Papers

Isolation measures in the hospital management of methicillin resistant *Staphylococcus aureus* (MRSA): systematic review of the literature

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Abstract

Objective To evaluate the evidence for the effectiveness of isolation measures in reducing the incidence of methicillin resistant *Staphylococcus aureus* (MRSA) colonisation and infection in hospital inpatients.

Design Systematic review of published articles.

Data sources Medline, Embase, CINAHL, Cochrane Library, System for Information on Grey Literature in Europe (SIGLE), and citation lists (1966-2000).

Review methods Articles reporting MRSA related outcomes and describing an isolation policy were selected. No quality restrictions were imposed on studies using isolation wards or nurse cohorting. Other studies were included if they were prospective or employed planned comparisons of retrospective data.

Results 46 studies were accepted; 18 used isolation wards, nine used nurse cohorting, and 19 used other isolation policies. Most were interrupted time series, with few planned formal prospective studies. All but one reported multiple interventions. Consideration of potential confounders, measures to prevent bias, and appropriate statistical analysis were mostly lacking. No conclusions could be drawn in a third of studies. Most others provided evidence consistent with a reduction of MRSA acquisition. Six long interrupted time series provided the strongest evidence. Four of these provided evidence that intensive control measures including patient isolation were effective in controlling MRSA. In two others, isolation wards failed to prevent endemic MRSA.

Conclusion Major methodological weaknesses and inadequate reporting in published research mean that many plausible alternative explanations for reductions in MRSA acquisition associated with interventions cannot be excluded. No well designed studies exist that allow the role of isolation measures alone to be assessed. None the less, there is evidence that concerted efforts that include isolation can reduce MRSA even in endemic settings. Current isolation measures recommended in national guidelines should continue to be applied until further research establishes otherwise.

Introduction

The incidence of hospital acquired methicillin resistant *Staphylococcus aureus* (MRSA) continues to rise globally.[1–4] Attempts to control this spread have relied principally on three measures: hand hygiene among healthcare workers, restriction of antibiotics, and the detection and isolation of infected or colonised patients. We consider the detection and isolation of infected or colonised patients, which is central to most national guidelines.[5–8]

Most transmission of MRSA from patient to patient is thought to be mediated by transiently colonised healthcare workers, although airborne dispersal and transmission through contacts with contaminated surfaces may also be important. Isolation measures for patients are intended to interrupt such transmission. The most intensive forms of isolating patients are isolation wards (designated for the treatment of known or suspected carriers of MRSA) and nurse cohorting (the physical segregation of MRSA patients in one part of a ward, with nursing by designated staff who care exclusively for these patients). Other isolation measures include the use of single bedded rooms, cohorts of patients on general wards (without designated nursing staff), and barrier precautions (use of aprons or gowns, gloves, and, in some cases, masks by healthcare workers as the only physical barrier to transmission).

Such control measures may place substantial burdens on hospital resources, and the value of their continued use has been questioned.[9] Earlier narrative reviews have been undertaken,[10 11] but the effectiveness of isolation measures in reducing transmission and controlling MRSA has not been assessed systematically. Moreover, as much of the research in this area is known to be of a quasi-experimental nature.[8 11] The associated threats to valid inferences need to be considered.[12–14] We therefore undertook a systematic review of the evidence for the effectiveness of isolation measures in the management of MRSA in hospitals.

Method

Search strategy

We developed a search strategy that covers the main subject areas of the review (MRSA, screening, and isolation of patients and control of infection). We searched the following databases, with no language restrictions: Medline 1966-December 2000, Embase 1980-December 2000, CINAHL 1982-May 2000, System for Information on Grey Literature in Europe (SIGLE) 1980-May 2000, and the *Cochrane Library* to December 2000. We also searched reference lists of retrieved articles and hand searched abstracts from key journals to verify the sensitivity of the search strategy.

Study selection

Two or three reviewers working together appraised abstracts. Full articles were obtained if abstracts mentioned endemic or epidemic MRSA and an attempt at control in a hospital setting.

