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NHS Scotland MRSA Screening Pathfinder Programme

Update Report

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by Health Protection Scotland

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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

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Designed and typeset by:
Graphics Team, Health Protection Scotland

1 Executive summary

This report presents an update on longer term monitoring of the implementation of universal Meticillin resistant *Staphylococcus aureus* (MRSA) screening in the NHSScotland Pathfinder Health boards, economics, and summary results of the two special studies within the Pathfinder programme [1;2]. This has been produced as a supplement to the MRSA Screening Pathfinder project report (Dec 2009) [3-6].

The debate about universal versus targeted MRSA screening continues and much of the literature published this year reinforces the findings of the Pathfinder programme. Editorials and some professional bodies are calling for decision making in the context of other emerging Antimicrobial Resistance (AMR) of concern, and investment in infection prevention and control interventions in the context of reducing HAI overall. Using public health principles for screening to support decision making in the context of overall healthcare expenditure therefore remains important.

Results from the Pathfinder study showed that MRSA infection incidence was 7.5 per 1,000 patient days over the year but, as with colonisation rates, significantly reduced within the year across the pathfinder boards. MRSA bacteraemia was already reducing in NHSScotland prior to the implementation of the pathfinder study, but there were early indications of a temporal association between the initiation of the universal screening and a decline in MRSA infections, as defined by the number of first clinical isolates from hospital based laboratory confirmed cases during the study. The reduction reached statistical significance within the combined pathfinder board data, although of course this does not necessarily prove that the screening caused the reduction. However, the decreasing trend persisted during the period after the introduction of the screening. Furthermore, the patients had similar baseline characteristics during the time of the study and the decreasing trend was not seen in the comparator control acute hospitals within the pathfinder NHS boards. No statistically significant change in meticillin sensitive *Staphylococcus aureus* (MSSA) occurred in any of the pathfinder boards. This is consistent with other smaller studies published to date, but required monitoring longer term.

Longer term monitoring in the six months since the Pathfinder report, indicated that nasal colonisation prevalence continued to reduce over the period of the special studies to 2%. This reduction in colonisation prevalence is a similar picture to the one which was projected within the model in the final report, although the effect has been earlier than projected by the model. There was a greater reduction in MRSA infection (measured by first new clinical MRSA isolates) after the implementation of universal screening in pathfinder hospitals, compared to hospitals that did not implement screening. Whilst within the time series analysis this did not reach statistical significance, this was important clinically as there were fewer infections overall.

A significant reduction in the total proportion of all *S. aureus* infections that were MRSA was shown within Pathfinder hospitals. This reduction reached statistical significance within all pathfinder hospitals, due to limitations of the study design it was not possible to attribute cause and effect. However, the decreasing trend persisted during the period after the introduction of the screening. Furthermore, the patients had similar baseline characteristics during the time of the study and the decreasing trend was not seen in the comparator control acute hospitals within the pathfinder NHS boards, although the sample size was smaller in the comparator boards. To further strengthen the association, no statistically significant reduction in meticillin sensitive *Staphylococcus aureus* (MSSA) occurred in any of the pathfinder boards, although the trend in each pathfinder board appeared different.

The results of the longer term monitoring are in line with the early indications of a possible temporal association between screening and reducing MRSA infection presented in the Pathfinder Report (2009) [5]. However, additional analyses of first new clinical isolates of MRSA in NHS Lothian (a non Pathfinder board) over the same period indicated a reducing trend without the implementation of universal screening. Whilst the rate of reduction in Pathfinders was greater post intervention the difference between NHS Lothian and the pathfinder boards did not reach statistical significance. There are a range of factors which may confound these findings, inclusive of the targeted MRSA screening activity already in place in NHS Lothian, and the evidence from the pathfinder boards about their inability to apply the interventions associated with screening in the time frame required to reduce risk of infection. The pathfinder study indicated that this was restricted by time to availability of result and short lengths of stay. These data must therefore be interpreted with caution, however it is not possible to conclude that the reduction seen in the pathfinder boards is attributable to the intervention of universal MRSA screening, nor is it possible on the balance of all the evidence to rule out an impact of the universal screening.

Identification of increased numbers of patients with MRSA inevitably leads to increased use of antibiotics to treat MRSA. It was considered important to monitor the possible emergence of resistance to these antibiotics particularly mupirocin. Extended monitoring of mupirocin resistance indicated no evidence of a significant difference in MRSA mupirocin resistance between Pathfinder and non Pathfinder health boards in the year of the study or in the year since the Pathfinder project. Whilst levels of resistance levels remain low at present, longer term monitoring is required, inclusive of organisms other than MRSA.

Universal nasal screening was recently estimated to cost around £8 million per year by SGHD [7], the cost per Quality Adjusted Life Year (QALY) was therefore estimated to be £15,325. Based on either National Institute for Health and Clinical Excellence (NICE) or Scottish Medicines Consortium (SMC) thresholds the universal MRSA screening programme appears to be acceptable in terms of QALYs. However a reduction in MRSA infection has been observed in most health boards over the period of the pathfinder programme and therefore the reduction in QALYs lost should be interpreted with due caution.

There were two special studies carried out to answer key questions on screening strategies within the pathfinder programme. The results from one of these studies indicated that universal nasal swabbing for MRSA appeared less effective than previously thought in identifying patients with MRSA carriage, with only 66% of 'gold standard' cases detected.

The studies also highlighted the potential for the Clinical Risk Assessment (CRA) questionnaire as a simple, economical and effective tool to identify true MRSA carriers within a small patient subgroup. An initial model was developed and tested, this was a weighted scoring system for 11 variables within four key questions and, whilst this had a reasonable sensitivity still required laboratory testing to be undertaken on 57% of admissions. However, there was the potential that a simple three question CRA was equivalent in terms of identifying true carriers, which would then proceed to swab screening and potential pre-emptive isolation or cohorting. This three question simple CRA model reduced those to be swabbed and isolated/cohorted to a more manageable 10% of all admissions including 68% of true positives; with 90% swabbing compliance and nasal and perineal swab positivity 50.4% of true positive gold standard. The increased efficiency of identifying true carriers through swabbing two body sites in this group made this option close to the other more complex CRA models performance, but with considerably reduced resource implications when compared to universal screening.

The discharge study indicated cross-transmission of MRSA occured in 1.3% of all patients admitted to the hospitals. An overall discharge prevalence of 2.9% of all patients discharged was observed. Of the patients who entered the hospital colonised with MRSA, just over half remained MRSA positive throughout their hospital stay. This finding reinforced the findings of the original Pathfinder study [5], which demonstrated that only a third of patients received both of the interventions associated with screening due to short length of stay and turn around time of the test results.

The discharge study did not indicate *net* acquisition at a population level: MRSA prevalence on discharge was not significantly higher than on admission. However on a patient level some patients acquired MRSA, some patients lost MRSA colonisation, and others remained MRSA colonised throughout hospital stay. Three risk factors for acquisition of MRSA were identified: age above 64 years, self-reported renal failure and self-reported presence of wounds or ulcers.

The special studies have provided evidence on the limitations of laboratory direct chromogenic agar screening, and on the use of clinical risk assessment in terms of value for money. As universal laboratory screening was the only strategy that has been fully tested in the real world, there was a requirement for reviewing the modelling work in order to undertake a 'like with like' comparison of the impact of the possible strategies which remained feasible options. These were reviewed not just in terms of value for money but also in terms of all aspects of the NHS Scotland Quality Strategy.

Three national screening strategy options remained on the table:

1. Universal screening
2. Clinical risk assessment of all admissions (using three questions and direct chromogenic agar nasal and perineal screening of all patients who answer yes to at least one question)
3. Clinical risk assessment (using three questions and direct chromogenic agar nasal and perineal screening all patients who answer yes to at least one question) and all those treated in specialties undertaking procedures which would have a high impact in quality of life and expected outcome.

More detailed examination of these options was required in order to make a decision regarding the best option in terms of cost of investment compared with effect on outcome. It was recognised that this should be based on the re-worked HTA model and the true cost effectiveness combined with the expected outcome and the results are presented in a subsequent report [8].

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5 Background

The Health Technology Assessment (HTA) report 'The clinical and cost effectiveness of screening for meticillin-resistant *Staphylococcus aureus* (MRSA)' was published in October 2007 [9]. This assessment examined alternative approaches to screening patients for MRSA on admission to acute hospitals. The clinical and cost effectiveness of screening different patient groups using three types of laboratory test and/or clinical risk assessment were compared. The results of systematic reviews of the literature, focus groups with staff and the public, a survey of hospital screening practices and an economic modelling were reported. The results of the economic model indicated that:

- Screening for MRSA colonisation in all patients admitted using a laboratory test is the most effective strategy in reducing prevalence and preventing infection
- Using chromogenic agar for direct culture of MRSA from clinical swabs is the most cost effective method of laboratory testing

The evidence and available data used in the HTA model was found to be of a sub optimal quality and not robust and consequently the strength of recommendations in the report were affected. There was therefore a need to examine and validate the assumptions in the model to test the robustness of the model in practice. The report recommended that a primary study be set up in acute inpatient care to assess outcome, i.e. whether screening all patients for MRSA was effective in preventing MRSA infection, as predicted by the economic model. This would involve an outcome evaluation study and in order to be robust will require at least one year of data collection.

A Pathfinder Project was established in NHSScotland to test the proposed model and test the assumptions and predictions of the NHS QIS HTA model and to examine the feasibility and implications for health boards of the proposals. A report on the findings of the Pathfinder project was delivered to the Scottish Government Health Directorate on the 31 December 2009. Within this report there was a recommendation for longer term monitoring of outcome and an identified need for further research, to inform any national policy decision. The SGHD funded the longer term monitoring and further research work, and this report presents the findings.

6 Vision

The vision of the MRSA screening programme in NHSScotland is to make changes to hospital MRSA screening practices which enable healthcare workers to identify and reduce MRSA colonisation in in-patients in acute care to a minimal level; whereupon, the risk of MRSA infection to hospital in-patients is low enough to prevent healthcare associated MRSA infection in the in-patient population; thereby reducing the negative impact on patients and any additional burden on healthcare resources.

7 Introduction

This report details the longer term monitoring within the Pathfinder project hospitals, and intelligence gathered from international literature on MRSA screening since the MRSA screening Pathfinder project report was submitted to Scottish Government Health Directorate (SGHD) in December 2009. This report also aims to summarise the findings of two research studies: the first examining optimal screening in terms of body sites and clinical risk assessment, and a second on cross transmission of MRSA during hospital stay. This report also examines the health economics of MRSA screening with a view to recommending future national MRSA Screening policy and practice in acute care in Scotland.

7.1 Literature published since final report

The role of MRSA screening in reducing HAI continues to be debated in the international literature. European and world leading organisations continue to focus on the public health threat of MRSA. The European Centre for Disease Control (ECDC) have acknowledged the bacterial challenge from organisms, such as MRSA, and called for action to narrow the gap between multidrug-resistant bacteria in the European Union (EU) inclusive of the development of new antibacterial agents [10].

The latest European data on MRSA [11] indicate that it remains a public health threat and many countries have high endemic proportions. The UK remains a country with high endemic proportions, although the proportion has been reducing over the last three years. In Scotland, data reported from the mandatory surveillance system [12] indicate that MRSA accounts for 24% of all *S. aureus* bacteraemias. The reducing proportions of selected organisms at country levels have resulted in some professional authorities to call for future efforts to focus on generic infection control interventions, which are not organism specific.

Despite this call there is a continued focus in the published literature on organism specific interventions. At the time of writing, 110 papers have been published on MRSA screening in 2010 so far. The main areas of focus are:

- Organisational issues and quality impact on patient (e.g. Isolation)
- Decolonisation (e.g. Success, drug resistance, body sites etc)
- Types of screening (Universal, targeted, search and destroy)
- Economic issues

Each of these will be addressed in turn.

7.2 Organisational issues and quality impact on patient (e.g. Tests used and facilities).

7.2.1 Tests

Since the production of the Pathfinder report ten months previously, there have been no new significant diagnostic technologies introduced. The mainstay of diagnosis remains the use of chromogenic agar and Polymerase Chain Reaction (PCR) [13]. The relative advantage of each method is inexpensive cost and speed respectively. Where PCR has been considered as a universal screening method, although providing a fast analytical result, the long pre-analytical phase and the high cost has precluded its adoption [14]. Although PCR has been indicated in some studies as useful in targeted screening in high risk groups.

The use of PCR based tests on previously known MRSA positive patients at readmission [14] was found to result in fewer unnecessary isolation days in a study in acute care, although the cost effectiveness of this approach is yet to be addressed.

