NHS Scotland MRSA Screening Pathfinder Programme

The Value of Nasal Swabbing versus Full Body Screening or Clinical Risk Assessment to Detect MRSA Colonisation at Admission to Hospital

1 Executive summary

Direct nasal swab screening combined with culture on chromogenic agar has been the routine methodology for detecting MRSA carriage in Scotland and in many other countries for some time. The first part of the current study was designed to determine the likely true sensitivity of nasal swabbing and the effect on ascertainment of undetected cases by swabbing additional body sites. This effectiveness was gauged against a 'gold standard' diagnosis of carriage, comprising swabs from nose, axilla, throat and perineum as well as swabs from wound or indwelling medical device sites, cultured both on standard chromogenic agar plates and enriched in broth with subsequent subculture onto chromorgenic agar to maximise MRSA identification. The second part of the study sought to develop and test a Clinical Risk Assessment (CRA) questionnaire which aimed to identify those most at risk of MRSA colonisation within a small subgroup of patient admissions, in order to greatly reduce the number of patients swabbed and to allow more efficient pre-emptive management of those at higher risk of colonisation.

Universal nasal swabbing for MRSA was found to be less effective than previously thought in identifying patients with MRSA carriage, with only 66% of 'gold standard' diagnoses detected. When combined with plausible rates for compliance with swabbing of 80% or 90%, only just over half of true carriers (53-59%) were likely to be identified in everyday practice. Using a combination of three body site swabs would increase ascertainment within a universal screening programme to a maximum of 90% (72-81% in practice with 80-90% swabbing compliance), but at a significant cost in terms of additional staff time and resources.

The CRA approach emerged as the most clinically effective option in the NHS QIS Health Technology Assessment model, but at less acceptable cost than nasal swab screening. The cost estimates used for CRA in the model were however, unrealistically high. The potential attractions of a CRA approach as a first line screening tool would be twofold, in terms of reducing swabbing/laboratory costs and of identifying a manageable proportion of patients who could be pre-emptively isolated; a second line screening system could then be applied to this subgroup using swabbing and culture.

The potential for the CRA questionnaire as a simple, economical and effective tool to identify most or all true carriers within a small patient subgroup has not been fully realised. The initial model developed and tested – a weighted scoring system for 11 variables within four key questions – appeared to perform no better than a simple three question CRA in terms of identifying true carriers, and delivered a much larger patient subgroup (57% of admissions), which would then proceed to swab screening and potential pre-emptive isolation or cohorting.

Using nasal plus perineal swabbing gave an 82.2% detection of carriage and therefore, in combination with 90% compliance with the CRA, would give a detection rate overall

of around 50.4% of true colonisations. This is marginally better than the first CRA model (48%). The three question simple CRA model reduced those to be swabbed and isolated/cohorted to a manageable 10% of admissions. The increased efficiency of identifying true carriers through swabbing two body sites in this group makes this option close in performance to universal nasal screening, but with considerably reduced resource implications.

Further economic modelling analyses around the various approaches suggested by this study are now in progress, and formed the basis for a subsequent report on national policy options [30].

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5 Background

MRSA infections are associated with increased mortality and morbidity, increased costs due to extended hospital stay. The 2005 Scottish point prevalence study of HAI (Healthcare Associated Infection) found the most prevalent laboratory-confirmed organism recorded to be *Staphylococcus aureus* (48%). Approximately one third of these infections were attributed to MSSA with a further two thirds attributable to MRSA [1]. MRSA is reported as the most frequently isolated organism in skin and soft tissue HAIs [2] and is second only to MSSA in hospital associated infections of bone, joint and surgical site [3;4]. MRSA infections also have a higher bacteraemia-associated mortality than MSSA [5;6] and a general in-hospital mortality which is higher than for MSSA alone [7]. In addition, the burden placed on the health service as a result of MRSA infections is greater due to extended patient length of stay and the increased cost associated with treatment. [8-10]

Those patients who are colonised with MRSA on admission are at higher risk of infection [11] and act as a reservoir for potential transmission to other patients. Screening for MRSA colonisation or infection on admission to hospital, if effective, could greatly reduce this risk of infection to both colonised and non-colonised patients through timely identification and implementation of targeted infection control measures [12]. For screening to be fully effective it has to be sensitive, accurate, and have a quick turnaround time for results in order to allow timely identification and intervention. The screening method can be conventional swab culture, molecular diagnostic techniques, or a CRA questionnaire.

In 2007 NHS Quality Improvement Scotland (NHS QIS) published a Health Technology Assessment (HTA) which modelled the clinical effectiveness and the cost effectiveness of screening for MRSA [13;14]. The HTA recommended that laboratory screening of all in-patient admissions using chromogenic agar was likely to be the most clinically and cost effective strategy for MRSA screening in NHS Scotland. During the Pathfinder project many of the assumptions which the HTA model had been based on were tested and investigated. However, as the preferred screening option of nasal swabbing alone was being employed, it was difficult to test any assumptions relating to other screening options. It was apparent that further robust and appropriate evidence had to be gathered on the efficacy of other screening options for use in NHS Scotland.

6   Introduction

CRA emerged from the HTA as the most clinically effective option, but was initially rejected within the HTA assessment on cost grounds. However, subsequent information from the Pathfinder project [15;16] strongly suggested that timing and resource values within the model were based on higher than were observed estimates. For both CRA and swab-based screening it is known from the HTA that a variety of approaches are already being used in NHS Scotland (though inconsistently in terms of coverage and approach). There was, therefore, a need to critically evaluate the sensitivity, specificity and applicability of swab-based screening from various body sites as well as CRA.

7 Study Aims and Objectives

The primary objectives of this study were:

1. To determine the proportion of MRSA detections identified by swabbing the anterior nares (nostrils) using currently recommended laboratory methods.

2. To determine the incremental effect of swabbing other anatomical sites: throat, axilla and perineum.

3. To determine the sensitivity and specificity of CRA. (see Appendix 1)

Secondary objectives of this study were:

1. To determine the proportion of MRSA detections identified in other clinically significant samples (from sites such as invasive device sites and open skin, lesions/ wounds) in the subpopulation where it was appropriate to screen these sites, compared with nasal swabbing alone.

2. To develop a validated CRA tool which best predicts MRSA colonisation in the total admission population.

8   Methods

8.1   Ethical approval

Ethical approval 09/MRE/0050 was obtained in June 2009 from the Scotland A Research Ethics Committee, subject to study modifications to include the provision of written informed consent for participating patients and GP notification of MRSA infection status on discharge.

8.2   Study population

The study was a cross sectional survey of elective and emergency admissions to inpatient care in three of the acute hospitals who participated in the Pathfinder project. These hospitals were considered to be representative of a large general hospital (Crosshouse Hospital) and a large teaching hospital (Aberdeen Royal Infirmary and Woodend Hospital).

Crosshouse Hospital has an average staffed bed occupancy of 590 beds, including 537 medical, surgical and high dependency unit beds. Aberdeen Royal Infirmary has an average staffed bed occupancy of 879 beds, comprising medical units, surgical units, accident and emergency, high dependency units, intensive care and specialty units such as communicable diseases. Woodend General Hospital has a staffed bed occupancy of 427 Orthopaedic and Care of the Elderly beds. Paediatric, obstetric and psychiatric beds were excluded from the study at both sites.

8.2.1   Inclusion and exclusion criteria

Patients were included in the study if they were aged 16 years or older and admitted electively or as an emergency to Crosshouse Hospital, Aberdeen Royal Infirmary, or Woodend General Hospital's orthopaedic department (essentially an annexe of Aberdeen Royal Infirmary). Further requirements included informed written consent from each patient and screening being undertaken within 48 hours of admission. Patients were included only if they consented to a swab from each body site.

Patients were also included if they were:

- Elective or emergency patients who stayed in a bed overnight

- Day patients who were subsequently admitted as inpatients

- Transferred from other hospitals

- Admitted as in-patients but discharged on the same day

- Patients having multiple admission episodes

Patients were excluded if they were:

- Defined as an adult with incapacity
- Younger than 16 years
- Day case patients
- Discharged before screening took place
- Patients in obstetrics and paediatric units
- Patients in psychiatric units

Patients who attended pre admission clinics did not have additional screening. Where patients were screened and found positive they were isolated where possible and managed according to standard local protocols. The only additional measures taken during the study involved notification to patients' GPs regarding MRSA status upon discharge from hospital (as required by ethical approval conditions).

8.3 Study design and approach

8.3.1 Sample size

For Objective one a minimum sample size of 7,680 admission episodes was required in order to ensure 95% confidence that the proportion of MRSA detections found on anatomical site screening was within +/- 5% of the actual proportion. This assumed MRSA prevalence in the admission population of 5% (interim findings of the pathfinder project) and the proportion of true MRSA colonisations detected to be in the region of 70%.

The CRA (Objective three) required an MRSA positive sample size sufficient both to develop the prediction model, which was arbitrarily ten times the number of predictive questions (13 questions from CRA and four from the data form, and 170 positive samples), and a further sample to test the sensitivity of the model. While the precision of anatomical site screening was likely to be within +/- 5%, it was unlikely that this degree of precision would be reached to test the CRA.

The Screening Working Group was, however, satisfied that a slightly lower precision would be acceptable since there was a wide range of estimated CRA sensitivities in the literature. As such, an achievable sample size of 10,000 admission episodes was proposed. This was based on the number of participants recruited during pathfinder and would allow 3,400 samples for priming the CRA model (i.e. 170 positive samples at a prevalence of 5% in the population) and a further 6,600 to test the model to provide a precision of the estimate in the region of +/- 5% (see Appendix 2).