As the number of studies was far greater than anticipated, we revised the original protocol (which had imposed no quality

Table 1 Characteristics of the 46 accepted studies

Highest level of isolation	Isolation ward	Nurse cohorting	Other isolation measures
No of studies	18	9	19
Range of study durations	3 months-15 years	3.5 months-4 years	1 month-9 years
Whole hospital setting	16	3	7
Hospital unit setting (such as burns, intensive care)	2	6	12
Other control measures			
Screening for MRSA	18	9	14
Topical eradication therapy	12	5	8
Hand hygiene programme	8	2	6
Antibiotic restriction	3	0	2
Study design			
Prospective interrupted time series	1	2	8
Retrospective interrupted time series	15	3	2
Hybrid retrospective and prospective interrupted time series	0	2	5
Retrospective cohort study	0	0	1
Non-comparative (one phase) studies	2	2	3

restrictions). We imposed the minimal requirement that accepted studies should include a component of prospective data collection. If they were entirely retrospective comparisons should have been planned and not prompted by part of the outcome data. No such restrictions were imposed for studies using the most intensive forms of isolation (isolation wards and nurse cohorting) as these have the greatest implications for the allocation of resources and organisation of services.

Two investigators reviewed the papers independently, to confirm that they met the above criteria. We rejected studies not mentioning an isolation policy or without relevant MRSA related outcomes.

Data extraction

We divided each study into phases, where appropriate, that were defined by major changes in isolation or other aspects of infection control policy and extracted data on study design, patient population, isolation details, screening, other infection control measures, and MRSA related outcomes for patients.

We documented potential threats to the internal validity of accepted studies. We considered the vulnerability of each study to selection, performance, detection, and attrition bias (see table 2). We documented measures taken to prevent bias and noted potential confounders and attempts to record and adjust for these. We documented threats to validity because of underlying trends, seasonal effects, and regression to the mean effects, which we defined as "a tendency for extreme measurements to be followed by less extreme measurements for imperfectly correlated variables that often results in wrong conclusions about the effects of interventions."[15] We assessed the appropriateness of any statistical analysis undertaken.

We wrote to authors when isolation or screening policies or their timing were unclear. We excluded studies if either the main isolation policy or the timing of interventions were unclear, or if the only outcome reported was MRSA colonisation but the screening policy was unclear or had changed sufficiently to make interpreting outcomes impossible.

Table 2 Selection, performance, detection and attrition bias

Type of bias	Cause	Studies vulnerable	Measures taken to identify or prevent bias
Selection bias	Differences in intervention groups on study entry	Studies without randomisation (39 studies)	Four of 35 interrupted time series studies where isolation or screening changed presented data allowing comparisons of patient characteristics between phases[26 34 40 57]
			Two described unquantified changes in case mix.[43 46] One study presented partial adjustment for confounders[30]
Performance bias	Differences in care for patients between treatment groups, apart from interventions under investigation	Studies where specified aspect of care was not under investigation:	
	Differences in antibiotic prescribing	31 interrupted time series studies	Four presented details of antibiotic use.[18 22 36 63] Two alluded to unquantified changes[46 54]
	Differences in lengths of stay	29 interrupted time series studies	Changes in length of stay could be assessed in four[33 36 47 61]
	Differences in bed occupancy and staff workload	31 interrupted time series studies	Comparisons of bed occupancy between phases possible in four[18 24 47 58] Changes in staffing levels or workloads could be assessed in five[18 24 26 32 47]
Detection bias	Differential outcome assessment between intervention groups:	All studies:	Three reported some blinding of outcome assessors[34 47 57]
	Differences in diagnosis of infections	26 studies	16 specified diagnostic criteria. 14 reported MRSA bacteraemias
	Differences in screening practices	10 studies with colonisation data only	In all cases screening effort either reported not to have changed or to have changed in opposite direction from outcomes, suggesting screening effort could not explain the changes
Attrition bias	Differential loss to follow up between treatment groups.	Studies where outcomes are infections (26 studies) and with substantial changes in length of stay	None: no studies followed up patients after discharge to detect hospital acquired infections
	Since hospital acquired infections may first become apparent after discharge, changes to length of stay could lead to attrition bias		