7.2.2 Isolation facilities

Gilligan et al [15] assessed median waiting times in Ireland from emergency admission wards to the hospital based on MRSA risk, and identified that being identified as previously MRSA positive resulted in delays to admission and therein treatment. They called for national and local policies to balance the welfare of patients in the emergency ward, with the need to comply with best practice when there are inadequate isolation facilities within an institution.

Testing of portable isolation systems on general wards [16], as an approach to addressing the lack of isolation facilities in the NHS estate, has recently indicated poor efficiency in reducing risk of MRSA transmission and is the subject of a clinical trial (Trial Identifier: ISRCTN02681602).

The psychological effects of isolation on patients with MRSA have been identified as an unintended negative consequence in previous literature. A recent study has identified that the quality of care, as perceived by the patients, was not negatively affected (74%). Short term isolation had no impact on Quality of Life (QoL) (anxiety/ depression) and patients perceived the intervention positively [17]. However the latest systematic review of the literature [18] indicates that, across the majority of studies published, isolation negatively impacts on several aspects of care including: wellbeing, satisfaction and safety.

7.3 Decolonisation as an intervention to reduce risk of MRSA infection

The latest systematic review of decolonisation (suppression of colonisation) has indicated that short term (4-7 days) topical nasal application of mupirocin is the most effective treatment for suppressing MRSA (success probability of 90% after one week). It is also proposed as safe and associated with a 1% risk of acquiring a drug resistant strain during treatment [19]. Studies published since this review, have indicated additional evidence on long term clearance, speciality specific and anatomical issues with respect to decolonisation. Although the long term clearance of MRSA carriage for most patients (post one year) has not been indicated [20].

The majority of studies published have been prospective cohort studies which are limited in design with respect to assessing effectiveness of interventions, and as a result report a variety of rates of success, nonetheless have indicated effectiveness rates as high as 81% in those receiving it. Of interest is the decolonisation failure noted, when colonisation is present in the throat and wounds, prior to commencement of the intervention [21]. Broek-Smits et al [22] note in some early histological work that presence of MRSA in hair follicles in the nares may present problems with relapse after decolonisation and this warrants further investigation if decolonisation strategies are to be optimised.

Continuing success of the decolonisation intervention in reducing infection in surgical specialties is noted. A statistically significant reduction in the rate of Surgical Site Infections (SSI) has been noted in universal surgical MRSA screening programmes using mupirocin as an intervention (3.4% (mupirocin) compared with 7.7% (placebo) (p=0.005)) [23].

Mupirocin resistance remains an issue of concern with respect to mass usage of an antimicrobial associated with MRSA screening interventions. Caffrey et al [24] have recently identified, in a case control study, a strong association between previous mupirocin exposure and subsequent mupirocin resistance in MRSA. Mupirocin susceptibility monitoring is therefore critical for national screening programmes.

7.4 Types of screening

The debate between universal and targeted screening continues in the literature.

7.4.1 Universal

Universal MRSA screening studies have been published this year with similar findings to the Pathfinder project in Scotland (i.e. association with reduced colonisation and infection during the period of the study are noted) [25-27].

7.4.2 Targeted

Specialty specific screening continues to be proposed in the literature. These studies usually focus on surgical and intensive care specialties. Study design, which is usually retrospective interrupted time series, continues to be a challenge in assessing the evidence from these studies [28].

Obstetrics (which were excluded in the HTA model) have been identified as a specialty for potential inclusion in universal screening programmes, although the authors note there is a need for more multi-centre studies [29].

Targeted 'at risk' MRSA screening based on clinical risk assessment, and other infection control interventions in France have been associated with a sustained country wide reduction in MRSA [30]. This has been further supported by a review of ten European countries practice with respect to reducing MRSA demonstrated vigorous management of MRSA in Intensive Care Units (ICUs) and surgical specialties were associated with a reduction in the prevalence of MRSA [31].

Community associated, hospital presenting MRSA is beginning to emerge as an issue in the literature. Countries with low endemic hospital associated MRSA are beginning to see community associated MRSA present in the hospital. Their existing search and destroy policies appear not to be effective, as the risk factors for colonisation are changing with the changing nature of acquisition [32]. Denmark, a country with historic low endemic proportions of MRSA, have reported on the aftermath of a MRSA ST22 hospital outbreak [33]. As a result of their follow up and analysis of risks, their search and destroy policy has been amended to include decolonisation of household members and the environment, to reduce long term carriage.

In the Netherlands, another country with low prevalence of carriage (0.94 per 1,000 inpatients), a clinical risk assessment tool has been developed based on two risk factors: professional contact with livestock, and stay in a foreign hospital [34].

7.4.3 MSSA screening

An interesting recent development is the role of screening for MSSA. A retrospective quasi experimental study in medical intensive care [35] indicated a reduction in incidence in *S. aureus* infection from 3.52 to 1.29 cases per 1,000 patient days when both MRSA and MSSA were screened for. Kim et al [36] had a similar finding in elective orthopaedic surgery (0.19% versus 0.455, p=0.0093). However these studies provide therapeutic level 3 evidence of benefit in selected settings only. A larger study in ICU [37] found that when other factors were accounted for, patients colonised with MRSA were more likely to develop infections than those with MSSA. Thus the evidence base for screening for MSSA is not as strong as that for MRSA [38].

7.4.4 Screening sites

Which sites to swab and how often to screen continues to have equivocal evidence. Papers continue to acknowledge the importance of getting the balance right between uptake and identification of colonisation. A recent USA study [39] examined the value (clinically and economically) of multiple surveillance cultures for MRSA in a low prevalence setting and concluded the sensitivity of admission swabs (groin and nasal) was 74.3%. Subsequent swabs taken within three days of hospital stay identified a further 49 colonised patients and the costs associated with taking multiple samples from all patients were $2,088 per additional patient identified.

Scheleyer et al [40] found a specificity and Positive Predictive Value (PPV) of 100% in nasal swabs in identifying skin and soft tissue infections where wounds could not be swabbed. However a comprehensive study by Lauderdale et al [41] has indicated that swabbing sites other than nares detected 18% more cases of colonisation than nares alone. Molecular typing indicated that multisite isolates were largely indistinguishable within each patient, although a few patients did have multiple subtypes and different clonotypes. This study also identified that the true positive colonisation prevalence can be enhanced by around 10% through the use of enrichment broth, in addition to direct plating. The authors have called for more epidemiology on the likelihood of subsequent HAI among colonised patients detected via nasal versus broth from multiple sites.

7.5 Economic issues

The burden of MRSA infection on healthcare services is significant, in particular because MRSA has not replaced susceptible Staphylococcal infection but is an additional problem. Treatment strategies for MRSA are suboptimal and compromise the care of patients. MRSA is associated with serious morbidity and mortality both within and outwith hospitals [42]. A recent review of the literature on costs of MRSA identified 32 papers [42]. Twenty-two studies could be classed as either a costing study, to establish the excess cost of MRSA infection or an estimate of the national burden (n=7), or an economic evaluation comparing the costs and benefits of an intervention with the pre-existing service (n=15). In this latter category all but one study evaluated screening in hospital, the exception being an evaluation of screening.

This review identified marked variation in estimates of costs attributable to MRSA and the interventions associated with these and identified that many of the studies published in the last 10 years in infection control have acknowledged the importance of costs, yet failed to address them within the context of their study. It also found that others have based infection prevention and control intervention recommendations on partial economic analysis, examining the gross cost of HAI, and not addressing cost effectiveness.

Modelling work has been published since this review was completed. Stochastic computer simulation of universal admission screening in adults was found to be cost effective at a wide range of prevalence (>1%) and transmission rate values (>0.25) [43]. However, stochastic

computer simulation of PCR compared with Clinical Risk Assessment (CRA) in surgical patients only indicated that PCR was not cost effective in low MRSA prevalence (<1%) settings [44].

While the literature on the costs of MRSA and its control is sub-optimal, it is clear the control of MRSA is highly desirable and likely to be cost effective. The literature suggests that decision making on the approach to screening and subsequent cost effectiveness should be guided by the prevalence of colonisation with in the country, i.e. the cost per positive case identified by screening will increase as colonisation prevalence decreases.

7.5.1 Summary of literature

The debate about strategies for MRSA screening continues and much of the literature published this year reinforces the findings of the Pathfinder programme. Editorials and some professional bodies are calling for decision making in the context of other emerging Antimicrobial Resistance (AMR) of concern, best 'bang for buck' in the context of reducing HAI overall, and prevalence of an organism within a country. Using public health principles for screening to support decision making, in the context of overall healthcare expenditure, therefore remains important [5].

8 Update on Pathfinder – longer term follow up

Within the final report of the Pathfinder study [5], clinical isolates were analysed in order to evaluate the impact on MRSA infection outcome. A full description of the Pathfinder study is described in the Final Report Volume 1 [5].Results from the Pathfinder study showed that MRSA infection incidence was 7.5 per 1,000 patient days over the year but, as with colonisation rates, significantly reduced within the year across the Pathfinder boards. MRSA bacteraemia was already reducing in NHSScotland prior to the implementation of the Pathfinder study, but there were early indications of a temporal association between the initiation of the universal screening and a decline in MRSA infections, as defined by the number of first new clinical isolates from hospital based laboratory confirmed isolates during the rolling year. This decreasing trend persisted during the 12 month period after the introduction of the screening in the Pathfinder hospitals. During the Pathfinder Study no statistically significant change in meticillin sensitive *Staphylococcus aureus* (MSSA) before and after implementation of MRSA screening occurred in any of the Pathfinder boards. This was consistent with other smaller studies published to date, but these findings required monitoring longer term. Laboratory data where examined for a further six months post completion of the Pathfinder study resulting in a time series of 18 months pre and post intervention.

8.1 Follow up time series analyses

The full data set was analysed from January 2006. Only first new clinical isolates were analysed and screening isolates were excluded from the data set. De-duplication was carried out on the full data set in the following order, separately for MSSA and for MRSA

1. De-duplicate entire data-set based on CHI number then date of birth
2. Allocate each remaining record to an acute Pathfinder, acute non Pathfinder, community or GP.
3. GP and community sourced first new clinical isolates were excluded
4. The acute Pathfinder and acute non Pathfinder were then compared
5. Data from January 2006 to January 2007 were then excluded as this ensured that the first months of the time series used the same exclusions as the final months. This minimised any potential bias resulting from an artificially high starting point pre the intervention

First new MRSA clinical isolates within a single year (in non-screening isolates) were used for time series analysis. If a patient had many samples taken and a number of those samples showed MRSA to be isolated, either within a single, or multiple admissions, only the first incidence of a new MRSA isolate was included within the analyses within a single year. This first new clinical isolate within a rolling year was used as a proxy count of MRSA infection [26].

Following the above noted analysis, a comparison of first new clinical isolates of MRSA within a year in Pathfinder hospitals for the eighteen months before and the eighteen months after was carried out to determine if there was a difference before and after universal screening was introduced.

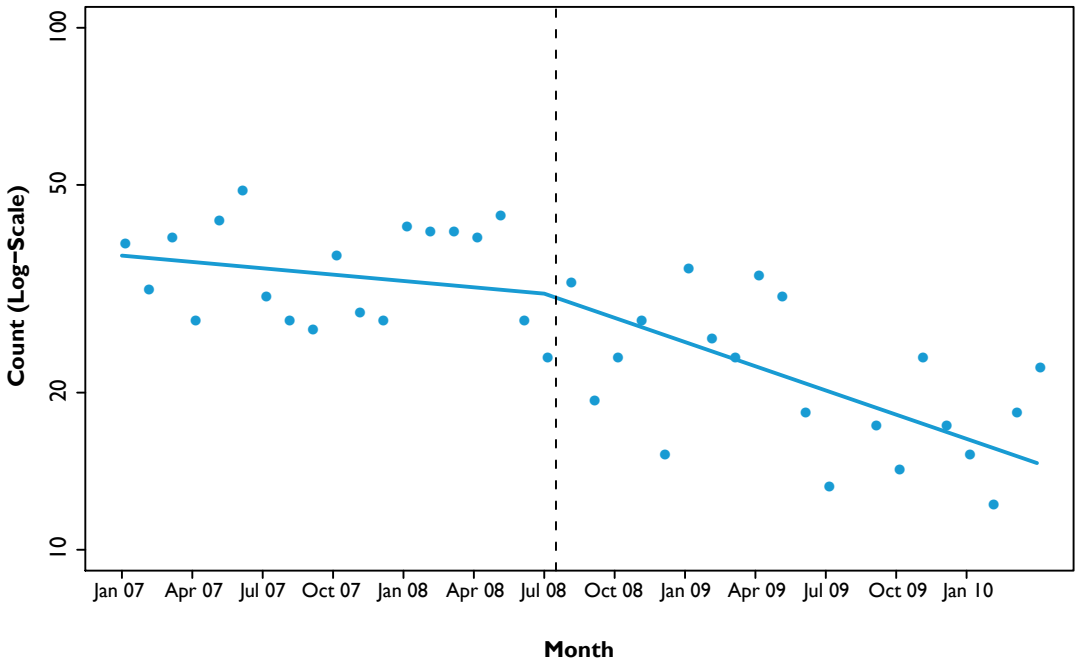
8.1.1 Historical Comparator

In Pathfinder hospitals a reduction in first new clinical isolates of MRSA was seen from the eighteen months prior to the introduction of universal screening compared to the eighteen months after. The magnitude of this reduction was 11.7% (95% CI 1.2%, 21.1%) (651 before to 575 after in Grampian, p=0.03), and 37.1% (95% CI 28.6%, 44.7%) (614 before to 386 after in Ayrshire and Arran, p<0.0001) (See Figure 8-4 for more information). In both NHS boards there was a significant reduction in first new MRSA clinical isolates after the introduction of screening and whilst this demonstrates a temporal association between the introduction of screening and the reduction in numbers of first new MRSA clinical isolates, this reduction cannot be fully attributed to the impact of universal screening, as the numbers may have been reducing without the introduction of intervention.

