healthier scotland
SCOTTISH GOVERNMENT

Health Protection Scotland

NHS National Services Scotland

NHS Scotland MRSA Screening Pathfinder Programme

Discharge testing for MRSA in Scottish hospitals: MRSA acquisition, description of acquired strains and risk factors for acquisition of MRSA in the hospital

Prepared for the Scottish Government HAI Task Force
by Health Protection Scotland

Delivered October 2010

Published March 2011 (Version 2)

NHS Ayrshire & Arran

NHS Grampian

Acknowledgements

This report would not have been completed successfully and within schedule without the cooperation and support of the staff in all of the participating Pathfinder hospitals. Their collaboration is gratefully acknowledged.

Final Report delivered to SGHD in October 2010

First published in February 2011

Version 2 published March 2011

ISBN 978-1-873772-38-6

For all enquiries please contact:

HAI & IC Group
1 Cadogan Square
Cadogan Street
Glasgow
G2 7HF

Tel: 0141 300 1100
Fax: 0141 300 1170

Email: nss.hps.enquires@nhs.net

Reference this report as:

Eva van Velzen, Jacqui Reilly, Kim Kavanagh, Gwen Allardice, Traiani Stari, Alistair Leanord, Giles Edwards, Kirsty Crockett, Ian Gould, Fiona MacKenzie, Robert Masterton: Health Protection Scotland, National Services Scotland, NHS Scotland MRSA Screening; Discharge testing for MRSA in Scottish hospitals: MRSA acquisition, description of acquired strains and risk factors for acquisition of MRSA in the hospital, 2011, Health Protection Scotland [Report]

Designed and typeset by:

Graphics Team, Health Protection Scotland

1 Executive summary

The objectives of this study were to estimate the proportion of patients who acquire MRSA whilst in hospital, to describe the MRSA strain types identified in these patients, and to identify risk factors for acquisition of MRSA. The study was designed as a multicentre retrospective cohort study and took place within hospitals in two Pathfinder Boards. Patients were screened for MRSA at multiple body sites on discharge using enrichment broth sub cultured on to Chromogenic agar (gold standard). The screening results were linked to their screening results on admission.

This study was the first of its kind and found that on discharge, 2.9% of patients were colonised with MRSA. In the cohort of patients screened on admission and discharge, this study found that 1.3 % of all patients acquired MRSA whilst in hospital. Evidence was also found of patients losing their MRSA colonisation during hospital stay: Twenty two patients (0.8%) were MRSA positive on admission and MRSA negative on discharge. The overall majority of patients (96.6%) were MRSA negative on admission and remained MRSA negative throughout their stay. There was no significant difference in MRSA acquisition between the study sites (p=0.86).

MRSA prevalence on admission was equal to MRSA prevalence on discharge on a population level, indicating no net acquisition. However, on a patient level some patients acquired MRSA, some patients lost MRSA colonisation and others remained MRSA colonised throughout hospital stay. Thirty-Five patients met the case definition of acquisition of MRSA whilst in hospital suggesting that cross transmission takes place in the general hospital population.

The majority of patients who were MRSA positive on admission remained colonised and all retained the same strain of MRSA throughout their hospital stay. Three risk factors for acquisition of MRSA were identified: age above 64, self reported renal failure, and self reported presence of open wounds.

The results indicate that cross-transmission of MRSA takes place in Scottish hospitals, even in the context of a universal MRSA screening programme. No other studies exist which allow a direct comparison of acquisition rates to be made, however other studies in selected groups of patients have published rates ranging from 1.7%-17%. In relation to the value of universal screening for MRSA on admission, this study reinforces the importance of infection prevention and control measures to prevent cross transmission during hospital stay; universal screening on admission is one part of the strategy required to reduce the number of MRSA colonisations (and subsequent MRSA infections).

This study raises several questions, such as how patients acquire MRSA during hospital stay, whether and when patients lose MRSA colonisation once out of the hospital, and to what extent they form a risk for onwards transmission to household members and fellow patients in case of re-admittance. Further work, including more analysis of the molecular epidemiology of MRSA acquisition, should address these questions.

2 Table of Contents

3 List of Figures

4 List of Tables

5 Background

Across the UK healthcare associated infections with Meticillin-resistant *Staphylococcus aureus* (MRSA) remain a cause for concern [1]. *S.aureus* is a Gram positive bacterium able to colonise the skin of humans and animals [2]. The bacterium is thought to be carried by approximately 25% - 30% of people in the general population without causing disease [3]. However upon entering the body, *S. aureus* can cause serious infections, ranging from localised skin infections to cellulitis, pneumonias and bacteraemias [4]. Due to resistance to commonly used antimicrobials, MRSA is significantly more difficult to treat than Meticillin-susceptible *S.aureus* (MSSA). However, recent literature suggests that both MRSA and MSSA cause substantial burden of disease [5]. Bacteraemias caused by *S.aureus*, including bacteraemias due to MRSA and MSSA infection have been monitored in Scotland since 2001.

In Scotland an estimated 9.5% of inpatients in acute hospitals have a healthcare associated infection (HAI) at any point in time, 17% of which are caused by MRSA and 9% by MSSA [6]. Prevention of HAI is therefore a priority for the Scottish Government and from 2005, a decline of 14.5% per year in bacteraemias due to MRSA has been observed [7]. Multiple infection prevention and control measures have been implemented in the past five years, including a national hand hygiene campaign, dissemination of infection prevention and control guidance, and implementation of care bundles [8].

An additional policy development on MRSA screening commenced after the publication of a Health Technology Assessment on the topic [9]. The effectiveness of universal screening for MRSA on admission remains controversial [10;11]. Therefore prior to implementing universal screening at admission for all hospitals in Scotland the Pathfinder Programme, a large intervention study was undertaken in Scottish hospitals to assess the effectiveness of universal screening for MRSA [12]. The study indicated a temporal association between the introduction of universal screening and a (further) reduced incidence of MRSA infections as a proportion of *S. aureus* infections [13].