8.3.2   Recruitment

In Crosshouse hospital all clinical tasks were undertaken by ward staff with additional ancillary staff allocated to the wards during the study to assist with the extra workload. Dedicated administrative staff were employed to assist in data collection. In Aberdeen Royal Infirmary and Woodend general hospital all clinical tasks were undertaken by dedicated nursing staff; dedicated screeners were employed to assist with the extra workload, and administrative staff were recruited to assist with data collection.

Those patients who had the capacity to consent were given the patient information leaflet by the nurses, who were available to answer any questions. Written consent was obtained thereafter from patients who were willing to take part, the CRA was administered, and responses recorded. Trained nurses and screening assistants took screening samples and prepared them for transport to the laboratory. Administration staff recorded patient admission information on the patient data form which was collated from the hospital Patient Administration System (PAS) and nursing notes. Project managers were employed to manage and oversee the project at both sites.

8.4   Data collection

These data were collected for each admission event following issue of the patient information leaflet and obtaining consent to participate:

Demographics and study management:

- CHI or hospital number
- Date of birth
- Hospital site of admission
- Gender
- Date of admission
- Type of admission (elective or emergency)
- Unit admitted to (high risk or low risk)
- Consent to CRA and swabbing
- Date swabs were obtained.

Clinical data:

- CHI
- Answers (Y/N/DK) to each clinical risk question

Microbiology:

- CHI

- Negative or positive results for each anatomical site on chromogenic agar

- Negative or positive result for all anatomical sites pooled in enrichment broth

- Negative or positive results for each 'clinically significant' site if appropriate (see below for definitions) on chromogenic agar

- Negative and positive results from swabs from anatomical sites and 'clinically significant' samples pooled in enrichment broth

- Unique laboratory result number for each sample

- Date of sample.

8.5   Swabbing

The following samples were collected using pre- moistened rayon tipped swabs:

- Nasal (left and right anterior nares using same swab)

- Axilla (left and right axilla using same swab)

- Throat

- Perineum

- Other 'clinically significant' samples e.g. swab from invasive device insertion sites, wounds (surgical and ulcers), urinary catheter site, and sputum samples where appropriate.

Ward nursing staff (Crosshouse) and screening nursing staff (ARI and Woodend) were responsible for assessing the requirement to obtain 'clinically significant' samples.

8.6   Microbiological methods

Swabs from anatomical sites and clinically significant sites were processed in the laboratory by inoculating directly onto Oxoid Brilliance MRSA Agar. In addition, samples from all anatomical sites and (where appropriate) clinically significant sites were pooled in Oxoid selective manitol enrichment broth and incubated at 37°C for 18-24 hours before plating onto Oxoid Brilliance MRSA agar. Confirmation of suspect colonies was by coagulase test using Prolex Staph Xtra Latex Kit: antibiotic susceptibility test carried out on the Vitek2 system and identification carried out on the Vitek2 system (see Appendix 3).

9 Data collection

Data collection forms, CRA and consent forms were scanned into a holding database using TELEform® scanning software. When visual and automatic validation was complete, data were committed to a bespoke SQL database which was designed and developed by HPS. Automatic validation was performed using preset validation rules embedded within the database. Where data errors could not be rectified at this stage, they were returned to the sites for correction prior to re-entry. Laboratory data were extracted from local Laboratory Information Management systems (LIMS) in excel format and sent via the secure NHS.net link to HPS. These data were imported into the SQL database.

Collation of data forms and laboratory results were carried out in the SQL database. A total of 12,889 admission data forms were obtained. Of these, 2,533 lacked valid consent forms and were excluded; patients without laboratory results, duplicate entries and those swabbed out with specified timeframes were all excluded. This gave a study population of 10,314 admissions; for the purposes of the main analysis patients were only included if they had a complete set of four body site swabs (N=10,077). Of those, a further 288 were excluded from the CRA analyses as their CRA data were missing, giving a denominator of 9,789 for the CRA analyses. This sift process is displayed in Figure 9-1.

Figure 9-1: Data collection flowchart

Total extract for combined
special studies
N=12,889

Consent at admission
less duplicated records
N=12,872 → Excluded N=17

Consent at admission
N=10,356 → Excluded N=2,516

Patients at least
one swab
Duplicates removed
N=10,345 → Excluded N=11

Eligible
timeframe only
N=10,314 → Excluded N=31

All body
sites swabbed
N=10,077 → Excluded N=237

CRA response → Excluded=288

Final Data set used for Analyses

All consenting
individuals
N=10,314

All individuals with
all body sites swabbed
N=10,077

All individuals with all
body sites swabbed
and CRA response
N=9,789

Training data set
N=6,534

Validation data set
N=3,255

10 Analysis

All statistical calculations were undertaken in STATA 9® (College station, Texas).

10.1   Proportions

The proportion of MRSA positive swabs identified per anatomical site and the additional benefit of screening at each anatomical site was based on the total number of patient admissions having all screens obtained e.g. nasal, axilla, throat, perineal swabs and one enrichment broth inoculated with samples from each site.

The performance of each anatomical site as an indicator of MRSA colonisation was carried out by comparing the detection in samples from each site against the 'gold standard', which acted as proxy for 'true' colonisation. For this purpose, a 'gold standard' positive result was defined as MRSA isolation from at least one anatomical site (nasal, axilla, throat, and perineum) or any other clinically significant sample such as sputum, urine or any device site, within 48 hours of admission, following culture on chromogenic agar or in enrichment broth. Difference in performance between the anatomical sites was assessed using McNemar's test for paired proportions.

Separate calculations were undertaken for the value of swabbing additional clinically relevant sites. This included only those patients who had additional clinically relevant sites and had samples from these sites included in the enrichment broth. Overall comparisons between responses in NHS boards were made using χ^2 test. Individual proportions for specific groups were compared using Z-tests for the equality of two proportions.

10.2   Clinical Risk Assessment

The CRA tool was developed by identifying risk factors associated with MRSA colonisation on admission then using these risk factors to develop a scoring system to identify individuals with a greater risk of MRSA colonisation.

Clustered multivariable logistic regression analysis was used to investigate the association between the patient's risk questionnaire responses and demographic information with MRSA colonisation on admission. Clustering, by patient was used to adjust for the lack of independence between episodes where the patient had been admitted more than once in the study period. Associations were estimated using a random two thirds selection of the study population (test population) to allow the CRA tool to be validated on the remaining third (validation population).

The independent variables considered are split into those from the CRA questionnaire and those available from the data forms. Those available from the questionnaire are; previous hospital admission in timeframe (six months, one year, not in the past year), previous care home admission, previous colonisation in the past (six months, one year, two years, never), previous antibiotics treatment in past year, presence of invasive devices, wounds, sores or

ulcers, diabetes, chronic obstructive pulmonary disease, and presence of renal failure. These variables all have 'yes', 'no' or 'don't know' responses. Data available from the hospital systems and/or the data form, and therefore regarded as validated in relation to patient reported data, comprised: age (< 49 yrs, 50-64, 65-79 >80 years), gender, type of admission (elective/emergency), the unit admitted to (high/low prevalence specialty as defined by Pathfinder project) and where the patient was admitted from (home, hospital, care home, other).

Prior to the multivariable model build, univariate screening of the variables was conducted to identify potentially important variables. All variables with p-values<0.3 were included in the multivariable analysis. Interactions between all pairs of independent variables deemed to be epidemiologically feasible were considered, with the inclusion p-value adjusted according to the Bonferroni correction[17], to account for multiplicity of testing. Any significant interactions were included in the multivariable model build.

The multivariable model build was implemented using backwards selection by hand. Variables were removed sequentially according to the p-value of the Wald test. For any variables where the 'don't know' response was the sole reason for maintaining inclusion, the variable was removed from the model regardless of the p-value of the Wald test. This was driven by the epidemiological unsuitability of using a 'don't know' response as a predictor of colonisation. Having developed the final model, risk scores were then assigned to each variable based on the coefficient of the variable. These risk scores were scaled and rounded to the nearest integer to provide a quick and easy method of assigning an overall risk score for each admission.

10.3   Sensitivity, specificity and ROC curve

The CRA tool was tested by assigning scores to each individual in the validation population. Individuals were recommended for screening if the score was greater than a defined cut off indicating a higher likelihood of MRSA colonisation. For a given cut off score, the sensitivity and specificity of the CRA tool was calculated by comparing the screening decision (yes/no) to the gold standard MRSA colonisation result. In this way, for every possible cut off, the sensitivity (true positive rate) and 1-specificity (false negative rate) were plotted to provide a ROC (Receiver Operating Characteristic) curve for the model. The accuracy of the model was then determined from the area under the curve (AUC). The greater the area under the curve (AUC) the more predictive the model is. The maximum AUC is 1 (implying a perfect model) whilst an AUC=0.5 implies that the model is diagnostically only as good as random chance.

11 Results

11.1   Demographics

A total of 10,314 admissions were screened during the study period. Of these 3,781 were from Crosshouse Hospital and 6,533 were from Aberdeen Royal Infirmary. Of the total admission population 10,077 had a full set of swabs obtained and were included in the analyses of anatomical sites screened. For development of the CRA tool, 9,789 admissions had a completed CRA form.

There were 4,926 male admissions and 5,388 female admissions in the study population. Age range proportions were distributed fairly evenly for males and females but with a slightly higher proportion of females in the higher age bands. Age range for males was 16 - 98 years and for females 16 -100 years. Median age for males was 63 years and for females was 61 years (IQR: males 50 - 73 years, females 46 - 74 years).

There was evidence of some variation in NHS Board specific demographics with regard to age and gender (Figure 11-1 and Figure 11-2). In Ayrshire and Arran there were 1,729 (45.7%) males and 2,052 (54.3%) females. Age ranged from 16-100 years (males 16-98 years, females 16-100 years). The median age for Ayrshire and Arran was 63 years for males and 63 years for females (IQR: males 48-73 years, females 48-75 years). In Grampian the population comprised 3,197 (48.9%) males and 3,336 (51.1%) females. Age ranged from 16-97 years for females and 17-96 years for males. The median age was 63 for males and 60 for females (IQR: males 51-74 years, females 45-73 years).