In order to investigate this reduction in MRSA further, a piecewise linear model was used to examine the trends in the numbers of first new MRSA clinical isolates month by month before and after screening was implemented from August 2008. The intervention point was therefore the end of July 2008. It should be noted that these time series have low power and thus a difference would need to be very big to be statistically significant.

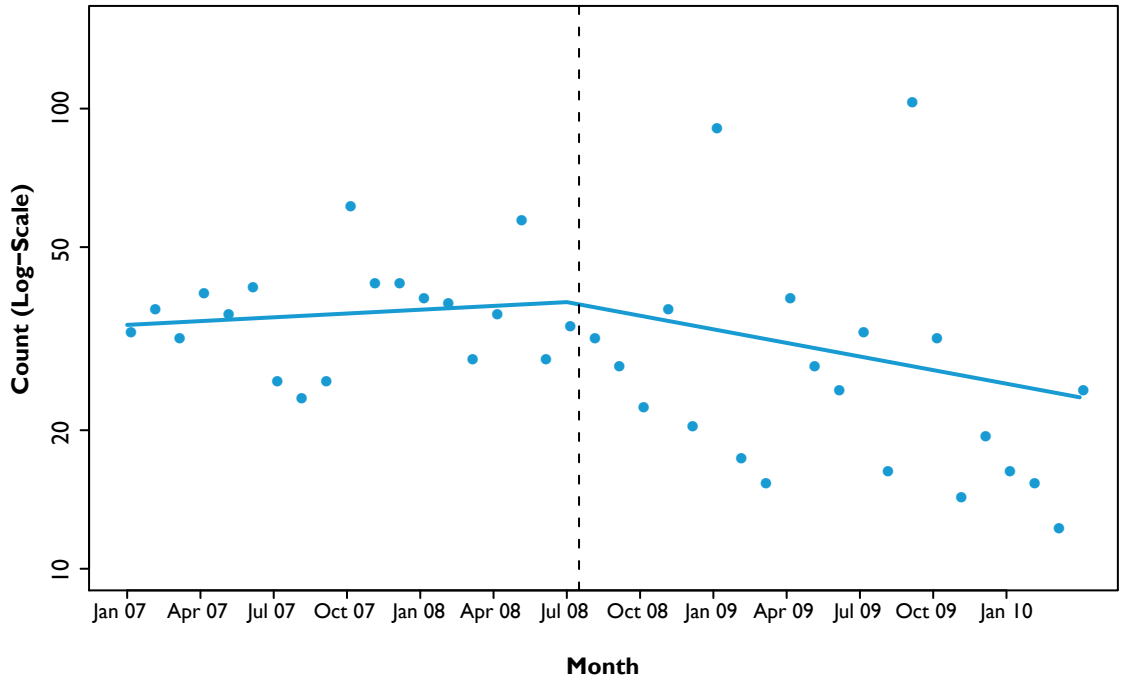
For Ayrshire and Arran using the piecewise linear model the decrease in rates of first new clinical isolates of MRSA was greater post the intervention of universal screening, however this reduction in rate was not statistically significant (p=0.077). In the Pathfinder hospitals there was a decrease of 0.009 per month before August 2008. From August 2008 onwards the log MRSA first new clinical isolates have decreased at a rate of 0.035. This demonstrates continued reduction since the final report and at a similar rate (0.041 within the Pathfinder final report) [5] (See Figure 8-1).

Figure 8-1: Comparison of MRSA first new clinical isolates in Ayrshire and Arran Pathfinder hospitals from January 2007 to April 2010 the change point (or date that universal screening was implemented) was July 2008 (Presented on a logarithmic scale).



For Grampian using the piecewise linear model there was a decrease in rates of first new MRSA clinical isolates post the intervention of universal screening, this reduction was not statistically significant (p=0.362). In the Pathfinder hospitals there was an increase of 0.006 per month before August 2008. From August 2008 onwards the log MRSA first new clinical isolates decreased at a rate of 0.023 per month.

Figure 8-2: Comparison of MRSA first new clinical isolates in Grampian Pathfinder hospitals from January 2007 to April 2010 the change point (or date that universal screening was implemented) was end of July 2008 (Presented on a logarithmic scale).



There was no statistical evidence that any of the trends in the piecewise linear model varied between Grampian and Ayrshire and Arran and so it was reasonable to pool the data over the two boards to display the trends.

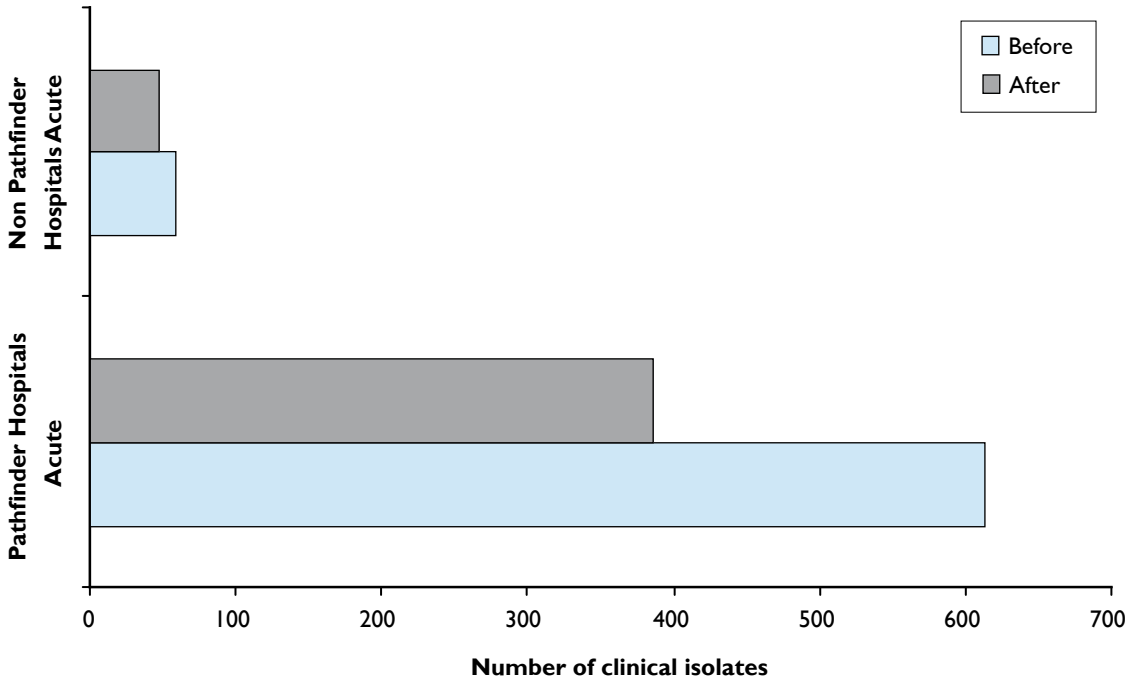
For the combined data using the piecewise linear model the decrease in rates of first new clinical isolates of MRSA was greater post the intervention of universal screening, however this reduction in rate was not statistically significant (p=0.147). There was a decrease of 0.001 per month before August 2008. From August 2008 onwards the log first new MRSA clinical isolates decreased at a rate of 0.028 per month. Whilst the magnitude of reduction was greater post the intervention of screening, and appeared to be greater than that reported in the final report (0.016), the change in rate reduction post the intervention did not reach statistical significance.

8.1.2 Non-pathfinder comparator

Within these analyses for the Pathfinder project, the best comparator hospitals were the small acute hospitals within the Pathfinder boards, but which were not part of the Pathfinder studies and therefore had not implemented universal screening. These were selected as it was considered likely that the patient population should have similar overall demographics, and the infection control policy would be the same in all sites. First new clinical isolate data which were used within these analyses were de duplicated using the protocol described in section 8.1. Poisson regression analyses were used to assess the relationship between the pre and post intervention period and the Pathfinder or non Pathfinder acute hospitals within each health board (see Figure 8-3 and Figure 8-4).

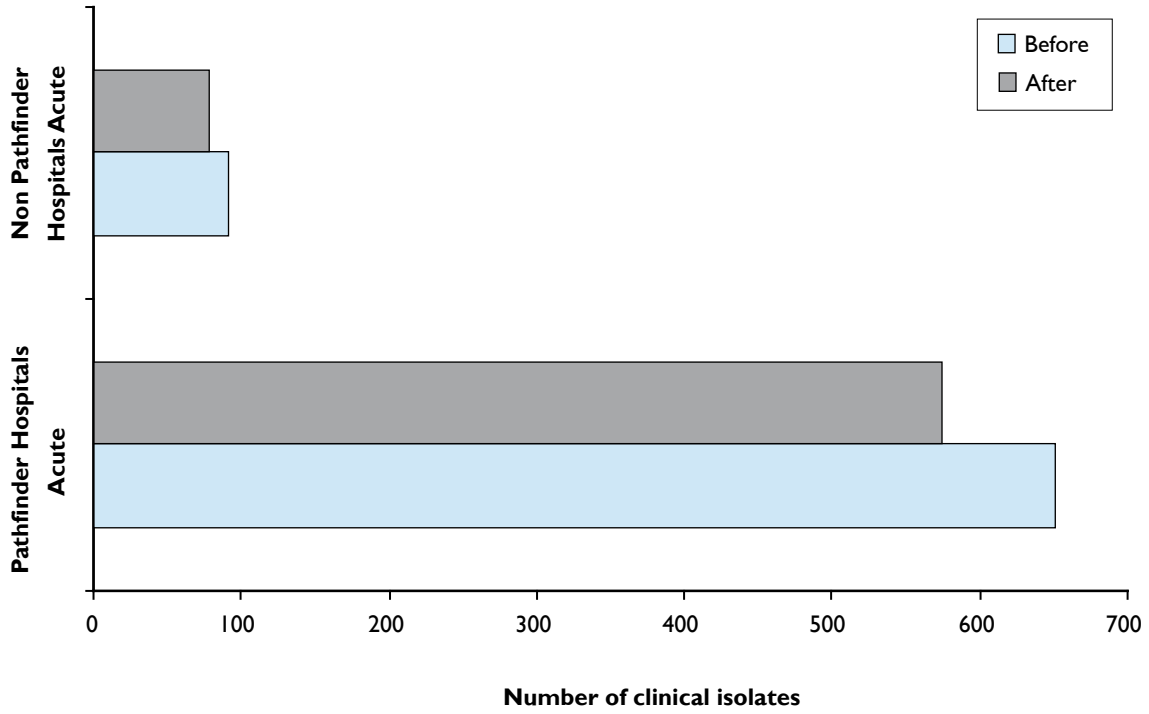
For Ayrshire and Arran, the reduction in number of first new clinical isolates was greater in Pathfinder hospitals, however there was no significant differences in the percentage change of MRSA first new clinical isolates, from before to after between the Pathfinder and non Pathfinder hospitals (p=0.250). The numbers were small in non Pathfinder hospitals therefore due caution must be taken when interpreting these data (see Figure 8-3).

Figure 8-3: Poisson regression of first new MRSA clinical isolates before and after implementation of Pathfinder project Ayrshire and Arran Pathfinder and non Pathfinder hospitals



For Grampian, the reduction in numbers of first new MRSA clinical isolates was greater in Pathfinder hospitals, however there was no significant differences in the percentage change of MRSA first new clinical isolates from before to after between the Pathfinder and non Pathfinder hospitals (p= 0.855). The numbers were small in non Pathfinder hospitals therefore due caution must be taken when interpreting these data. The probable confounder here is the movement of the patient population between the hospitals and therein the influence of MRSA burden in the Pathfinder Hospitals on the other hospitals [45].