Table 3 Studies providing stronger evidence

Study	Setting and study population	Design	Main interventions	Patient outcomes	Assessment of evidence
Coello et al, 1994[25]	Teaching hospital 1500 beds	Prospective interrupted time series. Three phases: 8, 8, and 26 months	Phases 1 and 2: minimal isolation and screening Phase 3: single room isolation and nurse cohorting, contact screening, prompt discharge of MRSA cases Topical eradication of MRSA carriage with neomcyin nasal cream in phase 1 and with mupirocin in phases 2 and 3	Figure: A 476 infected patients throughout	Evidence that a major outbreak was controlled by combined interventions. Lacks information on many potential confounders
Cosseron-Zerbib et al, 1998[26]	Paediatric ICU 20 beds	Hybrid retrospective and prospective interrupted time series. Two phases: 21 and 24 months.	Phase 1: screening for last 11 months Phase 2: single room isolation, cohorting, screening, feedback, handwashing education, barrier nursing, chlorhexidine soap, and other measures	Figure: B MRSA infections: Phase 1: 50 Phase 2: 6	Evidence that interventions reduced MRSA infections. Regression to mean and Hawthorne effects supply less plausible alternative explanations
Duckworth et al 1988,[28]	Teaching hospital 645 beds	Retrospective interrupted time series. Six phases: 4, 3, 13.5, 4, 1.5, 26 months	Initial isolation: mainly single rooms and some cohorting (phases 1-3), changing to mainly isolation ward (phases 4-6). Simultaneous changes to screening, eradication and other measures	Figure: C 408 MRSA infections throughout	Evidence supporting efficacy of combined measures in reducing incidence. Many potential confounders not recorded
Faoagali et al, 1992[31]	Teaching hospital 1200 beds	Retrospective interrupted time series. Two phases: 7 and 8 years	Isolation ward throughout Phase 1: minimal overflow from isolation ward Phase 2: overflow isolated in single rooms Additional measures in phase 2 include: pre-screening of admissions and transfers in; handwashing education; antibiotic restriction	Figure: D	Evidence that combined measures in both phases failed to prevent MRSA spreading and becoming endemic
Farrington et al, 1998[32]	Teaching hospital 1000 beds	Retrospective interrupted time series. Two phases: 9.5 and 2.5 years	Continual operation of isolation ward Phase 1: minimal overflow from isolation ward Phase 2: overflow cohorted and isolated in single rooms Screening, ward closure and eradication policies relaxed slightly in phase 2	Figure: E 221 MRSA acquisitions, 206 colonised on admission, 61 uncertain	Evidence supporting control of MRSA for 9.5 years by combined measures followed by eventual control failure related to rise in numbers colonised on admission or to change in strain rather than changed control measures
Harbath et al, 2000,[35] Pittet et al, 2000[36]	Teaching hospital 1300-1600 beds	Hybrid retrospective and prospective interrupted time series. Three phases: 4, 2, and 3 years	Phase 1:No control measures Phase 2: Single room isolation, screening, mupirocin Phase 3: as phase 2 + hand hygiene, education, and feedback programme	Figure: F 1771 MRSA colonisations and infections. 158 bacteraemias	Evidence supporting control by combined interventions Some potential confounders, but these provide less plausible explanations for the changes

Disagreements between reviewers were resolved by discussion and recourse to third parties. Reviewers were not permitted to play any part in appraising a study in which they had participated.

Data synthesis

Two reviewers independently evaluated the strength of evidence in each study by examining the study design, quality of data, and presence of plausible alternative explanations of outcomes. They characterised the evidence on a case by case basis as "none," "weak," "of intermediate strength," or "stronger." We considered formal meta-analysis inappropriate because of heterogeneity in outcome measures and patient populations. Full details of the search strategy, study selection, and data extraction are available in a technical report.[16]

Results

The electronic search selected 4382 abstracts. Hand searching produced no additional papers. Appraisal of abstracts selected 254 papers, including 20 in languages other than English. The final review included 46 studies (table 1).[17–63]