The Pathfinder project indicated that patients colonised with MRSA on admission were 15 times more likely to develop MRSA infection, in line with the literature [3]. However, the study indicated that half of the patients who developed an infection during hospital stay were not MRSA positive on admission, in line with a large Swiss study [14]. This suggested that many patients acquired MRSA through cross-transmission whilst in the hospital, assuming that the admission screening was reasonably sensitive to detect MRSA on admission. (Testing the latter assumption is the remit of another study within the MRSA Screening Programme – The MRSA Admission Study) [15]. Therefore there was also a need to determine the rate of MRSA acquisition during hospital stay to decide if there was need for further infection prevention and control interventions during hospital stay.

6 Introduction

Few studies have been published on MRSA acquisition rates in the general hospital population. Most research has focussed on a limited number of 'high risk' wards and acquisition rates found in these studies range from 1.7% to 3.2% in general wards [16-18] to 17% in an ICU setting [19]. The acquisition rate in the general hospital population is a very important parameter for decision making on the implementation of universal screening in hospitals. If many people acquire MRSA after a (negative) MRSA screen on admission through cross-transmission, the value of screening on admission is reduced.

The primary objective of this study was therefore to establish the MRSA acquisition rate within in-patients in two acute hospitals in Scotland whose population is expected to be representative of the general hospital population. This included not only patients who were MRSA negative on admission, but also those MRSA positive on admission; molecular techniques [20;21] allowed identification of new MRSA strains in the latter group. This is the first study to assess acquisition of MRSA in the general hospital wards' population which included patients who were found MRSA positive on admission. Discharge prevalence in this population was also assessed.

The second objective was to describe the strains identified in patients who were MRSA positive on discharge and to identify risk factors for acquisition of MRSA during admission in the hospital.

7 Methods

7.1 Study design and setting

In this multicentre retrospective cohort study, screening results were linked at discharge to screening results on admission. The latter were collected during the MRSA Admission Study which took place in parallel to this study; both studies formed part of The Pathfinder Programme.

Universal screening for MRSA took place in two acute care hospitals in two NHS Boards from February to August 2010 (seven months); one district general hospital (590 beds) and one large teaching hospital (893 beds). The elective orthopaedic ward of the latter hospital is located in an adjacent smaller hospital. Patients from this ward were included in the study population of the large teaching hospital. Both study hospitals applied a uniform study protocol.

7.2 Inclusion criteria

All patients aged 16 and older who were discharged from any ward in the two hospitals (except the Obstetrics, Paediatric or Psychiatric wards) were eligible for inclusion in the study. Discharge was defined as leaving the hospital to another hospital (external transfer), care home or home.

Day patients were not eligible for inclusion in the study; all patients stayed at least one night in hospital. Patients who had not been screened on admission were excluded from acquisition analysis, but were included in the discharge prevalence calculation.

All patients were required to give written informed consent to participate. Patients could be included in the study more than once. Therefore where we refer to an 'episode' we refer to one patient's stay in the hospital, but this individual may have been included in the study more than once during the study period.

7.3 Screening methods

All consenting patients were swabbed on admission at four body sites: anterior nares, perineum, axillae and throat. Where applicable, swabs also were taken from wounds and devices. Discharge screening took place within 24 hours prior to discharge. Admission swabbing took place as soon as possible after admission (within 48 hours maximum).

7.4 Clinical management

Patients who were found MRSA positive on admission were isolated whenever possible. If isolation was not possible, patients were cohorted, i.e. MRSA positive patients were grouped in one bay to reduce the risk of transmission to other patients.

MRSA positive patients were treated according to a standardised intervention protocol consisting of mupirocin nasal treatment (three times daily) for five days in conjunction with five days of use of antiseptic wash. After the decolonisation course, patients were re-tested for MRSA and prescribed a second decolonisation course if applicable. Re-test results did not form part of this study.

When patients were discharged prior to completing decolonisation treatment they were advised to finish the full decolonisation course after discharge.

7.5 Case definitions for MRSA colonisation and acquisition

A patient was considered MRSA positive i.e. colonised with MRSA if any of the swabs were MRSA positive per testing moment (on admission or discharge).

A patient was considered MRSA negative i.e. not colonised if none of their swabs were MRSA positive per testing moment (on admission or discharge).

A patient was considered to have acquired MRSA (i.e. became colonised with a new strain of MRSA) if one of three case definitions were met:

- The patient was MRSA negative on admission and MRSA positive on discharge.
- The patient was MRSA positive on both admission and discharge but acquired a new strain of MRSA during hospital stay (as shown by genotyping).
- The patient was MRSA negative on both admission and discharge, but developed an MRSA infection during hospital stay.

7.6 Data collection

Data were collected on demographics and risk factors for acquisition: gender, age, discharge specialty, length of stay, number of days in isolation facilities, patient movement through the hospital, co-morbidity and being on decolonisation treatment at discharge.

Information on co-morbidity was derived from an admission risk assessment administered on admission. Data were captured in standardised data forms.

Laboratory results were collected separately from the two hospital laboratories and the national reference laboratory where genotyping took place. Data derived from the different data sources were validated and linked in a SQL database at Health Protection Scotland (HPS).

7.7 Laboratory methods

All specimens from one patient were inoculated onto Oxoid's Brilliance MRSA Agar medium. Thereafter they were pooled and inoculated into Oxoid's selective manitol enrichment broth. After 18 – 24 hours incubation period, a sample from the broth was plated on Oxoid Brilliance MRSA agar. Therefore, individual results per patient (admission or discharge) were obtained for each body site and enrichment broth result consisting of pooled swabs.

All MRSA isolates (confirmed by Vitek 2 AST/ID testing) were sent to the MRSA reference laboratory for genotyping. All MRSA isolates found at discharge were genotyped. In addition the admission isolates from patients found MRSA positive on discharge were genotyped to allow identification of a newly acquired MRSA strain in patients positive on admission and discharge.

