

Impact of rapid screening tests on acquisition of meticillin resistant *Staphylococcus aureus*: cluster randomised crossover trial

Dakshika Jeyaratnam,^{1,2} Christopher J M Whitty,³ Katie Phillips,¹ Dongmei Liu,³ Christina Orezzi,¹ Uchechukwu Ajoku,¹ Gary L French^{1,2}

EDITORIAL by Wilcox

¹Department of Infection, Guys and St Thomas' NHS Foundation Trust, London

²Department of Infectious Diseases, King's College London School of Medicine

³Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London

Correspondence to: D Jeyaratnam, Health Protection Agency Regional Laboratory (Microbiology), King's College Hospital NHS Foundation Trust, London SE5 9RS
dakshika.jeyaratnam@kcl.ac.uk

BMJ 2008;336:927-30
doi:10.1136/bmj.39525.579063.BE

This article is an abridged version of a paper that was published on bmj.com. Cite this article as: BMJ 2008, doi: 10.1136/bmj.39525.579063.BE

ABSTRACT

Objective To determine whether introducing a rapid test for meticillin resistant *Staphylococcus aureus* (MRSA) screening leads to a reduction in MRSA acquisition on hospital general wards.

Design Cluster randomised crossover trial.

Setting Medical, surgical, elderly care, and oncology wards of a London teaching hospital on two sites.

Main outcome measure MRSA acquisition rate (proportion of patients negative for MRSA who became MRSA positive).

Participants All patients admitted to the study wards who were MRSA negative on admission and screened for MRSA on discharge.

Intervention Rapid polymerase chain reaction based screening test for MRSA compared with conventional culture.

Results Of 9608 patients admitted to study wards, 8374 met entry criteria and 6888 had full data (82.3%); 3335 in the control arm and 3553 in the rapid test arm. The overall MRSA carriage rate on admission was 6.7%. Rapid tests led to a reduction in median reporting time from admission, from 46 to 22 hours ($P<0.001$). Rapid testing also reduced the number of inappropriate pre-emptive isolation days between the control and intervention arms (399 v 277, $P<0.001$). This was not seen in other measurements of resource use. MRSA was acquired by 108 (3.2%) patients in the control arm and 99 (2.8%) in the intervention arm. When predefined confounding factors were taken into account the adjusted odds ratio was 0.91 (95% confidence interval 0.61 to 1.234). Rates of MRSA transmission, wound infection, and bacteraemia were not statistically different between the two arms.

Conclusion A rapid test for MRSA led to the quick receipt of results and had an impact on bed usage. No evidence was found of a significant reduction in MRSA acquisition and on these data it is unlikely that the increased costs of rapid tests can be justified compared with alternative control measures against MRSA.

Trial registration Clinical controlled trials ISRCTN75590122.

INTRODUCTION

It is widely recommended that patients at risk of meticillin resistant *Staphylococcus aureus* (MRSA) carriage should be screened on or before hospital admission to guide the implementation of control measures.¹⁻⁶ Universal screening has been suggested for UK national policy.⁷

Conventional culture methods for MRSA take 1-5 days to produce a positive result. Polymerase chain reaction based systems are now available that detect MRSA within usually one day. The strong political pressure to reduce MRSA rates means that rapid screening, which is significantly more costly—about £10 (€13; \$21) compared with less than £2 for conventional tests—is under consideration.

Current evidence is insufficient to extend rapid testing to universal screening given the substantial implications on resources. We tested whether universal, rapid screening for MRSA leads to a reduction in MRSA acquisition on general wards.

METHODS

We randomised 10 wards (see bmj.com) of a London teaching hospital to either rapid screening for MRSA or conventional culture. The wards swapped screening methods after the first intervention and a washout period. Patients were screened at the nares, axillae, and groin (swabs were pooled); skin breaks; and clinically indicated sites.

The intervention was a polymerase chain reaction test (BD GeneOhm MRSA Assay; Becton Dickinson, NJ, USA), which produces a result for MRSA in less than two hours. The control was conventional culture, which produces a positive result for MRSA after at least 72 hours and a negative result after 24 hours.