Study design

We found no randomised controlled trials and only four prospective planned comparison studies with predefined study phases.[22 40 52 63] Most designs were interrupted time series—that is, time series of outcome measures recorded before and after one or more interventions. However, eight of 38 interrupted time series studies presented only collapsed data, summarising time series from each phase in a single data point. One retrospective cohort study used survey data from all Dutch hospitals.[30]

Ten studies did not compare isolation or screening measures with respect to isolation or screening.[17 33 37 41 44 49 56 59 60 62] Review of the 36 studies allowing comparisons between isolation policies indicated that in 27 the comparisons being made were dependent on knowledge of the outcome data. Short retrospective studies with successful outcomes were particularly vulnerable to this problem; in at least seven the decision to intervene was influenced by part of the outcome data reported. This, and the predominance of unplanned retrospective reports, shows that reporting bias is likely to be important.

Threats to internal validity of evidence

In the absence of cluster randomised trials, all comparative studies were vulnerable to selection bias, yet recording and adjustment of potential confounders was minimal (table 2). In two cases we considered reported changes in case mix to represent a plausible explanation for changes in the incidence of MRSA.[43 46]

We identified changes in antibiotic prescribing, staff workload and ratios of staff to patients, and lengths of stay as the main potential sources of performance bias. Again, few studies reported data allowing an assessment of these, and none provided adjustment in the analysis (table 2). In a few cases some

Table 4 Studies providing intermediate levels of evidence

Study	Setting and study population	Design	Main interventions	Outcomes	Assessment of evidence
Arnow et al, 1982[18]	Burns unit, 8 beds	Hybrid retrospective and prospective interrupted time series. Two phases of 8.5 months each	Phase 1: barrier precautions only Phase 2 nurse cohorting, handwashing education, increased screening	MRSA cases: 39 (phase 1); 6 (phase 2). No new cases occurred during periods when nurse cohorting was complete	Evidence supporting control by interventions. Variation in patient-bed days is a plausible alternative explanation. Regression to the mean effects are possible
Blumberg et al, 1995[22]	Intensive care unit (20 beds), paediatric oncology (15 beds), and non-targeted areas of a tertiary care hospital (~3000 beds)	Hybrid interrupted time series. One year cohort study with non-equivalent concurrent controls, one year historical controls, and one year follow up	No control measures before study (historical controls). During intervention year eradication, screening and patient isolation (single rooms and staff cohorting) used in ICU and paediatric oncology. Measures largely abandoned in follow up year.	299 MRSA bacteraemias (43 in areas with interventions) Bacteraemias fell in the intervention year in targeted areas, then rose to intermediate levels in the post-intervention year. They increased each year in non-targeted areas	Evidence supporting control by interventions. Regression to the mean effects likely, and study vulnerable to changes in length of stay