Two molecular methods for genotyping were applied: pulse-field gel electrophoresis (PFGE) method and multilocus VNTR analysis (MLVA sequencing). MLVA was applied when PFGE strains were considered identical i.e. if they showed six or less DNA fragment differences [21].

7.8 Statistical analysis

STATA9® software was used for data analysis. The following statistical tests were applied: the chi-square test for comparing proportions in categorical variables, the two sample t-test for estimating differences in mean statistics such as age, the Mann Whitney test for comparing median length of stay and the McNemar test for testing differences in paired samples.

Clustered logistic regression was employed for the univariate risk factor screening. Variables with p <0.3 (overall p-value for all levels of the variable, tested using Wald test) were included in the clustered multivariate logistic regression model [22]. Clustering, by unique patient identifier was used to adjust the standard errors to account for multiple entries of individual patients in the study. All biologically plausible interactions between risk factors were tested for inclusion, with the p-value adjusted using the Bonferroni method of correcting for multiple testing [23].

Twelve potential risk factors were included in the univariate analysis: gender, age, discharge specialty (as a proxy for admission indication), length of stay, whether patient had been isolated during hospital stay, patient movement (i.e. the number of wards the patient had been in during hospital stay) and whether the patient was on MRSA decolonisation treatment on the moment of discharge screening. These seven factors were derived from the data collection form.

In addition, five potential risk factors were derived from the 'clinical risk assessment' (Admission Study) administered on admission, in which patients were asked to indicate whether they had received antibiotics in the year prior to admission to the hospital and whether they suffered from co-morbidity: the presence of diabetes, renal failure, Chronic Obstructive Pulmonary Disease (COPD) and open wounds / sores / ulcers were recorded.

7.9 Ethical approval

The Scotland A Research Ethics Committee, Edinburgh, approved the study protocol (A REC reference number 09/MRE00/50, R&D reference NRS09BA01).

8 Results

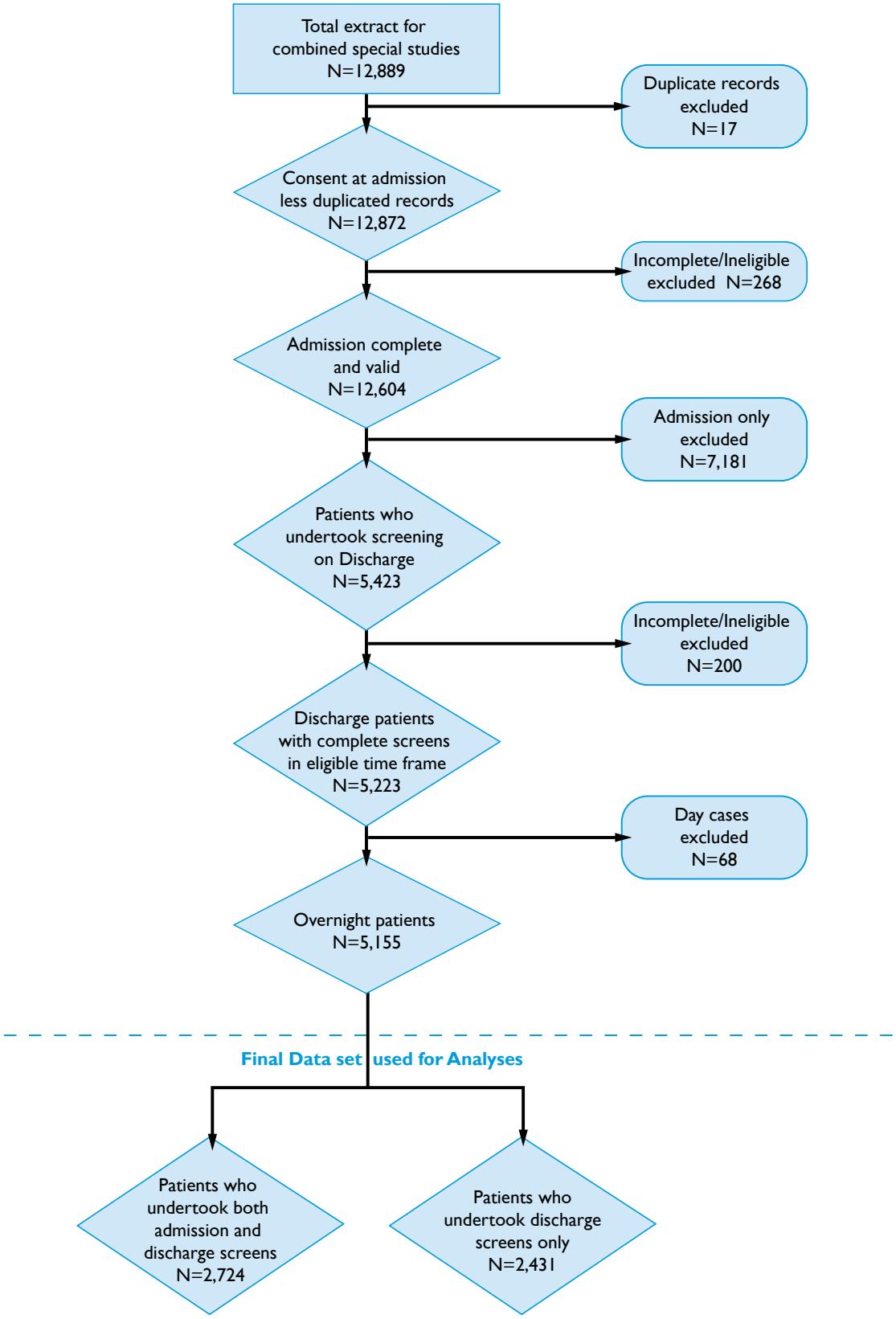
8.1 Study population and demographics

In total, 12,872 episodes were included in the study after data cleaning and de-duplication. These episodes were split into three separate cohorts:

- The admisson-discharge cohort: patients who were screened on admission and discharge.
- The discharge-only cohort: patients who were only screened on discharge.
- The admission-only cohort: patients who were only screened on admission.