Table 11-1 shows the age distribution and the epidemiological characteristics for the study populations at each hospital site. Grampian patients had a higher rate of admission from other hospitals (2.3% vs. 0.7%), a higher proportion of elective admissions (41.6% vs. 24%), and a greater proportion of patients in 'low risk' specialties (58.2% vs. 10.6%) than Ayrshire and Arran patients (all *p* values <0.001). These differences are probably characteristic of the different types of hospital involved.

Figure 11-1: Population pyramid for study population in NHS Ayrshire and Arran N= 3,781
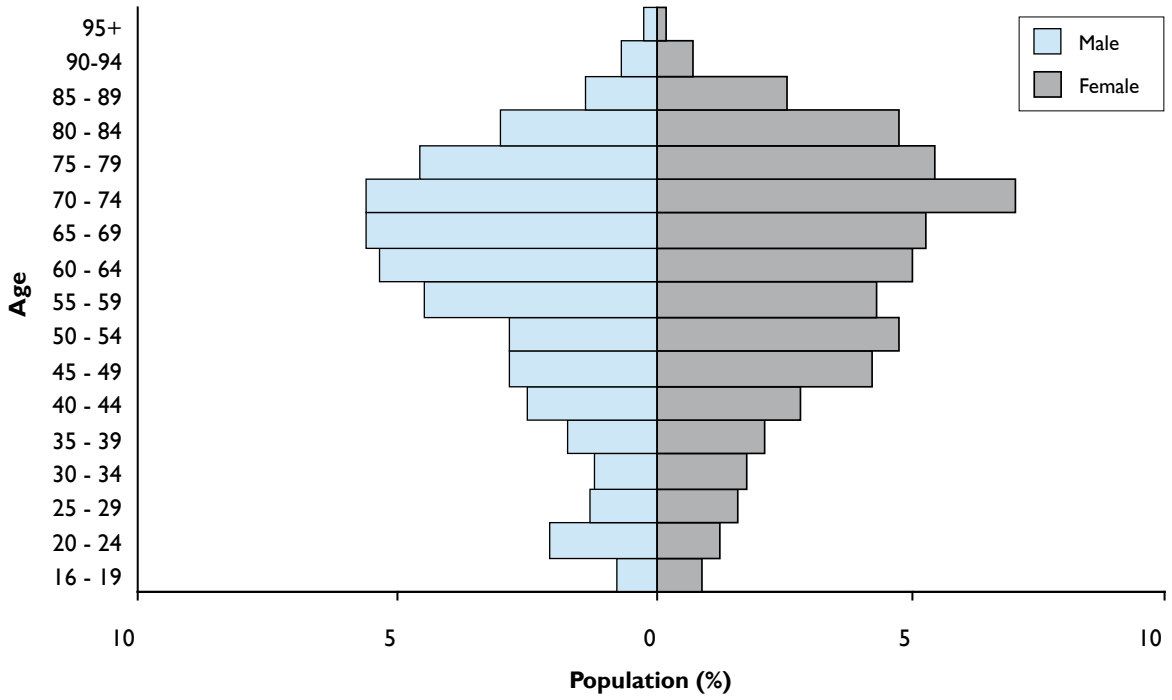
Figure 11-2: Population pyramid for study population in NHS Grampian N = 6,533
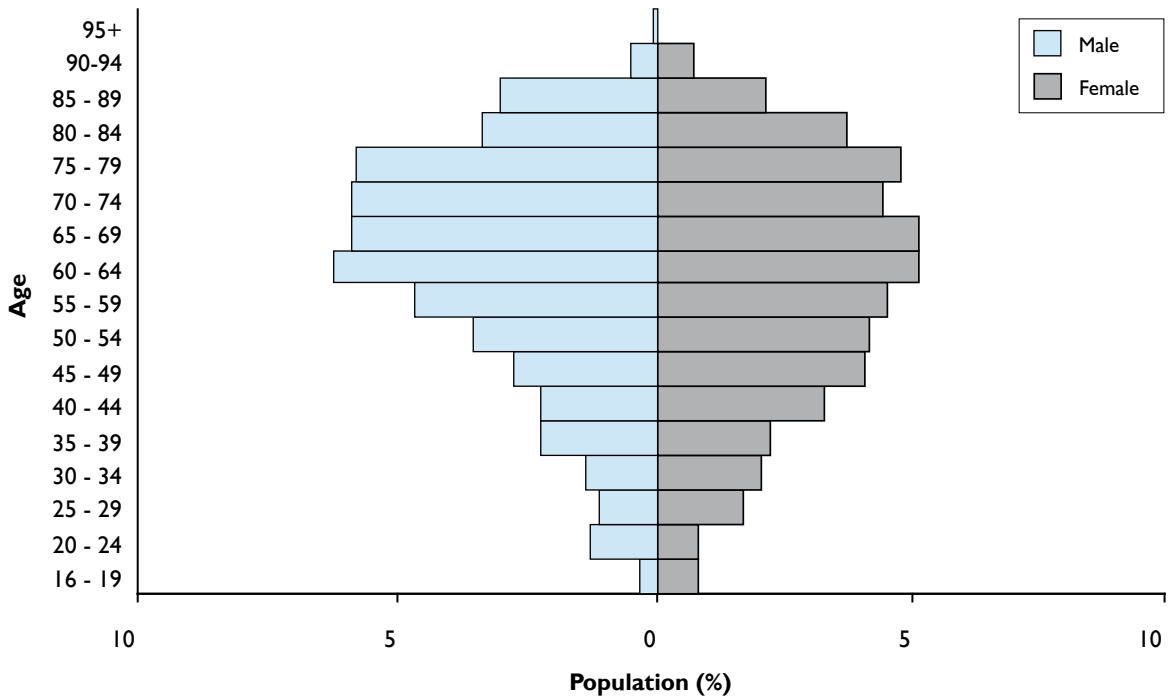
Table 11-1: Epidemiological characteristics of study sites N= 10,314

Characteristic		Ayrshire and Arran			Grampian		
		n	%	95% CI	n	%	95% CI
Gender	Male	1,729	45.7	(44.16, 50.15)	3,197	48.9	(47.72, 50.15)
	Female	2,052	54.3	(52.66, 55.84)	3,336	51.1	(49.85, 52.28)
Age	<=49	1,008	26.7	(25.25, 28.07)	1,789	27.4	(26.33, 28.50)
	50 - 64	1,006	26.6	(25.17, 27.99)	1,859	28.5	(27.35, 29.54)
	65 - 79	1,257	33.3	(31.82, 34.83)	2,096	32.1	(30.93, 33.20)
	>=80	510	13.5	(12.35, 14.53)	789	12.1	11.28, 12.87)
Admitted from	Home	3,737	98.8	(98.49, 99.18)	6,315	96.7	(96.27, 97.14)
	Other hospital	26	0.7	(0.47, 0.10)	148	2.27	(1.91, 2.64)
	Care home	11	0.3	(0.16, 0.52)	14	0.21	(0.10, 0.33)
	Other	7	0.2	(0.09, 0.38)	53	0.81	(0.58, 10.17)
	Unknown	0	0.0	-	3	0.05	(0.02, 0.13)
Type of admission	Elective	923	24.4	(23.06, 25.80)	2,715	41.6	(40.31, 42.71)
	Emergency	2,856	75.6	(74.20, 76.94)	3,816	58.4	(57.29, 56.69)
	Unknown	2	0.1	(0.0, 0.19)	2	0.0	(0.008, 0.11)
Admitted to	Low risk	3,369	89.1	(88.42, 90.39)	3,802	58.2	(57.29, 59.69)
	High risk	399	10.6	(1.58, 9.61)	2,698	41.3	(40.31, 42.71)
	Unknown	13	0.3	-	33	0.5	-

11.2 Objective 1

11.2.1 To determine the proportion of MRSA detections identified by swabbing the anterior nares (nostrils) using currently recommended laboratory methods

Table 11-2 shows total MRSA detections by individual anatomical sites using chromogenic agar and by enrichment broth culture and by geographical site for 10,314 admissions with any test result. MRSA was detected from the nares more frequently than any other site and detected least frequently from the axillae.

Only those patients with a complete set of four swabs were included in subsequent analyses, and Table 11-3 shows the number of positives from chromogenic agar culture (n=273) for these 10,077 admissions by anatomical site.

Comparing NHS boards, there were no statistically significant differences in positivity for the nasal swabs ($p=0.963$) or the axilla swabs ($p=0.923$). The difference in positivity for the perineum swabs (1.29% vs. 0.91%) was also not found to be statistically significant, ($p=0.068$). Broth and throat positivity was found to vary significantly between the sites ($p=0.022$) and $p=0.003$ respectively), with higher positivity in Ayrshire and Arran than Grampian.

Table 11-2: Admissions screened and number and percentage positive at each anatomical site. Total detections n=273 excluding broth, n=303 including broth; total admissions tested N=10,314

Anatomical site	Ayrshire and Arran, N=3,781			Grampian, N= 6,533			Total, N=10,314	
	Total Screens	Positive	(%)	Total Screens	Positive	(%)	Total MRSA positivity	(%)
Nares	3,767	74	1.96	6,509	127	1.95	201	1.96
Axilla	3,750	9	0.24	6,508	15	0.23	24	0.23
Throat	3,752	53	1.41	6,511	52	0.80	105	0.56
Perineum	3,718	48	1.29	6,492	59	0.91	107	1.05
"All sites in enrichment broth "	3,741	102	2.73	6,520	132	2.02	234	2.28

Table 11-3: MRSA detection by anatomical site swab using chromogenic agar culture. Total detections n=273 (excluding broth); total admissions tested N=10,077

Site	Detections	% of total
Nares	198	72.5
Axilla	23	8.4
Throat	103	37.7
Perineum	107	39.1

The positive results from anatomical site swabs plus the' clinically significant' site swabs (for those with wounds or devices etc) plus the enrichment broth isolates collectively gave the 'gold standard' best approximation of true positives for comparison purposes. Some 298 positive colonisations were detected within the combined gold standard total, giving 2.96% prevalence within the 10,077 patients with complete anatomical swab sets.