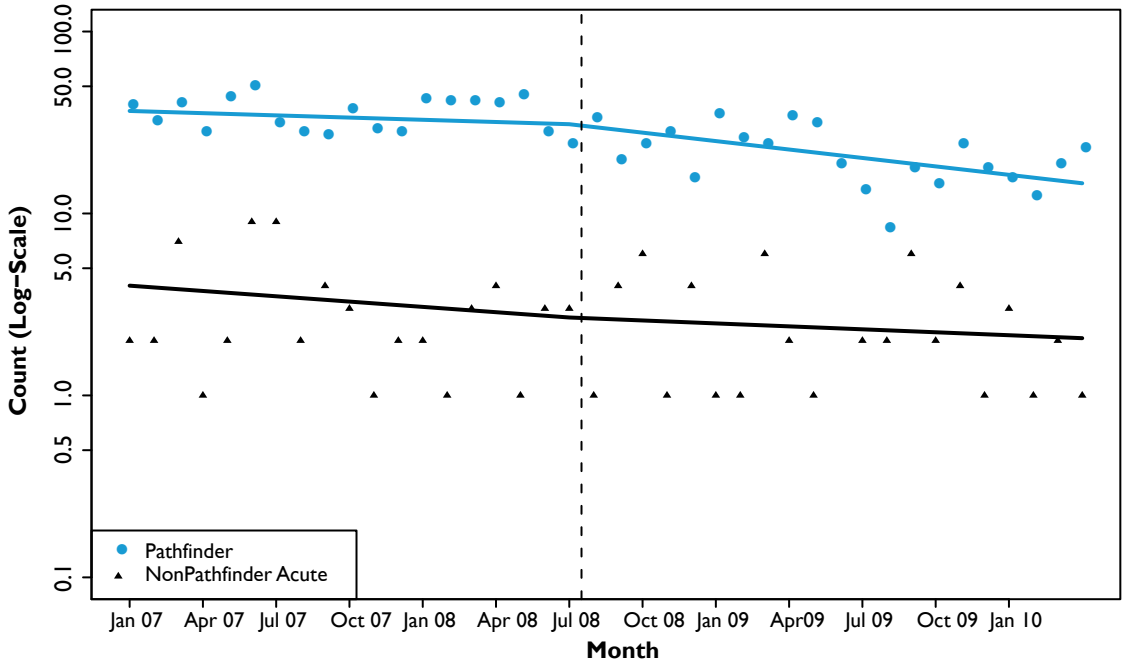
Figure 8-4: Poisson regression of first new MRSA clinical isolates before and after implementation of Pathfinder project Grampian Pathfinder and non Pathfinder hospitals



In addition to comparing the eighteen months before with the eighteen months after screening was implemented, these data were analysed using a piecewise linear model to examine trends in the numbers of first new MRSA clinical isolates month by month. These trends were examined before and after screening was implemented in August 2008, and between Pathfinder and non Pathfinder hospitals.

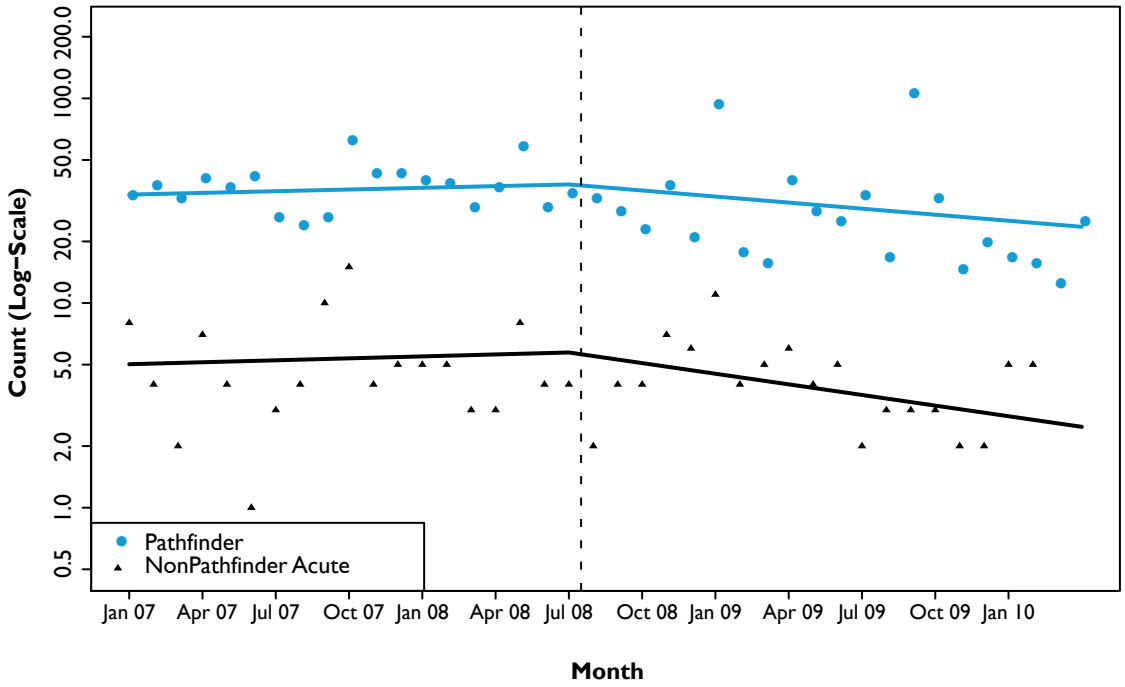
Before the intervention of universal screening in Pathfinder hospitals in Ayrshire and Arran, the non Pathfinder acute hospitals log MRSA first new clinical isolates decreased at a rate of 0.022 per month while in the Pathfinder hospitals there was a decrease of 0.009 per month. From August 2008 onwards the log MRSA first new clinical isolates decreased in non Pathfinder acute hospitals at a rate of 0.012 per year. In Pathfinder hospitals post implementation of universal MRSA screening from August 2008 there was a decrease in the log MRSA rates of 0.036 per month. A reduction was seen in the Pathfinder hospitals and not in non Pathfinder hospitals after the implementation of screening, and whilst the magnitude of reduction was greater in Pathfinder hospitals, the difference in rates was not statistically significant (p= 0.427) (Figure 8-5).

Figure 8-5: Comparison of MRSA first new clinical isolates in Ayrshire and Arran Pathfinder hospitals compared with Ayrshire and Arran non Pathfinder acute hospitals from January 2007 to April 2010 the change point (or date that universal screening was implemented) was end of July 2008 (Presented on a logarithmic scale).



Before the intervention of universal screening in Pathfinder hospitals in Grampian, the non Pathfinder acute hospitals log MRSA first new clinical isolates increased at a rate of 0.007 per month while in the Pathfinder hospitals there was an increase of 0.006 per month. From August 2008 onwards the log MRSA first new clinical isolates decreased in non Pathfinder acute hospitals at a rate of 0.040 per month. In Pathfinder hospitals post implementation of universal MRSA screening from August 2008 there was a decrease of 0.023 log MRSA rates per month. Whilst this longer term monitoring identified a reduction post intervention in Pathfinder hospitals there was no statistical evidence the trends from August 2008 onwards were different in Pathfinder and non Pathfinder hospitals (p= 0.793) (See Figure 8-6).

Figure 8-6: Comparison of MRSA first new clinical isolates in Grampian Pathfinder hospitals compared with Grampian non Pathfinder acute hospitals from January 2007 to April 2010 the change point (or date that universal screening was implemented) was end of July 2008 (Presented on a logarithmic scale).



8.1.3 Overall S. aureus comparator

In order to examine the impact of the intervention of MRSA screening on outcome, the reduction in first new MRSA clinical isolates as a proportion of all first new *S. aureus* first new clinical isolates was examined.

Pearson Chi-squared tests were conducted to test for association between the period pre and post implementation and the proportion of all first new isolates of *S. aureus* which was MRSA for the eighteen months before and eighteen months after August 2008. For both Pathfinder hospitals there was a statistically significant reduction in the proportion of all *S. aureus* first new clinical isolates which was MRSA. This indicates that the percentage change in the first new MRSA clinical isolates count from 18 months before to 18 months after was significantly different to the percentage change in the count of all first new *S. aureus* over the

same time period (p<0.0001 for Ayrshire and Arran and p=0.002 for Grampian respectively). The same analyses were undertaken for non Pathfinder hospitals and the results indicated no significant difference in the proportion of first new *S. aureus* clinical isolates which was MRSA in eighteen months before intervention compared to eighteen months after the intervention (p= 0.497) for Ayrshire and Arran and (p=0.216) for Grampian respectively.

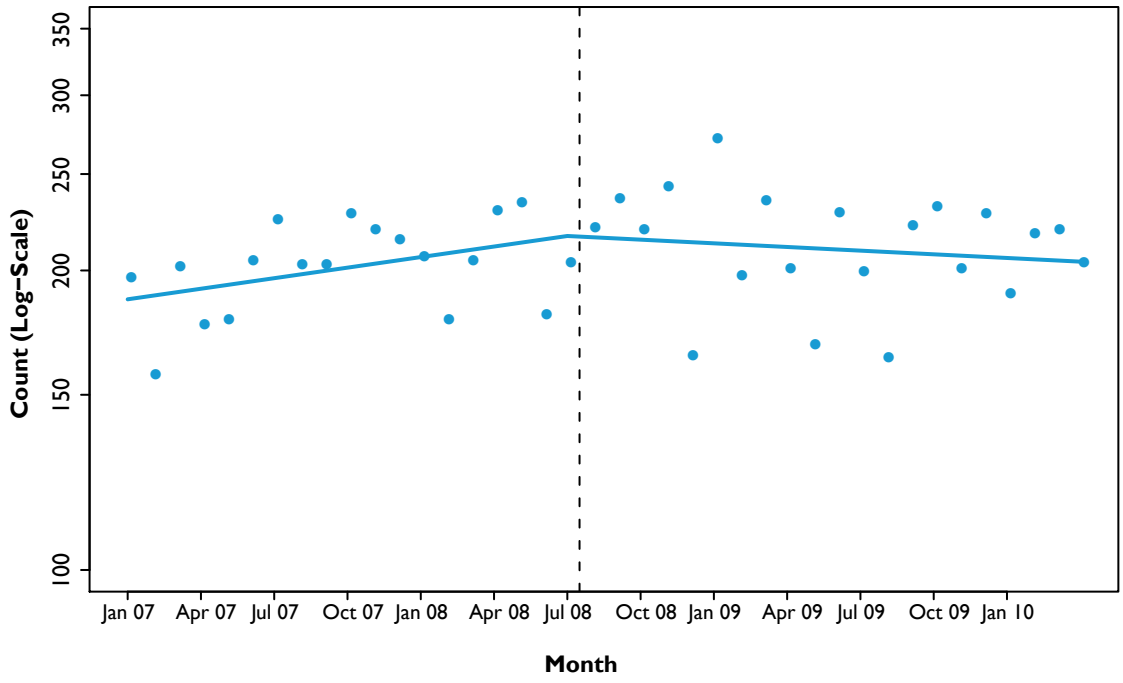
These results suggest a temporal association between the intervention of MRSA screening and reducing MRSA as a proportion of all first new *S. aureus* clinical isolates in the Pathfinder hospitals.

8.2 MSSA

8.2.1 Historical comparator

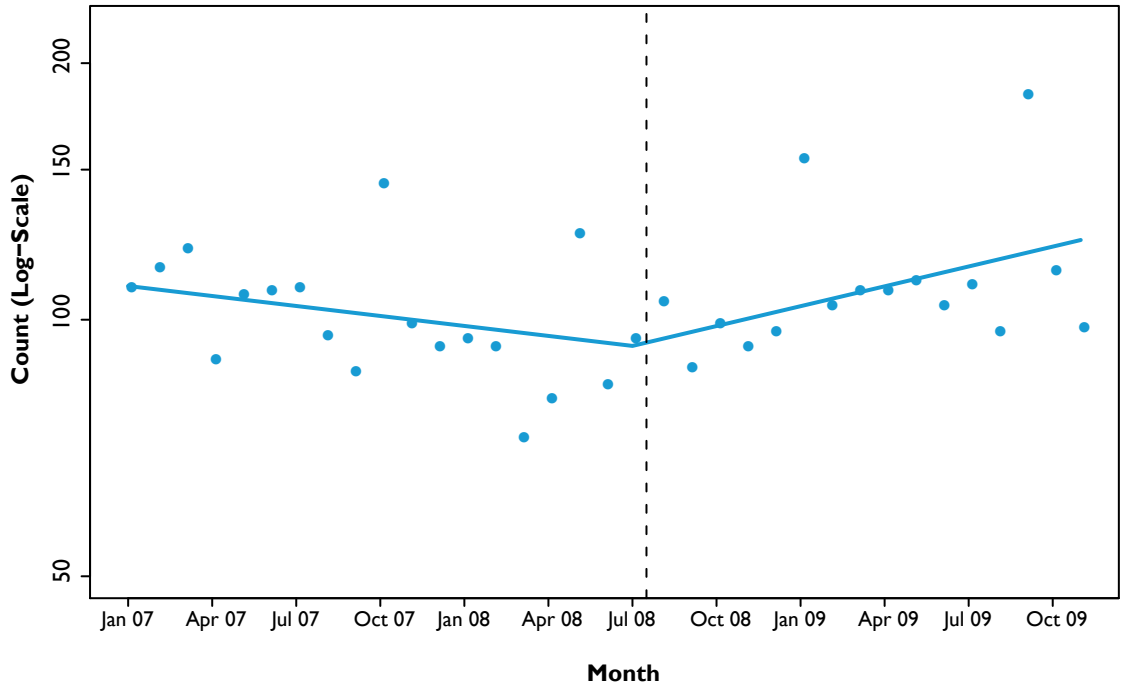
In Ayrshire and Arran there was an increase in first new MSSA clinical isolates of 0.008 per month before August 2008. From August 2008 onwards the log of first new MSSA clinical isolates decreased in Pathfinder hospitals at a rate of 0.004. Using the piecewise linear model there was no evidence that the trend in the rates in Pathfinder hospitals before and after August 2008 was significantly different (p=0.089).