Of all patients screened on admission, 268 episodes were excluded because they did not have a full screen or the timing of the screen did not meet the inclusion criteria. Then the patients who were screened on admission-only were excluded, and 200 discharge episodes were excluded for incompleteness or inappropriate timing. Finally, 68 day patients were excluded, because only patients who stayed at least one night in the hospital were eligible for inclusion. Figure 8-1 summarises the inclusion of episodes in the analysis.

Figure 8-1: Flow chart of patients included in the analysis[i]



i NB: Figure 8-1 was amended on 25/02/2011

Table 8-1 presents the baseline characteristics of the three cohorts. Patients included in the admisson-discharge cohort were on average slightly older than admission-only patients and slightly younger than patients in the discharge-only cohort.The wards they were admitted to and discharged from varied significantly from the admission-only and discharge-only cohort, respectively (both $p<0.001$). Notably, patients in the admisson-discharge cohort were more likely to be admitted to or discharged from the orthopaedic wards compared to patients in the other cohorts.

The admission prevalence in the admisson-discharge cohort was lower than in the admission-only cohort ($p=0.004$), which may be explained by the generally lower MRSA prevalence in the orthopaedic wards compared to other wards (not in table).

Table 8-1: Baseline characteristics of the admisson-discharge cohort (middle column) comparing patients' characteristics to the admission-only, admission-discharge and discharge-only cohorts (N=12,336).

Demographic		Admission-only cohort	Admisson-discharge cohort	Discharge-only cohort	p-value (χ2 test)
N		7,181	2,724	2,431	
Mean age (95% CI)		59.4 (59.0 , 59.8)	61.4 (60.7, 62.0)	62.6 (61.9 , 63.3)	
Age (on admission)	<=49 yrs	2,058 (28.7%)	616 (22.6 %)		<0.001
	50-64 yrs	1,966 (27.4%)	791 (29.0 %)		
	65 -79 yrs	2,248 (31.3%)	969 (35.6%)		
	>=80 yrs	909 (12.7%)	348 (12.8%)		
Age (on discharge)			616 (22.6 %)	571 (23.5 %)	<0.001
			790 (29.0 %)	592 (24.3 %)	
			969 (35.6%)	825 (33.9 %)	
			349 (12.8%)	443 (18.2 %)	
Gender (%)	Male	3,385 (47.1%)	1,357 (49.8%)		0.02
	Female	3,795 (52.9%)	1,376 (50.2%)		
	Male		1,357 (49.8%)	1,170 (48.2%)	0.23
	Female		1,376 (50.2%)	1,261 (51.9%)	
Admission specialty (%)	A&E	141 (2.0%)	53 (2.0%)		
	Medicine	2,813 (39.2%)	780 (28.6%)		
	Orthopaedics	936 (13.0%)	729 (26.8%)		
	Surgery	2,597 (36.2%)	893 (32.8%)		
	Other	694 (9.7%)	269 (9.9%)		<0.001
Discharge specialty (%)	A&E		41 (1.5%)	41 (1.7%)	
	Medicine		616 (22.6%)	663 (27,3%)	
	Orthopaedics		737 (27.1%)	444 (18.3%)	
	Surgery		901 (33.1%)	745 (30.7%)	
	Other		429 (15.8%)	538 (22.1%)	<0.001
Admission prevalence		3.2%	2.1%		0.004
Discharge prevalence			2.6%	3.2%	0.20

8.2 Discharge prevalence

A total of 5,155 patients from the admisson-discharge and discharge-only cohort were pooled for calculation of the discharge prevalence. Out of these, 147 patients were MRSA positive on discharge. This resulted in a 2.9% discharge prevalence (95% CI 2.43, 3.34). There was no significant difference between the discharge prevalence in either cohort (Table 8-1, p=0.20).

8.3 Acquisition analysis

In total we included 2,724 episodes in the admisson-discharge cohort including 2,649 (97%) individual patients who were included once and 75 patients (3%) who were included more than once in the cohort (indicating that the overall majority of episodes were indeed individual patients, which justifies referring to them as 'patients'). Table 8-2 shows the baseline characteristics by NHS Board.

Table 8-2 Demographics of patients included in the admisson-discharge cohort (N=2,724) by NHS Board.

Demographic		Ayrshire & Arran	Grampian	p-value (χ2 test)
N (total 2,724)		1,127 (41%)	1,597 (59%)	
Mean age (95% CI)		60.7 (59.6, 61.7)	61.8 (61.0, 62.6)	0.09*
Gender (%)	Male	538 (47.7%)	819 (51,3%)	0.07
	Female	589 (52.3%)	778 (48,7%)	
Admission specialty (%)	A&E	51 (4.5%)	2 (0.1%)	
	Medicine	384 (34.0%)	396 (24.8%)	
	Orthopaedics	310 (27.5%)	419 (26.2%)	
	Surgery	286 (25.4%)	607 (38.0%)	
	Other	96 (8.5%)	173 (10.8%)	< 0.001
Discharge specialty (%)	A&E	41 (3.6%)	0	
	Medicine	272 (24.1%)	344 (21.5%)	
	Orthopaedics	312 (27.7%)	425 (26.6%)	
	Surgery	282 (25.0%)	619 (38.7%)	
	Other	220 (19.5%)	209 (13.1%)	< 0.001
Length of stay (days)	median	3 [25% 1, 75% 7]	5 [25% 3, 75% 8]	< 0.001**
Admission prevalence (95% CI)		2.0% (1.29, 2.94)	2.3% (1.63, 3.10)	0.59
Discharge prevalence (95% CI)		2.8 (1.94, 3.88)	2.4% (1.79, 3.32)	0.62

* two sample t-test
** Mann Whitney test

Table 8-2 illustrates that the two study sites were different: admission specialty, discharge specialty and median length of stay were significantly different (all p <0.001). This was anticipated; a multicentre approach of the study was chosen to account for differences in the general Scottish hospital population. There was no age difference between patients in both sites (p=0.09), or a difference between MRSA prevalence on either admission (p=0.59) or discharge (p=0.62) between the two study sites.