Cox et al, 1995[27]	One general hospital (hospital A) and two long stay or rehab hospitals (B and C). 750 beds in total	Retrospective interrupted time series. Three phases (at hospital A): 5, 4, and 11 months	Phase 1: single rooms and cohorting Phase 2 and 3: isolation wards Eradication and extensive screening throughout, including pre-admission from phase 2	83 MRSA infected patients, 334 colonisations. Hospital A: 1-4 infections/month in all phases. Last month of data collection showed very low colonisation incidence Hospital B: Continual detection of MRSA cases. No clear trend Hospital C: apparent elimination of MRSA 14 months after isolation ward opened	Evidence that combined measures in all phases failed to prevent sustained spread at hospital A. No evidence of control at hospital B. Weak evidence of control at hospital C. Interpretation of hospital B and C data difficult without colonisation on admission data due to interhospital transfers
Esveld et al, 1999[30]	Dutch hospitals with index MRSA cases responding to a questionnaire. 231 returned questionnaires	Two year retrospective cohort study based on systematically collected survey data	Two cohorts defined by isolation policy Isolation cohort: index cases isolated on admission according to Dutch guidelines Non-isolation cohort: other isolation policy or delayed isolation	Isolation cohort: 4 out of 73 cases led to secondary spread Non-isolation cohort: 19 out of 95 cases led to secondary spread. Odds ratio 4.3 (95% CI 1.3 to 18.2)	Evidence that immediate isolation contributed to control. Other plausible explanations include: differences in strains (prompt isolation was associated with strains originating abroad); differences in characteristics of cohorts and settings; and bias introduced by differential response rates to questionnaires
Jernigan et al, 1996[38]	Neonatal intensive care unit, 33 beds	Hybrid retrospective and prospective interrupted time series. Two phases: 12 days and 9 months	Phase 1: contact isolation (gloves, gowns, masks and use of two bedded side-room if possible) Phase 2: as phase 1 plus eradication from selected patients; weekly screening; handwashing education	Total cases: 16 (5 in phase1, 11 in phase 2). Large fall in incidence after additional control measures Relative risk of transmission from an unisolated compared to an isolated source 15.6 ((95% CI 5.3 to 45.6), P<0.0001	Evidence supporting reduction in MRSA transmission by isolation measures Potential bias as no blinding to the isolation status of patients when assessing transmission sources Regression to the mean effects possible
Kac et al, 2000[40]	Wound care centre, 51 beds	Prospective interrupted time series. Two phases: 3 months and 2 years	Phase 1: no measures Phase 2: gowns and gloves, handwashing education, feedback of infection rates, MRSA wounds dressed last	15 wound infections. Reduction in proportion of patients acquiring MRSA wound infections from 6/70 (9%) to 9/583 (1.5%)	Evidence that control measure reduced infection rates, but limited by short baseline and vulnerable to pre-existing trends (due to lack of time series data). Impossible to distinguish cross-infection and autoinfection
Murray Leisure et al, 1990[46]	General hospital, 884 beds	Retrospective interrupted time series. two phases: 32 and 12 months	Phase 1:Single room isolation Phase 2: Isolation ward and changes to screening	177 new MRSA cases MRSA cases increased throughout phase 1 then fell to low levels in phase 2	Evidence consistent with control by isolation ward and screening, but change in numbers colonised on admission provides a plausible alternative explanation
Selkon et al, 1980[54]	Teaching hospital, 1000 beds	Retrospective interrupted time series. Two phases of 5.5 years each	Phase 1: single room isolation Phase 2: isolation ward	965 MRSA infections MRSA infections increased before the opening of isolation ward, and subsequently decreased	Evidence consistent with control by isolation ward Changing antibiotic use provides a plausible alternative explanation