Figure 8-7: Comparison of MSSA first new clinical isolates in Ayrshire and Arran Pathfinder hospitals from January 2007 to April 2010 the change point (or date that universal screening was implemented) was August 2008 (Presented on a logarithmic scale).



In Grampian in the Pathfinder hospitals there was a decrease in MSSA first new clinical isolates of 0.009 per month before August 2008. From August 2008 onwards the log first new MSSA clinical isolates increased in Pathfinder hospitals at a rate of 0.027 per month. Using the piecewise linear model there was evidence that the trend in the rates in Pathfinder hospitals before and after August 2008 was significantly different (p=0.040), although the trend did not appear to be the same as that in MRSA.

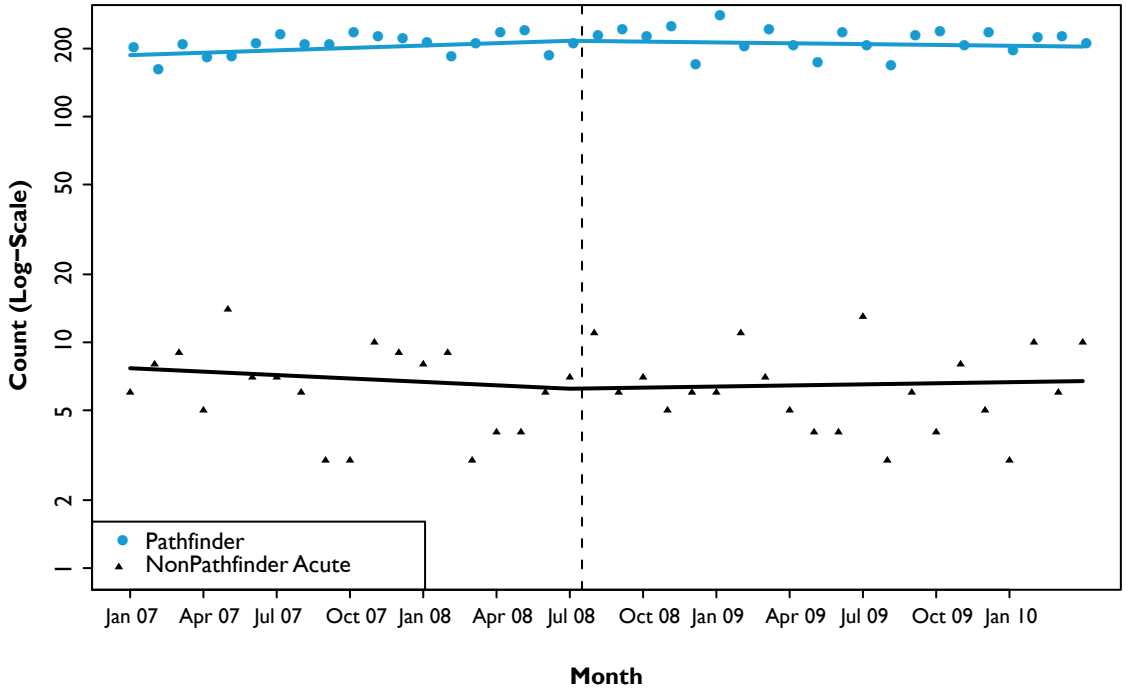
Figure 8-8 Comparison of MSSA first new clinical isolates in Grampian Pathfinder hospitals from January 2007 to April 2010 the change point (or date that universal screening was implemented) was July 2008 (Presented on a logarithmic scale).



8.2.2 Non-pathfinder comparator

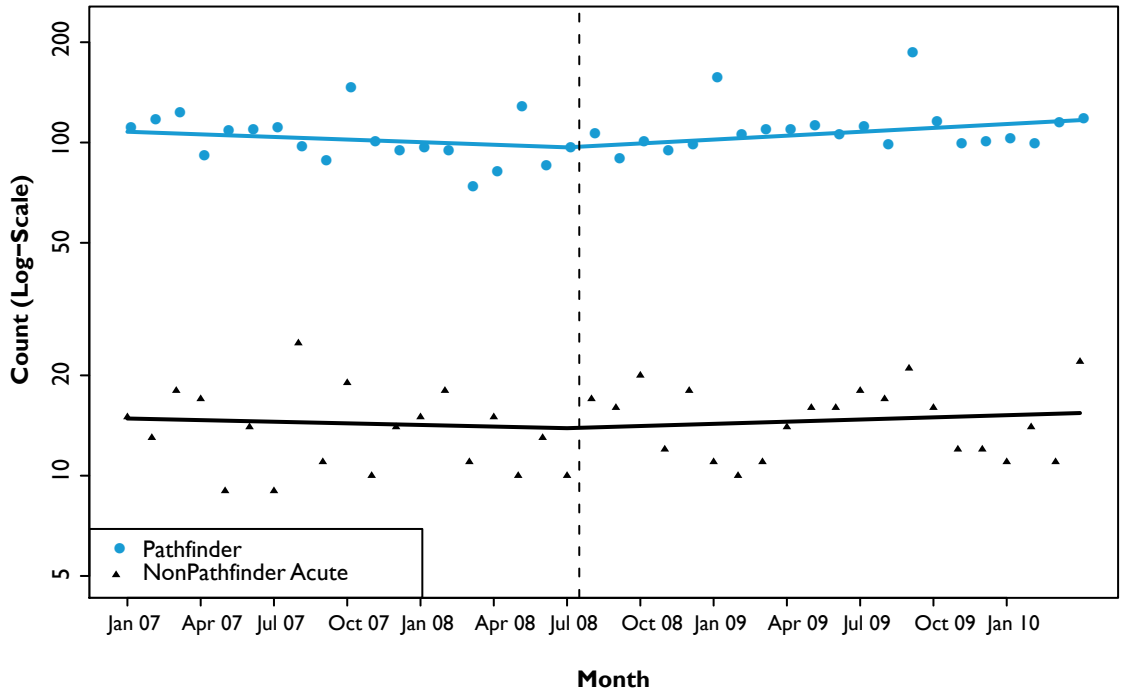
As indicated previously, for these analyses the non Pathfinder comparator hospitals were the small acute hospitals within the Pathfinder health board areas, but were not part of the Pathfinder studies, i.e. did not have universal MRSA screening implemented. In Ayrshire and Arran there was no significant difference in the trends in first new clinical isolate of MSSA before (p=0.277) or after August 2008 (p= 0.384) in Pathfinder and non Pathfinder hospitals.

Figure 8-9: Comparison of MSSA first new clinical isolates in Ayrshire and Arran Pathfinder hospitals compared with Ayrshire and Arran non Pathfinder acute hospitals from January 2007 to April 2010 the change point (or date that universal screening was implemented) was July 2008 (Presented on a logarithmic scale).



In Grampian there was no significant difference in the trends in first new clinical isolates of MSSA from before (p=0.875) or after August 2008 (p=0.792) in Pathfinder and non Pathfinder hospitals (Figure 8-10).

Figure 8-10: Comparison of MSSA first new clinical isolates in Grampian Pathfinder hospitals compared with Grampian non Pathfinder acute hospitals from January 2007 to April 2010 the change point (or date that universal screening was implemented) was July 2008 (Presented on a logarithmic scale).



Key summary point:

There was a significant reduction in MRSA infections (measured by first new clinical isolates) within the pathfinder hospitals, post the intervention of universal screening. There was also a greater reduction in MRSA infection (measured by first new clinical isolates) after the implementation of universal screening in Pathfinder hospitals, compared to hospitals that did not implement universal screening. Whilst within the time series analysis this did not reach statistical significance, this was important clinically as there were fewer infections overall.

A significant reduction in the total proportion of all *S. aureus* first new clinical isolates that were MRSA was shown within Pathfinder hospitals. This reduction reached statistical significance within all Pathfinder hospitals, although of course this does not necessarily prove that the screening caused the reduction. However, the decreasing trend persisted during the period after the introduction of the screening. Furthermore, the patients had similar baseline characteristics during the time of the study and the decreasing trend was not seen in the comparator control acute hospitals within the Pathfinder NHS boards, although the sample size was smaller in the comparator boards.

To further strengthen the association, no statistically significant reduction in MSSA occurred in any of the Pathfinder boards, although the trend in each Pathfinder board appeared different.

The results of the longer term monitoring are in line with the early indications of a possible temporal association between screening and reducing MRSA infection presented in the Pathfinder Report (2009) [5].

8.3 To compare with trends in clinical isolates from a non Pathfinder Board

8.3.1 Introduction

In order to further verify the findings from the pathfinder study, data were examined from a board which did not participate in the pathfinder study. Data for these analyses were kindly provided by NHS Lothian, directly from the Laboratory information system. De-duplication of the clinical isolates data was carried out following the same protocol used for the clinical isolates analysis described within the Final Pathfinder Report (see Section 8) [5] and used within the update on Pathfinder hospitals. It should also be noted that targeted MRSA screening was in place in NHS Lothian at the baseline. The volume of screening increased when the interim national policy was introduced (this was introduced in a phased plan and was fully implemented by January 2009), thus there is possible confounding effect. No board wide changes were made to MRSA management in August 2008 (this was the date that universal screening was implemented within the Pathfinder NHS Boards).

Initially the three Lothian acute hospitals were compared (Western General Hospital (WGH) in Edinburgh, Royal Infirmary Edinburgh (RIE), and St John's Hospital (SJH), Livingston. The Western General Hospital has far more patients that require complex and prolonged hands-on care. Royal Infirmary Edinburgh is a new acute hospital and is larger than the Western General Hospital and St John's Hospital. It has a large ITU and Medical and Surgical Wards.

8.3.2 Analyses

Statistical analysis was carried out using a Poisson regression model, the same as that for the Pathfinder boards and Final Pathfinder Report [5]. This model showed a change of trend within each hospital in Lothian in August 2008 though as stated above there was no alteration in MRSA management at this time and it is unlikely that this was due to the effect of screening for MRSA. The aim of this analysis was to examine if the trends, observed in the pathfinder hospitals, were also observed in NHS Lothian. If they were then this might indicate that there was a limited effect of universal screening. If the trends in NHS Lothian were different, and specifically if the rate of decrease in new MRSA clinical isolates post August 2008 was slower than in the pathfinder hospitals, then this might indicate an effect of screening. Of course this would be a temporal association and there may be other possible interpretations. The statistical modelling presented here used data from all three hospitals from August 2007 until July 2010.