Table 8-3 contains the results of the MRSA acquisition analysis. Thirty-four patients (1.2%) were MRSA negative on admission and MRSA positive on discharge. One patient was MRSA negative both on admission and discharge, but developed MRSA infection during hospital stay. Thus, 35 patients (1.3 %, 95% CI 0.93, 1.78) met the case definitions for acquiring MRSA. This equates to an incidence rate of 2.1 per 1,000 Acute Occupied Bed Days (AOBDs) (95% CI 1.5, 2.9).

Out of the 58 patients who entered the hospital MRSA positive, 36 (62%) remained MRSA positive throughout their hospital stay. Genotype results (i.e. strain types) were available for 18 patients (50%). Strain typing did not reveal acquisition of a new MRSA strain in these patients hence no acquisition could be proven in this group of 'positive-positive' patients.

Evidence was also found of patients losing their MRSA colonisation during hospital stay: 22 patients (0.8%) were MRSA positive on admission and MRSA negative on discharge. The overall majority of patients (96.6%) were MRSA negative on admission and remained MRSA negative throughout their stay. There was no significant difference in MRSA acquisition between the study sites (p=0.86).

Of all the patients admitted to the study hospitals, 1.3% acquired MRSA whilst in hospital.

Table 8-3: Admisson-discharge cohort results of screening on admission and discharge, (N = 2,724)

Results on admission and discharge			Number (%)	No. of new strains	Acquisition*
Admission result	Discharge result	Infection*			
MRSA negative	MRSA positive	NA	34 (1.2 %)		Yes
MRSA positive	MRSA positive	NA	36 (1.3 %)	0 / 18	No
MRSA positive	MRSA negative	NA	22 (0.8 %)		No
MRSA negative	MRSA negative	No MRSA infection	2,631 (96.6 %)		No
MRSA negative	MRSA negative	MRSA infection	1 (0.04%)		Yes
Total			**2,724 (100 %)**		

** refer to case definition of 'acquisition'*

8.4 Net acquisition

Table 8-4 compares MRSA discharge prevalence to MRSA prevalence on admission within the admisson-discharge cohort, per study site (N=2,724). No significant difference was found in MRSA prevalence in either site (p=0.74 in Grampian, p=0.08 in Ayrshire & Arran) nor in the combined sample (p=0.14, McNemar test). This indicates that on a *population level* net acquisition cannot be proven, i.e. MRSA prevalence on discharge equalled MRSA prevalence on admission. However, at a *patient level*, results indicated that patients acquired MRSA, lost MRSA colonisation, or remained colonised with MRSA throughout their hospital stay.

Table 8-4 'Net acquisition' by NHS Board

	Total number of episodes	Number MRSA positive on admission	Admission prevalence (95% CI)	Number MRSA positive on discharge	Discharge prevalence (95% CI)	p-value of prevalence difference (Mc Nemar test)
Ayrshire and Arran	1,127	22	2.0% (1.29, 2.94)	31	2.8 (1.94, 3.88)	0.08
Grampian	1,597	36	2.3% (1.63, 3.10)	39	2.4% (1.79, 3.32)	0.74

8.5 Molecular analysis (strain typing)

Strains

The MRSA strains identified in 18 out of 36 patients (50%) who remained MRSA positive (the 'positive-positive group') were genotyped; six patients in Ayrshire and Arran, 12 in Grampian. No acquisition of new strains could be proven in any of the 18 patients; patients kept their admission strain until discharge. Sixteen out of 18 (89%) patients carried a EMRSA15 strain, two patients (12%) carried the EMRSA16 strain, corresponding to common strain types found in the Scottish population [24].

Subtypes

There was much variation between strains on subtyping identified in patients from the two study sites. Only one patient in each NHSBoard shared the same strain on subtyping. In Ayrshire and Arran, three patients shared an MRSA PFGE which is known to be common in that NHS Board. Of the 12 patients in Grampian six carried unique strains as identified by sub typing. The other six patients fell into three groups containing two indistinguishable stains in each group on subtyping. The generally more discriminatory MLVA typing [20], performed on all isolates from the positive-positive group, subdivided a few of the identified PFGE types but did not alter the overall interpretation that no acquisition had taken place.

Body Sites

Substantial variation was noted in body site colonisation patterns within patients, even in patients who were admitted for a short time period. For instance, in three out of five patients who remained MRSA positive and had stayed only one day in hospital, the same strain of MRSA was found on different body sites on discharge compared to the colonised body sites on admission.

8.6 Risk factor analysis

Table 8-5 shows the result of univariate risk factor analysis for MRSA acquisition whilst in hospital. Four risk factors were significantly associated with acquisition of MRSA: increasing age above 64 (odds ratio =10 for people aged above 80), having been in three wards during hospitalisation, renal failure and open wounds.

Table 8-5: Univariate risk factor analysis for MRSA acquisition (N=2,724)

Risk factor	Categories	OR	*p*-value	95% CI	Combined *p*-value (Wald test)
Gender	Male	1			na
	Female	1.18	0.63	(0.60, 2.31)	na
Age (years)	≤ 49	1			
	50 - 64	2.74	0.21	(0.57, 13,26)	
	65 - 79	4.83	0.04	(1.09, 21.19)	
	≥ 80	9.99	0.003	(2.20, 45.36)	0.005
Discharge specialty	Medicine	1			
	A&E	1.52	0.70	(0.19, 12.14)	
	Cardiology	0.53	0.41	(0.11, 2.42)	
	Care of the elderly	2.42	0.26	(0.52, 11.37)	
	Oncology	1.06	0.95	(0.13, 8.50)	
	Orthopedics	0.41	0.11	(0.14, 1.22)	
	Nephrology	1.73	0.48	(0.38, 7.92)	
	Surgery	0.82	0.64	(0.35, 1.91)	0.45
Length of stay	1 night	1			
	2-3 nights	0.61	0.52	(0.14, 2.73)	
	4-7 nights	1.92	0.31	(0.55, 6.73)	
	≥ 8 nights	2.52	0.15	(0.72, 8.84)	0.06
Patient has been isolated	No	1			na
	Yes	0.51	0.53	(0.62, 4.20)	na
Patient movement	1 ward	1			
	2 wards	1.59	0.24	(0.73, 3.44)	
	3 wards	2.75	0.04	(1.04, 7.22)	
	≥ 4 wards	2.64	0.13	(0.75, 9.30)	0.15
CRA* co-morbidity: diabetes		0.83	0.71	(0.29, 2.35)	na
CRA* co-morbidity: COPD		1.73	0.26	(0.67, 4.52)	na
CRA* co-morbidity: wounds / ulcers		2.94	0.012	(1.27, 6.81)	na
CRA* co-morbidity: renal failure		4.43	0.006	(1.52, 12.87)	na
CRA* patient indicating antibiotic use in year prior to discharge	No	1			na
	Yes	1.70	0.130	(0.85, 3.39)	na
Decolonisation treatment on discharge	No	1			na
	Yes	3.92	0.19	(0.51,30.10)	na