information was available that implied that performance bias could plausibly explain changes in MRSA outcomes.[54 18 22 33]

Similarly, studies took few measures (such as blinding of outcome assessors) to prevent detection bias, although we considered studies reporting infections with specified diagnostic criteria and bacteraemias as primary outcomes to be less vulnerable to this bias.

Trends, regression to the mean, and seasonal effects

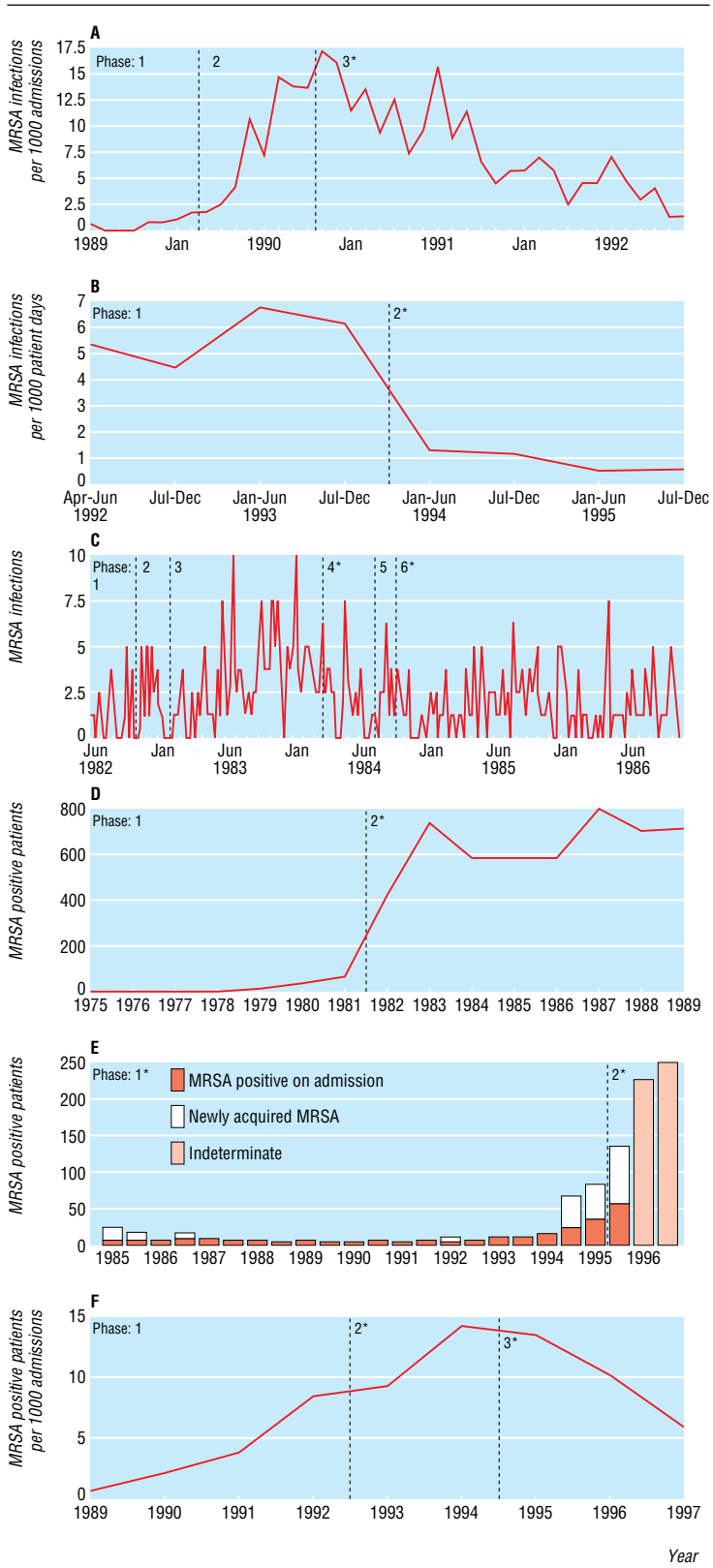
Of 30 studies with two or more phases and pre-intervention time series, clear trends were apparent in 13. In all cases the trend was for increasing MRSA levels before major interventions.

Trends in the number of patients colonised on admission may also complicate interpretation of outcomes. Of 35 studies presenting time series data, only five of the 18 studies that assessed whether patients were colonised on admission presented sufficient data to assess trends. In two cases there was an increasing trend,[32 50] in one a decreasing trend,[46] and in two no clear trend.[33 40] In two cases these trends provided a plausible explanation for changes in outcome measures.[32 46]

Regression to the mean effects were considered likely when unusually high MRSA incidence data prompted the intervention and when these data were included in the study. We considered this threat to provide a plausible explanation of outcomes in seven studies.[18 22 23 24 47 48 58]

Inspection showed that seasonal effects may have been important in two[23 58] of 14 studies with time series of 18 months or more. In the 21 studies with shorter time series it was not possible to disentangle seasonal from intervention effects.

Changes in MRSA strain types may explain changes in outcomes. Fourteen studies reported no typing details. In one study we considered the documented introduction of a new strain believed to have greater epidemic potential to plausibly explain increased MRSA incidence and control failure.[32]



Outcome of studies considered to present the strongest evidence Interrupted time series for A: Coello et al[25] B: Cosseron Zerbib et al[26] C: Duckworth et al[28] D: Faoagli et al[31] E: Farrington et al[32] F: Harbath et al.[35 36] Table 3 gives explanatory text. Asterisks indicate phases with most intensive isolation policies. In D and E isolation policies in both phases were similar (isolation wards), but in the second phase the capacities of the isolation wards were exceeded in both cases, and the overflow was cohorted or isolated in single rooms

Statistical validity

Of the 38 interrupted time series, 24 reported results of statistical analysis. In all but one study[38] where the analysis could be assessed patient outcomes were assumed by authors to be independent. Such assumptions are inappropriate when transmission from patient to patient occurs and would cause inflated rates of type I errors. In one study we considered the independence assumption to be justified as outcomes at hospital level from distinct hospitals were used.[30]

Evidence for control of MRSA

In 45 of the 46 studies multiple simultaneous control measures were apparent. It was not possible to assess the relative contribution of individual measures.