Ward staff screened patients for MRSA on admission and at discharge. We considered specimens taken within 48 hours of admission and discharge (after ward transfer) as valid (see bmj.com for exclusions). Patients positive for MRSA were isolated and contact precautions applied. Isolation was in a side room or in a designated ward area, usually in bays with other MRSA positive patients (cohorting).³ MRSA positive patients

received decolonisation treatment. They were rescreened weekly and were considered MRSA positive until results were negative on three, consecutive, weekly screens. Patients considered high risk for MRSA carriage (see bmj.com) were pre-emptively isolated or cohort nursed from the time of admission, pending screening results; this was stopped if they were MRSA negative on admission screening.

Outcome measures

The primary outcome was the rate of MRSA acquisition (patient became MRSA culture positive on screens or specimens taken >48 hours after admission and ≤48 hours after discharge). Major secondary outcomes were rate of MRSA acquisition per 1000 patient days at risk, MRSA transmission rate, the number of patients with MRSA wound infection, and the number with bacteraemia acquired during the ward stay. We considered one infection per patient per admission.

Resource outcomes were the number of days that patients were pre-emptively nursed with precautions but were not MRSA positive on admission (“inappropriately isolated or cohorted”), or nursed without precautions and were MRSA positive on admission (“inappropriately open”). We determined the sensitivity and specificity of rapid testing on the admission specimen, which included swabs of nares, axillae, and groin compared with conventional culture.

Intervention and control arms

In the control arm, samples were taken on admission for culture only. In the rapid test arm two samples were taken on admission, one for rapid testing and the other for culture. Swabs taken on discharge were processed only by culture and we compared the results with admission culture results.

MRSA positive results were communicated to the wards as soon as possible. We define the turnaround time as the time between admission to the study ward and the result of the admission sample that determined MRSA status.

Data collection

We collected data on potential confounders for patients (see bmj.com). We collected potential ward confounders monthly: compliance with hand hygiene policy, bed occupancy, antibiotic use, staffing numbers, temporary staff levels, number of beds and side rooms open, number of MRSA culture positive patients with and without isolation precautions, percentage of patients MRSA positive on admission that were isolated at admission, and MRSA importation pressure—proportion of patients who were MRSA positive on admission.

Statistical analysis

We designated patients who were not correctly swabbed at discharge as “lost to follow-up.” We calculated unadjusted odds ratios and then adjusted them in a generalised estimating equation regression

model, with logit link for acquisition rate taking into account the cluster randomised design, with the predefined potential confounding factors of age, sex, American Society of Anesthesiology score, ward type, and length of stay on the study ward. We adjusted standard errors for correlation within wards. Odds ratios of regression coefficients are reported. To check for significant differences in sampling across wards, we constructed a summary score, taking potential factors likely to affect within ward and between ward transmission pressure and tested the homogeneity of the distribution score across wards. We carried out a further restricted primary outcome analysis, where we excluded all patients with any MRSA culture positive specimen within three months before admission, and those with MRSA positive discharge screens taken within 48 hours of a negative admission swab (see bmj.com). In the resource analysis we included patients who were MRSA positive on admission and those lost to follow-up.

RESULTS

The study ran from January 2006 to March 2007 and comprised a baseline period, first intervention period, washout period, and second intervention period. During the intervention periods 9608 patients were admitted to the study wards; 637 (6.6%) did not meet the inclusion criteria (see bmj.com). Overall, 597 (6.7%) swabbed patients were culture positive for MRSA on admission (298 in the control arm, 299 in the rapid test arm). In total, 6888 patients had full data and were eligible: 3335 (81.4%) in the control arm and 3553 (83.1%) in the rapid test arm. The intervention was carried out in 4528 (99.0%) patients (see bmj.com for characteristics of patients and study wards).

MRSA was acquired by 108 (3.2%) patients in the control arm and 99 (2.8%) in the intervention arm. The arms did not differ for MRSA acquisition rate (unadjusted odds ratio 0.88, 95% confidence interval 0.52 to 1.46), MRSA acquisition rate per 1000 patient days at risk (4.9 in the control arm *v* 4.4; incidence rate ratio 0.90, 95% confidence interval 0.69 to 1.2) and transmission rate (0.36 in the control arm *v* 0.33, 0.85, 0.64 to 1.12). This was unchanged when the acquisition rate was adjusted using generalised estimating equation regression for the predefined confounders (adjusted odds ratio 0.91, 95% confidence interval 0.61 to 1.34).

MRSA wound infections occurred in 22 patients in the control arm and 21 patients in the rapid test arm (odds ratio 0.91, 0.48 to 1.7). Two MRSA bacteraemias occurred during the control phase and one during the intervention phase (0.49, 0.01 to 9.1).