* Data derived from a risk assessment questionnaire administered on admission. Patients indicate co-morbidity; this risk factor does not refer to medically verified co-morbidity.

Eight variables (highlighted in table 8-5) with a (Wald test) *p*-value <0.3 were included in the clustered multivariable regression model. Three risk factors remained significantly associated with acquisition of MRSA after correction for the influence of all other risk factors (Table 8-6). We tested for biologically plausible interactions between the variables included in the model; no interactions reached the (multiple test) adjusted threshold of statistical significance.

Since the prevalence of MRSA was low, the odds ratio could be interpreted as risk ratio. Thus the risk of acquiring MRSA was 5 times higher for a person above 64, compared to somebody younger than 50 years. For a person above 80 years old the risk was increased more than 10 times.

A person admitted to the hospital with self reported open wounds or ulcers were almost three times more at risk for MRSA acquisition than somebody with intact skin. This risk was comparable to the increased risk for a patient with self reported renal failure (OR=3).

Table 8-6: Multivariable analysis of risk factors for acquisition of MRSA

Risk factor	Catergories	Adjusted OR	*p*-value	95% CI
Age (years)	≤ 49	1		
	50 - 64	2.95	0.190	(0.59, 14.64)
	65 - 79	5.14	0.030	(1.14, 23.17)
	≥ 80	10.54	0.003	(2.20, 50.56)
CRA* co-morbidity: wounds / ulcers	No	1		
	Yes	2.92	0.016	(1.22, 7.00)
CRA* co-morbidity: renal failure	No	1		
	Yes	3.11	0.046	(1.02, 9.51)

* Data derived from a risk assessment questionnaire administered on admission. Patients indicate co-morbidity; this risk factor does not refer to medically verified co-morbidity.

9 Discussion

This is the first study to examine MRSA acquisition in the general hospital population. A number of other studies into MRSA acquisition have been published to date; they were confined to either a number of general wards [17;18] or specific high risk wards such as the ICU [19;25]. One study included both general wards and an ICU but the population was (related to) military personnel [16].

A multicentre retrospective cohort study was conducted among patients admitted to acute Scottish hospitals. This study found that in a large cohort (including more than 5,000 patients) 2.9% of patients were MRSA positive on discharge. Discharge screening results could be linked to admission screening results in 2,724 patients; acquisition of MRSA was investigated in this cohort. Thirty-five patients (1.3%) acquired MRSA during hospital stay with a confidence interval ranging from 0.9% to 1.8%. This proportion is relatively low compared to other studies; estimates vary from 1.7% in a military hospital [16] to 2.8% in a large cross-over trial [17] to 17% in an ICU [19], but the studies vary significantly in design and population which makes direct comparison difficult. One prospective cohort study, whose population might be best comparable to this study, found an acquisition of 3.1% with a 95% confidence interval ranging from 1.8% to 4.4%; the confidence intervals of both studies just overlap [18].

No net acquisition in the admission-discharge study cohort could be proven, indicating that MRSA prevalence on admission was equal to MRSA prevalence on discharge on a population level. However on a patient level some patients acquired MRSA, some patients lost MRSA colonisation, and others remained MRSA colonised throughout their hospital stay. Thirty-Five patients met the case definition of acquisition of MRSA whilst in hospital suggesting that cross transmission takes place in the general hospital population.

The remaining patients were already MRSA positive on admission and remained colonised, despite the (unquantified) implementation of interventions such as universal screening on admission and consequent isolation and decolonisation treatment for MRSA positive patients. This group of 36 patients constituted more than 60% of all patients (n=58) who had entered the hospital MRSA positive. Strain typing of MRSA strains identified in this group did not indicate new acquisition of MRSA; it showed that patients kept their admission MRSA strain. These findings reinforce the importance of implementing infection control measures in the hospital for the prevention of cross-transmission, rather than focusing solely on screening on admission.

In a multivariable logistic regression model, three risk factors for acquiring MRSA were identified: being of older age (over 64, with increased risk for age above 80 years), self reported renal failure, and self reported presence of wounds. Only one other study reported risk factors for acquisition of MRSA, adjusted for interactions in a multivariable analysis in a non-ICU environment: in line with this study, Rioux *et al.*[18] found a significant association between the presence of chronic skin breaks at admission and acquisition of MRSA. Notably, neither this study nor the Rioux study found a significant association between the length of stay in the hospital and acquisition of MRSA in the multivariable analysis. Two other studies did identify an association with length of stay in the hospital [16;19] but these were only tested in univariate analyses.

This study has reasonable external validity; the study sites were selected in the Pathfinder Project [13] because together they were considered to be representative of the general Scottish in-patient population. The two study sites were indeed different in the proportions of patients admitted and discharged from certain specialties, however important parameters such as the mean age of patients and the admission and discharge prevalence were not different. Therefore it was justified to combine the two samples in this multi-centre study as being representative of the target population.