11.3   Objective 2

11.3.1   To determine the incremental effect of swabbing other anatomical sites: throat, axilla and perineum.

Table 11-4 shows the detections for each anatomical site and the incremental benefit of swabbing additional body sites in comparison with the gold standard. Nasal swabbing alone identified 66.4% (198 /298) of MRSA positive admissions. For an additional second swab this increased by 2.4% by adding axilla screening, by 10.1% by adding throat screening, and by 15.8% by adding perineal screening. Optimum numbers of MRSA colonisation were detected by screening all four sites (91.6% of gold standard positives) but excluding axilla screening reduced this only minimally (90.3%).

Table 11-4: The number of positive samples by anatomical site (chromogenic agar) and the percentage positive compared with gold standard, N= 10,077, n= 298

Anatomical site(s)	MRSA Positive samples n= 298	% of gold standared positivity identified	% gold standard positivity 95% CI	"% of additional MRSA detection compared to nasal alone (95% CI)"
Nares alone	198	66.4	(60.902, 71.564)	
Nares/axilla	205	68.8	(63.320, 73.785)	+2.4 (0.95, 4.8)
Nares/throat	228	76.5	(71.378, 80.967)	+10.1(6.9, 14.1)
Nares/perineum	245	82.2	(77.471, 86.138)	+15.8 (11.8, 20.4)
Nares/throat/axilla	234	78.5	(73.500, 82.800)	+12.1 (8.6, 16.3)
Nares/throat/perineum	269	90.3	(86.300, 93.400)	+23.8 (19.1, 29.1)
Nares/axilla/perineum	250	83.9	(79.291, 87.630)	+17.5 (13.3, 22.2)
Nares/throat/axilla/ perineum	273	91.6	(87.909, 94.253)	+25.2 (20.3, 30.5)

Of the total admission population 1.6% (162/10,077) had swabs taken from other 'clinically significant' sites, e.g. wounds or indwelling devices. Of these, 15.4% (25/162) were positive as determined by the gold standard. For these 25 colonised admissions, 40% (10/25) were identified on nasal swabbing alone and 84% (21/25) from wound/device site swabs. Nasal and wound/device site swabbing in combination identified all gold standard colonisations for patients with wounds/devices (Table 11-5).

Table 11-5: The number of positive samples (n=25) from admissions with wounds/devices (n=162) by anatomical site of swabbing and the additional detection rate for each site

Anatomical site	Number positive samples n=25	% of gold standard positivity	% gold standard positivity 95% CI	% of additional MRSA detection compared to nasal alone (95% CI)
Nares	10	40	(23.4, 59.2)	
Axilla	5	20	(8.8, 39.1)	
Throat	8	32	(0.17, 0.51)	
Perineum	11	44	(26.6, 62.9)	
Wound or device	21	84	(84.0, 93.6)	
Nares/ axilla	13	52	(33.4, 69.9)	+12 (4.2, 29.9)
Nares/throat	12	48	(30.0, 66.5)	+8 (2.2, 24.9)
Nares/perineum	17	68	(48.4, 82.7)	+28 (14.2, 57.6)
Nares/axilla/throat	15	60	(40.7, 76.5)	+20 (8.9, 39.1)
Nares/axilla/perineum	19	76	(56.5, 88.5)	+36 (20.2, 55.5)
Nares/throat perineum	18	72	(52.4, 85.7)	+32 (17.2, 51.6)
Nares/axilla/throat/perineum	20	80	(60.8, 91.1)	+40 (23.4, 59.3)
Nares/wound/device site	25	100	(86.6, 100.0)	+60 (40.7, 76.6)

11.4   Objective 3

11.4.1   To determine the sensitivity and specificity of CRA

The development of the CRA tool was undertaken in two stages: the CRA was developed using a 'training' cohort of 6,532 admissions (adjusted for 6,173 clusters) and tested on a 'validation' cohort of 3,255 admissions.

The CRA form and selected variables from the data recording sheet were investigated for risk impact. Table 11-6 shows the number and percent positive for each variable, and Table 11-7 shows the impact of each risk independently in the univariate analysis. The most significant independent factors identified were age group on admission, previous colonisation, admitted from anywhere other than home, previous hospital admission, frequency of admission, specialty admitted to, type of admission, antibiotics administered in previous year, presence of indwelling device, presence of wounds or ulcers, and presence of diabetes or chronic obstructive pulmonary disease. The recorded answer to the renal failure question with a significantly increased odds ratio was 'don't know or not answered'. All significant variables were included in the multivariable logistic regression analysis. No interactions were found to be significant.

11.4.2 To determine the sensitivity and specificity of CRA

Table 11-6: MRSA positivity by risk variable for training set of study population during study period

Variable	Subgroup	Total	"Total MRSA +ve "	"% MRSA +ve "	95% CI
Gender	Male	3114	91	2.92	(2.39, 3.57)
	Female	3419	99	2.90	(2.38, 3.51)
Age group	<=49 years	1759	32	1.82	(1.29, 2.56)
	50-64 years	1811	31	1.71	(1.21, 2.42)
	65-79 years	2135	70	3.28	(2.6, 4.12)
	80+	829	57	6.88	(5.34, 8.80)
Origin of patient	Home	6364	172	2.70	(2.33, 3.13)
	Hospital transfer	116	8	6.90	(3.54, 13.0)
	Nursing home	17	5	29.41	(13.28, 53.1)
	Other	35	5	14.29	(6.26, 29.38)
Type of admission	Elective	2327	54	2.32	(1.7, 3.0)
	Emergency	4203	135	3.21	(2.72, 3.79)
Previous MRSA colonisation	Never	6006	82	1.37	(1.1, 1.69)
	Past year	192	70	36.46	(29.98, 43.47)
	Past 2 year	59	10	16.95	(9.48, 28.46)
	More than 2 years	158	24	15.19	(10.42, 21.6)
	Not known	*	*	3.36	(1.31, 8.32)
More than two admissions in past year	Yes	80	15	18.75	(11.7, 28.66)
	No	6365	169	2.66	(2.29, 3.02)
	Not known	89	6	6.74	(3.12, 13.93)
Specialty admitted to	High risk	4543	108	2.38	(1.97, 2.86)
	Low risk	1965	80	4.07	(3.28, 5.04)
Previous hospital admission	Past 6 months	2234	110	4.92	(4.1, 5.9)
	Past 6 – 12months	708	24	3.39	(2.29, 4.99)
	Not in past year	3505	51	1.46	(1.10, 1.90)
	Not known	87	5	5.75	(2.48, 12.76)
Resident in care home in past year	Yes	1253	79	6.30	(5.09, 7.89)
	No	5091	105	2.06	(1.71, 2.49)
	Don't know or not answered	190	6	3.16	(1.46, 6.72)
Received antibiotics in past year	Yes	3346	131	3.92	(3.31, 4.62)
	No	2895	48	1.66	(1.28, 2.23)
	Don't know or not answered	293	11	3.75	(2.11, 6.60)

Variable	Subgroup	Total	"Total MRSA +ve "	"% MRSA +ve "	95% CI
Presence of indwelling device	Yes	927	46	4.96	(3.74, 6.56)
	No	5532	142	2.57	(2.18, 3.02)
	Don't know or not answered	*	*	2.67	(0.73, 9.21)
Presence of open wounds/ sores /ulcers	Yes	542	32	5.90	(4.21, 8.21)
	No	5908	155	2.62	(2.24, 3.06)
	Don't know or not answered	*	*	3.57	(1.22, 9.98)
Diabetes	Yes	885	38	4.29	(3.14, 5.83)
	No	5567	149	2.68	(2.28, 3.13)
	Don't know or not answered	*	*	3.66	(1.25, 10.21)
Chronic Obstructive Pulmonary Disease	Yes	577	34	5.89	(4.25, 8.12)
	No	5849	150	2.56	(2.19, 3.06)
	Don't know or not answered	108	6	5.56	(25.71, 11.59)
Renal Failure	Yes	229	8	3.49	(1.78, 6.74)
	No	6177	171	2.77	(2.39, 3.21)
	Don't know or not answered	128	11	8.59	(4.87, 14.73)

* Indicates values that have been suppressed due to the potential risk of disclosure