In 14 studies it was impossible to draw any conclusions about the effect of interventions. Most of the remaining 32 reported evidence consistent with reduction in MRSA transmission. The evidence in 18 of these we considered weak, because of poor study design or clear alternative explanations. This often applied to small and successfully controlled outbreaks managed by isolation wards or nurse cohorting.[17 19 39 50 51 53 55 56 61] None the less, it remains possible that immediate deployment of nurse cohorting or an isolation ward may be successful. Fourteen studies provided "stronger" evidence or evidence of intermediate strength (tables 3 and 4).

The strongest evidence came from six longer time series, with detailed information on interventions and fewer plausible alternative explanations (table 3, figure). In four cases major outbreaks were controlled or MRSA numbers substantially reduced over prolonged periods[25 26 28 35 36]; the main isolation measures were single room in two studies,[26 35 36] nurse cohorting in one,[25] and isolation ward in one.[28] Another isolation ward study reported failure to control the spread of MRSA,[31] and another reported control by an isolation ward for many years followed by eventual failure.[32]

We considered eight studies (table 4) to present evidence of reduction of MRSA by measures that included an isolation ward,[46 54] nurse cohorting,[16 20] or other interventions.[30 38 40] One presented data indicating the failure of an isolation ward to control MRSA.[27] However, these studies either had plausible alternative explanations or reported smaller changes in MRSA and did not record some important potential confounders. The evidence was therefore considered weaker than that from the first six. We found evidence from only one study that supported the hypothesis that MRSA replaces methicillin-sensitive *Staphylococcus aureus* (MSSA).[43] MRSA and MSSA bacteraemia data from the longer time series[31 32 36] contradicted this and showed that MRSA added to the total burden of infection.

Discussion

Our primary conclusion is that major methodological weaknesses and inadequate reporting in research into the effectiveness of isolation measures mean that many plausible alternative explanations for reductions in MRSA cannot be excluded. We have produced guidelines to facilitate the planning and publication of better quality studies.[16]

The secondary conclusion is that, despite the limitations of existing research we found evidence that concerted interventions that include isolation measures can reduce MRSA transmission substantially, even in settings with endemic MRSA. We found no evidence to show that current isolation measures recommended in many countries[5–8] are ineffective at reducing transmission from isolated patients: the only two studies that directly measured this reported large reduction in the transmission rate per source.[30 38] None the less, we found reports of control failure despite the employment of intensive isolation measures including isolation wards.[31 32] These studies indicate a need to investigate precisely how such isolation measures should be used. We address this question in detail elsewhere, using mathematical models to explore the effectiveness and cost effectiveness of isolation wards under different assumptions.[16]

What is already known on this topic

National guidelines in many countries recommend patient isolation to control the spread of MRSA

Traditional narrative reviews differ as to its effectiveness

Most of the research is of a quasi-experimental nature, and no review has systematically assessed the threats to valid inference associated with such studies

What this study adds

The shortcomings of existing research are rigorously evaluated through a systematic comprehensive search strategy, data extraction, and documentation of component threats to validity

Major methodological weaknesses and inadequate reporting in many studies mean that plausible alternative explanations for reductions in MRSA cannot be excluded

There is evidence that interventions that include isolation can achieve major reductions in MRSA, even when endemic, but there are no well designed studies that allowed the role of isolation measures alone to be assessed

Studies considered to provide stronger evidence or evidence of intermediate strength provide testable hypotheses for future well planned studies

Guidelines have been produced to facilitate such research (www.hta.nhsweb.nhs.uk)

Strengths of the study

In contrast with narrative reviews,[3 10 11 64–67] where study selection may be biased, our systematic comprehensive search strategy, data extraction and documentation of component threats to validity provided a rigorous evaluation of the shortcomings of existing research. In particular, no studies tell us anything about the relative effectiveness or cost effectiveness of individual measures in different clinical situations. These would be fertile areas for further research.

