et al.* Rapid screening of methicillin-resistant *Staphylococcus aureus* (MRSA) using PCR and chromogenic agar: a prospective study to evaluate costs and effects. *Clin Microbiol Infect* 2010; 16: 1754–1761.
10. Batra R, Eziefula AC, Wyncoll D, Edgeworth J. Throat and rectal swabs may have an important role in MRSA screening of critically ill patients. *Intensive Care Med* 2008; 34: 1703–1706.
11. Harbarth S, Schrenzel J, Renzi G, Akakpo C, Ricou B. Is throat screening necessary to detect methicillin-resistant *Staphylococcus aureus* colonization in patients upon admission to an intensive care unit? *J Clin Microbiol* 2007; 45: 1072–1073.
12. Ide L, Lootens J, Thibo P. The nose is not the only relevant MRSA screening site. *Clin Microbiol Infect* 2009; 15: 1192–1193.
13. Marshall C, Spelman D. Re: is throat screening necessary to detect methicillin-resistant *Staphylococcus aureus* colonization in patients upon admission to an intensive care unit? *J Clin Microbiol* 2007; 45: 3855.
14. Bignardi GE, Lowes S. MRSA screening: throat swabs are better than nose swabs. *J Hosp Infect* 2009; 71: 373–374.
15. van Griethuysen A, de Neeling H, Vandenbroucke-Grauls C, Vos G, Kluytmans J. Richtlijn Detectie van methicillineresistente *Staphylococcus aureus* in Nederland. *Ned Tijdschr Med Microbiol* 2003; 11: 58–65.
16. Mertz D, Frei R, Jaussi B *et al.* Throat swabs are necessary to reliably detect carriers of *Staphylococcus aureus*. *Clin Infect Dis* 2007; 45: 475–477.
17. Wertheim HF, Melles DC, Vos MC *et al.* The role of nasal carriage in *Staphylococcus aureus* infections. *Lancet Infect Dis* 2005; 5: 751–762.
18. Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks. *Clin Microbiol Rev* 1997; 10: 505–520.
19. Nilsson P, Ripa T. *Staphylococcus aureus* throat colonization is more frequent than colonization in the anterior nares. *J Clin Microbiol* 2006; 44: 3334–3339.
20. Tacconelli E, De Angelis G, de Waure C, Cataldo MA, La Torre TG, Cauda R. Rapid screening tests for meticillin-resistant *Staphylococcus aureus* at hospital admission: systematic review and meta-analysis. *Lancet Infect Dis* 2009; 9: 546–554.
21. Conterno LO, Shymanski J, Ramotar K *et al.* Real-time polymerase chain reaction detection of methicillin-resistant *Staphylococcus aureus*: impact on nosocomial transmission and costs. *Infect Control Hosp Epidemiol* 2007; 28: 1134–1141.
22. Buhlmann M, Bogli-Stuber K, Droz S, Muhlemann K. Rapid screening for carriage of methicillin-resistant *Staphylococcus aureus* by PCR and associated costs. *J Clin Microbiol* 2008; 46: 2151–2154.

23. Murthy A, De Angelis G, Pittet D, Schrenzel J, Uckay I, Harbarth S. Cost-effectiveness of universal MRSA screening on admission to surgery. *Clin Microbiol Infect* 2010; 16: 1747–1753.
24. Jeyaratnam D, Whitty CJ, Phillips K *et al.* Impact of rapid screening tests on acquisition of meticillin resistant *Staphylococcus aureus*: cluster randomised crossover trial. *BMJ* 2008; 336: 927–930.
25. Harbarth S, Masuet-Aumatell C, Schrenzel J *et al.* Evaluation of rapid screening and pre-emptive contact isolation for detecting and controlling methicillin-resistant *Staphylococcus aureus* in critical care: an interventional cohort study. *Crit Care* 2006; 10: R25.
26. Aldeyab MA, Kearney MP, Hughes CM *et al.* Can the use of a rapid polymerase chain screening method decrease the incidence of nosocomial meticillin-resistant *Staphylococcus aureus*? *J Hosp Infect* 2009; 71: 22–28.
27. de San N, Denis O, Gasasira MF, de Mendonça R, Nonhoff C, Struelens MJ. Controlled evaluation of the IDI-MRSA assay for detection of colonization by methicillin-resistant *Staphylococcus aureus* in diverse mucocutaneous specimens. *J Clin Microbiol* 2007; 45: 1098–1101.
28. Boyce JM, Havill NL. Comparison of BD GeneOhm methicillin-resistant *Staphylococcus aureus* (MRSA) PCR versus the CHROMagar MRSA assay for screening patients for the presence of MRSA strains. *J Clin Microbiol* 2008; 46: 350–351.
29. Snyder JW, Munier GK, Johnson CL. Comparison of the BD GeneOhm methicillin-resistant *Staphylococcus aureus* (MRSA) PCR assay to culture by use of BBL CHROMagar MRSA for detection of MRSA in nasal surveillance cultures from intensive care unit patients. *J Clin Microbiol* 2010; 48: 1305–1309.
30. Grmek-Kosnik I, Ihan A, Dermota U, Rems M, Kosnik M, Jorn KH. Evaluation of separate vs pooled swab cultures, different media, broth enrichment and anatomical sites of screening for the detection of methicillin-resistant *Staphylococcus aureus* from clinical specimens. *J Hosp Infect* 2005; 61: 155–161.
31. Jeyaratnam D, Gottlieb A, Ajoku U, French GL. Validation of the IDI-MRSA system for use on pooled nose, axilla, and groin swabs and single swabs from other screening sites. *Diagn Microbiol Infect Dis* 2008; 61: 1–5.
32. Kelley PG, Grabsch EA, Howden BP, Gao W, Grayson ML. Comparison of the Xpert methicillin-resistant *Staphylococcus aureus* (MRSA) assay, BD GeneOhm MRSA assay, and culture for detection of nasal and cutaneous groin colonization by MRSA. *J Clin Microbiol* 2009; 47: 3769–3772.
33. Svent-Kucina N, Pirs M, Mueller-Premru M, Cvitkovic-Spik V, Kofol R, Seme K. One-year experience with modified BD GeneOhm MRSA assay for detection of methicillin-resistant *Staphylococcus aureus* from pooled nasal, skin, and throat samples. *Diagn Microbiol Infect Dis* 2009; 63: 132–139.
34. Yang ES, Tan J, Eells S, Rieg G, Tagudar G, Miller LG. Body site colonization in patients with community-associated methicillin-resistant *Staphylococcus aureus* and other types of *S. aureus* skin infections. *Clin Microbiol Infect* 2010; 16: 425–431.