Table 11-7: Univariate analysis for each risk variable

Variable	Subgroup	Odds ratio	Pvalue	95% CI
Gender	Male	1	-	-
	Female	0.99	0.952	(0.72 - 1.35)
Age group	<=49 years	1	-	-
	50-64 years	0.94	0.827	(0.53 - 1.63)
	65-79 years	1.83	0.014	(1.13 - 2.96)
	80+	3.98	<0.001	(2.44 - 6.50)
Origin of patient	Home	1.00	-	-
	Hospital transfer	2.67	<0.001	(1.28 - 5.57)
	Nursing home	15.00	<0.001	(5.21 - 43.1)
	Other	6.00	<0.001	(1.54 - 23.3)
Type of admission	Elective	1.00	-	-
	Emergency	1.40	0.047	(1.00 - 1.94)
Previous MRSA colonisation	Never	1	-	-
	Past year	41.45	<0.001	(28.6 - 60.1)
	Past 2 year	14.74	<0.001	(7.21 - 30.1)
	More than 2 years	12.93	<0.001	(7.92 - 21.1)
	Not known	2.51	0.077	(0.90 - 6.98)
Specialty admitted to	High risk	1	-	-
	Low risk	1.74	<0.001	(1.29 - 2.35)
Previous hospital admission	Not in past year	1	-	-
	Past 6 months	3.51	<0.001	(2.49 - (4.95)
	Past 6 – 12months	2.38	<0.001	(1.43, 3.94)
	Not known	4.13	<0.001	(1.60 - 10.6)
Resident in care home in past year	No baseline	1	-	-
	Yes	8.46	<0.001	(4.73, 15.13)
	Don't know or not answered	2.65	0.024	(1.14, 6.17)
Received antibiotics in past year	No baseline	1	-	-
	Yes	2.42	<0.001	(1.72 - 3.39)
	Don't know or not answered	2.31	0.014	(1.18 - 4.52)
Presence of indwelling device	No baseline	1	-	-
	Yes	1.98	<0.001	(1.40 - 2.79)
	Don't know or not answered	1.04	0.957	(0.25 - 4.28)

Variable	Subgroup	Odds ratio	Pvalue	95% CI
Presence of open wounds/ sores /ulcers	No baseline	1	-	-
	Yes	2.33	0.000	(1.57 - 3.44)
	Don't know or not answered	1.37	0.592	(0.42 - 4.47)
Diabetes	No baseline	1	-	-
	Yes	1.63	0.011	(1.12 - 2.37)
	Don't know or not answered	1.38	0.588	(0.43 - 4.43)
Chronic Obstructive Pulmonary Disease	No Baseline	1	-	-
	Yes	2.38	<0.001	(1.56 - 3.61)
	Don't know or not answered	2.23	0.061	(0.96 - 5.18)
Renal Failure	No Baseline	1	-	-
	Yes	1.27	0.554	(0.57 - 2.81)
	Don't know or not answered	3.30	0.000	(1.74 - 6.23)

The results of the multivariable logistic regression analysis are shown in Table 11-8. As the univariate analysis established that the effect of age was insignificant in those under 65 yrs, the ≤ 49 and the 50-64 yr old age groups were combined. After adjusting for other variables, the four statistically significant factors in predicting MRSA colonisation on admission to hospital were age group at admission, previous colonisation with MRSA, admission frequency and where the patient was admitted from.

Table 11-8: Results of multivariable clustered logistic regression analysis of risk factors for MRSA colonisation during study period February 2010-July 2010 N= 6,532

Variable	Subgroup	Odds Ratio	Confidence Intervals 95%	Regression Coefficient	P value
Age Group	65-79 years	1.606	(1.081, 2.384)	0.473	0.019
	>= 80 years	2.915	(1.901, 4.470)	1.070	<0.001
Previous colonisation	Not known/ not answered	2.057	(0.706, 5.990)	0.721	0.186
	Past year	33.56	(22.372, 50.351)	3.513	<0.000
	Past two years	11.35	(5.056, 25.481)	2.429	<0.000
	More than two years ago	11.61	(6.764, 19.924)	2.451	<0.000
Admission frequency	More than two admissions in past year	1.44	(1.003, 2.058)	0.362	0.048
	Don't know/ not answered	1.09	(0.419, 2.820)	0.843	0.862
Admitted from	Hospital	2.80	(1.181, 6.637)	1.029	0.019
	Care home	8.18	(1.484, 45.105)	2.102	0.016
	Other	7.65	(1.803, 32.468)	2.034	0.006

The scoring system used to validate the model was based on the regression coefficients which were scaled and rounded to provide an easy scoring system for use in practice (Table 11-9).

Table 11-9: Scaling and rounding of coefficients to establish scoring system

Variable	Subgroup	Coeff	Scaled coeff (X3)	Scaled and rounded coeff
Age Category	65 years- 79 years	0.473727	1.421182	1
	80+ years	1.070013	3.210039	3
Admitted from	Hospital	1.029354	3.088062	3
	Care home	2.102009	6.306027	6
	Other	2.034755	6.104265	6
More than two admissions in previous year	Yes	0.362683	1.088049	1
	Don't know/not answered	0.084365	0.253094	0
Previous colonisation	Don't know/not answered	0.721357	2.164071	2
	Past year	3.513435	10.54031	11
	Past 2 years	2.429363	7.288089	7
	More than 2 years	2.45184	7.35552	7

These scores were then assigned to all admissions in the validation cohort i.e. each admission was allocated an overall score depending on the cumulative score for each applicable risk. The overall sensitivity and 1-specificity of each score was then established using the gold standard as a proxy for true positive or true negative MRSA status. The sensitivity and 1-specificity for each score was then plotted to provide a ROC curve for the model. The ROC curve was used to determine which score provides the best trade off in terms of sensitivity and specificity to identify those most likely to be MRSA positive for isolation and screening on admission. The area under the curve for the ROC model was 0.7648. The best cut off point in terms of trade-off is the highest point closest to the Y axis as indicated in Figure 11-3. This corresponds to a sensitivity of 54.8%, specificity of 91.1% and a cut-off value for the risk score of four.

Figure 11-3: ROC curve for the CRA tool as tested on the validation cohort N= 3,255. Optimal cut-off area circled
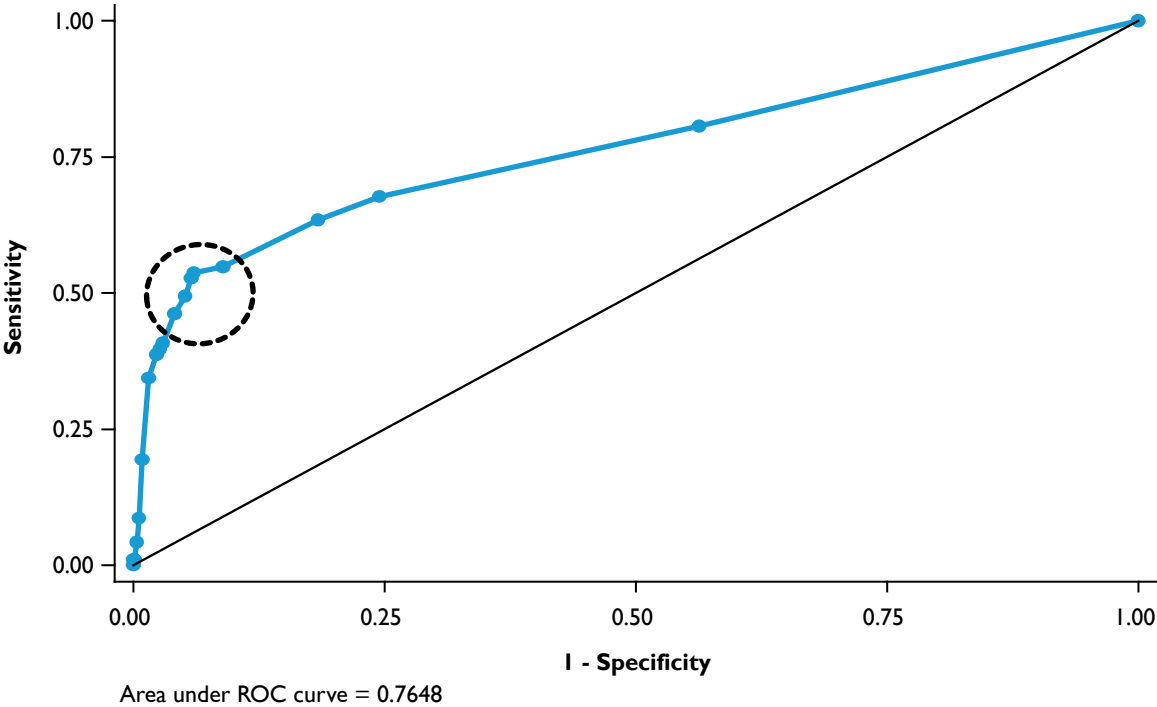

Area under ROC curve = 0.7648

Figure 11-4 shows an alternative representation of the model's performance. The histograms represent, for each risk score, the number of admissions with that score who were positive or negative for MRSA colonisation. The dotted line is the optimal cut off indicated by the ROC curve. The proportion of positives to the left of the line in the upper histogram represents those who were positive but would not be screened at this cut off point (false negatives). Similarly, in the lower histogram the proportion of negatives to the right of the line represents those who were negative but would be screened (false positives). The low number of false positives reflects the high specificity of the CRA tool. Higher levels of sensitivity can, however, only be achieved if the cut off is reduced further leading to more false positives and higher numbers of individuals screened.