Nevertheless, a lack of evidence of an effect associated with specific measures should not be mistaken for evidence of lack of effect. Having considered the evidence we believe isolation measures recommended in national guidelines should therefore continue to be applied until further research establishes otherwise.

The six studies[25 26 28 31 32 35 36] we considered to present the strongest evidence for assessing the effect of isolation, although they often failed to consider potentially important confounders, provide testable hypotheses that could be assessed in future studies.

Priority for research

MRSA is associated with substantial morbidity and mortality.[8 68] The emergence of glycopeptide resistant *Staphylococcus aureus*

strains,[69] which further reduce therapeutic options,[70] makes the implementation of well designed interventional studies to inform the choice of control measures a research priority.

Contributors: SPS coordinated writing grant proposal and conduct of review. BSC was employed as a full time postdoctorate research fellow. RL developed the search strategy together with CCK and SPS. BSC, SPS, and CCK jointly appraised abstracts. BSC and SPS independently appraised articles initially. BSC appraised articles fully and extracted data for all papers, with one of SPS, CCK, BDC, JR, GFM, and GD chosen in accordance with area of expertise. BSC with SPS and the other reviewers analysed the data. Writing up of the Health Technology Assessment report was done principally by SPS and BSC, with review and input from the whole review team. SE advised on systematic review methods in grant application and throughout review and writing up phase. The study was funded for two years by the Health Technology Assessment Board of the NHS R&D HTA Programme.

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Commentary: Golden rules

Geoff Watts

Few events in biology offer a more powerful demonstration of the wonders of natural selection than the spread of antibiotic resistance. Hospital staff struggling to contain the golden staph may, of course, take a more jaundiced view of its triumph.

Fortunately the microbe is not invincible. This week's review by Cooper and colleagues is a reminder that strict isolation measures can limit the spread of methicillin resistant *Staphylococcus aureus* (MRSA).[1] In a similar vein we have the recent report of a successful attempt at eradicating the organism by "ring fencing" elective orthopaedic beds.[2] The consequent drop in the incidence of postoperative infection allowed surgeons to do more joint replacements. Better research is urgently needed.

The literature on infection control began with Ignaz Semmelweis, a Hungarian physician, in the mid 19th century, and is now extensive. A review by Muto et al on behalf of the Society for Healthcare Epidemiology of America provides a useful insight into our current understanding of the spread of MRSA, and so what needs to be done to combat it.[3] The key to interrupting transmission is, of course, a firm understanding of what makes it possible. Do dirty rooms, dirty equipment, or dirty habits make the greatest contribution?

As many studies of MRSA have testified, hands (gloved or otherwise) are still the leading culprit. And transmission does not have to be direct. One investigation showed that almost half of the gloves worn by a group of nurses became contaminated with MRSA when they touched not the patients themselves, but various surfaces in the rooms where those patients were being nursed. Another study found the microbe on the keyboards of computers used only by clinicians.

There's evidence too of MRSA from gowns, white coats, all manner of portable equipment from stethoscopes to pagers, domestic items such as mops and furniture, and many types of environmental surface. In one hospital more than a quarter of 350 surfaces tested in the rooms of 38 patients colonised by MRSA were positive for the organism.

All this one might have suspected; more worrisome is the period for which the microbe can continue to pose a threat. One study of the outer surfaces of packages of sterile goods revealed the presence of MRSA that had survived for more than 38 weeks.

Given the part that antibiotics have played in fostering the emergence of resistant strains, it comes as something of a disappointment to learn that strict policies to limit their use are not enough to reverse the trend. Once MRSA has gained a foothold, there is, it seems, little correlation between its prevalence and the parsimonious use of antibiotics. Finland, the United Kingdom, and Italy all consume roughly the same amounts of these drugs, but they have big differences in the proportion of methicillin resistant isolates.

In short, while antibiotics do give the golden genie a selective advantage over its susceptible brethren once it has escaped its bottle, squeezing it back from whence it came depends principally on sustained efforts at preventing transmission. When it comes to regular hand washing, at least one survey has suggested that doctors are more blameworthy than nurses.

So, once more unto the sink, dear friends, once more . . .

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