8.3.3 Results

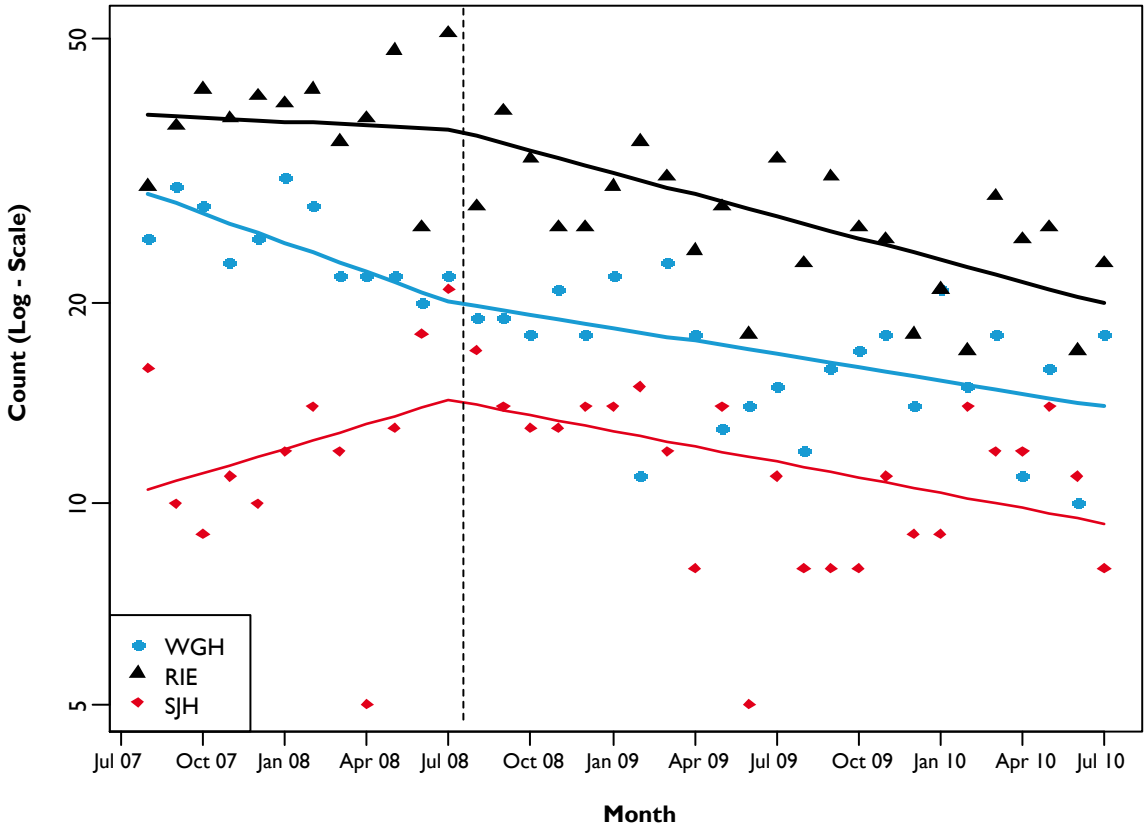
The numbers of new first clinical isolates of MRSA and MSSA per month were analysed separately for the three hospitals in Lothian. Finally the proportion of all *S. aureus* new first clinical isolates which was MRSA was investigated. These analyses were then compared to the findings from Pathfinder Hospitals during the same period.

8.3.4 Time Series Analyses. Historical comparator (Lothian)

MRSA

The numbers of new first clinical isolates of MRSA were reducing in both of the Edinburgh hospitals. The reduction was a steady, almost linear (0.0198), decline since the beginning of the data series Representing a decrease of 1.96% (95% CI 1.55%, 2.37%) per month. Furthermore there was no evidence of a significant change in rate of reduction at August 2008 (p= 0.59). In St Johns Hospital (Livingston) there was an increase in the number of new clinical isolates of MRSA before August 2008. The trends in Lothian hospitals new first MRSA clinical isolates were significantly different pre August 2008 among the three hospitals (p=0.009). This was due to the different pattern in St John's Hospital compared to the two Edinburgh hospitals (Figure 8-11). In St John's Hospital the decrease in MRSA isolates per month post August 2008 was 1.77% per month which is virtually identical to that in Western General Hospital and Royal Infirmary Edinburgh.

Figure 8-11: Piecewise linear Poisson Regression Model for first new MRSA clinical isolates counts in Lothian

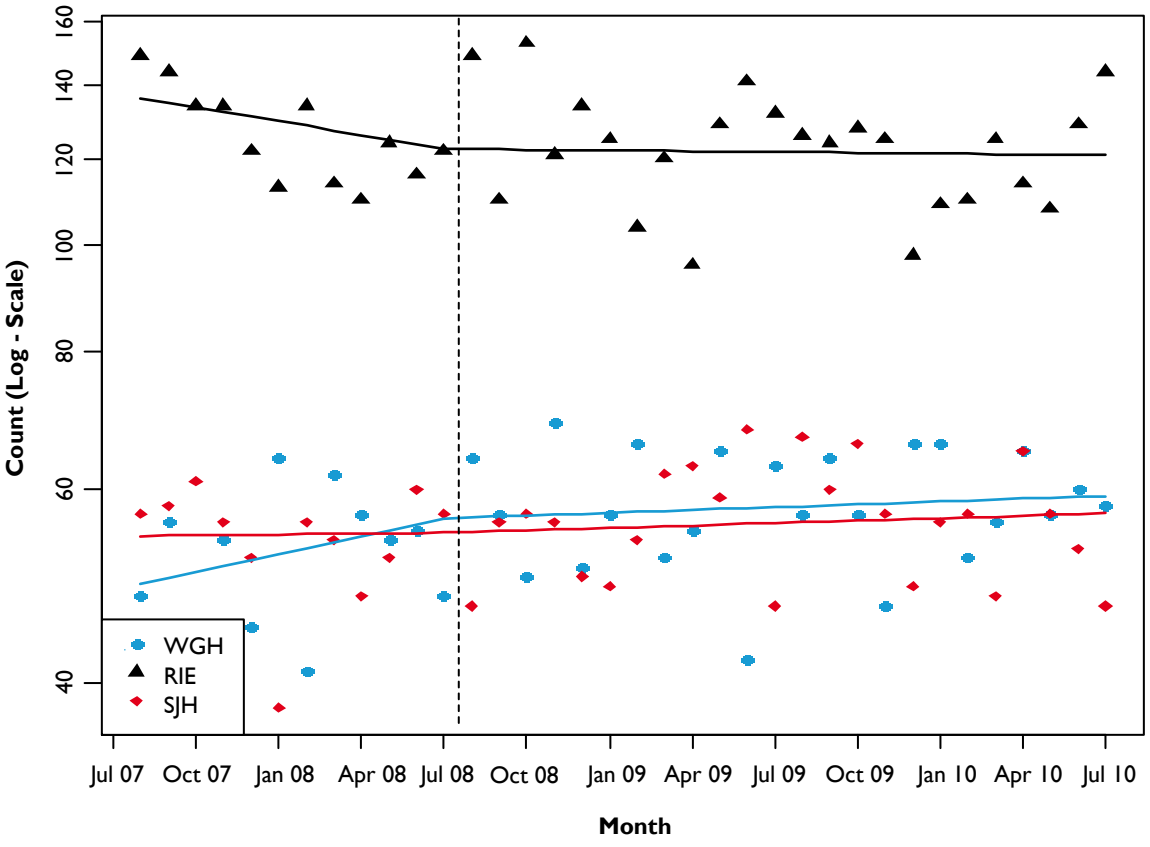


MSSA

There were differences between the hospitals with similar levels of new first clinical isolates for MSSA in the Western General Hospital as in St John's Hospital and both of these are at about one third the level of the Royal Infirmary Edinburgh. The discrepancy between the numbers of MSSA first new clinical isolates for St John's Hospital and Western General Hospital may potentially be explained in terms of patient mix, as Western General Hospital serves more patients that need complex and prolonged hands-on care and potentially display more of the risk factors associated with *S. aureus* infection.

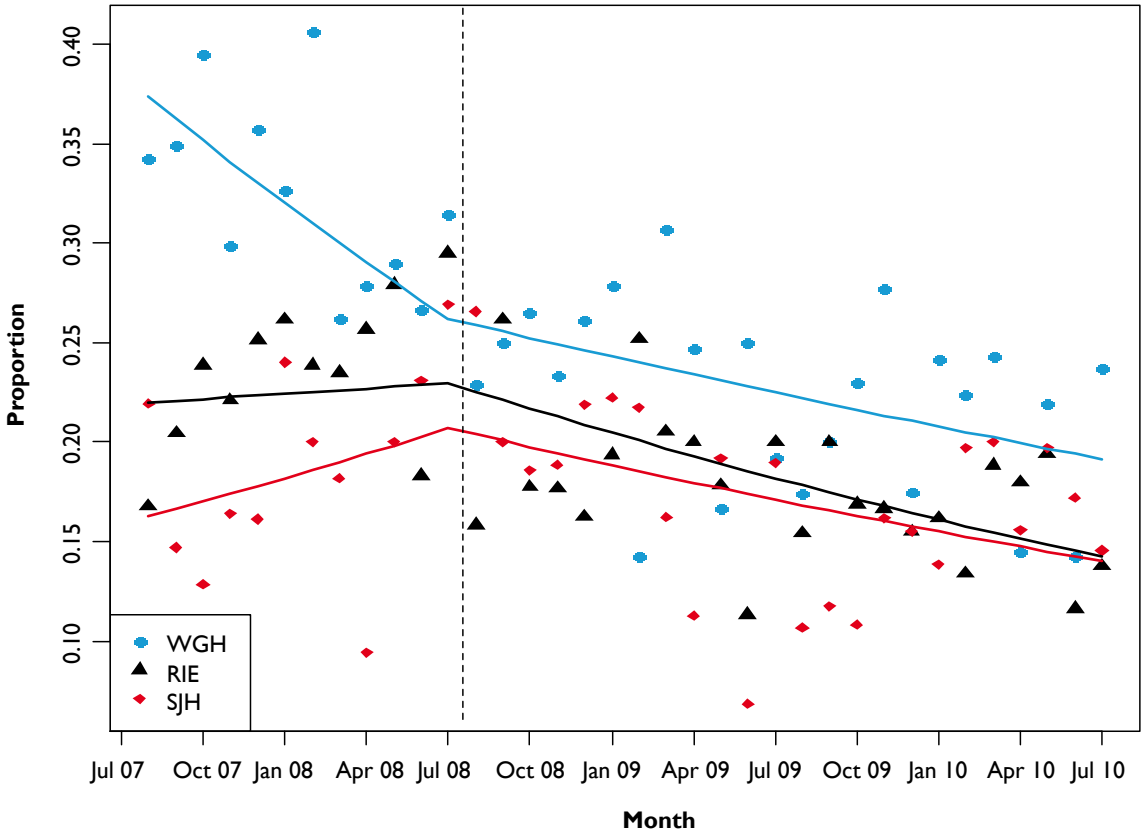
In all three hospitals the numbers of first new MSSA clinical isolates increased very slightly over time since August 2007. Furthermore the temporal trends in Western General Hospital and Royal Infirmary Edinburgh for MSSA were not the same pre August 2007 compared to post August 2007.

Figure 8-12: Piecewise linear Poisson Regression Model for first new MSSA clinical isolate counts in Lothian



Since April 2006 the percentage of new first *S. aureus* clinical isolates which were MRSA for the Royal Infirmary Edinburgh and St John's Hospital were comparable over time but the proportions for the Western General Hospital were higher. There was a downward trend in all three hospitals after August 2008.

Figure 8-13: Piecewise linear Logistic Regression Model for proportion of first new S. aureus clinical isolates which are MRSA in Lothian



8.3.5 Conclusions and comparison to Pathfinder data

These analyses have demonstrated that the number of new first clinical isolates of MRSA have been decreasing steadily in Lothian since 2006, a health board which was not part of the Pathfinder project, at a rate of just under 2% per month. This decrease cannot be attributed to universal MRSA screening, but some targeted screening was in place and this may be confounding.

In the pathfinder hospitals within the two pathfinder boards the decrease in MRSA cases per month was 2.8% (95% CI -0.8%, 6.2%). This wide confidence interval overlaps with the 1.96% (95% CI 1.55%, 2.37) the confidence interval in Lothian. Whilst the rate reduction in the pathfinder hospitals was greater than that in the five non pathfinder hospitals post August 2008, there is no evidence this reduction is statistically significant (p=0.54).

Modelling the two pathfinder hospitals and the two non pathfinder hospitals in Ayrshire and Arran and Grampian along with the three Lothian hospitals indicates no evidence of different trends post August 2008 in the seven hospitals (p = 0.87), nor pre August 2008 (p=0.49).

There was no overall change in the numbers of first new MSSA isolates and consequently the proportion of all new *S. aureus* isolates which were MRSA has also decreased. The same decrease was observed in all three hospitals in Lothian after August 2009.

These analyses provide an indication that universal MRSA screening with nasal swab may not be associated with a reduction in infection. There are a number of limitations to be noted. The time series were low powered as the comparator hospitals in pathfinder boards were small and this study is observational. The hospitals are not truly comparable and there are many factors which may be confounding inclusive of: the introduction of enhanced screening in non pathfinder hospitals, hand hygiene campaigns and the implementation of the Scottish Patient Safety Programme (SPSP) care bundles all within the same time period.

Key Summary Point:

Whilst the rate of reduction of MRSA first new clinical isolates post screening was greater in Pathfinder hospitals, this reduction did not reach statistical significance when compared to a board not participating in the pathfinder project (NHS Lothian). There are a range of factors which may confound these findings and these data must be interpreted with caution, however, on balance of evidence it is not possible to rule out an impact of MRSA screening reducing the number of first new clinical isolates of MRSA.