Figure 11-4: Histogram of risk scores for MRSA positive and MRSA negative admissions, N=3,255
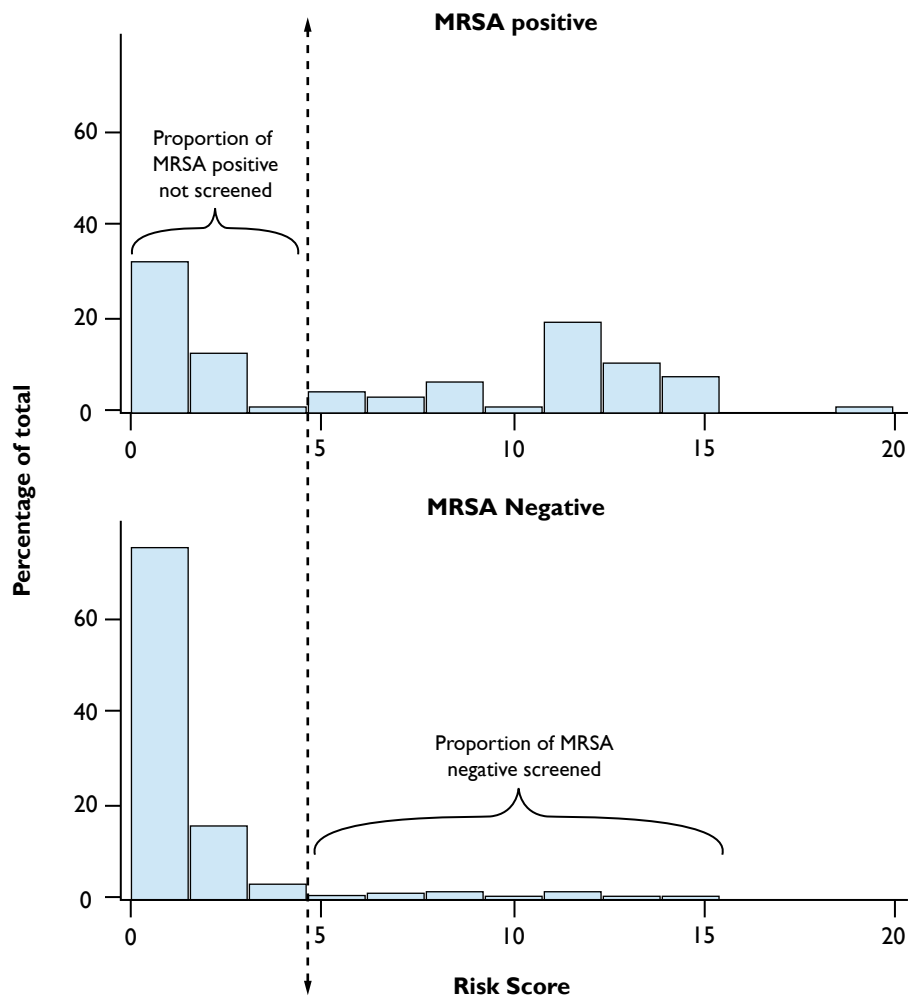
Table 11-10 shows the effect of altering the cut off point for scores in terms of sensitivity (true positives detected) and specificity, and the proportion of patients who would require subsequent swab screening. The first cut off indicates that at best only 80.7% of true MRSA carriers would be included in this group, and this would require isolation and swab screening of 57% of patients. Reducing the screening population to 10% of patients would result in 45% of true MRSA cases being missed.

Table 11-10: Sensitivity Specificity and validation population screened for each risk score value

Cut off point Risk score	Sensitivity %	Specificity %	Validation population screened %
0	100	0	100
1	80.7	43.7	57
2	67.7	75.5	25.7
3	63.4	81.6	19.7
4	54.8	91.1	10.2
5	53.8	94	7.4
6	52.7	94.3	7.1
7	49.5	94.8	6.5
8	46.2	96	5.3
9	40.9	97.1	4
10	39.8	97.3	3.7
11	38.7	97.2	3.3
12	34.4	98.5	2.5

The interplay between sensitivity, specificity and the proportion of patients identified for swab screening is shown graphically in Figure 11-5.

Figure 11-5: Sensitivity specificity and percentage screened by cut off point for CRA model's performance using the validation population N= 3,255
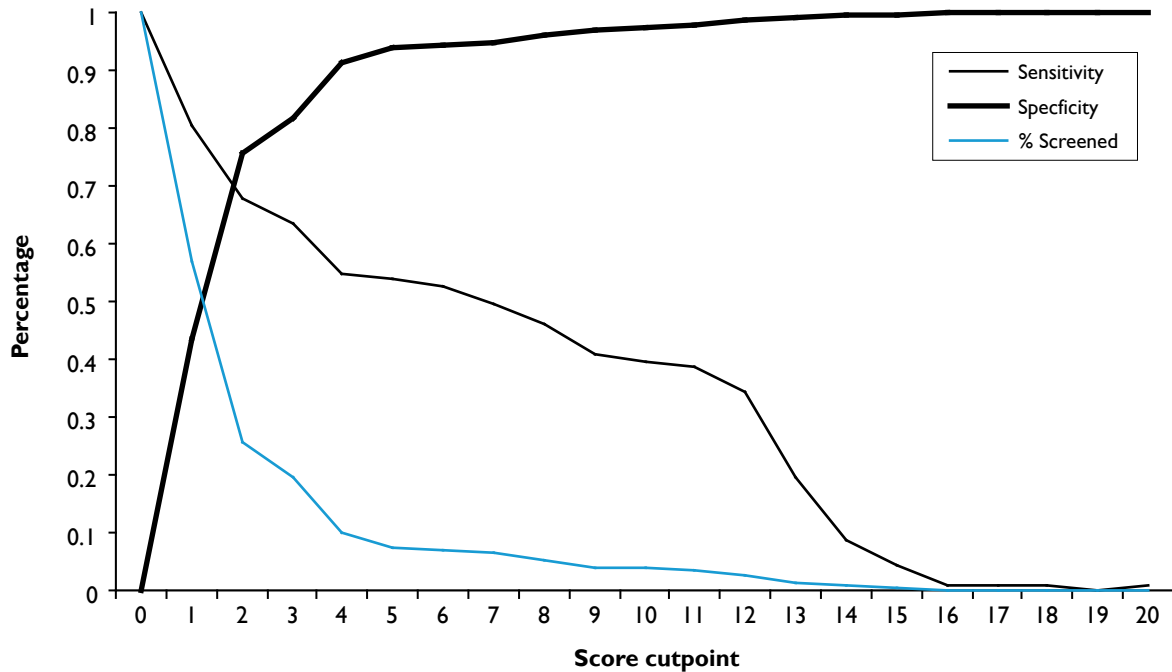
11.4.3   Simple prioritisation using selected risk factors

Given that the model was less predictive of colonisation than anticipated as demonstrated in the validation population, an approach of combining the scoring elements into a simple yes/no for each of the four key risk factors was tested for its' performance in identifying a more manageable proportion of the population for isolation and screening. This would potentially reduce patient mixing to an extent, and would be preferable to having no patient separation pending laboratory confirmation of MRSA status. If, in addition these risk factors were identifiable on admission from patient information systems rather than from patient recall, this would permit inclusion of all patients and not merely those who could give accurate responses to questions.

Table 11-11 shows the key risk factor information which could be available on admission, and the impact of applying this in terms of MRSA ascertainment and minimising the size of the 'at risk' group. Looking at the individual coefficients the best single predictor of positivity is a previous history of colonisation or infection. Patient answers indicating previous history of MRSA colonisation or infection at any time in the past identified 150/298 cases (50.4%); laboratory confirmed data for any history of MRSA identified 188/298 cases (63.1%) within 6.3% of the study population. Adding additional risk factors brought incremental

increases in both the number of true positives captured and the proportion of admissions which could be prioritised for pre-emptive isolation and swab screening (Table 11-11). Any positive response to a combination of previous laboratory positives, those not admitted from home and those with wounds or devices would identify 68.1% of positives within 9.7% of admissions. Adding age >80 to the first two risk factors increased sensitivity to 76.2%, but this effectively doubled (19.2% of admissions) the number of patients who would be identified for isolation and swab screening.

Table 11-11: Numbers of MRSA gold standard cases identified by risk factor (single and in combination), and number of patients requiring isolation and swab screening for confirmation (study population N=10,077, gold standard positive n=298

Risk factor	MRSA negative	MRSA positive	Total requiring swab screening	% of admissions requiring isolation/screening	95% CI	% of gold standard MRSA detected	95% CI
1. Known previous positive (laboratory)	449	188	637	6.3	(5.86, 6.81)	63.1	(57.5, 68.4)
2. Not admitted from home	227	23	250	2.5	(2.19, 2.80)	7.7	(5.19, 1.13)
1. + 2.	660	198	858	8.5	(7.98, 9.07)	66.4	(60.9, 71.5)
3. Age >80	1193	79	1272	12.6	(11.9, 13.2)	26.5	(21.8, 31.7)
1. + 2. + 3.	1704	227	1931	19.2	(18.4, 19.9)	76.2	(71.0, 80.6)
4. Wounds or devices	137	25	162	1.6	(1.37, 1.87)	8.9	(5.74, 12.0)
1. + 2.+ 4.	775	203	978	9.7	(9.14, 1.02)	68.1	(62.6, 73.1)

12 Discussion

12.1 Introduction to discussion

Nasal swab screening combined with culture on agar has been the routine methodology for detecting MRSA carriage in Scotland and in many other countries for some time. It is however, costly in terms of staff time and laboratory processing and the sensitivity of the technique in detecting true carriers in the patient population is poorly understood. The current study sought to determine the likely true sensitivity of nasal swabbing and the effect on ascertainment of swabbing additional body sites.

The CRA approach emerged as the most clinically effective option in the NHS QIS Health Technology Assessment model, but at less acceptable cost than nasal swab screening [13]. The cost estimates used for CRA in the model were unrealistically high. The potential attractions of a CRA approach as a first line screening tool would be twofold in terms of reducing swabbing/laboratory costs and of identifying a manageable proportion of patients who could be pre-emptively isolated; a second line screening system could then applied using swabbing and culture.

12.2 Nasal screening and multiple body site screening

One of the more surprising findings in this study was that nasal swabbing alone the standard routine screening method appeared only to detect 66% of 'true' positive cases as assessed by the gold standard measure (all body site swabs on chromogenic agar plus broth enrichment combined). This efficiency of identifying MRSA carriers will be further reduced in the real-time hospital environment by the difficulty in ensuring compliance with swabbing – 90% and 80% compliance with universal nasal swabbing would for example at best detect 59% and 53% of true cases respectively. This implies that even with universal nasal screening almost half of true MRSA carriers would go undetected in reality.

MRSA colonisation was detected most frequently on nasal screening and least frequently on axilla screening. For a two-swab approach the combination of nasal plus perineum produced a significantly better detection rate (82.2%) than nasal alone (66.4%); nasal plus throat swabbing also produced a better detection rate than nasal alone (76.5%) but this difference was not statistically significant.