10 Limitations

The study has a number of limitations. Patients whom, at the moment of discharge, were unable to give written informed consent could not be included in the study due to ethical approval conditions. Likewise, patients who could participate in the study on discharge but who had been too unwell to be screened on admission could not be included in the acquisition cohort. This may have resulted in a selection bias towards relatively healthier patients in the acquisition cohort which could have lead to an underestimation of the proportion of patients acquiring MRSA. The discharge prevalence of MRSA in both cohorts was not statistically different, implying there was no clear selection bias at the moment of inclusion to the study at discharge.

The study design accounted for the time from admission to screening as observed in the Pathfinder project [13]. This meant that an assumption was made that hospital associated acquisition occurred after day two, this is in line with internationally accepted definitions of hospital associated infection, but may have underreported true acquisition occurring between admission and this period.

Inclusion of study participants in the study was not constant over time; the hospital sites included proportionally more patients towards the end of the study period, which may have resulted in bias. However, this bias was not quantified when analysing the prevalence over time (p=0.67, Poisson regression).

This study could not include data on potentially important confounding factors such as individual antibiotic consumption or the reason for admission in the risk factor analysis. As a result we may have been unable to account for potentially relevant confounding effects in the multivariable model. The multivariable analysis was also limited by the low number of acquisitions compared to the study population; this is reflected in the wide confidence intervals around the estimated odds ratios.

Unfortunately, strain type results were not available for all patients who remained colonised. However, based on results of fifty per cent of these patients, it seems unlikely that many of the other 18 patients in this group will have acquired MRSA on top of their pre-existing colonisation.

In this study two co-morbidity risk factors (renal failure and the presence of open wounds) were significantly associated with acquisition of MRSA, in addition to increasing age over 64. Data collection for these risk factors relied on self-reporting of patients. The validity of these reports by patients is unknown; the increased risk should be interpreted with caution as it is uncertain whether this ascertainment bias would result in under or overestimation of the risk.

The study raises several questions, such as how patients acquire MRSA during hospital stay, whether and when patients lose MRSA colonisation once out of the hospital, and to what extent they form a risk for onwards transmission to household members and fellow patients in case of re-admittance. Further work, including more analysis of the molecular epidemiology of MRSA acquisition, should address these questions.

11 Conclusions

We conclude that cross-transmission of MRSA takes place in Scottish hospitals, in the context of a universal MRSA screening programme; 1.3 % of all patients admitted to the hospitals acquired MRSA whilst in hospital. This study found an overall discharge prevalence of 2.9% of all patients discharged. Of the patients who entered the hospital colonised with MRSA, the majority remained MRSA positive throughout their hospital stay. No acquisition could be proven in these patients.

This study did not indicate *net* acquisition at a population level: MRSA prevalence on discharge was not significantly higher than on admission. Three risk factors for acquisition of MRSA were identified: age above 64, self-reported renal failure, and self-reported presence of wounds or ulcers.

In relation to the value of universal screening for MRSA on admission, these findings support the notion that universal screening has a role as part of broader strategy in hospitals to reduce the number of MRSA colonisations (and subsequent MRSA infections). Screening on admission is important to identify MRSA positive patients, but if these patients remain MRSA colonised despite intervention measures, as this study indicates, onward transmission to other patients can not be prevented through the implementation of screening alone. Therefore infection prevention and control measures to prevent cross transmission in the hospital remain very important, in addition to an ongoing focus on reduction of antimicrobial resistance development in the hospital environment.

12 Potential conflicts of interest

HPS declares no conflicts of interest.

The study was funded by the Scottish Government Health Directorate, HAI Task Force.

13 References

[1] Boyce JM, Cookson B, Christiansen K, Hori S, Vuopio-Varkila J, Kocagoz S, et al. Meticillin-resistant *Staphylococcus aureus*. Lancet Infect Dis 2005 Oct;5(10):653-63.

[2] Morgan M. Methicillin-resistant *Staphylococcus aureus* and animals: zoonosis or humanosis? J Antimicrob Chemother 2008 Dec;62(6):1181-7.

[3] Wertheim HF, Melles DC, Vos MC, van LW, van BA, Verbrugh HA, et al. The role of nasal carriage in *Staphylococcus aureus* infections. Lancet Infect Dis 2005 Dec;5(12):751-62.

[4] Klevens RM, Morrison MA, Nadle J, Petit S, Gershman K, Ray S, et al. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. JAMA 2007 Oct 17;298(15):1763-71.

[5] Ben-David D, Novikov I, Mermel LA. Are there differences in hospital cost between patients with nosocomial methicillin-resistant *Staphylococcus aureus* bloodstream infection and those with methicillin-susceptible *S. aureus* bloodstream infection? Infect Control Hosp Epidemiol 2009 May;30(5):453-60.

[6] Reilly J, Stewart S, Allardice G, Noone A, Robertson C, Walker A, et al. NHSScotland national HAI prevalence survey. Final report. Glasgow: Health Protection Scotland; 2007.

[7] Health Protection Scotland. The annual report of healthcare associated infection report January - December 2009. Glasgow: Health Protection Scotland; 2010 Apr.

[8] The Scottish Governments's Healthcare Associated Infection (HAI) Task Force. Scottish Government 2009 March 24 [cited 2010 Oct 28];Available from: URL: http://www.scotland.gov.uk/Topics/Health/NHS-Scotland/19529/2005

[9] Ritchie K, Craig J, Eastgate J, Foster L, Kohli H, Iqbal K, et al. The clinical and cost effectiveness of screening for meticillin-resistant *Staphylococcus aureus* (MRSA). Edinburgh: NHS Quality Improvement Scotland; 2007.

[10] Gopal Rao G, Michalczyk P, Nayeem N, Walker G, Wigmore L. Prevalence and risk factors for meticillin-resistant *Staphylococcus aureus* in adult emergency admissions--a case for screening all patients? J Hosp Infect 2007 May;66(1):15-21.

[11] Peterson LR, Diekema DJ. To screen or not to screen for methicillin-resistant *Staphylococcus aureus*. J Clin Microbiol 2010 Mar;48(3):683-9.