MRSA was endemic on the study wards (see bmj.com). Ward results varied but no systematic significant difference was found in MRSA acquisition or transmission rates between the study arms on individual wards, except during an MRSA outbreak that occurred on one ward during the control phase and another during the intervention phase.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Universal screening for MRSA has been suggested by the UK Department of Health

Rapid tests are under consideration but the expense of these means they require proper investigation: currently available data cannot be extrapolated to general wards

WHAT THIS STUDY ADDS

Compared with conventional methods, universal rapid screening for MRSA on admission did not reduce MRSA rates on general wards where pre-emptive isolation was in place, to a level of public health significance, given the cost implications

Although an impact was found on isolation and barrier nursing, formal cost effectiveness analysis is needed

Universal rapid screening for MRSA across the NHS is not recommended on the data presented

A univariable analysis (see bmj.com) showed that MRSA acquisition was associated with compliance with hand hygiene, the number of days that MRSA culture positive patients were cohort nursed on the open ward, and the number of days that MRSA culture positive patients were on the open ward but were not cohort nursed. When these potential independent factors were included in the generalised estimating equation regression model the adjusted odds ratio for MRSA acquisition was 0.85 (95% confidence interval 0.65 to 1.13).

The control and intervention arms differed significantly in number of inappropriately isolated or cohorted days (399 *v* 277, respectively, $P < 0.001$). In the control arm 303 days inappropriately isolated or cohorted (75.9%) and in the intervention arm 221 such days (79.8%) were spent in side rooms. The proportion of patients who were pre-emptively isolated or cohort nursed was similar between the arms (5% in control arm, 4.7% in rapid test arm). A small, statistically insignificant difference was found for the number of inappropriate open days between the two arms (389 in control arm *v* 351, $P = 0.08$). Using culture only (comparing like with like) the difference in the number of inappropriate open days between the two arms was statistically significant (389 in control arm *v* 213, $P < 0.001$).

Overall, the sensitivity of the rapid test compared with conventional culture was 87.8% and the specificity was 96.3% (positive predictive value 55.1%, negative predictive value 99.4%; see bmj.com).

The median (interquartile range) turnaround time from admission was 46.4 hours (39.1-66.1) for conventional culture and 21.8 hours (17.9-25.4) for the rapid test ($P < 0.001$). The time between a positive result being available electronically and being telephoned to the ward during the rapid phase was calculated for 260 MRSA positive patients; four (1.5%) were telephoned the day before the result, 217 (83%) the same day, 31 (11%) the day after, six (2.3%) two days after, and one (0.38%) each three and four days after.

Seven of the included patients who were MRSA culture negative on admission and MRSA culture positive by discharge were positive on admission using the polymerase chain reaction test; these cases were counted as MRSA acquisitions by study definitions. When these patients were excluded from the analysis the difference in MRSA acquisition between the two arms remained statistically insignificant ($P = 0.13$).

DISCUSSION

Reducing cross infection with meticillin resistant *Staphylococcus aureus* (MRSA) is a major priority of the National Health Service. This randomised trial found that under operational conditions rapid testing for MRSA reduced the time taken for wards to get results and had an impact on patient isolation and cohort nursing. We found no evidence of a significant reduction of MRSA acquisition (3.2% *v* 2.8%, $P = 0.61$). This magnitude of reduction (four per 1000 patients) is unlikely to be large enough, even if it were statistically significant, to influence policy on MRSA control given the cost implications and the evidence of effective, cheaper, alternatives. MRSA transmission and infection rates were also not significantly different between the study arms.

Potential confounders did not explain the lack of a difference. In this hospital, patients positive for MRSA are either isolated or cohort nursed on the open ward and decontaminated, following national guidelines. We found no evidence that deploying universal rapid testing would improve usefully on universal culture testing to reduce rates of MRSA.