Throat screening is relatively acceptable to patients and is easy and quick to perform. Perineal colonisation is a proxy measure for rectal colonisation, which is reported as more likely to cause environmental contamination and has been associated with high dispersal [18;19]. Perineal swabbing on this basis would be the site of choice for second swab screening given this propensity for transmission; however, it may be less acceptable to patients than throat screening and more demanding of staff time (patients may require assistance to undress and manoeuvre and may also require perineal hygiene prior to screening).

A broad range of individual site detection rates are quoted in the literature and are generally higher than identified in the current study [20-22]. However, these studies vary in their population samples, and detection methods used to determine colonisation. Some were undertaken with in-patients at higher risk of colonisation or combining clinical samples with screening samples. The actual clinical impact of relatively inefficient detection of MRSA carriage is unknown, but the Pathfinder project [23] suggests that around half of the MRSA infections diagnosed in hospital are in patients not known to be colonised on admission. Those patients will be partly undiagnosed carriers and partly true negatives who acquire their colonisation or infection directly or indirectly from patients who are colonised at admission. The dynamics of this are unquantifiable from the current study but there may be additional insights into this issue in the findings of the linked discharge [24] study .

12.3   Screening wounds and indwelling device sites

For those admissions with indwelling devices or wounds (surgical wounds, pressure ulcers, diabetic ulcers etc) MRSA detection is considerably improved by including appropriate site swabbing in the screening strategy. The total number of admissions with wounds or devices swabbed was 162 (1.6%) of which MRSA colonisation or infection was identified in 25 (15.4%). Nasal swabbing alone identified 10 (40%) positive MRSA admissions in this sub group but in combination with wound/device swabbing 100% of patients were identified without the addition of perineal screening. For a small group however, the simpler practicalities of applying a two swab (nasal plus perineal) regimen to all patients probably outweigh the marginal financial benefits of using nasal swabs only in this group. Wound/device site screening is a current UK recommendation [25] but the current study provides further evidence for reinforcing this measure in a small group at substantially higher risk of colonisation as part of any screening policy.

12.4   Clinical risk assessment

Clinical Risk Assessment if effective, would identify those most at risk of MRSA colonisation on admission to hospital in order to efficiently target pre-emptive isolation and anatomical site screening to confirm MRSA status. This would help interrupt the transmission cycle by reducing patient mixing in the 24-48 hour period required for routine laboratory confirmation of swab testing. The ideal CRA first line screening tool would be a short list of questions which would (singly or in combination) detect all true positive MRSA carriers in as small a subgroup of patients as possible, which would be a relatively manageable number to pre-emptively manage and apply second line swab based screening. This is a broad principle in screening programmes generally; breast cancer screening in Scotland, for example, identifies 10% of those invited for first mammography screening as requiring further more detailed investigation [26].

The CRA tool in this study was developed using a broad range of known risks for colonisation on admission which were indicated in the literature [24;27-32]. The CRA questionnaire required patient responses (positive, negative or unknown) and was complemented by a data form which administrative staff completed with known or confirmed information as available in the patient's medical notes or from patient information systems. The operational aim was to develop a tool which was short and easy to complete with information which was readily available at the point of admission, to which a weighted scoring system was applied.

A number of different models and scoring methods were explored in the development of the CRA tool. The model which provided the most sensitive indicator of MRSA colonisation included 11 indicators within four risk factors with the highest regression coefficients; these risk factors have been well documented in the literature [27-29;31-33] and comprise: age category on admission to hospital (the 80+ year age category being particularly predictive); those admitted from another other hospital, care home or other institutions such as prison or hostels; frequency of hospital admission; and if previously colonised or infected with MRSA. Of the four key risks identified, two were obtained from the CRA questionnaire (previous colonisation and inpatient episodes in the past year) and two were obtained from the data form (age and where admitted from). Information on previous MRSA positivity was also collected from laboratory information management systems. Although the questionnaire was designed to be administered on admission, if patient information systems were able to provide this information with ease and in a timely manner this would be preferable to reliance on patient recall. Previous colonisation was identified here as the dominant predictor of current MRSA colonisation and was included as such in original HTA model [13] .

The ROC curve showed an area under the curve of 0.76 which indicates good but not excellent predictive properties for this weighted scores model. The tool performed better in terms of specificity than sensitivity i.e. it efficiently identified those who are truly negative at the expense of identifying those truly positive but sensitivity is the key attribute of a primary screening tool. The majority of negative cases are identified at the 'optimum' cut off point but with a considerable proportion of positive patients missed. The best sensitivity which could be achieved by application of the weighted scores CRA tool was at a cut off score of 1.0 with 81% sensitivity but with 57% of the population requiring isolation and swab screening. Moreover, when combined with 66% sensitivity for nasal screening and less than 100% compliance (e.g. 90% which was the compliance rate at the end of the Pathfinder project [16]) this tool would only identify 48% of true positives in return for nasal swab screening of more than half of admissions.

Given that the single most predictive element of the model was a history of previous colonisation or infection at any time this question was used as a first step in a second very simple model for risk assessment. This 'previous positive' group (identified from laboratory confirmation data) included 63% of true positives within only 6.3% of total admissions. Adding two smaller groups with a high prevalence of colonisation (wounds/indwelling devices and those admitted from locations other than home) captured 68.1% of true positives

within 9.7% of admissions (Table 11-11). The other strong indicator for carriage (age >80) increased the numbers detected but at the expense of doubling the number of patients who would be targeted for isolation and swab screening. The three formal questions comprising the short CRA would therefore be:

- Has the patient any past history of MRSA colonisation or MRSA infection at any time?

- Is the patient currently resident in a care home or institutional setting, or transferred from another hospital?

- Does the patient have a wound/ulcer or indwelling medical device which was present before admission to this hospital?

Within a subgroup of 10% of patients employing a two-swab regimen becomes financially attractive in comparison with universal nasal swabbing of a much larger group. Using nasal plus perineal swabbing to give 82.2% detection of carriage in combination with 90% compliance would give a detection rate overall of around 50.4% of true positives, marginally better than the first CRA model (48%) but at substantially lower cost. This approach additionally identifies a much more manageable subgroup in terms of pre-emptive isolation. This very simple model – answering 'yes' to any of the three questions above –would also enable risk assessment of patients who were unconscious or otherwise incapacitated.

13 Limitations

In line with research ethics requirements this study did not include those patients who were unfit to participate in the study on admission to hospital due to incapacity. It is plausible that this subpopulation would be at higher risk of colonisation on admission. As such, exclusion of these patients may have altered the efficacy of detection of the CRA in the study making the estimates more conservative. Conversely these patients may be particularly likely to be picked up by the simple three question CRA model.

The CRA has only been validated in a subsection of the total admission population and the specialty distribution was not the same as recorded in the Pathfinder project – different proportions for example were admitted from home or admitted to 'high risk' specialties as defined in the Pathfinder project [23]. There is probably a need for the risk assessment tool to be more rigorously validated with other hospital populations. In addition the CRA was validated in hospitals where universal nasal screening had been continuously employed during the 18 months prior to the study, which may have reduced the overall incidence of carriage (and thereby adversely affected sensitivity values) – again, giving a more conservative estimate of true efficacy of the CRA.

The data from the CRA questionnaire on indwelling devices/wounds were not used as the number of positive responses (13.6% of patients were recorded as having invasive devices) was clinically judged to be unrealistically high and very much higher than the number of wound/device swabs received by laboratories. It is possible the phrasing of the question allowed erroneous recording of peripheral venous cannulas inserted on admission for example; these cannulas could also have been inserted just prior to admission by paramedical ambulance staff. The number of swabs submitted for wound/device testing (162, 1.6% of admissions) was taken as a proxy for the true number of such patients, but this is likely to be an underestimate which reflected the degree of compliance with swabbing.

A further unexpected anomaly was that the 'not known' answer to some questions appeared significant in determining likelihood of colonisation These questions included previous hospital admission during a time period, presence of renal failure, and previous use of antibiotics. The reason for increased likelihood of MRSA in these patients is unclear but may relate to lowered recall secondary to pre-existing illness in some patients who were thereby at higher risk of colonisation.

Finally, the variable and often unpredictable nature of the evolution of micro-organisms and the speed with which they change is a limitation to future success and is unpredictable. Whether similar risk characteristics will be prognostic of MRSA colonisation in the future is uncertain – community acquired strains of MRSA affect very different risk groups than hospital-acquired strains for example.

14 Conclusions

Universal nasal swabbing for MRSA appeared less effective than previously thought in identifying patients with MRSA carriage, with just over half of true carriers likely to be identified in practice. Using a combination of body site swabs would increase ascertainment within a universal screening programme but at a significant cost in terms of staff time and resources.

The ideal of the CRA questionnaire as a simple, economical and effective tool to identify most true carriers within a small patient subgroup has not been fully realised. The initial model developed and tested – a weighted scoring system for 11 variables within four key questions – appeared to perform no better than a simple three question CRA in terms of identifying carriers and delivered a much larger patient group which would then proceed to swab screening and pre-emptive risk management. The three question simple CRA model reduced those to be swabbed and isolated/cohorted to a more manageable 10% of admissions and the increased efficiency of identifying true carriers through swabbing two body sites in this group makes this option closer to more complex CRA models and the performance to universal nasal screening, but probably with considerably reduced resource implications.