8.4 Trends in pathfinder board laboratory confirmed infection data on organisms other than MRSA

The recorded annual counts of six key selected causative organism bacteraemias were examined in the 2009 report and are updated here. These were chosen because these have been identified by EARSS as the ones most closely related to emerging resistance and posing a heavy burden on healthcare. Year one was the year before the Pathfinder project year; two and three are the years after implementation of the Pathfinder project.

A Chi Squared test indicated significant differences for *E. coli*, *K. pneumoniae*. Using a trend test to see if the trends were different over the three years between the pathfinder and non pathfinder boards, *P. aeruginosa* and *S. pneumoniae* exhibited different trends as well as *E. coli, K. pneumoniae*. In all cases the tables of the percentages indicate that the percentages of organisms reported from pathfinder boards were increasing relative to the non pathfinder boards.

Data from bacteraemias reported to HPS over a three year period, July 2007 to June 2010, showed a year on year increase in the Gram negative organisms (*E. coli*, *K. pneumoniae* and *P. aeruginosa*) and the Gram positive organisms (*E. faecalis*, *E. faecium* and *S. pneumoniae*) from both pathfinder and non-pathfinder boards.

Although there was an increase in the totals for *S. pneumonia*, *E. faecalis* and *E. faecium* over the three year period, no difference was seen between the pathfinder and non-pathfinder boards.

Over this period not all laboratories were reporting through the ECOSS electronic reporting system, thus it is important that these data are not over interpreted. From July 09 to June 2010, the first year that complete data were available, all laboratories in Scotland reported bacteraemia isolated via the ECOSS system.

Continued monitoring these organisms, which are capable of causing significant morbidity and mortality, using 2009 - 2010 as the baseline, will be worthwhile to monitor any trends in the causation of bacteraemia within Scotland.

Table 8-1: Causative organism of bacteraemia by Pathfinder year one and two and non pathfinder year one and two showing P values from Pearson Chi-squared test

Organism	Pathfinder Cases Year 1	Pathfinder Cases Year 2	Pathfinder Cases Year 3	Non Pathfinder Cases Year 1	Non Pathfinder Cases Year 2	Non Pathfinder Cases Year 3	*P* value
Enterococcus faecalis	42	65	59	234	423	357	0.7664
Enterococcus faecium	36	45	36	198	248	202	0.9962
Escherichia coli	208	416	573	1636	2779	3347	0.0019
Klebsiella pneumoniae	47	86	136	318	554	571	0.0034
Pseudomonas aeruginosa	14	25	42	153	159	232	0.1039
Streptococcus pneumoniae	67	88	98	460	516	457	0.0700

Key summary point:

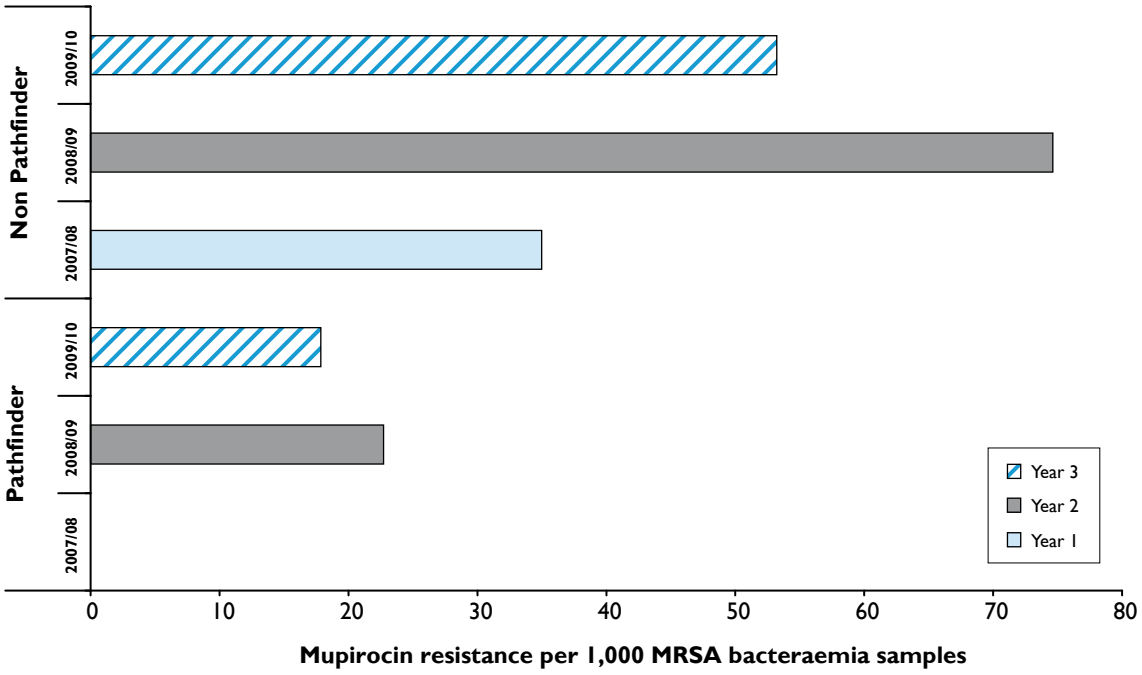
Continued monitoring of the organisms closely related to emerging resistance and posing a heavy burden on healthcare is worthwhile in order to monitor any trends in the causation of bacteraemias within Scotland.

8.5 To monitor any change in mupirocin resistance

The use of mupirocin to suppress carriage and shedding of MRSA is promoted by UK guidance [46] as a strategy for preventing infection and transmission. The risk of such a strategy is the selection for mupirocin resistance. Selection pressure for resistance will increase if there is increased use of mupirocin as a consequence of a universal screening programme [47]. The national MRSA reference laboratory monitored mupirocin resistance of isolates as part of their remit. The laboratory also provided historical and comparator data for non pathfinder hospitals from the routine and snapshot study samples submitted from NHS laboratories in Scotland for the year before and after the intervention of universal screening.

Poisson regression analyses were carried out on the Scottish MRSA reference laboratory data. Year 2007/8 was the year before implementation of the Pathfinder project and was considered to be the baseline, 2008/9 was year one post Pathfinder implementation and 2009/10 was year two post implementation. While the rates were higher in the non pathfinder boards compared to the pathfinder boards there was no statistical evidence of a change in rates from 2007/8 to 2008/9 and 2009/10 in the pathfinder and non pathfinder boards. Essentially there were similar increases in both groups of boards, (p=0.41, Chi squared deviance test).

Figure 8-14: Mupirocin resistance as a proportion of all MRSA bacteraemia by Pathfinder and non Pathfinder sites pre 2007/8 and post implementation of universal screening (2008/9 and 2009/10)



Selection of drug resistant strains of MRSA may arise as a result of usage of antibiotics for both prophylaxis and treatment. The time course for evolution and spread of an antibiotic resistant strain is unpredictable. Prescribing of antibiotics needs to reflect local resistance patterns as captured through local surveillance whilst taking note of national trends [48]. The frequency of resistance at which an antimicrobial drug ceases to be the empirical choice in a patient group is debateable, but ten percent resistance has been used as a guide for seeking an alternative [49]. This level of resistance was not found during the study period. It should however be noted that the short time period over which this work has been conducted may not be long enough to detect any changes of resistance to mupirocin.

Other data from the reference laboratory indicate that resistance levels within NHSScotland remain low, but an upward trend has been seen in the last few years. This trend varies between NHS boards, and there is considerable local variation within boards.

International literature has noted the emergence of mupirocin resistance with unrestricted prescribing policies, although this has not been universally observed [47]. In some studies the use of a restrictive policy has resulted in mupirocin resistance levels decreasing or remaining low despite continuing use for decolonisation in the context of a single hospital with a universal screening programme [47].

If clinical use of mupirocin increases nationwide, in the context of a national screening programme, it is the possible that prevalence of resistance will increase. A strategy for the on going monitoring of the prevalence of mupirocin resistance within NHSScotland should therefore be developed by the MRSA reference laboratory and HPS as part of the national rollout of MRSA screening.

Research studies are required to quantify the efficacy, effectiveness and unintended consequences of mupirocin use as an MRSA infection prevention strategy.

Key summary point:

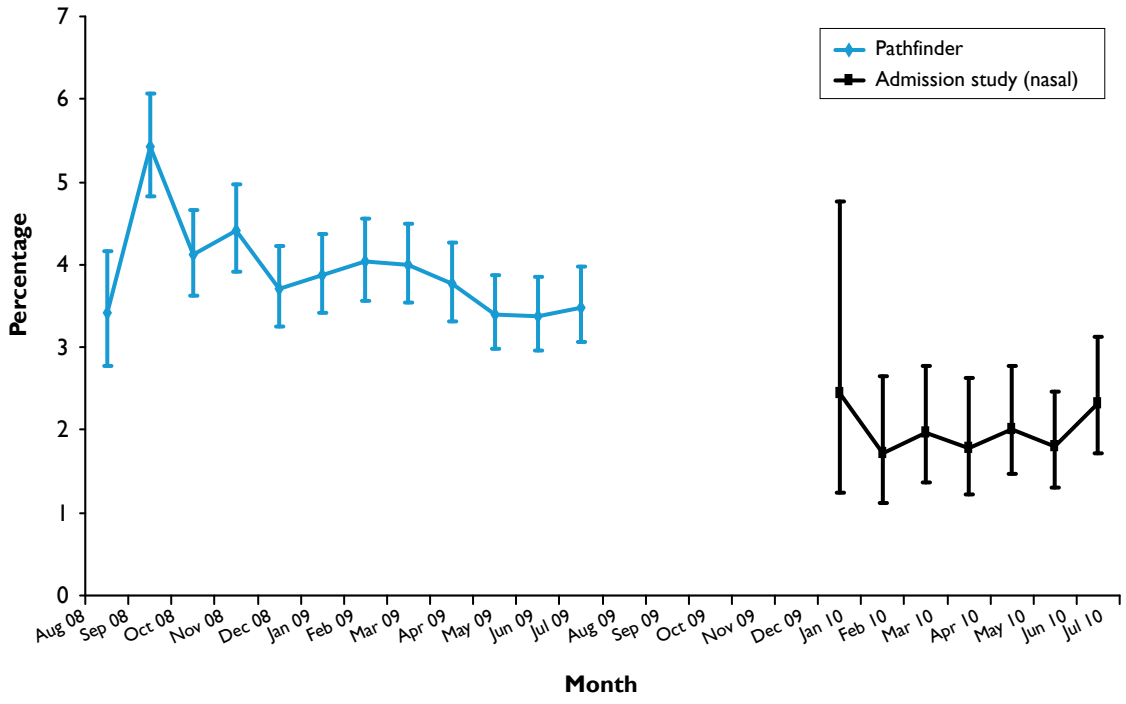
There was no evidence of a different change in rates of mupirocin resistance from 2007/8 to 2008/9 and 2009/10 in the pathfinder and non pathfinder boards. There were similar increases in both groups of boards. Whilst levels of resistance levels remain low at present, longer term monitoring is required.

8.6 Nasal Colonisation

Pathfinder data collection commenced in August 2008 and completed in July 2009. The admission and discharge studies commenced data collection in January 2010. Nasal colonisation prevalence is presented here for the special studies from January 2010 to July 2010. It is important to note that the population of the Pathfinder project did not exactly match the population within the special studies due to ethical constraints.

Over the period of the Pathfinder project there was a decrease in nasal colonisation on admission and the last month of the study (July 2009) recorded a prevalence of 3.5%.The data from the special studies indicated that nasal colonisation prevalence reached a prevalence of less than two percent which was not expected to be achieved by the HTA model within Pathfinder hospitals until at least year three [6].

Figure 8-15: Nasal colonisation during Pathfinder programme August 2008 to July 2010.



Key summary point:

Nasal colonisation prevalence has continued to reduce over the period of the special studies and has levelled out at about 2%; this is a similar picture to the one which was projected within the model in the final report, although the effect has been earlier than projected by the model.

8.7 Cost of MRSA Screening and the consequences on clinical outcome.

8.7.1 Methods

One important aspect of the discussion around introduction of MRSA screening is "What effect does MRSA screening have in terms of cost of investment in screening compared with infections prevented?". There is very little good quality information within the literature on MRSA infections in terms of Quality Adjusted Life Years (QALY). The HTA [9] noted QALYs would be helpful to decision-makers because a range of other health services, mainly new medicines, have been evaluated in terms of costs and QALYs. Thus, estimates of the costs and QALYs of different MRSA screening options would allow a comparison of this use of NHS resources with other options. One reason for the lack of QALY estimates in MRSA is the range of possible infections that MRSA can cause and the range of consequences to the overall health of a patient as a result of that infection and that the majority of studies focus on a particular infection type. At the time of the HTA [9] there was no literature available to allow the estimation of QALYs within the model. However in the time since this HTA, the pathfinder study has gathered much intelligence to inform the development of QALYs.