Our results are contrary to theoretical expectations and differ from a non-controlled study in an intensive care unit.⁸ Another uncontrolled study in intensive care units showed a reduction in MRSA infections when pre-emptive isolation was added to rapid testing.⁹ A third non-randomised study reduced the potential advantage of the test by prolonging the turnaround time and found a statistically insignificant difference in MRSA rates.¹⁰ Another uncontrolled study associated a reduction of MRSA bacteraemia and wound infection rates with the introduction of rapid tests, although the authors state that causality could not be confirmed.¹¹ A prospective study in surgical patients found that universal, rapid MRSA screening in addition to standard infection control measures did not reduce nosocomial MRSA infection rates when compared with standard infection control measures alone.¹²

We found no evidence that our study hospitals responded less well to a positive MRSA result than other UK hospitals. Most patients with MRSA were isolated in side rooms and we found no evidence of an increased risk of MRSA acquisition when positive patients were nursed on the open ward (data not shown). Importation pressure was similar to another, local hospital¹³ and to the centres that reported a reduction of MRSA rates with rapid MRSA screening.^{8,9,11} Rates for hand hygiene were similar to or better than those found at other UK hospitals.^{14,15}

Robust data on MRSA acquisition and transmission rates are lacking¹⁶ and as these measurements depend on ward case mix, comparison is difficult. Our rates are in keeping with good, non-outbreak studies that include general wards^{17,18} and do not suggest unusually poor MRSA control. The wards were chosen as representative of the settings where MRSA transmission occurs in the UK.

In principle, rapid detection of MRSA will have the greatest effect when control measures are relatively weak for patients with undiagnosed MRSA carriage on admission. In the present study 30% of patients subsequently found to be MRSA culture positive on admission were pre-emptively isolated before test results were available, but this is not universal practice elsewhere. Additionally, our policy is to nurse all patients with standard precautions for their hospital stay. It is therefore possible that a more positive result would be seen for rapid testing in settings where these practices are used only for those identified as having MRSA.

The rapid test performed well. In common with most operational studies of diagnostic tests its sensitivity was lower in routine practice than initial validation studies, but our results are similar to those reported by others.^{19,20} The test is validated for use on nasal swabs only and we optimised it for multiple site specimens.

Efficient use of limited isolation resources is important for the control of nosocomial infections. In this study there were fewer inappropriately isolated or cohorted days with rapid testing, most of which were in side rooms. This was, however, countered by isolation or cohort nursing of patients detected as positive only by the rapid test. This is a potential further cost of polymerase chain reaction based tests in addition to the substantially higher consumable costs.¹⁰

In this study on general wards a rapid MRSA screening result did not, by itself, reduce MRSA rates to a degree likely to justify the cost. This hospital has MRSA practices similar to or more intensive than comparable NHS institutions. Rapid testing may have a role in outbreak control, emergency surgical screening, or high risk patients such as those on intensive care units. In general medical and surgical settings prioritising rapid testing over optimising other control measures such as pre-emptive isolation of patients at high risk of MRSA is not supported by this study.

We thank the patients and staff on the following wards—Alan Apley, Alexandra, Aston Key, Blundell, Dorcas, Henry, Hedley Atkins, Luke, Page, Samaritan, and Stanley, and the surgical admissions lounge; the Department of Infection; Ghaseem Yadeghafar, Florence Bunting, Sarah Sacks, Edel Dunkerley, and other staff of Electronic Patient Records; the staff of performance management; and the staff of the information team in the human resources department.

Contributors: See bmj.com.

Funding: This study was funded by the UK Department of Health and sponsored by Guy's and St Thomas' NHS Foundation Trust. The funding source did not have any role in the study design, execution, analysis, writing of the manuscript or conclusions.

Competing interests: None declared.

Ethical approval: Ethical approval was given by the Guy's and St Thomas' central office for research ethics committees.

Provenance and peer review: Not commissioned; externally peer reviewed.