Further study of the parameters and the economic modelling around the various approaches suggested by this study is required to inform national policy options and is presented in a subsquent report [29]

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16 Appendix 1

Crosshouse Hospital

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MRSA Study Clinical Risk Assessment On Admission

Complete the forms using black ink
For text questions, write clearly and in block capitals
For choice questions, place only one cross ☒ in the applicable box, unless instructed otherwise

1.1 Patient identification code (CHI)

1.2 Patient Date Of Birth (dd/mm/yyyy)

1.3 Gender
☐ Male   ☐ Female

1.4 Hospital Unit Number (only if patient has no CHI number))

1.5 Admission Date

2. Clinical Risk Assessment

Where clinical case notes are used to verify a response please cross 'verified'. Please ensure **all** questions are answered. If response is no\unknown, please check relevant box, no boxes should be left blank.

	yes	no	unk	verified
1. Has the patient been an 'in patient' in hospital during the past year?	☐	☐	☐	☐
2. If so,was this during the past 6 months?	☐	☐	☐	☐
3. Has the patient had more than two 'in patient' episodes during the past year?	☐	☐	☐	☐
4. Has the patient been resident in a care home during the past year?	☐	☐	☐	☐
5. Has the patient had a confirmed MRSA infection or colonisation reported in the past?	☐	☐	☐	☐
6. If so, was this within the past year?	☐	☐	☐	☐
7. If so, was this within 2 years?	☐	☐	☐	☐
8. Has the patient received antibiotic treatment during the past year?	☐	☐	☐	☐
9. Does the patient currently have an indwelling urinary catheter or other invasive device(s) in situ e.g. PEG feeding tube,central line, tracheostomy tube etc?	☐	☐	☐	☐
10. Does the patient have any open wounds/sores/ulcers?	☐	☐	☐	☐
11. Does the patient have diabetes?	☐	☐	☐	☐
12. Does the patient have COPD?	☐	☐	☐	☐
I3. Does the patient have renal failure?	☐	☐	☐	☐

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17 Appendix 2

Sample size calculation

Sample sizes were calculated using the formula

Equation i: Sample size calculation for clinical risk assessment

$$z * \sqrt{\frac{p*(1-p)}{n}}$$

Where z represents the Standard Normal distribution of approximately 1.96 for 95% confidence intervals

Where p represents the proportion to be estimated i.e. the test sensitivity

Where n represents the prevalence in the population i.e. 5% as per interim pathfinder results

The clinical risk assessment will require an arbitrary estimate of 170 positive samples (17 questions x 10 positive results) to prime the model. At a 5% MRSA prevalence in the admission population this would require an actual admission sample size of 3,400 admissions. If an overall sample size of 10,000 admission events was obtained this would allow a sample size of 6,600 admission events to test the sensitivity of the CRA. Given a mid point sensitivity of 70% this would provide a precision of the estimate of the sensitivity of the CRA of +/- 5% (4.9%).

$$196 * \sqrt{\frac{0.7 * 0.3}{330}} = 0.49$$

18 Appendix 3

Laboratory SOP: Examination for MRSA on hospital admission and discharge (part of MRSA screening studies)

1. Purpose of examination

Meticillin resistant *Staphylococcus aureus* (MRSA) is a major cause of hospital acquired infection. It is easily spread by person to person contact. Patients found to be infected can carry the organism for a considerable length of time making them reservoirs of infection. Accurate and rapid detection of meticillin resistance is necessary for successful containment and treatment of these organisms and so screening of patients is vital.

2. Principle of examination

Specimens are plated onto a selective agar that encourages the growth of MRSA. All suspect colonies are identified and can be tested against a range of antibiotics.

3. Specimen requirements

3.1 A screen for MRSA carriage should include swabs / samples from:

- Anterior nares

- Throat

- Perineum

- Axilla

- Swab from invasive device site: central line, PEG tube, tracheotomy site

- CSU if applicable

- Swab from open skin / wound / ulcer

- Sputum if applicable

- Where the patient has previously been infected with MRSA, for example in a urine specimen, this should also be included.

3.2 Medical Wire sterile wooden shafted cotton swab (code MW 104) should be used for taking specimens. The cotton swab should be moistened with sterile saline.

4. Media and supplies

4.1 All specimens will be individually inoculated directly onto Oxoid's Brilliance MRSA Agar which uses a chromogen that produces a blue colour as a result of phosphatise activity. This enzyme is present in many staphylococci including *S. aureus*. To allow the medium to differentiate MRSA accurately, it contains a combination of antibacterial compounds to inhibit the growth of a wide variety of competitor organisms and meticillin sensitive *S. aureus* (MSSA).

4.2 All specimens from a single patient will then immediately be pulled and added to a single tube of Oxoid's selective manitol enrichment broth, incubated at 37°C for 18 – 24 hours and the broths then plated onto Oxoid's Brilliance agar. This is thought to increase the sensitivity of MRSA screening by 10 – 20% although, when dealing with multiple swabs, it is uncertain if it will yield significantly more MRSA positive patients. If an enrichment broth is found to be positive, the patient should be re-screened to assess the specific body sites that are MRSA positive by enriching the specimens in separate tubes of enrichment broth and then plating each broth onto the selective agar.

4.3 Each new batch of selective medium should be quality controlled by the laboratory before routine use and quality controlled on a daily basis using the following controls:

– MRSA strain ATCC 43300

– MSSA strain ATCC 25923

– *E. coli* ATCC 25922

4.4 Confirmation of suspect colonies should be carried out by coagulase test using the Prolex Staph Xtra Latex Kit (Pro-Lab Diagnostics product code PL.1080 / PL.1081).

5. MRSA screen

5.1 Each specimen should be inoculated directly onto an Oxoid Brilliance agar plate and incubated at 37°C for 18 – 24 hours according to local policies.

5.2. All specimens from a single patient should then be added to one bottle of Oxoid's selective manitol enrichment broth, incubated at 37°C for 18 – 24 hours and the broth then plated onto Oxoid Brilliance agar.

5.3. Presumptive MRSA colonies are blue on Oxoid Brilliance agar.

5.4. A coagulase test should be performed on suspect colonies. If the suspect colony is coagulase positive and from a new case, identification and susceptibility testing should be carried out. Coagulase positive colonies from an old case should be reported as MRSA without performing identification and susceptibility testing unless the patient fits the criteria as described below in Section 6 (i.e. is assumed a new case).

All coagulase positive colonies should be stored and sent to the ref lab, irrespective of the patient's prior MRSA status and confirmation test.

6. Confirmation: Identification and Sensitivity Testing of MRSA

Confirmatory tests should be carried out on MRSA screen positive bacterial isolates from a) patients not previously know to carry / be infected with MRSA and b) patients previously known to be MRSA positive but who have had either three negative screens or no MRSA isolated for over one year.

6.1 Identification of all MRSA screen positive isolates should be confirmed on the Vitek 2 system using the Gram Positive ID card.

6.2. Antimicrobial susceptibility testing should be carried out on the Vitek 2 system using the Staphylococcal card AST 578 (Ref: 22 219).

7. Special Studies MRSA isolates: Isolates to be saved locally and sent to SMRSARL

7.1 All MRSA isolates from all body sites and from all patients (regardless of whether or not that patient has ever been MRSA positive in the past) should be sent to the SMRSARL for further testing. A further clinical report should be issued when the strain is positive for the Pantene Valentine Leukocidin (PVL) producing gene or when certain antibiotics tested only at the reference lab are found to be resistant, e.g. mupiricin resistance (high level only).

7.2 All MRSA isolates from all body sites and from all patients (regardless of whether or not that patient has ever been MRSA positive in the past) should be stored locally at -20°C / -70°C in an appropriate cryogenic storage medium.

7.3 It is sufficient to store / send away a sweep from the primary plate if the isolate would not normally require ID confirmation and antibiotic susceptibility testing.

8. Nasal only (Pathfinder) MRSA isolates:

8.1 In addition to storing MRSA isolates from Special Studies full body screens, isolates from any nasal only screens (Pathfinder protocol) carried out in the Special Studies eligible hospital / wards should also be stored. All MRSA isolates grown from admission nasal screens from all patients (regardless of whether or not that patient has ever been MRSA positive in the past) should be stored locally at -20°C / -70°C in an appropriate cryogenic storage medium. These isolates should then be sent to SMRSARL when requested.

8.2 It is sufficient to store / send away a sweep from the primary plate if the isolate would not normally require ID confirmation and antibiotic susceptibility testing.

12. Genotyping

MRSA isolates will be genotyped by the ref lab (applying both PFGE and MLVA techniques).

When there are paired admission and discharge isolates from the same patient they will be compared by PFGE which is the most discriminatory of established MRSA typing methods. If both isolates have the same PFGE type and subtype and this is a common subtype then they will be compared by MLVA (multilocus VNTR analysis) which is more discriminatory.

10. Data confidentiality

All data will be held in line with HPS Confidentiality Guidelines and with the Data Protection Act 1998.

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10a. Abstract : [Maximum 200 words]

This study was designed to determine the likely true sensitivity of nasal swabbing and the effect on ascertainment of undetected cases by swabbing additional body sites. It also sought to develop and test a Clinical Risk Assessment (CRA) questionnaire which aimed to identify those most at risk of MRSA colonisation within a small subgroup of patient admissions, in order to greatly reduce the number of patients swabbed and to allow more efficient pre-emptive management of those at higher risk of colonisation. Universal nasal swabbing for MRSA was found to be less effective than previously thought in identifying patients with MRSA carriage, with only 66% of 'gold standard' diagnoses detected on chromogenic agar. The potential for the CRA questionnaire as a simple, economical and effective tool to identify most or all true carriers within a small patient subgroup has not been fully realised. However a three question simple CRA model reduced those to be swabbed and isolated/cohorted to a manageable 10% of admissions. The increased efficiency of identifying true carriers through swabbing two body sites in this group makes this option close in performance to universal nasal screening, but with considerably reduced resource implications.

Authorisation *(complete as applicable)*

Role	Name
Head of Division/ Delegated owner	Mary Morgan
Lead Consultant	Prof. Jacqui Reilly
Project/Programme Manager	Sally Stewart
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