The approach used was as follows:

- Using data from the Pathfinder project, it was possible to estimate the change in the number of MRSA infections before and after screening
- The consequences of MRSA infection were considered in terms of the patient's health and whether this was likely to be fatal, to have lasting consequences for the patient's quality of life, or whether the infection could be successfully treated.
- A QALY loss for each of the three types of consequence was estimated from the literature.
- The QALY losses were weighted according to how frequent each one would be and thus derived an average QALY loss per infection
- This was then applied this to the change in the number of infections estimated from Pathfinder data.

The Pathfinder project was the data source for these analyses wherever possible. During the Pathfinder project the number of infections observed during year one of implementing universal screening was recorded each month. MRSA infections were recorded by the local data collection teams and defined in terms of CDC HAI infection classification [50]. It was possible to estimate the number of infections prevented in one year by calculating the incidence of HA infection in month two of the Pathfinder project as a baseline (month two was selected to ensure that the programme was fully implemented in all areas). The incidence of infection in month 12 was used to calculate MRSA infections after one year of universal screening. It is important to note that there was a reduction within the year of implementation of the screening and therefore these are point estimates and would not be expected to exactly match the pathfinder data.

The CDC HA infection classes were then mapped into one of the three categories of infection consequence based on discussion with a MRSA screening clinical expert group from the pathfinder programme, as follows:

Table 8-2: Categories of consequence of MRSA infection and proportion of those observed during the Pathfinder project

Consequences of MRSA Infection	Percentage of MRSA infections
Fatal	2.7
Long-term consequences (loss of health)	2.4
Treatable (short-term consequences)	94.9

For the purposes of this work it was assumed that the distribution of infection types seen over the whole year of Pathfinder would remain consistent regardless of the overall prevalence of colonisation, i.e. as the number of infections reduced there would always be 34% of the total HA infections that would be skin and soft tissue, no matter how many infections occurred.

The fatal category included a mortality rate of 30% of people with MRSA bacteraemia and 20-30% of people with MRSA pneumonia. The long term consequences were defined as all bone and joint infections (bone, joint and disc space) and surgical site infections (deep incisional and organ space). The remainder were included in the short term consequences category (this include the remaining proportion of blood stream infections and pneumonias as well as skin sort tissue infection, urinary tract infections etc).

This logic allowed a calculation based on total annual overnight admissions to hospital (rounded to 1,000,000) and an incidence value with screening (from month 12 of the Pathfinder project) and without screening (from month two of the Pathfinder project) to calculate the total of each infection consequence that would be expected with each strategy. Utility values for each type of MRSA infection consequence were then applied.

Table 8-3: Published utility values for MRSA infection

	1=full health, 0= as bad as dead [50]
Surgical site infection	0.64
Urinary tract infection	0.73
Pneumonia	0.58
Amputation	0.44
Abscess/osteomyelitis	0.59

8.7.2 Assumptions

The quality-of-life (utility) values for a QALY are based on a value of 1.0 representing full health and 0 representing a health state that is considered close to death. Population surveys have shown that older people report their health as falling slightly below 1.0, with values of 0.75 to 0.85 being typical.

For a fatal infection it was assumed that, if a patient had not died, they would have lived another 10 years with about 80% Quality of Life (QoL). This was consistent with the age of those with bacteraemia infections being 75-years on average.

For long-term consequence infections the patient was assumed to live another 10 years and lose 30% of their QoL. Life Expectancy (LE) was as defined in Table 8-4, QoL was based on that defined by Lee et al. [51]. It was also assumed that short-term consequence infections resulted in a 20% QoL loss for two weeks.

Table 8-4: Calculated Quality of Life reduction and number of years to generate QALY for each infection type

Infection type	QoL loss on 0 to 1 scale	Years	QALYs
Fatal	0.8	10	6.65
Long-term	0.3	10	2.49
Short-term	0.2	0.04	0.01

Applying the QALY loss to each category, the resulting average per case was 0.24

Table 8-5: Calculations to derive the total number of QALYs saved per year in Scotland

Infection (in absence of screening)	Number of cases per million admissions without screening incidence =0.60	Number of cases per million admissions with screening incidence =0.39	Infections reduced during implementation of screening	QALYs lost per case	Total QALYs gained by screening
Fatal	162.0	105.3	56.7	6.7	377.0
Long-term	144.0	93.6	50.4	2.5	125.0
Short-term	5694.0	3701.1	1992.9	0.0	20.0
Total	6000.0	3900.0	2100.0		522.0

Within one year in Scotland the total QALY loss due to MRSA infection with status quo screening would be 1,491 (assuming that incidence of MRSA infection remained static over that year). It was estimated that MRSA screening, implemented in Scotland in overnight admissions, would impact as follows; 58 fewer deaths, 50 fewer long-term consequences, 2,042 fewer to be treated (short-term impact). This would produce a total QALY gain of 522 per year.

The National Institute for Health and Clinical Excellence (NICE) and Scottish Medicines Consortium (SMC) use a threshold value of £20-30k per QALY respectively to evaluate a new treatment as reasonable to implement. Within the HTA [9] NHSQIS estimated universal screening cost to be £15 million pounds per year.

In order to achieve £30k for each QALY the overall programme must save 500 QALYs per year. In order to achieve £20k a total of 750 QALYs must be saved per year. This suggests the cost per QALY of MRSA screening would be in the range £20k to £30k. However, the cost of £15 million included the cost of isolation rooms, some of which is already incurred, as well as opportunity costs for staff time. If screening cost £8 million, which is a more accurate estimate of the total costs of screening (excluding the cost of isolation of patients and the time releasing costs), only 267 QALYS would need to be saved to reach a value of £30K per QALY and 400 QALYs would be need to be saved to get to £20k per QALY. Under this scenario MRSA screening is likely to cost less than £20k per QALY.

It should be noted that these results make the assumption that the reduction in infection can be attributed to the intervention of screening. There may be confounding variables not taken account of in these analyses and therefore they should be interpreted with care.

Key Summary Point

Assuming universal screening will cost around £8 million per annum, the cost per QALY would be £15,325. Based on either NICE or SMC thresholds the universal MRSA screening programme appears to be acceptable in terms of QALYs on the assumption that the reduction in infection is associated with the screening intervention.

9 Summary of findings from the special studies

9.1 Admission study

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 [8].

9.2 Discharge Study

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. On admission, 58 patients were MRSA positive and on discharge 70 patients were MRSA positive. This confirms that cross-transmission of MRSA 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.

10 Conclusion

Evidence for the implementation of a national MRSA Screening Programme gathered since the final report on the Pathfinder project in December 2009 indicates that there may be some value in screening patients; however there appears to be equal value in universal CRA in terms of clinical effectiveness.

Two strands of evidence support the value in some type of universal assessment: the reworked model indicated an increased benefit in screening compared with the do nothing option, there was a decrease in MRSA as a proportion of all *S. aureus* first new clinical isolates within the Pathfinder hospitals. No negative consequences have as yet been identified in association with the screening programme, however continued monitoring is required. This evidence has to be balanced with the cost of prevention of infection. The work around QALYs assumes that the incidence of infection seen at the start of the Pathfinder project was similar to that seen in all other boards in NHS Scotland now; there are no national data to support this assumption.

The evidence to support a universal nasal screening programme by direct chromogenic agar laboratory testing is weak, a prevalence of now 2% (by nasal screen alone) in Pathfinders hospitals means that 98% of nasal swab laboratory tests are negative, only one third of patients found positive receive both of the interventions of decolonisation and isolation or cohorting. Also it is now known that only two thirds of gold standard positives are identified by nasal swab testing alone.

Although the principle of universal screening within the context of the HTA model looked preferable, the limitations of the current healthcare system mean that the opportunity for intervention (given length of stay, observed turn around times of the test, and availability of isolation facilities) means that the effectiveness of the approach is limited. This limited ability to intervene in a timely manner so as to reduce risk of cross transmission of colonisation, calls into question the value of the large financial investment which is required to effectively implement universal laboratory screening for all admissions.

Universal screening has a potential temporal association with reducing infection and appears to meet the criteria required for QALYs, indicating it would be an acceptable investment balancing with the benefit in outcome. However it cannot be attributed on its own for the reduction in MRSA infections observed during the Pathfinder study. There is also a burden of MRSA acquisition during hospital stay which requires to be managed with additional interventions. Further the prevalence of colonisation is lower than that predicted by the HTA, and length of stay (LOS) precludes many of those found positive from getting the interventions during their stay. These factors mean that the ability of healthcare workers to reducing risk of infection or cross transmission is severely limited. The clinical benefit of the investment in universal laboratory based screening is therefore in question, particularly in the current economic climate.

CRA was proposed by the HTA as the most clinically effective strategy and appears to show promise as an approach for implementation in NHSScotland. It appears that it would provide a similar clinical effect but would require significantly less investment and no capital investment. It also allows the possibility of improved timely patient placement, so as to reduce the risk of cross transmission during stay.

The pathfinder study together with the two special studies has demonstrated the value of MRSA screening in reducing risk of infection. The special studies have provided solid evidence on the limitations of both laboratory chromogenic agar screening, and on the use of clinical risk assessment in terms of value for money. The only strategy that has been fully tested in a real world setting, as it would be implemented, is universal screening, therefore there is a requirement for reviewing the modelling work in order to undertake a like with like comparison of the impact of the possible strategies which remain feasible options. These should be reviewed not just in terms of value for money but also in terms of all the aspects of the NHS Scotland Quality Strategy.

11 Recommendation

Three national screening strategy options remain on the table:

1. Universal screening
2. Clinical risk assessment of all admissions (using three questions and chromogenic agar screening all patients who answer yes to one question)
3. Clinical risk assessment (using three questions and chromogenic agar screening all patients who answer yes to one question) and swab all those treated in specialties undertaking procedures which would have a high impact in quality of life and expected outcome.

A detailed examination of these options was required in order to make a policy decision regarding the best option in terms of cost of investment compared with effect on outcome. This was based on the re-worked HTA model and the true cost effectiveness combined with the expected outcome and the output of this is presented in an economic analysis report [8].

There has been much debate around whether a threshold value for cost per QALY should be used in order to make a decision. In their paper on NICE [52] Culyer et al argue that the decision should be for parliament to decide. This decision making will necessarily be in the context of alternative public spend. The role of economic evaluation is to provide guidance on the optimal incremental cost effectiveness ratio that is "consistent with the aim of maximising population health".

The economic analysis presented in the supplementary report [8] aims to inform the programme board and ultimately SGHD, using the best information available for determining the shape of a future national MRSA Screening policy. The resulting recommendation [53] has been made based on the public health principles, patient safety, acceptability of the approach, efficacy in detecting true MRSA carriage, clinical effectiveness and the cost.

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13 Acronyms

CRA	Clinical Risk Assessment
ECDC	European Centre for Disease Control
EU	European Union
HTA	Health Technology Assessment
ICU	Intensive Care Units
ITU	Intensive Therapy Unit
MoE	Medicine of the Elderly
GI	Gastro Intestinal
LE	Life Expectancy
MRSA	meticillin-resistant *Staphylococcus aureus*
MSSA	meticillin-sensitive *Staphylococcus aureus*
NICE	National Institute for Health and Clinical Excellence
PCR	Polymerase Chain Reaction
QALY	Quality Adjusted Life Year
SMC	Scottish Medicines Consortium
SHEA	Society for Healthcare Epidemiology of America
SSI	Surgical Site Infections
WGH	Western General Hospital
RIE	Royal Infirmary Edinburgh
SJH	St John's Hospital Livingston
SPSP	Scottish Patient Safety Programme
PPV	Positive Predictive Value

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10a. Abstract : [Maximum 200 words]

This report presents an update on longer term monitoring of areas of concern relating to the implementation of universal MRSA screening in the NHSScotland Pathfinder Health boards, and a summary results of the two special studies within the pathfinder programme. The MRSA screening programme appears to be acceptable in terms of QALYs. However a reduction in MRSA infection has been observed in all health boards and therefore the reduction in QALYs lost is not necessarily attributable to universal screening. Universal nasal swabbing for MRSA appears less effective than previously thought in identifying patients with MRSA carriage, with only 66% of 'gold standard' cases detected. The potential for the Clinical Risk Assessment questionnaire as a simple, economical and effective tool to identify true carriers within a small patient subgroup has not been fully realised. The discharge study showed cross-transmission of MRSA takes place in Scottish hospitals. The discharge study did not indicate *net* acquisition at a population level; these studies have provided solid evidence on the limitations of both laboratory chromogenic agar screening and on the use of clinical risk assessment in terms of value for money.

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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