[12] Health Protection Scotland. NHS Scotland MRSA screening pathfinder programme - Interim report. Glasgow: Health Protection Scotland; 2009.

[13] Health Protection Scotland on behalf of Pathfinder Health Boards. Final report volume 1: An investigation of the clinical effectiveness of MRSA screening. Glasgow: Health Protection Scotland; 2009 Dec. Report No.: Vol. 1

[14] 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 Mar 12;299(10):1149-57.

[15] Health Protection Scotland. The value of nasal swabbing versus full body screening or clinical risk assessment to detect MRSA colonisation at admission to hospital. Glasgow: Health Protection Scotland; 2010 Oct.

[16] Fishbain JT, Lee JC, Nguyen HD, Mikita JA, Mikita CP, Uyehara CF, et al. Nosocomial transmission of methicillin-resistant *Staphylococcus aureus*: a blinded study to establish baseline acquisition rates. Infect Control Hosp Epidemiol 2003 Jun;24(6):415-21.

[17] Jeyaratnam D, Whitty CJ, Phillips K, Liu D, Orezzi C, Ajoku U, et al. Impact of rapid screening tests on acquisition of meticillin resistant *Staphylococcus aureus*: cluster randomised crossover trial. BMJ 2008 Apr 26;336(7650):927-30.

[18] Rioux C, Armand-Lefevre L, Guerinot W, Andremont A, Lucet JC. Acquisition of methicillin-resistant *Staphylococcus aureus* in the acute care setting: incidence and risk factors. Infect Control Hosp Epidemiol 2007 Jun;28(6):733-6.

[19] Scriven JM, Silva P, Swann RA, Thompson MM, Naylor AR, Bell PR, et al. The acquisition of methicillin-resistant *Staphylococcus aureus* (MRSA) in vascular patients. Eur J Vasc Endovasc Surg 2003 Feb;25(2):147-51.

[20] Rivero-Perez B, Perez-Roth E, Mendez-Alvarez S. Evaluation of multiple-locus variable-number tandem-repeat analysis for typing a polyclonal hospital-acquired methicillin-resistant *Staphylococcus aureus* population in an area where such infections are endemic. J Clin Microbiol 2010 Aug;48(8):2991-4.

[21] Tenover FC, Arbeit RD, Goering RV, Mickelsen PA, Murray BE, Persing DH, et al. Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol 1995 Sep;33(9):2233-9.

[22] Juul S. An Introduction to Stata for Health Researchers. 2nd ed. Texas: Stata Press; 2008.

[23] Bland M. An Introduction to Medical Statisitics. 2nd ed. New York: Oxford University Press; 1995.

[24] Holmes A, Edwards GF, Girvan EK, Hannant W, Danial J, Fitzgerald JR, et al. Comparison of two multilocus variable-number tandem-repeat methods and pulsed-field gel electrophoresis for differentiating highly clonal methicillin-resistant *Staphylococcus aureus* isolates. J Clin Microbiol 2010 Oct;48(10):3600-7.

[25] Warren DK, Guth RM, Coopersmith CM, Merz LR, Zack JE, Fraser VJ. Epidemiology of methicillin-resistant *Staphylococcus aureus* colonization in a surgical intensive care unit. Infect Control Hosp Epidemiol 2006 Oct;27(10):1032-40.

1. Originator's report number:	HPS/HAIIC/MRSA/2011/02/7
1a. Additional Report Number:	E.g. If published under EU contract
2. Publishers Name and Location:	National Services Scotland Health Protection Scotland Room, 1 Cadogan Square, Cadogan Street, Glasgow G27HF
3. Funding source and period covered:	SGHD HAITF Delivery Plan DELIVERY April 2008 to March 2011 AREA 4: GUIDANCE AND STANDARDS Item 4.3
4. Sponsor's Name and Address:	Nursing Advisor HAI Chief Nursing Officer Directorate St Andrew's House
5. Report Classification and Caveats in use	UNLIMITED
5a. Date written:	31 October 2010
5b. Date published	Version 1 - February 2011 Version 2 - March 2011
5c. Pagination:	30
7a. Report Title:	NHS Scotland MRSA Screening Pathfinder Programme: Discharge testing for MRSA in Scottish hospitals: MRSA acquisition, description of acquired strains and risk factors for acquisition of MRSA in the hospital
7b. ISBN	978-1-873772-38-6
7b. Conference details (if part of conference then give conference particulars):	Not Applicable
7c. Part of Series	MRSA Screening Programme
7d Supersedes document	Not Applicable
7e Review date	
8. Authors:	MRSA Screening Programme Team
9. Descriptors/Key words should be terms from the HPS taxonomy	MRSA; Screening; Epidemiology; Statistics, Cohort Study, Healthcare; Healthcare Associated Infection; Infection Control, Scotland

10a. Abstract : [Maximum 200 words]

The objectives of this study were to estimate the proportion of patients who acquire MRSA whilst in hospital, to describe the MRSA strain types identified in these patients, and to identify risk factors for acquisition of MRSA. The study was designed as a multicentre retrospective cohort study and took place within hospitals in two Pathfinder Boards. Patients were screened for MRSA on multiple body sites on discharge using Chromogenic agar and nutrient broth (gold standard). The screening results were linked to their screening results on admission. MRSA prevalence on admission was equal to MRSA prevalence on discharge on a population level, indicating no net acquisition. However on a patient level some patients acquired MRSA, some patients lost MRSA colonisation and others remained MRSA colonised throughout hospital stay. The majority of patients who were MRSA positive on admission remained colonised and retained the same strain of MRSA throughout hospital stay. Three risk factors for acquisition of MRSA were identified: age above 64, self reported renal failure and self reported presence of open wounds.

Authorisation *(complete as applicable)*

Role	**Name**
Head of Division/ Delegated owner	Mary Morgan
Lead Consultant	Prof. Jacqui Reilly
Project/Programme Manager	Sally Stewart
Document Business Classification	Active Projects and Programmes, Healthcare Associated Infections and Infection Control, Epidemiology and Statistics