- Ritchie K, Bradbury I, Eastgate J, Foster L, Iqbal, K, MacPherson K, et al. *Consultation report on health technology. Clinical and cost effectiveness of screening for MRSA.* NHS Quality Improvement Scotland, 2006.
- Rubinovitch B, Pittet D. Screening for methicillin-resistant *Staphylococcus aureus* in the endemic hospital: what have we learned? *J Hosp Infect* 2001;47:9-18.
- Coia JE, Duckworth GJ, Edwards DI, Farrington M, Fry C, Humphreys H, et al. Joint Working Party of the British Society of Antimicrobial Chemotherapy; Hospital Infection Society; Infection Control Nurses Association. Guidelines for the control and prevention of methicillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities. *J Hosp Infect* 2006;63(suppl 1):S1-44.
- Duckworth G, Cookson B, Humphreys H, Heathcock R. Revised methicillin-resistant *Staphylococcus aureus* infection control guidelines for hospitals. Report of a Working Party of the British Society for Antimicrobial Chemotherapy, the Hospital Infection Society and the Infection Control Nurses Association. *J Hosp Infect* 1998;39:253-90.
- Mulligan ME, Murray-Leisure KA, Ribner BS, Standiford HC, John JF, Korvick JA, et al. Methicillin-resistant *Staphylococcus aureus*: a consensus review of the microbiology, pathogenesis, and epidemiology with implications for prevention and management. *Am J Med* 1993;94:313-28.
- Muto CA, Jemigan JA, Ostrowsky BE, Richet HM, Jarvis WR, Boyce JM, et al. SHEA guidelines for preventing nosocomial transmission of multi-drug resistant strains of *Staphylococcus aureus* and *Enterococcus*. *Infect Control Hosp Epidemiol* 2003;24:362-86.
- Department of Health. *Screening for methicillin-resistant Staphylococcus aureus (MRSA) colonisation. A strategy for NHS trusts: a summary of best practice.* London: DoH, 2007.
- Cunningham R, Jenks P, Northwood J, Wallis M, Ferguson S, Hunt S. Effect on MRSA transmission of rapid PCR testing of patients admitted to critical care. *J Hosp Infect* 2007;65:24-8.
- Harbarth S, Masuet-Aumatell C, Schrenzel J, Francois P, Akakpo C, Renzi G, 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 Med* 2006;10:R25.
- Cotner LO, Shymanski J, Ramotar K, Toye B, van Walraven C, Coyle D, et al. Real-time polymerase chain reaction detection of methicillin-resistant *Staphylococcus aureus*: impact on nosocomial transmission and costs. *Infect Control Hosp Epidemiol* 2007;28:1134-41.
- Keshtgar MR, Khalili A, Coen PG, Carder C, Macrae B, Jeanes A, et al. Impact of rapid molecular screening for methicillin-resistant *Staphylococcus aureus* in surgical wards. *Br J Surg* 2008;95:381-6.
- Harbarth S, Fankhauser C, Schrenzel J, Christenson J, Gervaz P, Bandiera-Clerc C, et al. Universal screening for methicillin-resistant *Staphylococcus aureus* at hospital admission and nosocomial infection in surgical patients. *JAMA*. 2008;299:1149-57.
- Gopal Rao, Michalczyk P, Nayeem N, Walker G, Wigmore L. Prevalence and risk factors for methicillin-resistant *Staphylococcus aureus* in adult emergency admissions: a case for screening all patients? *J Hosp Infect* 2007;66:15-21.
- Cepeda J, Whitehouse T, Cooper B, Hails J, Jones K, Kwaku F, et al. Isolation of patients in single rooms or cohorts to reduce spread of MRSA in intensive-care units: prospective two-centre study. *Lancet* 2005;365:295-304.
- MacDonald A, Dinah F, MacKenzie D, Wilson A. Performance feedback of hand hygiene, using alcohol gel as the skin decontaminant, reduces the number of inpatients newly affected by MRSA and antibiotic costs. *J Hosp Infect* 2004;56:56-63.
- Cooper BS, Medley GF, Stone SP, Kibbler CC, Cookson BD, Roberts JA, et al. Methicillin-resistant *Staphylococcus aureus* in hospitals and the community: stealth dynamics and control catastrophes. *Proc Natl Acad Sci* 2004;101:10223-8.
- Farrington M, Redpath C, Trundle C, Coomber S, Brown NM. Winning the battle but losing the war: methicillin-resistant *Staphylococcus aureus* (MRSA) infection at a teaching hospital. *Q J Med* 1998;91:539-48.
- Rioux C, Armand-Lefevre L, Guerinet W, Andremont A, Lucet J-C. Acquisition of methicillin-resistant *Staphylococcus aureus* in the acute care setting: incidence and risk factors. *Infect Control Hosp Epidemiol* 2007;28:733-6.
- Bishop E, Grabsch EA, Ballard SA, Mayall B, Xie S, Martin R, et al. Concurrent analysis of nose and groin swab specimens by the IDI-MRSA PCR assay is comparable to analysis by individual specimen PCR and routine culture assays for detection of colonization by methicillin-resistant *Staphylococcus aureus*. *J Clin Microbiol* 2006;44:2904-8.
- Warren DK, Liao RS, Merz LR, Eveland M, Dunne WM. Detection of methicillin-resistant *Staphylococcus aureus* directly from nasal swab specimens by a real-time PCR assay. *J Clin Microbiol* 2004;42:5578-81.

Accepted: 7 March 2008